p-ジクロロベンゼンのラット及びマウスを用いた
吸 入 に よ る が ん 原 性 試 験 報 告 書

APPENDIX

(J1～Q2)

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIX J 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0158
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control				20 ppm				75 ppm				300 ppm			
		No. of Animals on Study	17				16				21				32			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
nasal cavit			<17>				<16>				<21>				<32>			
	thrombus		5 (29)	0 (0)	0 (0)	0 (0)	7 (44)	0 (0)	0 (0)	0 (0)	4 (19)	0 (0)	0 (0)	0 (0)	12 (38)	0 (0)	0 (0)	0 (0)
	mineralization		14 (82)	0 (0)	0 (0)	0 (0)	11 (69)	0 (0)	0 (0)	0 (0)	13 (62)	0 (0)	0 (0)	0 (0)	18 (56)	0 (0)	0 (0)	0 (0)
	inflammation		1 (6)	0 (0)	0 (0)	0 (0)	2 (13)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)	3 (9)	0 (0)	0 (0)	0 (0)
	eosinophilic change:olfactory epithelium		9 (53)	0 (0)	0 (0)	0 (0)	3 (19)	0 (0)	0 (0)	0 (0)	4 (19)	0 (0)	0 (0)	0 (0)	13 (41)	1 (3)	0 (0)	0 (0)
	eosinophilic change:respiratory epithelium		1 (6)	0 (0)	0 (0)	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)
	inflammation:foreign body		3 (18)	0 (0)	0 (0)	0 (0)	7 (44)	0 (0)	0 (0)	0 (0)	4 (19)	0 (0)	1 (5)	0 (0)	8 (25)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:olfactory 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)	3 (9)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:gland		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)

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 17				20 ppm 16				75 ppm 21				300 ppm 32			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
nasopharynx		<a>	<17>				<16>				<21>				<32>			
	inflammation:foreign body		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)
lung		<a>	<17>				<16>				<21>				<32>			
	congestion		0	0	0	0	1	0	0	0	5	0	0	0	2	2	0	0
		(c)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(24)	(0)	(0)	(0)	(6)	(6)	(0)	(0)
	edema		0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
		(c)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)
	accumulation of foamy cells		1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
		(c)	(6)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	pneumonia:NOS		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(c)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	interstitial penumonia		2	1	0	0	1	0	0	0	0	0	0	0	3	1	0	0
		(c)	(12)	(6)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(9)	(3)	(0)	(0)
	bronchiolar-alveolar cell hyperplasia		1	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
		(c)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
[Hematopoietic system]																		
bone marrow		<a>	<17>				<16>				<21>				<32>			
	fibrosis		2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(c)	(12)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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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 17				20 ppm 16				75 ppm 21				300 ppm 32			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Hematopoietic system]																		
bone marrow			<17>				<16>				<21>				<32>			
	increased hematopoiesis		1	1	7	0	3	1	5	0	2	2	6	0	13	1	6	0
			(6)	(6)	(41)	(0)	(19)	(6)	(31)	(0)	(10)	(10)	(29)	(0)	(41)	(3)	(19)	(0)
lymph node			<17>				<16>				<21>				<32>			
	lymphadenitis		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)	(0)	(0)	(0)	(0)	(0)
spleen			<17>				<16>				<21>				<32>			
	atrophy		9	0	0	0	4	0	0	0	4	0	0	0	8	0	0	0
			(53)	(0)	(0)	(0)	(25)	(0)	(0)	(0)	(19)	(0)	(0)	(0)	(25)	(0)	(0)	(0)
	hemorrhage		1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(6)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	deposit of hemosiderin		0	6	2	0	4	2	3	0	1	8	0	0	7	8	0	0 *
			(0)	(35)	(12)	(0)	(25)	(13)	(19)	(0)	(5)	(38)	(0)	(0)	(22)	(25)	(0)	(0)
	fibrosis		1	0	0	0	0	0	0	0	1	0	0	0	2	1	0	0
			(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(6)	(3)	(0)	(0)
	extramedullary hematopoiesis		3	2	2	2	4	2	2	0	8	2	3	0	9	9	3	1
			(18)	(12)	(12)	(12)	(25)	(13)	(13)	(0)	(38)	(10)	(14)	(0)	(28)	(28)	(9)	(3)

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Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 17				20 ppm 16				75 ppm 21				300 ppm 32			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Hematopoietic system]																		
spleen		<a>	<17>				<16>				<21>				<32>			
	mobilization of mesothelial cell	b	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
		(c)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
[Circulatory system]																		
heart		<a>	<17>				<16>				<21>				<32>			
	thrombus	b	1	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
		(c)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
	necrosis	b	0	3	0	0	0	0	0	0	0	0	0	0	4	0	0	0 *
		(c)	(0)	(18)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(13)	(0)	(0)	(0)
	myocardial fibrosis	b	10	2	0	0	8	1	0	0	12	2	0	0	12	2	0	0
		(c)	(59)	(12)	(0)	(0)	(50)	(6)	(0)	(0)	(57)	(10)	(0)	(0)	(38)	(6)	(0)	(0)
	myocarditis	b	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
		(c)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)
	mineralization:artery	b	0	2	1	0	0	1	0	0	1	0	0	0	6	1	0	0
		(c)	(0)	(12)	(6)	(0)	(0)	(6)	(0)	(0)	(5)	(0)	(0)	(0)	(19)	(3)	(0)	(0)
artery/aort		<a>	<17>				<16>				<21>				<32>			
	mineralization	b	0	2	0	0	0	0	1	0	1	1	0	0	5	4	0	0
		(c)	(0)	(12)	(0)	(0)	(0)	(0)	(6)	(0)	(5)	(5)	(0)	(0)	(16)	(13)	(0)	(0)

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Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 17				20 ppm 16				75 ppm 21				300 ppm 32			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
tooth			<17>				<16>				<21>				<32>			
	dysplasia		6	0	0	0	7	0	0	0	11	0	0	0	16	0	0	0
			(35)	(0)	(0)	(0)	(44)	(0)	(0)	(0)	(52)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
tongue			<17>				<16>				<21>				<32>			
	arteritis		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)
	mineralization:artery		0	3	0	0	2	1	0	0	4	1	0	0	9	4	0	0
			(0)	(18)	(0)	(0)	(13)	(6)	(0)	(0)	(19)	(5)	(0)	(0)	(28)	(13)	(0)	(0)
salivary gl			<17>				<16>				<21>				<32>			
	inflammatory infiltration		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)
stomach			<17>				<15>				<21>				<32>			
	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)
	mineralization		0	0	3	0	0	0	1	0	0	1	0	0	2	1	7	0
			(0)	(0)	(18)	(0)	(0)	(0)	(7)	(0)	(0)	(5)	(0)	(0)	(6)	(3)	(22)	(0)
	ulcer:forestomach		0	3	3	1	1	1	3	0	2	0	4	0	6	2	3	0
			(0)	(18)	(18)	(6)	(7)	(7)	(20)	(0)	(10)	(0)	(19)	(0)	(19)	(6)	(9)	(0)

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Organ	Findings	Group Name	Control				20 ppm				75 ppm				300 ppm			
		No. of Animals on Study	17				16				21				32			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
stomach			<17>				<15>				<21>				<32>			
	hyperplasia:forestomach		1	4	0	0	3	3	0	0	3	3	0	0	2	4	0	0
			(6)	(24)	(0)	(0)	(20)	(20)	(0)	(0)	(14)	(14)	(0)	(0)	(6)	(13)	(0)	(0)
	erosion:glandular stomach		3	0	0	0	3	0	0	0	0	0	0	0	1	0	0	0
			(18)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
	ulcer:glandular stomach		2	2	0	0	1	1	0	0	4	1	0	0	4	2	2	0
			(12)	(12)	(0)	(0)	(7)	(7)	(0)	(0)	(19)	(5)	(0)	(0)	(13)	(6)	(6)	(0)
	hyperplasia:glandular stomach		2	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(12)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
small intes			<17>				<16>				<21>				<32>			
	ulcer		0	1	0	0	1	0	0	0	0	0	0	0	0	1	0	0
			(0)	(6)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(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)
large intes			<17>				<16>				<21>				<32>			
	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)

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			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver			<17>				<16>				<21>				<32>			
	herniation		1	0	0	0	1	0	0	0	0	0	0	0	2	0	0	0
			(6)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
	poliosis-like lesion		4	1	0	0	1	0	0	0	4	1	0	0	6	0	0	0
			(24)	(6)	(0)	(0)	(6)	(0)	(0)	(0)	(19)	(5)	(0)	(0)	(19)	(0)	(0)	(0)
	necrosis:central		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)	(0)	(0)	(0)
	fatty change:peripheral		3	0	2	0	2	1	0	1	1	1	1	0	2	2	0	0
			(18)	(0)	(12)	(0)	(13)	(6)	(0)	(6)	(5)	(5)	(5)	(0)	(6)	(6)	(0)	(0)
	degeneration:central		1	1	0	0	1	0	0	0	1	3	0	0	3	2	0	0
			(6)	(6)	(0)	(0)	(6)	(0)	(0)	(0)	(5)	(14)	(0)	(0)	(9)	(6)	(0)	(0)
	extramedullary hematopoiesis		1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
	acidophilic cell focus		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)	(9)	(0)	(0)	(0)
	basophilic cell focus		0	0	0	0	0	0	0	0	5	1	0	0	2	2	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(24)	(5)	(0)	(0)	(6)	(6)	(0)	(0)

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		No. of Animals on Study	17				16				21				32			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver			<17>				<16>				<21>				<32>			
	vacuolated cell focus		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)
	bile duct hyperplasia		14 (82)	1 (6)	1 (6)	0 (0)	11 (69)	1 (6)	0 (0)	0 (0)	18 (86)	2 (10)	0 (0)	0 (0)	27 (84)	4 (13)	0 (0)	0 (0)
	hepatocellular hypertrophy:central		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	5 (16)	0 (0)	0 (0)	0 (0)
pancreas			<17>				<16>				<21>				<32>			
	atrophy		0 (0)	0 (0)	0 (0)	0 (0)	7 (44)	1 (6)	0 (0)	0 (0) **	3 (14)	2 (10)	0 (0)	0 (0)	6 (19)	2 (6)	1 (3)	0 (0)
[Urinary system]																		
kidney			<17>				<16>				<21>				<32>			
	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)	1 (3)	0 (0)	0 (0)
	ossification		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)	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 17				20 ppm 16				75 ppm 21				300 ppm 32			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Urinary system]																		
kidney			<17>				<16>				<21>				<32>			
	chronic nephropathy		0	5	0	12	0	5	6	4 *	0	3	8	9 *	0	6	7	19
			(0)	(29)	(0)	(71)	(0)	(31)	(38)	(25)	(0)	(14)	(38)	(43)	(0)	(19)	(22)	(59)
	hydronephrosis		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)
	mineralization:papilla		0	0	0	0	1	0	0	0	0	0	0	0	26	1	0	0 **
			(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(81)	(3)	(0)	(0)
	urothelial hyperplasia:pelivis		4	0	0	0	0	0	0	0	4	0	0	0	17	0	0	0
			(24)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(19)	(0)	(0)	(0)	(53)	(0)	(0)	(0)
[Endocrine system]																		
pituitary			<17>				<16>				<21>				<32>			
	angiectasis		2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(12)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	cyst		2	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(12)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyperplasia		2	0	0	0	0	0	0	0	2	0	0	0	1	0	0	0
			(12)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(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	Grade	Control 17				20 ppm 16				75 ppm 21				300 ppm 32			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Endocrine system]																		
pituitary			<17>				<16>				<21>				<32>			
	Rathke pouch		0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
thyroid			<17>				<15>				<21>				<32>			
	ultimibranchial body remanet		1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
	follicular hyperplasia		0	0	0	0	0	0	0	0	0	1	0	0	1	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)	(3)	(3)	(0)	(0)
	C-cell hyperplasia		6	1	0	0	7	0	0	0	7	0	0	0	15	0	0	0
			(35)	(6)	(0)	(0)	(47)	(0)	(0)	(0)	(33)	(0)	(0)	(0)	(47)	(0)	(0)	(0)
parathyroid			<17>				<16>				<21>				<32>			
	hyperplasia		1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(6)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
panc islet			<17>				<16>				<21>				<32>			
	islet cell hyperplasia		1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
adrenal			<17>				<16>				<21>				<32>			
	peliosis-like lesion		1	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(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				20 ppm				75 ppm				300 ppm			
		No. of Animals on Study	17				16				21				32			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]																		
adrenal			<17>				<16>				<21>				<32>			
	necrosis		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)
	hyperplasia:cortical cell		1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
	hyperplasia:medulla		5	0	0	0	0	0	0	0	5	0	0	0	10	1	0	0
			(29)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(24)	(0)	(0)	(0)	(31)	(3)	(0)	(0)
	focal fatty change:cortex		3	1	0	0	3	0	0	0	2	1	0	0	4	0	0	0
			(18)	(6)	(0)	(0)	(19)	(0)	(0)	(0)	(10)	(5)	(0)	(0)	(13)	(0)	(0)	(0)
[Reproductive system]																		
testis			<17>				<16>				<21>				<32>			
	atrophy		1	0	5	0	0	0	0	0 *	0	0	5	0	0	0	4	0
			(6)	(0)	(29)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(24)	(0)	(0)	(0)	(13)	(0)
	arteritis		0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	interstitial cell hyperplasia		7	0	0	0	1	0	0	0	5	1	0	0	4	0	0	0
			(41)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(24)	(5)	(0)	(0)	(13)	(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 17				20 ppm 16				75 ppm 21				300 ppm 32			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Reproductive system]																		
semin ves			<17>				<16>				<21>				<32>			
	mineralization		0	0	0	0	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)
	hyperplasia		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)
prostate			<17>				<16>				<21>				<32>			
	hemorrhage		0	0	0	0	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)
	inflammation		5	7	0	0	2	6	1	0	6	8	1	0	4	14	1	0
			(29)	(41)	(0)	(0)	(13)	(38)	(6)	(0)	(29)	(38)	(5)	(0)	(13)	(44)	(3)	(0)
mammary gl			<17>				<16>				<21>				<32>			
	hyperplasia		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)	(0)	(0)	(0)	(0)
	galactocele		1	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0
			(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(3)	(0)	(0)
[Nervous system]																		
brain			<17>				<16>				<21>				<32>			
	hemorrhage		0	0	0	0	2	0	0	0	3	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(13)	(0)	(0)	(0)	(14)	(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 17				20 ppm 16				75 ppm 21				300 ppm 32			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Nervous system]																		
brain			<17>				<16>				<21>				<32>			
	hyaline body		7	0	0	0	6	0	0	0	11	0	0	0	15	0	0	0
			(41)	(0)	(0)	(0)	(38)	(0)	(0)	(0)	(52)	(0)	(0)	(0)	(47)	(0)	(0)	(0)
	gliosis		2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(12)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spinal cord			<17>				<16>				<21>				<32>			
	necrosis:focal		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)	(0)
[Special sense organs/appandage]																		
eye			<17>				<16>				<21>				<32>			
	cataract		0	0	3	0	0	0	0	0	0	0	0	0	1	0	1	0
			(0)	(0)	(18)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(3)	(0)
	retinal atrophy		0	0	0	2	0	0	0	0	0	1	0	0	0	1	2	0
			(0)	(0)	(0)	(12)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(3)	(6)	(0)
	keratitis		0	2	0	0	0	0	0	0	1	0	0	0	3	2	0	0
			(0)	(12)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(9)	(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

Organ	Findings	Group Name	Control				20 ppm				75 ppm				300 ppm			
		No. of Animals on Study	17				16				21				32			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Special sense organs/appandage]																		
eye			<17>				<16>				<21>				<32>			
	iritis		1	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
			(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
Harder gl			<17>				<16>				<21>				<32>			
	degeneration		0	0	0	0	1	0	0	0	1	0	0	0	1	4	0	0
			(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(3)	(13)	(0)	(0)
	inflammation		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)	(0)	(0)	(0)	(0)
	lymphocytic infiltration		0	0	0	0	1	0	0	0	0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
nasolacr d			<17>				<16>				<21>				<32>			
	inflammation		0	0	0	0	1	0	0	0	2	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Musculoskeletal system]																		
muscle			<17>				<16>				<21>				<32>			
	necrosis		1	1	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(6)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(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				20 ppm				75 ppm				300 ppm			
		No. of Animals on Study	17				16				21				32			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
[Musculoskeletal system]																		
muscle			<17>				<16>				<21>				<32>			
	mineralization:artery		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)	(0)
[Body cavities]																		
adipose			<17>				<16>				<21>				<32>			
	granulation		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

APPENDIX J 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 12				20 ppm 16				75 ppm 12				300 ppm 14			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
nasal cavit			<12>				<16>				<12>				<14>			
	thrombus		2	0	0	0	3	0	0	0	5	0	0	0	3	0	0	0
			(17)	(0)	(0)	(0)	(19)	(0)	(0)	(0)	(42)	(0)	(0)	(0)	(21)	(0)	(0)	(0)
	mineralization		2	0	0	0	2	0	0	0	0	0	0	0	5	0	0	0
			(17)	(0)	(0)	(0)	(13)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(36)	(0)	(0)	(0)
	eosinophilic change:olfactory epithelium		10	1	0	0	7	5	0	0	3	3	4	0 *	2	9	3	0 **
			(83)	(8)	(0)	(0)	(44)	(31)	(0)	(0)	(25)	(25)	(33)	(0)	(14)	(64)	(21)	(0)
	eosinophilic change:respiratory epithelium		0	0	0	0	0	0	0	0	3	0	0	0	7	0	0	0 *
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(25)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
	inflammation:foreign body		2	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
			(17)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)
	respiratory metaplasia:gland		1	0	0	0	0	0	0	0	1	0	0	0	7	0	0	0
			(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
larynx			<12>				<16>				<12>				<14>			
	inflammation		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)	(0)	(0)	(0)	(0)
lung			<12>				<16>				<12>				<14>			
	congestion		2	0	0	0	4	0	0	0	0	0	0	0	0	0	0	0
			(17)	(0)	(0)	(0)	(25)	(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				20 ppm 16				75 ppm 12				300 ppm 14			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
lung			<12>				<16>				<12>				<14>			
	accumulation of foamy cells		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	pneumonia:NOS		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 (7)	0 (0)
	interstitial penumonia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Hematopoietic system]																		
bone marrow			<12>				<16>				<12>				<14>			
	necrosis		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)	0 (0)	0 (0)	0 (0)
	fibrosis		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)
	increased hematopoiesis		3 (25)	2 (17)	2 (17)	0 (0)	1 (6)	1 (6)	5 (31)	0 (0)	1 (8)	4 (33)	4 (33)	0 (0)	5 (36)	2 (14)	0 (0)	0 (0)
lymph node			<12>				<16>				<12>				<14>			
	deposit of hemosiderin		0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	1 (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				20 ppm 16				75 ppm 12				300 ppm 14			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Hematopoietic system]																		
spleen			<12>				<16>				<12>				<14>			
	atrophy		1 (8)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	2 (17)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)
	hemorrhage		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	infarct		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)	0 (0)
	deposit of hemosiderin		2 (17)	4 (33)	3 (25)	0 (0)	1 (6)	4 (25)	3 (19)	0 (0)	4 (33)	3 (25)	0 (0)	0 (0)	0 (0)	2 (14)	8 (57)	0 (0)
	fibrosis		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)
	extramedullary hematopoiesis		6 (50)	3 (25)	2 (17)	0 (0)	4 (25)	3 (19)	1 (6)	1 (6)	3 (25)	2 (17)	2 (17)	0 (0)	8 (57)	0 (0)	3 (21)	0 (0)
[Circulatory system]																		
heart			<12>				<16>				<12>				<14>			
	necrosis		0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (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				20 ppm 16				75 ppm 12				300 ppm 14			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Circulatory system]																		
heart			<12>				<16>				<12>				<14>			
	necrosis:focal		0 (0)	0 (0)	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)
	myocardial fibrosis		4 (33)	0 (0)	0 (0)	0 (0)	3 (19)	0 (0)	0 (0)	0 (0)	3 (25)	0 (0)	0 (0)	0 (0)	4 (29)	0 (0)	0 (0)	0 (0)
	mineralization:artery		0 (0)	0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
artery/aort			<12>				<16>				<12>				<14>			
	mineralization		1 (8)	1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Digestive system]																		
tooth			<12>				<16>				<12>				<14>			
	dysplasia		2 (17)	0 (0)	0 (0)	0 (0)	2 (13)	0 (0)	0 (0)	0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	3 (21)	0 (0)	0 (0)	0 (0)
tongue			<12>				<16>				<12>				<14>			
	mineralization:artery		0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (8)	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 12				20 ppm 16				75 ppm 12				300 ppm 14			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
stomach			<12>				<16>				<12>				<14>			
	mineralization		0 (0)	0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)
	basal cell activation		0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)
	ulcer:forestomach		0 (0)	0 (0)	0 (0)	1 (8)	1 (6)	0 (0)	1 (6)	0 (0)	5 (42)	1 (8)	0 (0)	0 * (0)	0 (0)	2 (14)	0 (0)	1 (7)
	hyperplasia:forestomach		1 (8)	1 (8)	0 (0)	0 (0)	2 (13)	4 (25)	0 (0)	0 (0)	2 (17)	2 (17)	0 (0)	0 (0)	1 (7)	1 (7)	0 (0)	0 (0)
	erosion:glandular stomach		0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	ulcer:glandular stomach		0 (0)	0 (0)	0 (0)	0 (0)	3 (19)	2 (13)	0 (0)	0 (0)	3 (25)	1 (8)	0 (0)	0 (0)	1 (7)	1 (7)	0 (0)	0 (0)
	hyperplasia:glandular stomach		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
small intes			<12>				<16>				<12>				<14>			
	ulcer		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)	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				20 ppm 16				75 ppm 12				300 ppm 14			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver			<12>				<16>				<12>				<14>			
	herniation		3 (25)	0 (0)	0 (0)	0 (0)	3 (19)	0 (0)	0 (0)	0 (0)	2 (17)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)
	necrosis:central		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	necrosis:focal		0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)
	fatty change:peripheral		2 (17)	0 (0)	0 (0)	0 (0)	1 (6)	1 (6)	0 (0)	0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	1 (7)	0 (0)
	degeneration:central		0 (0)	0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	2 (14)	1 (7)	0 (0)
	granulation		0 (0)	2 (17)	0 (0)	0 (0)	3 (19)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (14)	0 (0)	0 (0)	0 (0)
	clear cell focus		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)	0 (0)
	basophilic cell focus		1 (8)	0 (0)	0 (0)	0 (0)	4 (25)	0 (0)	0 (0)	0 (0)	0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	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 / No. of Animals on Study / Grade	Control 12				20 ppm 16				75 ppm 12				300 ppm 14			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver			<12>				<16>				<12>				<14>			
	vacuolated cell focus		0 (0)	0 (0)	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)
	bile duct hyperplasia		3 (25)	0 (0)	0 (0)	0 (0)	3 (19)	0 (0)	0 (0)	0 (0)	1 (8)	1 (8)	0 (0)	0 (0)	2 (14)	0 (0)	0 (0)	0 (0)
	hepatocellular hypertrophy:central		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (21)	0 (0)	0 (0)	0 (0)
pancreas			<12>				<16>				<11>				<14>			
	atrophy		1 (8)	0 (0)	0 (0)	0 (0)	3 (19)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)
[Urinary system]																		
kidney			<12>				<16>				<12>				<14>			
	thrombus		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	chronic nephropathy		2 (17)	3 (25)	2 (17)	1 (8)	3 (19)	7 (44)	2 (13)	0 (0)	3 (25)	2 (17)	3 (25)	0 (0)	2 (14)	6 (43)	1 (7)	3 (21)

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				20 ppm				75 ppm				300 ppm			
		No. of Animals on Study	12				16				12				14			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Urinary system]																		
kidney			<12>				<16>				<12>				<14>			
	hydronephrosis		0 (0)	0 (0)	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)
	tubular necrosis		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)
	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)
[Endocrine system]																		
pituitary			<12>				<16>				<12>				<14>			
	angiectasis		2 (17)	0 (0)	0 (0)	0 (0)	2 (13)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	cyst		1 (8)	0 (0)	0 (0)	0 (0)	5 (31)	0 (0)	0 (0)	0 (0)	6 (50)	0 (0)	0 (0)	0 (0)	2 (14)	0 (0)	0 (0)	0 (0)
	hyperplasia		1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
thyroid			<12>				<16>				<12>				<13>			
	C-cell hyperplasia		5 (42)	0 (0)	0 (0)	0 (0)	8 (50)	0 (0)	0 (0)	0 (0)	6 (50)	0 (0)	0 (0)	0 (0)	6 (46)	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				20 ppm				75 ppm				300 ppm			
		No. of Animals on Study	12				16				12				14			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]																		
adrenal			<12>				<16>				<12>				<14>			
	peliosis-like lesion		7	2	0	0	3	1	0	0 *	5	1	0	0	6	0	0	0
			(58)	(17)	(0)	(0)	(19)	(6)	(0)	(0)	(42)	(8)	(0)	(0)	(43)	(0)	(0)	(0)
	hyperplasia:cortical cell		1	0	0	0	2	0	0	0	0	0	0	0	1	0	0	0
			(8)	(0)	(0)	(0)	(13)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)
	hyperplasia:medulla		1	0	0	0	0	1	0	0	3	0	0	0	4	0	0	0
			(8)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(25)	(0)	(0)	(0)	(29)	(0)	(0)	(0)
	focal fatty change:cortex		2	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(17)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Reproductive system]																		
uterus			<12>				<16>				<12>				<14>			
	angiectasis		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)
	hyperplasia:epithelium		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)	(0)	(0)	(0)	(0)
	cystic endometrial hyperplasia		0	0	0	0	0	0	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)

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				20 ppm 16				75 ppm 12				300 ppm 14			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Reproductive system]																		
mammary gl			<12>				<16>				<12>				<14>			
	hyperplasia		3 (25)	0 (0)	0 (0)	0 (0)	2 (13)	0 (0)	0 (0)	0 (0)	2 (17)	0 (0)	0 (0)	0 (0)	4 (29)	0 (0)	0 (0)	0 (0)
[Nervous system]																		
brain			<12>				<16>				<12>				<14>			
	hemorrhage		0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	necrosis:focal		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)
	deposit of calcium		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)	0 (0)
	hyaline body		5 (42)	0 (0)	0 (0)	0 (0)	7 (44)	0 (0)	0 (0)	0 (0)	9 (75)	0 (0)	0 (0)	0 (0)	7 (50)	0 (0)	0 (0)	0 (0)
spinal cord			<12>				<16>				<12>				<14>			
	gliosis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (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	Control				20 ppm				75 ppm				300 ppm			
		No. of Animals on Study	12				16				12				14			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Special sense organs/appandage]																		
eye			<12>				<16>				<12>				<14>			
	hemorrhage		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)	0 (0)	0 (0)	0 (0)
	cataract		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	retinal atrophy		0 (0)	0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	1 (6)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)
	keratitis		1 (8)	0 (0)	0 (0)	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)
Harder gl			<12>				<16>				<12>				<14>			
	degeneration		1 (8)	0 (0)	0 (0)	0 (0)	3 (19)	0 (0)	0 (0)	0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	1 (7)	1 (7)	0 (0)	0 (0)
	inflammation		0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)
nasolacr d			<12>				<16>				<12>				<14>			
	inflammation		2 (17)	0 (0)	0 (0)	0 (0)	4 (25)	0 (0)	0 (0)	0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	1 (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				20 ppm				75 ppm				300 ppm			
		No. of Animals on Study	12				16				12				14			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Musculoskeletal system]																		
muscle			<12>				<16>				<12>				<14>			
	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)
bone			<12>				<16>				<12>				<14>			
	increased hematopoiesis		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)	(0)	(0)	(0)
	osteosclerosis		1	2	0	0	3	1	1	0	1	0	2	0	2	2	0	0
			(8)	(17)	(0)	(0)	(19)	(6)	(6)	(0)	(8)	(0)	(17)	(0)	(14)	(14)	(0)	(0)
[Body cavities]																		
adipose			<12>				<16>				<12>				<14>			
	granulation		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)

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 J 3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0158
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control				20 ppm				75 ppm				300 ppm			
		No. of Animals on Study	33				34				29				18			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Integumentary system/appandage]																		
skin/app			<33>				<34>				<29>				<18>			
	inflammation		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)
	hyperplasia:epidermis		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)
	epidermal cyst		0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Respiratory system]																		
nasal cavit			<33>				<34>				<29>				<18>			
	thrombus		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)
	mineralization		27 (82)	0 (0)	0 (0)	0 (0)	21 (62)	0 (0)	0 (0)	0 (0)	15 (52)	0 (0)	0 (0)	0 * (0)	7 (39)	0 (0)	0 (0)	0 ** (0)
	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)	1 (6)	0 (0)	0 (0)	0 (0)
	eosinophilic change:olfactory epithelium		23 (70)	1 (3)	0 (0)	0 (0)	17 (50)	1 (3)	1 (3)	0 (0)	15 (52)	1 (3)	1 (3)	0 (0)	6 (33)	6 (33)	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				20 ppm				75 ppm				300 ppm			
		No. of Animals on Study	33				34				29				18			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
nasal cavit			<33>				<34>				<29>				<18>			
	eosinophilic change:respiratory epithelium		3	0	0	0	1	0	0	0	5	0	0	0	2	0	0	0
			(9)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(17)	(0)	(0)	(0)	(11)	(0)	(0)	(0)
	inflammation:foreign body		12	0	0	0	14	0	0	0	11	0	0	0	1	0	0	0 *
			(36)	(0)	(0)	(0)	(41)	(0)	(0)	(0)	(38)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
	respiratory metaplasia:gland		2	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)	(0)
nasopharynx			<33>				<34>				<29>				<18>			
	inflammation:foreign body		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)	(6)	(0)	(0)	(0)
lung			<33>				<34>				<29>				<18>			
	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)	(3)	(0)	(0)	(0)	(0)	(0)	(0)
	inflammatory infiltration		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)
	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 / No. of Animals on Study / Grade	Control 33				20 ppm 34				75 ppm 29				300 ppm 18			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
lung			<33>				<34>				<29>				<18>			
	accumulation of foamy cells		1	0	0	0	1	0	0	0	1	0	0	0	1	0	0	0
			(3)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
[Hematopoietic system]																		
bone marrow			<33>				<34>				<29>				<18>			
	hemorrhage		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)	(0)	(0)	(0)
	granulation		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)
	fibrosis		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)
	increased hematopoiesis		7	12	8	0	15	7	4	0	6	10	3	0	11	5	0	0 *
			(21)	(36)	(24)	(0)	(44)	(21)	(12)	(0)	(21)	(34)	(10)	(0)	(61)	(28)	(0)	(0)
lymph node			<33>				<34>				<29>				<18>			
	lymphadenitis		2	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0
			(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(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 33				20 ppm 34				75 ppm 29				300 ppm 18			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Hematopoietic system]																		
spleen			<33>				<34>				<29>				<18>			
	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)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	infarct		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)
	deposit of hemosiderin		11	0	0	0	24	3	0	0 **	16	5	0	0 **	12	1	0	0 *
			(33)	(0)	(0)	(0)	(71)	(9)	(0)	(0)	(55)	(17)	(0)	(0)	(67)	(6)	(0)	(0)
	fibrosis		2	2	0	0	3	0	0	0	2	0	0	0	2	2	1	0
			(6)	(6)	(0)	(0)	(9)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(11)	(11)	(6)	(0)
	extramedullary hematopoiesis		18	11	2	0	19	9	1	1	21	7	0	0	13	3	0	0
			(55)	(33)	(6)	(0)	(56)	(26)	(3)	(3)	(72)	(24)	(0)	(0)	(72)	(17)	(0)	(0)
[Circulatory system]																		
heart			<33>				<34>				<29>				<18>			
	necrosis		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)
	myocardial fibrosis		14	3	0	0	20	4	0	0	15	7	0	0	6	0	0	0
			(42)	(9)	(0)	(0)	(59)	(12)	(0)	(0)	(52)	(24)	(0)	(0)	(33)	(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 33				20 ppm 34				75 ppm 29				300 ppm 18			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Circulatory system]																		
heart			<33>				<34>				<29>				<18>			
	arteritis		2	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)	(0)
	mineralization:artery		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)
artery/aort			<33>				<34>				<29>				<18>			
	mineralization		0	0	0	0	2	0	0	0	3	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	arteritis		0	0	0	0	0	2	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)
[Digestive system]																		
tooth			<33>				<34>				<29>				<18>			
	dysplasia		15	0	0	0	14	0	0	0	21	0	0	0	9	0	0	0
			(45)	(0)	(0)	(0)	(41)	(0)	(0)	(0)	(72)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
tongue			<33>				<34>				<29>				<18>			
	granulation		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)	(6)	(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				20 ppm				75 ppm				300 ppm			
		No. of Animals on Study	33				34				29				18			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
tongue			<33>				<34>				<29>				<18>			
	arteritis		3	0	0	0	8	0	0	0	5	0	0	0	6	0	0	0
			(9)	(0)	(0)	(0)	(24)	(0)	(0)	(0)	(17)	(0)	(0)	(0)	(33)	(0)	(0)	(0)
	mineralization:artery		4	0	0	0	13	0	0	0 *	18	0	0	0 **	7	0	0	0
			(12)	(0)	(0)	(0)	(38)	(0)	(0)	(0)	(62)	(0)	(0)	(0)	(39)	(0)	(0)	(0)
salivary gl			<33>				<34>				<29>				<18>			
	atrophy		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)
stomach			<33>				<34>				<29>				<18>			
	mineralization		0	0	0	0	0	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)
	inflammation		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)
	basal cell activation		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)
	epidermal 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)

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				20 ppm				75 ppm				300 ppm			
		No. of Animals on Study	33				34				29				18			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
stomach			<33>				<34>				<29>				<18>			
	ulcer:forestomach		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)	1 (6)	1 (6)	0 (0)
	hyperplasia:forestomach		0 (0)	1 (3)	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)
	erosion:glandular stomach		0 (0)	0 (0)	0 (0)	0 (0)	2 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (11)	0 (0)	0 (0)	0 (0)
	ulcer:glandular stomach		1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	2 (11)	0 (0)	0 (0)	0 (0)
	hyperplasia:glandular stomach		3 (9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
large intes			<33>				<34>				<29>				<18>			
	mineralization		1 (3)	0 (0)	0 (0)	0 (0)	2 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
liver			<33>				<34>				<29>				<18>			
	herniation		5 (15)	0 (0)	0 (0)	0 (0)	2 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	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				20 ppm				75 ppm				300 ppm			
		No. of Animals on Study	33				34				29				18			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
liver			<33>				<34>				<29>				<18>			
	peliosis-like lesion		8	1	0	0	5	0	0	0	3	0	0	0	5	0	0	0
			(24)	(3)	(0)	(0)	(15)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(28)	(0)	(0)	(0)
	fatty change:peripheral		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)	(3)	(0)	(0)	(0)	(0)	(0)	(0)
	granulation		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)	(6)	(0)	(0)	(0)
	clear 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)	(6)	(0)	(0)	(0)
	acidophilic cell focus		7	2	0	0	16	0	0	0 *	5	0	0	0	7	2	0	0
			(21)	(6)	(0)	(0)	(47)	(0)	(0)	(0)	(17)	(0)	(0)	(0)	(39)	(11)	(0)	(0)
	basophilic cell focus		5	1	0	0	15	1	0	0 *	6	1	0	0	6	2	0	0
			(15)	(3)	(0)	(0)	(44)	(3)	(0)	(0)	(21)	(3)	(0)	(0)	(33)	(11)	(0)	(0)
	vacuolated cell focus		0	0	0	0	3	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(9)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)
	mixed cell focus		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 33				20 ppm 34				75 ppm 29				300 ppm 18			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver			<33>				<34>				<29>				<18>			
	bile duct hyperplasia		31	2	0	0	29	3	0	0	26	1	0	0	18	0	0	0
			(94)	(6)	(0)	(0)	(85)	(9)	(0)	(0)	(90)	(3)	(0)	(0)	(100)	(0)	(0)	(0)
pancreas			<33>				<34>				<29>				<18>			
	atrophy		14	1	0	0	11	0	1	0	8	0	0	0	9	0	0	0
			(42)	(3)	(0)	(0)	(32)	(0)	(3)	(0)	(28)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
	inflammation		0	0	0	0	0	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)
	hyperplasia:acinar cell		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)
[Urinary system]																		
kidney			<33>				<34>				<29>				<18>			
	chronic nephropathy		0	3	18	12	0	3	14	17	0	0	18	11	0	0	7	11
			(0)	(9)	(55)	(36)	(0)	(9)	(41)	(50)	(0)	(0)	(62)	(38)	(0)	(0)	(39)	(61)
	hydronephrosis		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)	(6)	(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 33				20 ppm 34				75 ppm 29				300 ppm 18			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Urinary system]																		
kidney			<33>				<34>				<29>				<18>			
	tubular necrosis		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)	(0)
	mineralization:papilla		0	0	0	0	0	0	0	0	0	0	0	0	14	0	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(78)	(0)	(0)	(0)
	tubular cell hyperplasia:cystic		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)
	urothelial hyperplasia:pelivis		3	0	0	0	8	0	0	0	9	0	0	0	15	0	0	0 **
			(9)	(0)	(0)	(0)	(24)	(0)	(0)	(0)	(31)	(0)	(0)	(0)	(83)	(0)	(0)	(0)
[Endocrine system]																		
pituitary			<33>				<34>				<29>				<18>			
	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)	(6)	(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)	(6)	(0)	(0)	(0)
	cyst		2	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0
			(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(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 33				20 ppm 34				75 ppm 29				300 ppm 18			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Endocrine system]																		
pituitary			<33>				<34>				<29>				<18>			
	hyperplasia		5	1	0	0	6	0	0	0	6	0	0	0	3	0	0	0
			(15)	(3)	(0)	(0)	(18)	(0)	(0)	(0)	(21)	(0)	(0)	(0)	(17)	(0)	(0)	(0)
	Rathke pouch		0	0	0	0	4	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(12)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
thyroid			<32>				<34>				<29>				<18>			
	follicular hyperplasia		1	0	0	0	3	0	0	0	2	0	0	0	2	0	0	0
			(3)	(0)	(0)	(0)	(9)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(11)	(0)	(0)	(0)
	C-cell hyperplasia		23	0	0	0	26	0	0	0	22	0	0	0	13	0	0	0
			(72)	(0)	(0)	(0)	(76)	(0)	(0)	(0)	(76)	(0)	(0)	(0)	(72)	(0)	(0)	(0)
panc islet			<33>				<34>				<29>				<18>			
	islet cell hyperplasia		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)
adrenal			<33>				<34>				<29>				<18>			
	hyperplasia:cortical cell		3	1	0	0	3	0	0	0	4	0	0	0	3	0	0	0
			(9)	(3)	(0)	(0)	(9)	(0)	(0)	(0)	(14)	(0)	(0)	(0)	(17)	(0)	(0)	(0)
	hyperplasia:medulla		12	2	0	0	11	0	0	0	8	3	0	0	6	0	0	0
			(36)	(6)	(0)	(0)	(32)	(0)	(0)	(0)	(28)	(10)	(0)	(0)	(33)	(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 33				20 ppm 34				75 ppm 29				300 ppm 18			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Endocrine system]																		
adrenal			<33>				<34>				<29>				<18>			
	focal fatty change:cortex		6 (18)	0 (0)	0 (0)	0 (0)	5 (15)	1 (3)	0 (0)	0 (0)	9 (31)	1 (3)	0 (0)	0 (0)	3 (17)	0 (0)	0 (0)	0 (0)
[Reproductive system]																		
testis			<33>				<34>				<29>				<18>			
	atrophy		0 (0)	0 (0)	2 (6)	0 (0)	0 (0)	0 (0)	6 (18)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	4 (22)	0 (0)
	arteritis		0 (0)	1 (3)	0 (0)	0 (0)	2 (6)	2 (6)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)
	interstitial cell hyperplasia		6 (18)	0 (0)	0 (0)	0 (0)	2 (6)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	2 (11)	0 (0)	0 (0)	0 (0)
prostate			<33>				<34>				<29>				<18>			
	inflammation		11 (33)	4 (12)	0 (0)	0 (0)	14 (41)	6 (18)	0 (0)	0 (0)	7 (24)	12 (41)	0 (0)	0 * (0)	2 (11)	4 (22)	1 (6)	0 (0)
	hyperplasia		2 (6)	1 (3)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	3 (10)	0 (0)	0 (0)	0 (0)	2 (11)	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				20 ppm				75 ppm				300 ppm			
		No. of Animals on Study	33				34				29				18			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Reproductive system]																		
mammary gl			<33>				<34>				<29>				<18>			
	hyperplasia		1	0	0	0	1	0	0	0	2	0	0	0	0	0	0	0
			(3)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	galactocele		0	0	0	0	2	0	0	0	2	0	1	0	0	0	0	0
			(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(7)	(0)	(3)	(0)	(0)	(0)	(0)	(0)
[Nervous system]																		
brain			<33>				<34>				<29>				<18>			
	hemorrhage		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)
	deposit of calcium		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)	(0)	(0)	(0)	(0)
	hyaline body		19	0	0	0	22	0	0	0	17	0	0	0	9	0	0	0
			(58)	(0)	(0)	(0)	(65)	(0)	(0)	(0)	(59)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
spinal cord			<33>				<34>				<29>				<18>			
	gliosis		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 33				20 ppm 34				75 ppm 29				300 ppm 18			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Special sense organs/appandage]																		
eye			<33>				<34>				<29>				<18>			
	cataract		0	0	2	0	0	3	0	0	0	0	0	0	0	0	1	0
			(0)	(0)	(6)	(0)	(0)	(9)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)
	retinal atrophy		3	0	2	1	0	0	3	0	0	0	0	0	0	0	0	1
			(9)	(0)	(6)	(3)	(0)	(0)	(9)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)
	keratitis		1	0	0	0	1	0	0	0	3	1	0	0	0	0	0	0
			(3)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(10)	(3)	(0)	(0)	(0)	(0)	(0)	(0)
Harder gl			<33>				<34>				<29>				<18>			
	degeneration		2	0	0	0	2	0	0	0	2	0	0	0	1	0	0	0
			(6)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
	inflammation		1	0	0	0	0	0	0	0	1	0	0	0	1	1	0	0
			(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(6)	(6)	(0)	(0)
	lymphocytic infiltration		0	0	0	0	1	0	0	0	1	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(11)	(0)	(0)	(0)
nasolacr d			<33>				<34>				<29>				<18>			
	inflammation		2	0	0	0	2	0	0	0	3	0	0	0	0	0	0	0
			(6)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(10)	(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 J 4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

Organ	Findings	Group Name	Control				20 ppm				75 ppm				300 ppm			
		No. of Animals on Study	38				34				38				36			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Integumentary system/appandage]																		
skin/app			<38>				<34>				<38>				<36>			
	inflammation		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)
subcutis			<38>				<34>				<38>				<36>			
	epidermal cyst		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)
[Respiratory system]																		
nasal cavit			<38>				<34>				<38>				<36>			
	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)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	thrombus		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)
	mineralization		5	0	0	0	1	0	0	0	1	0	0	0	11	0	0	0
			(13)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(31)	(0)	(0)	(0)
	inflammation		6	0	0	0	1	0	0	0	2	0	0	0	0	0	0	0 *
			(16)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(5)	(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				20 ppm				75 ppm				300 ppm			
		No. of Animals on Study	38				34				38				36			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
nasal cavit			<38>				<34>				<38>				<36>			
	eosinophilic change:olfactory epithelium		12	20	6	0	10	22	2	0	4	13	19	0 **	1	18	17	0 **
			(32)	(53)	(16)	(0)	(29)	(65)	(6)	(0)	(11)	(34)	(50)	(0)	(3)	(50)	(47)	(0)
	eosinophilic change:respiratory epithelium		11	0	0	0	10	0	0	0	11	0	0	0	31	0	0	0 **
			(29)	(0)	(0)	(0)	(29)	(0)	(0)	(0)	(29)	(0)	(0)	(0)	(86)	(0)	(0)	(0)
	inflammation:foreign body		3	0	0	0	7	0	0	0	2	0	0	0	2	0	0	0
			(8)	(0)	(0)	(0)	(21)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
	respiratory metaplasia:gland		4	0	0	0	4	0	0	0	3	0	0	0	26	0	0	0 **
			(11)	(0)	(0)	(0)	(12)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(72)	(0)	(0)	(0)
lung			<38>				<34>				<38>				<36>			
	foreign body granuloma		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)
[Hematopoietic system]																		
bone marrow			<38>				<34>				<38>				<36>			
	granulation		1	1	0	0	0	2	0	0	6	2	0	0	4	0	0	0
			(3)	(3)	(0)	(0)	(0)	(6)	(0)	(0)	(16)	(5)	(0)	(0)	(11)	(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				20 ppm				75 ppm				300 ppm			
		No. of Animals on Study	38				34				38				36			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Hematopoietic system]																		
bone marrow			<38>				<34>				<38>				<36>			
	increased hematopoiesis		10 (26)	4 (11)	1 (3)	0 (0)	2 (6)	1 (3)	1 (3)	0 * (0)	6 (16)	7 (18)	1 (3)	0 (0)	5 (14)	9 (25)	1 (3)	0 (0)
	osteosclerosis		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)
lymph node			<38>				<34>				<38>				<36>			
	deposit of hemosiderin		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)
spleen			<38>				<34>				<38>				<36>			
	atrophy		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)
	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)
	deposit of hemosiderin		13 (34)	18 (47)	4 (11)	0 (0)	13 (38)	21 (62)	0 (0)	0 (0)	8 (21)	26 (68)	2 (5)	0 (0)	8 (22)	19 (53)	4 (11)	0 (0)
	fibrosis		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)	1 (3)	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				20 ppm				75 ppm				300 ppm			
		No. of Animals on Study	38				34				38				36			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
spleen			<38>				<34>				<38>				<36>			
	extramedullary hematopoiesis		20	13	3	0	8	20	2	0	18	17	1	0	19	11	1	0
			(53)	(34)	(8)	(0)	(24)	(59)	(6)	(0)	(47)	(45)	(3)	(0)	(53)	(31)	(3)	(0)
[Circulatory system]																		
heart			<38>				<34>				<38>				<36>			
	myocardial fibrosis		10	1	0	0	10	1	0	0	14	1	0	0	10	0	0	0
			(26)	(3)	(0)	(0)	(29)	(3)	(0)	(0)	(37)	(3)	(0)	(0)	(28)	(0)	(0)	(0)
[Digestive system]																		
tooth			<38>				<34>				<38>				<36>			
	dysplasia		4	1	0	0	3	1	0	0	6	1	0	0	5	0	0	0
			(11)	(3)	(0)	(0)	(9)	(3)	(0)	(0)	(16)	(3)	(0)	(0)	(14)	(0)	(0)	(0)
tongue			<38>				<34>				<38>				<36>			
	inflammation		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)
	arteritis		4	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0
			(11)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(14)	(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				20 ppm 34				75 ppm 38				300 ppm 36			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
stomach			<38>				<34>				<38>				<36>			
	basal cell activation		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 (3)	0 (0)	0 (0)	0 (0)
	hyperplasia:forestomach		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	1 (3)	0 (0)	0 (0)
	ulcer:glandular stomach		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)
large intes			<38>				<34>				<38>				<36>			
	dilatation		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)
liver			<38>				<34>				<38>				<36>			
	herniation		4 (11)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)	2 (6)	0 (0)	0 (0)	0 (0)
	peliosis-like lesion		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)
	necrosis:focal		1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	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 / No. of Animals on Study / Grade	Control 38				20 ppm 34				75 ppm 38				300 ppm 36			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver			<38>				<34>				<38>				<36>			
	fatty change:peripheral		4 (11)	0 (0)	0 (0)	0 (0)	3 (9)	0 (0)	0 (0)	0 (0)	4 (11)	0 (0)	0 (0)	0 (0)	2 (6)	0 (0)	0 (0)	0 (0)
	degeneration:central		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)
	granulation		9 (24)	2 (5)	0 (0)	0 (0)	11 (32)	3 (9)	0 (0)	0 (0)	15 (39)	4 (11)	0 (0)	0 (0)	10 (28)	1 (3)	0 (0)	0 (0)
	clear cell focus		3 (8)	0 (0)	0 (0)	0 (0)	7 (21)	0 (0)	0 (0)	0 (0)	5 (13)	1 (3)	0 (0)	0 (0)	1 (3)	1 (3)	0 (0)	0 (0)
	acidophilic cell focus		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)	1 (3)	0 (0)	0 (0)
	basophilic cell focus		6 (16)	0 (0)	0 (0)	0 (0)	12 (35)	1 (3)	0 (0)	0 (0)	9 (24)	2 (5)	0 (0)	0 (0)	20 (56)	3 (8)	0 (0)	0 (0) **
	mixed cell focus		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)
	bile duct hyperplasia		5 (13)	0 (0)	0 (0)	0 (0)	10 (29)	0 (0)	0 (0)	0 (0)	7 (18)	2 (5)	0 (0)	0 (0)	11 (31)	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				20 ppm				75 ppm				300 ppm			
		No. of Animals on Study	38				34				38				36			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
pancreas			<38>				<34>				<38>				<36>			
	atrophy		7	0	0	0	7	0	0	0	5	1	0	0	6	1	0	0
			(18)	(0)	(0)	(0)	(21)	(0)	(0)	(0)	(13)	(3)	(0)	(0)	(17)	(3)	(0)	(0)
	hyperplasia:acinar cell		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)
[Urinary system]																		
kidney			<38>				<34>				<38>				<36>			
	chronic nephropathy		6	14	14	1	6	14	14	0	2	22	13	0	7	15	12	2
			(16)	(37)	(37)	(3)	(18)	(41)	(41)	(0)	(5)	(58)	(34)	(0)	(19)	(42)	(33)	(6)
[Endocrine system]																		
pituitary			<38>				<34>				<38>				<36>			
	angiectasis		5	0	0	0	2	0	0	0	6	0	0	0	7	0	0	0
			(13)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(16)	(0)	(0)	(0)	(19)	(0)	(0)	(0)
	cyst		3	0	0	0	11	0	0	0 *	14	0	0	0 **	10	0	0	0
			(8)	(0)	(0)	(0)	(32)	(0)	(0)	(0)	(37)	(0)	(0)	(0)	(28)	(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 38				20 ppm 34				75 ppm 38				300 ppm 36			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Endocrine system]																		
pituitary			<38>				<34>				<38>				<36>			
	hyperplasia		3 (8)	0 (0)	0 (0)	0 (0)	1 (3)	1 (3)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	3 (8)	0 (0)	0 (0)	0 (0)
	Rathke pouch		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)
thyroid			<35>				<34>				<37>				<36>			
	ultimibranchial body remanet		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)	0 (0)
	follicular hyperplasia		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)
	C-cell hyperplasia		25 (71)	0 (0)	0 (0)	0 (0)	26 (76)	0 (0)	0 (0)	0 (0)	27 (73)	0 (0)	0 (0)	0 (0)	27 (75)	0 (0)	0 (0)	0 (0)
panc islet			<38>				<34>				<38>				<36>			
	islet cell hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
adrenal			<38>				<34>				<38>				<36>			
	peliosis-like lesion		19 (50)	9 (24)	0 (0)	0 (0)	19 (56)	5 (15)	0 (0)	0 (0)	22 (58)	4 (11)	0 (0)	0 (0)	21 (58)	3 (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	Control				20 ppm				75 ppm				300 ppm			
		No. of Animals on Study	38				34				38				36			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Endocrine system]																		
adrenal			<38>				<34>				<38>				<36>			
	hyperplasia:cortical cell		5 (13)	0 (0)	0 (0)	0 (0)	8 (24)	0 (0)	0 (0)	0 (0)	6 (16)	2 (5)	0 (0)	0 (0)	4 (11)	0 (0)	0 (0)	0 (0)
	hyperplasia:medulla		6 (16)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	5 (13)	0 (0)	0 (0)	0 (0)	8 (22)	0 (0)	0 (0)	0 (0)
	focal fatty change:cortex		8 (21)	0 (0)	0 (0)	0 (0)	2 (6)	0 (0)	0 (0)	0 (0)	9 (24)	0 (0)	0 (0)	0 (0)	6 (17)	0 (0)	0 (0)	0 (0)
[Reproductive system]																		
ovary			<38>				<34>				<38>				<36>			
	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 (3)	0 (0)	0 (0)	0 (0)
uterus			<38>				<34>				<38>				<36>			
	inflammation		1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)
	hyperplasia:gland		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)

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				20 ppm 34				75 ppm 38				300 ppm 36			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Reproductive system]																		
uterus			<38>				<34>				<38>				<36>			
	cystic endometrial hyperplasia		3 (8)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)	1 (3)	2 (6)	0 (0)	0 (0)
mammary gl			<38>				<34>				<38>				<36>			
	hyperplasia		7 (18)	0 (0)	0 (0)	0 (0)	4 (12)	0 (0)	0 (0)	0 (0)	6 (16)	0 (0)	0 (0)	0 (0)	9 (25)	0 (0)	0 (0)	0 (0)
	galactocele		1 (3)	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)	0 (0)	0 (0)
[Nervous system]																		
brain			<38>				<34>				<38>				<36>			
	hemorrhage		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 (3)	0 (0)	0 (0)	0 (0)
	vacuolic change		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)
	deposit of calcium		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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 38				20 ppm 34				75 ppm 38				300 ppm 36			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Nervous system]																		
brain			<38>				<34>				<38>				<36>			
	hyaline body		25	0	0	0	22	0	0	0	23	0	0	0	23	0	0	0
			(66)	(0)	(0)	(0)	(65)	(0)	(0)	(0)	(61)	(0)	(0)	(0)	(64)	(0)	(0)	(0)
[Special sense organs/appandage]																		
eye			<38>				<34>				<38>				<36>			
	cataract		0	0	0	0	0	1	0	0	1	2	1	0	1	0	1	1
			(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(3)	(5)	(3)	(0)	(3)	(0)	(3)	(3)
	retinal atrophy		4	0	1	0	3	1	1	0	0	0	3	1	1	1	1	2
			(11)	(0)	(3)	(0)	(9)	(3)	(3)	(0)	(0)	(0)	(8)	(3)	(3)	(3)	(3)	(6)
	keratitis		2	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0
			(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
Harder gl			<38>				<34>				<38>				<36>			
	degeneration		8	0	0	0	5	0	0	0	10	0	0	0	11	0	0	0
			(21)	(0)	(0)	(0)	(15)	(0)	(0)	(0)	(26)	(0)	(0)	(0)	(31)	(0)	(0)	(0)
	inflammation		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 38				20 ppm 34				75 ppm 38				300 ppm 36			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Special sense organs/appandage]																		
Harder gl			<38>				<34>				<38>				<36>			
	lymphocytic infiltration		1 (3)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	2 (6)	0 (0)	0 (0)	0 (0)
nasolacr d			<38>				<34>				<38>				<36>			
	inflammation		5 (13)	0 (0)	0 (0)	0 (0)	3 (9)	0 (0)	0 (0)	0 (0)	5 (13)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Musculoskeletal system]																		
bone			<38>				<34>				<38>				<36>			
	increased hematopoiesis		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)
	osteosclerosis		1 (3)	6 (16)	3 (8)	0 (0)	7 (21)	5 (15)	5 (15)	0 (0)	11 (29)	3 (8)	1 (3)	0 * (0)	6 (17)	6 (17)	1 (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

APPENDIX J 5

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOSUE : MALE : DEAD AND MORIBUND ANIMALS

MOSUE (2-YEAR STUDY)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 22				20ppm 25				75ppm 26				300ppm 24			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
nasal cavit			<22>				<25>				<26>				<24>			
	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)
	eosinophilic change:olfactory epithelium		4 (18)	0 (0)	0 (0)	0 (0)	4 (16)	1 (4)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)
	eosinophilic change:respiratory epithelium		11 (50)	0 (0)	0 (0)	0 (0)	16 (64)	5 (20)	0 (0)	0 * (0)	16 (62)	5 (19)	1 (4)	0 * (0)	19 (79)	2 (8)	0 (0)	0 * (0)
	respiratory metaplasia:olfactory epithelium		1 (5)	0 (0)	0 (0)	0 (0)	4 (16)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	8 (33)	0 (0)	0 (0)	0 * (0)
	respiratory metaplasia:gland		2 (9)	0 (0)	0 (0)	0 (0)	2 (8)	0 (0)	0 (0)	0 (0)	4 (15)	0 (0)	0 (0)	0 (0)	9 (38)	1 (4)	0 (0)	0 * (0)
larynx			<22>				<25>				<25>				<24>			
	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)
lung			<22>				<25>				<26>				<24>			
	congestion		1 (5)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	3 (12)	0 (0)	0 (0)	0 (0)	3 (13)	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 22				20ppm 25				75ppm 26				300ppm 24			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
lung			<22>				<25>				<26>				<24>			
	hemorrhage		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 (8)	0 (0)	0 (0)	0 (0)
	inflammation		0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	accumulation of foamy cells		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)
	respiratory metaplasia:olfactory 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)	2 (8)	0 (0)	0 (0)	0 (0)
[Hematopoietic system]																		
bone marrow			<22>				<25>				<26>				<24>			
	atrophy		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)
	increased hematopoiesis		15 (68)	0 (0)	0 (0)	0 (0)	11 (44)	0 (0)	0 (0)	0 (0)	14 (54)	0 (0)	0 (0)	0 (0)	16 (67)	0 (0)	0 (0)	0 (0)
	erythropoiesis:increased		0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	1 (4)	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				20ppm				75ppm				300ppm			
		No. of Animals on Study	22				25				26				24			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
bone marrow			<22>				<25>				<26>				<24>			
	reticulosis		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)	(0)
	granulopoiesis:increased		2	0	0	0	4	0	0	0	2	0	0	0	1	0	0	0
			(9)	(0)	(0)	(0)	(16)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
lymph node			<22>				<25>				<26>				<24>			
	lymphadenitis		0	1	0	0	0	1	0	0	1	0	0	0	0	0	0	0
			(0)	(5)	(0)	(0)	(0)	(4)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen			<22>				<25>				<26>				<24>			
	deposit of melanin		2	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(9)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	extramedullary hematopoiesis		2	1	8	1	2	1	11	0	4	5	8	2	3	2	11	1
			(9)	(5)	(36)	(5)	(8)	(4)	(44)	(0)	(15)	(19)	(31)	(8)	(13)	(8)	(46)	(4)
[Circulatory system]																		
heart			<22>				<25>				<26>				<24>			
	thrombus		0	1	0	0	0	1	1	0	0	1	0	0	0	0	0	0
			(0)	(5)	(0)	(0)	(0)	(4)	(4)	(0)	(0)	(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	Control				20ppm				75ppm				300ppm			
		No. of Animals on Study	22				25				26				24			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
[Circulatory system]																		
heart			<22>				<25>				<26>				<24>			
	mineralization		2	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(9)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	myocardial fibrosis		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)	(0)
[Digestive system]																		
tooth			<22>				<25>				<26>				<24>			
	dysplasia		1	1	0	0	0	3	0	0	6	1	0	0	5	2	0	0
			(5)	(5)	(0)	(0)	(0)	(12)	(0)	(0)	(23)	(4)	(0)	(0)	(21)	(8)	(0)	(0)
stomach			<22>				<25>				<26>				<24>			
	hyperkeratosis:forestomach		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)
	hyperplasia:glandular stomach		2	8	7	0	3	9	8	0	4	14	4	0	5	9	7	0
			(9)	(36)	(32)	(0)	(12)	(36)	(32)	(0)	(15)	(54)	(15)	(0)	(21)	(38)	(29)	(0)
liver			<22>				<25>				<26>				<24>			
	herniation		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)	(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 22				20ppm 25				75ppm 26				300ppm 24			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver			<22>				<25>				<26>				<24>			
	angiectasis		2 (9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)
	necrosis:central		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	necrosis:focal		1 (5)	1 (5)	0 (0)	0 (0)	2 (8)	0 (0)	0 (0)	0 (0)	2 (8)	0 (0)	0 (0)	0 (0)	1 (4)	1 (4)	0 (0)	0 (0)
	necrosis:single cell		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)
	fatty change:central		0 (0)	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)
	deposit of ceroid		2 (9)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	4 (17)	0 (0)	0 (0)	0 (0)
	granulation		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)	0 (0)
	acidophilic cell focus		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 (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 22				20ppm 25				75ppm 26				300ppm 24			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver			<22>				<25>				<26>				<24>			
	basophilic cell focus		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 (8)	0 (0)	0 (0)	0 (0)
	biliary cyst		0 (0)	0 (0)	0 (0)	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)
	hepatocellular hypertrophy:central		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)
[Urinary system]																		
kidney			<22>				<25>				<26>				<24>			
	infarct		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)
	hyaline droplet		6 (27)	1 (5)	0 (0)	0 (0)	5 (20)	0 (0)	0 (0)	0 (0)	14 (54)	0 (0)	0 (0)	0 (0)	6 (25)	0 (0)	0 (0)	0 (0)
	basophilic 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)	1 (4)	0 (0)	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)	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 22				20ppm 25				75ppm 26				300ppm 24			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Urinary system]																		
kidney			<22>				<25>				<26>				<24>			
	hyaline cast		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)	(0)
	lymphocytic infiltration		0	0	0	0	1	0	0	0	2	0	0	0	1	1	0	0
			(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(4)	(4)	(0)	(0)
	inflammatory polyp		2	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(9)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hydronephrosis		0	1	1	0	1	1	1	0	0	1	0	0	0	0	0	0
			(0)	(5)	(5)	(0)	(4)	(4)	(4)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)
	tubular necrosis		0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:papilla		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)	(8)	(0)	(0)	(0)
	dilatation:tubular lumen		0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	glomerulosclerosis		0	0	2	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(9)	(0)	(4)	(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 22				20ppm 25				75ppm 26				300ppm 24			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Urinary system]																		
urin bladd			<22>				<25>				<26>				<24>			
	dilatation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	1 (4)	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)	2 (8)	0 (0)	0 (0)	0 (0)
[Endocrine system]																		
pituitary			<22>				<25>				<26>				<24>			
	angiectasis		0 (0)	0 (0)	0 (0)	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)
	cyst		2 (9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (8)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)
	hyperplasia		0 (0)	1 (5)	0 (0)	0 (0)	1 (4)	1 (4)	0 (0)	0 (0)	2 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	Rathke pouch		2 (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)
adrenal			<22>				<25>				<26>				<24>			
	thrombus		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)

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				20ppm				75ppm				300ppm			
		No. of Animals on Study	22				25				26				24			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]																		
adrenal			<22>				<25>				<26>				<24>			
	spindle-cell hyperplasia		0	18	0	0	5	19	0	0 *	6	19	0	0 *	7	16	0	0 *
			(0)	(82)	(0)	(0)	(20)	(76)	(0)	(0)	(23)	(73)	(0)	(0)	(29)	(67)	(0)	(0)
	hyperplasia:medulla		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)	(0)	(0)	(0)	(0)
[Reproductive system]																		
ovary			<22>				<25>				<26>				<24>			
	congestion		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)	(0)	(0)	(0)
	hemorrhage		0	0	0	0	0	0	1	0	1	0	0	0	0	0	1	0
			(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(4)	(0)
	cyst		2	1	1	0	4	3	1	0	1	2	0	0	3	3	1	0
			(9)	(5)	(5)	(0)	(16)	(12)	(4)	(0)	(4)	(8)	(0)	(0)	(13)	(13)	(4)	(0)
	cystic endometrial hyperplasia		0	1	0	0	2	0	0	0	0	0	0	0	0	0	0	0
			(0)	(5)	(0)	(0)	(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
uterus			<22>				<25>				<26>				<24>			
	cystic endometrial hyperplasia		5	0	0	0	6	1	0	0	8	1	2	0	6	1	1	0
			(23)	(0)	(0)	(0)	(24)	(4)	(0)	(0)	(31)	(4)	(8)	(0)	(25)	(4)	(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 22				20ppm 25				75ppm 26				300ppm 24			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Reproductive system]																		
mammary gl			<22>				<25>				<26>				<24>			
	galactocele		0 (0)	0 (0)	0 (0)	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)
prep/cli gl			<22>				<25>				<26>				<24>			
	duct ectasia		4 (18)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (12)	0 (0)	0 (0)	0 (0)	4 (17)	0 (0)	0 (0)	0 (0)
[Nervous system]																		
brain			<22>				<25>				<26>				<24>			
	hemorrhage		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)
	deposit of calcium		6 (27)	0 (0)	0 (0)	0 (0)	13 (52)	0 (0)	0 (0)	0 (0)	10 (38)	0 (0)	0 (0)	0 (0)	7 (29)	0 (0)	0 (0)	0 (0)
	hyaline body		11 (50)	0 (0)	0 (0)	0 (0)	9 (36)	0 (0)	0 (0)	0 (0)	14 (54)	0 (0)	0 (0)	0 (0)	12 (50)	0 (0)	0 (0)	0 (0)
	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)	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 22				20ppm 25				75ppm 26				300ppm 24			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Nervous system]																		
brain		<22>	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	arteritis		(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spinal cord		<22>	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	congestion		(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Special sense organs/appandage]																		
eye		<22>	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
	keratitis		(5)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	degeneration:cornea		1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(5)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:cornea		0	0	0	0	3	0	0	0	4	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(12)	(0)	(0)	(0)	(15)	(0)	(0)	(0)	(13)	(0)	(0)	(0)
Harder gl		<22>	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	hyperplasia		(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
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

APPENDIX J 6

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOSUE : FEMALE : DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0159
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				20ppm				75ppm				300ppm			
		No. of Animals on Study	10				18				18				19			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Integumentary system/appandage]																		
skin/app			<10>				<18>				<18>				<19>			
	inflammation		0	2	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)
	hyperkeratosis		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)
[Respiratory system]																		
nasal cavit			<10>				<18>				<18>				<19>			
	eosinophilic change:olfactory epithelium		2	0	0	0	8	0	0	0	3	0	0	0	4	0	0	0
			(20)	(0)	(0)	(0)	(44)	(0)	(0)	(0)	(17)	(0)	(0)	(0)	(21)	(0)	(0)	(0)
	eosinophilic change:respiratory epithelium		3	0	0	0	5	0	0	0	4	0	0	0	0	0	0	0
			(30)	(0)	(0)	(0)	(28)	(0)	(0)	(0)	(22)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		3	0	0	0	9	0	0	0	10	0	0	0	2	2	0	0
			(30)	(0)	(0)	(0)	(50)	(0)	(0)	(0)	(56)	(0)	(0)	(0)	(11)	(11)	(0)	(0)
	respiratory metaplasia:gland		5	1	0	0	11	2	0	0	10	5	1	0	10	3	0	0
			(50)	(10)	(0)	(0)	(61)	(11)	(0)	(0)	(56)	(28)	(6)	(0)	(53)	(16)	(0)	(0)
	atrophy:olfactory epithelium		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)

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 10				20ppm 18				75ppm 18				300ppm 19			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
lung			<10>				<18>				<18>				<19>			
	congestion		1	0	0	0	0	0	0	0	2	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(5)	(0)	(0)	(0)
	hemorrhage		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)	(0)
	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)	(6)	(0)	(0)	(0)	(0)	(0)	(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)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Hematopoietic system]																		
bone marrow			<10>				<18>				<18>				<19>			
	erythropoiesis:increased		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)	(0)	(0)	(0)	(0)
	reticulosis		0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)
	granulopoiesis:increased		3	1	0	0	3	0	0	0	6	0	0	0	1	0	0	0
			(30)	(10)	(0)	(0)	(17)	(0)	(0)	(0)	(33)	(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	Control				20ppm				75ppm				300ppm			
		No. of Animals on Study	10				18				18				19			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Hematopoietic system]																		
lymph node			<10>				<18>				<18>				<19>			
	lymphadenitis		1 (10)	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 (11)	0 (0)	0 (0)
spleen			<10>				<18>				<18>				<19>			
	atrophy		1 (10)	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)
	deposit of melanin		0 (0)	0 (0)	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)
	extramedullary hematopoiesis		1 (10)	1 (10)	5 (50)	0 (0)	3 (17)	5 (28)	3 (17)	1 (6)	3 (17)	3 (17)	7 (39)	2 (11)	3 (16)	3 (16)	8 (42)	4 (21)
[Circulatory system]																		
heart			<10>				<18>				<18>				<19>			
	thrombus		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)
	necrosis:focal		0 (0)	0 (0)	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)

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				20ppm				75ppm				300ppm			
		No. of Animals on Study	10				18				18				19			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Circulatory system]																		
heart			<10>				<18>				<18>				<19>			
	mineralization		1	0	0	0	1	0	0	0	2	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(5)	(0)	(0)	(0)
	myocardial fibrosis		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)
	arteritis		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)
[Digestive system]																		
tooth			<10>				<18>				<18>				<19>			
	dysplasia		5	0	0	0	8	1	0	0	6	2	0	0	9	4	0	0
			(50)	(0)	(0)	(0)	(44)	(6)	(0)	(0)	(33)	(11)	(0)	(0)	(47)	(21)	(0)	(0)
tongue			<10>				<18>				<18>				<19>			
	arteritis		0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)	(0)
stomach			<10>				<18>				<18>				<19>			
	arteritis		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)

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				20ppm				75ppm				300ppm			
			10				18				18				19			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
stomach			<10>				<18>				<18>				<19>			
	hyperkeratosis:forestomach		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:glandular stomach		1 (10)	2 (20)	5 (50)	0 (0)	4 (22)	4 (22)	6 (33)	0 (0)	0 (0)	5 (28)	6 (33)	0 (0)	3 (16)	9 (47)	7 (37)	0 (0)
large intes			<10>				<18>				<18>				<19>			
	inflammation		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)	0 (0)	0 (0)
liver			<10>				<18>				<18>				<19>			
	congestion		0 (0)	0 (0)	1 (10)	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)
	angiectasis		1 (10)	0 (0)	0 (0)	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)
	necrosis:central		0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	1 (5)	1 (5)	0 (0)	0 (0)
	necrosis:focal		1 (10)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	2 (11)	0 (0)	1 (6)	0 (0)	1 (5)	1 (5)	1 (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	Control				20ppm				75ppm				300ppm			
		No. of Animals on Study	10				18				18				19			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver			<10>				<18>				<18>				<19>			
	necrosis:single cell		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 (11)	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 (6)	0 (0)	0 (0)	0 (0)	3 (16)	0 (0)	0 (0)	0 (0)
	deposit of ceroid		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	3 (16)	0 (0)	0 (0)	0 (0)
	granulation		0 (0)	0 (0)	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)
	arteritis		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)	0 (0)	0 (0)
	clear cell focus		0 (0)	0 (0)	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)
	basophilic cell focus		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	biliary cyst		1 (10)	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				20ppm				75ppm				300ppm			
		No. of Animals on Study	10				18				18				19			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
[Digestive system]																		
liver			<10>				<18>				<18>				<19>			
	hepatocellular hypertrophy:central		0	0	0	0	0	0	0	0	0	0	0	0	4	3	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(21)	(16)	(0)	(0)
gall bladd			<10>				<18>				<18>				<19>			
	eosinophilic change		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)	(0)	(0)	(0)	(0)
pancreas			<10>				<18>				<18>				<19>			
	arteritis		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)
[Urinary system]																		
kidney			<10>				<18>				<18>				<19>			
	infarct		0	1	0	0	0	0	0	0	1	0	1	0	0	0	0	0
			(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(6)	(0)	(0)	(0)	(0)	(0)
	hyaline droplet		0	0	0	0	2	0	0	0	2	0	0	0	4	0	0	0
			(0)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(21)	(0)	(0)	(0)
	basophilic change		5	0	0	0	3	0	0	0	8	0	0	0	2	1	0	0
			(50)	(0)	(0)	(0)	(17)	(0)	(0)	(0)	(44)	(0)	(0)	(0)	(11)	(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 10				20ppm 18				75ppm 18				300ppm 19			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Urinary system]																		
kidney			<10>				<18>				<18>				<19>			
	deposit of hemosiderin		0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)
	lymphocytic infiltration		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)
	inflammatory polyp		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)
	arteritis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (11)	0 (0)	0 (0)	1 (6)	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)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	vacuolization of proximal tubule		6 (60)	0 (0)	0 (0)	0 (0)	10 (56)	0 (0)	0 (0)	0 (0)	12 (67)	0 (0)	0 (0)	0 (0)	11 (58)	3 (16)	0 (0)	0 (0)
	hydronephrosis		0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	2 (11)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)
	retention cyst		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)

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 10				20ppm 18				75ppm 18				300ppm 19			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Urinary system]																		
kidney			<10>				<18>				<18>				<19>			
	pyelonephritis		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)	0 (0)	0 (0)
	papillary necrosis		0 (0)	0 (0)	1 (10)	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:papilla		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)
	dilatation:tubular lumen		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 (11)	0 (0)	0 (0)	0 (0)
urin bladd			<10>				<18>				<18>				<19>			
	dilatation		0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	4 (21)	0 (0)
	hemorrhage		0 (0)	0 (0)	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)
urethra			<10>				<18>				<18>				<19>			
	inflammation		1 (10)	0 (0)	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)

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				20ppm				75ppm				300ppm			
		No. of Animals on Study	10				18				18				19			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																		
urethra			<10>				<18>				<18>				<19>			
	xanthogranuloma		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)	(0)	(0)	(0)	(0)
[Endocrine system]																		
pituitary			<10>				<18>				<18>				<19>			
	cyst		0	0	0	0	4	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(22)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	Rathke pouch		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)
adrenal			<10>				<18>				<18>				<19>			
	deposit of amyloid		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)
	spindle-cell hyperplasia		4	0	0	0	3	0	0	0	4	0	0	0	3	0	0	0
			(40)	(0)	(0)	(0)	(17)	(0)	(0)	(0)	(22)	(0)	(0)	(0)	(16)	(0)	(0)	(0)
[Reproductive system]																		
testis			<10>				<18>				<18>				<19>			
	mineralization		6	0	0	0	11	0	0	0	15	0	0	0	16	0	0	0
			(60)	(0)	(0)	(0)	(61)	(0)	(0)	(0)	(83)	(0)	(0)	(0)	(84)	(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				20ppm				75ppm				300ppm			
		No. of Animals on Study	10				18				18				19			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Reproductive system]																		
epididymis			<10>				<18>				<18>				<19>			
	spermatogenic granuloma		1	0	0	0	2	0	0	0	2	0	0	0	3	0	0	0
			(10)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(16)	(0)	(0)	(0)
semin ves			<10>				<18>				<18>				<19>			
	inflammation		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)	(0)	(0)	(0)	(0)
	xanthogranuloma		0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
prostate			<10>				<18>				<18>				<19>			
	inflammation		2	0	0	0	0	0	0	0	1	1	0	0	0	1	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(6)	(0)	(0)	(0)	(5)	(0)	(0)
	xanthogranuloma		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)	(0)	(0)	(0)
prep/cli gl			<10>				<18>				<18>				<19>			
	duct ectasia		0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)
[Nervous system]																		
brain			<10>				<18>				<18>				<19>			
	hemorrhage		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)	(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				20ppm				75ppm				300ppm			
		No. of Animals on Study	10				18				18				19			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Nervous system]																		
brain			<10>				<18>				<18>				<19>			
	deposit of calcium		4	0	0	0	8	0	0	0	5	0	0	0	4	0	0	0
			(40)	(0)	(0)	(0)	(44)	(0)	(0)	(0)	(28)	(0)	(0)	(0)	(21)	(0)	(0)	(0)
	hyaline body		4	0	0	0	10	0	0	0	8	0	0	0	6	0	0	0
			(40)	(0)	(0)	(0)	(56)	(0)	(0)	(0)	(44)	(0)	(0)	(0)	(32)	(0)	(0)	(0)
	arteritis		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)
[Special sense organs/appandage]																		
eye			<10>				<18>				<18>				<19>			
	keratitis		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)
	degeneration:cornea		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)	(0)
	mineralization:cornea		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)	(0)	(0)	(0)	(0)
Harder gl			<10>				<18>				<18>				<19>			
	degeneration		0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(6)	(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				20ppm				75ppm				300ppm			
		No. of Animals on Study	10				18				18				19			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Special sense organs/appandage]																		
Harder gl			<10>				<18>				<18>				<19>			
	hyperplasia		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)	(0)	(0)	(0)	(0)
[Body cavities]																		
retroperit			<10>				<18>				<18>				<19>			
	hemorrhage		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)	(0)	(0)
[All other systems]																		
other			<10>				<18>				<18>				<19>			
	congestion		0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(6)	(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

APPENDIX J 7

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOSUE : MALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0159
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control				20ppm				75ppm				300ppm			
		No. of Animals on Study	39				31				32				30			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Integumentary system/appandage]																		
skin/app			<39>				<31>				<32>				<30>			
	inflammation		2	0	0	0	1	1	0	0	0	1	0	0	0	0	0	0
			(5)	(0)	(0)	(0)	(3)	(3)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)
subcutis			<39>				<31>				<32>				<30>			
	inflammatory infiltration		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)
[Respiratory system]																		
nasal cavit			<39>				<31>				<32>				<30>			
	eosinophilic change:olfactory epithelium		15	0	0	1	9	0	0	0	10	0	0	0	5	0	0	0
			(38)	(0)	(0)	(3)	(29)	(0)	(0)	(0)	(31)	(0)	(0)	(0)	(17)	(0)	(0)	(0)
	eosinophilic change:respiratory epithelium		17	0	0	0	19	0	0	0	20	0	0	0	12	0	0	0
			(44)	(0)	(0)	(0)	(61)	(0)	(0)	(0)	(63)	(0)	(0)	(0)	(40)	(0)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		20	0	0	0	21	0	0	0	27	1	0	0 **	20	0	0	0
			(51)	(0)	(0)	(0)	(68)	(0)	(0)	(0)	(84)	(3)	(0)	(0)	(67)	(0)	(0)	(0)
	respiratory metaplasia:gland		23	8	0	0	18	10	1	0	17	13	1	0 *	20	8	0	0
			(59)	(21)	(0)	(0)	(58)	(32)	(3)	(0)	(53)	(41)	(3)	(0)	(67)	(27)	(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 39				20ppm 31				75ppm 32				300ppm 30			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
nasal cavit			<39>				<31>				<32>				<30>			
	atrophy:olfactory epithelium		1 (3)	0 (0)	0 (0)	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)
lung			<39>				<31>				<32>				<30>			
	granulation		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)
	hyperplasia		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)
[Hematopoietic system]																		
bone marrow			<39>				<31>				<32>				<30>			
	granulation		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)
	erythropoiesis:increased		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)
	granulopoiesis:increased		4 (10)	0 (0)	0 (0)	0 (0)	3 (10)	0 (0)	0 (0)	0 (0)	4 (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				20ppm				75ppm				300ppm			
		No. of Animals on Study	39				31				32				30			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
lymph node			<39>				<31>				<32>				<30>			
	lymphadenitis		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)
spleen			<39>				<31>				<32>				<30>			
	deposit of melanin		1	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
			(3)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
	extramedullary hematopoiesis		10	4	2	0	9	3	6	1	9	3	3	0	14	6	2	0
			(26)	(10)	(5)	(0)	(29)	(10)	(19)	(3)	(28)	(9)	(9)	(0)	(47)	(20)	(7)	(0)
	follicular hyperplasia		1	0	0	0	1	1	0	0	2	0	0	0	1	0	0	0
			(3)	(0)	(0)	(0)	(3)	(3)	(0)	(0)	(6)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
[Digestive system]																		
tooth			<39>				<31>				<32>				<30>			
	dysplasia		23	7	1	0	16	5	2	1	15	8	0	2	14	6	0	0
			(59)	(18)	(3)	(0)	(52)	(16)	(6)	(3)	(47)	(25)	(0)	(6)	(47)	(20)	(0)	(0)
	endothelial cell hyperplasia		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 / No. of Animals on Study / Grade	Control 39				20ppm 31				75ppm 32				300ppm 30			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
tongue			<39>				<31>				<32>				<30>			
	arteritis		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)
stomach			<39>				<31>				<32>				<30>			
	inflammatory infiltration		2 (5)	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)
	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)
	erosion:glandular stomach		5 (13)	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		4 (10)	14 (36)	19 (49)	0 (0)	3 (10)	8 (26)	19 (61)	0 (0)	1 (3)	10 (31)	21 (66)	0 (0)	2 (7)	11 (37)	17 (57)	0 (0)
	ectopia:glandular stomach		1 (3)	0 (0)	0 (0)	0 (0)	3 (10)	0 (0)	0 (0)	0 (0)	2 (6)	0 (0)	0 (0)	0 (0)	3 (10)	0 (0)	0 (0)	0 (0)
liver			<39>				<31>				<32>				<30>			
	angiectasis		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)

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 39				20ppm 31				75ppm 32				300ppm 30			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver			<39>				<31>				<32>				<30>			
	necrosis:zonal		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)
	necrosis:focal		2 (5)	0 (0)	0 (0)	0 (0)	3 (10)	1 (3)	0 (0)	0 (0)	3 (9)	0 (0)	0 (0)	0 (0)	4 (13)	1 (3)	0 (0)	0 (0)
	necrosis:single cell		1 (3)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	5 (17)	0 (0)	0 (0)	0 (0)
	fatty change:central		2 (5)	0 (0)	0 (0)	0 (0)	1 (3)	1 (3)	0 (0)	0 (0)	2 (6)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)
	deposit of ceroid		1 (3)	0 (0)	0 (0)	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)
	inflammatory infiltration		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)
	granulation		23 (59)	0 (0)	0 (0)	0 (0)	12 (39)	1 (3)	0 (0)	0 (0)	15 (47)	0 (0)	0 (0)	0 (0)	3 (10)	0 (0)	0 (0)	0 ** (0)
	clear cell focus		2 (5)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	2 (6)	0 (0)	0 (0)	0 (0)	2 (7)	1 (3)	0 (0)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
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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 / No. of Animals on Study / Grade	Control 39				20ppm 31				75ppm 32				300ppm 30			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver			<39>				<31>				<32>				<30>			
	acidophilic cell focus		2	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
	basophilic cell focus		0	0	0	0	1	2	0	0	1	1	0	0	1	1	0	0
			(0)	(0)	(0)	(0)	(3)	(6)	(0)	(0)	(3)	(3)	(0)	(0)	(3)	(3)	(0)	(0)
	biliary cyst		1	0	0	0	1	0	0	0	3	0	0	0	0	0	0	0
			(3)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(9)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hepatocellular hypertrophy:central		0	0	0	0	0	0	0	0	0	0	0	0	21	6	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(70)	(20)	(0)	(0)
gall bladd			<39>				<31>				<32>				<30>			
	eosinophilic change		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)	(0)	(7)	(0)	(0)	(0)
pancreas			<39>				<31>				<32>				<30>			
	arteritis		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)
[Urinary system]																		
kidney			<39>				<31>				<32>				<30>			
	infarct		0	0	0	0	0	1	0	0	2	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(6)	(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				20ppm				75ppm				300ppm			
		No. of Animals on Study	39				31				32				30			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																		
kidney			<39>				<31>				<32>				<30>			
	spongiosis		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)
	hyaline droplet		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)
	basophilic change		30	0	0	0	26	0	0	0	29	0	0	0	22	0	0	0
			(77)	(0)	(0)	(0)	(84)	(0)	(0)	(0)	(91)	(0)	(0)	(0)	(73)	(0)	(0)	(0)
	deposit of hemosiderin		0	0	0	0	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)
	lymphocytic infiltration		3	0	1	0	6	0	0	0	4	0	0	0	1	0	0	0
			(8)	(0)	(3)	(0)	(19)	(0)	(0)	(0)	(13)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
	inflammatory polyp		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)
	vacuolization of proximal tubule		34	0	0	0	27	0	0	0	28	2	0	0	22	7	0	0 **
			(87)	(0)	(0)	(0)	(87)	(0)	(0)	(0)	(88)	(6)	(0)	(0)	(73)	(23)	(0)	(0)
	hydronephrosis		0	1	2	0	0	1	0	0	1	0	0	0	0	0	1	0
			(0)	(3)	(5)	(0)	(0)	(3)	(0)	(0)	(3)	(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
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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				20ppm				75ppm				300ppm			
		No. of Animals on Study	39				31				32				30			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																		
kidney			<39>				<31>				<32>				<30>			
	retention cyst		1	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
			(3)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
	pyelitis		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)
	mineralization:papilla		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)
	glomerulosclerosis		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)
	tubular cell hyperplasia:cystic		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)
urin bladd			<39>				<31>				<32>				<30>			
	lymphocytic infiltration		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)
	polyp		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)
urethra			<39>				<31>				<32>				<30>			
	inflammation		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 39				20ppm 31				75ppm 32				300ppm 30			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Urinary system]																		
urethra			<39>				<31>				<32>				<30>			
	xanthogranuloma		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)
[Endocrine system]																		
pituitary			<39>				<31>				<32>				<30>			
	cyst		3	0	0	0	5	0	0	0	4	0	0	0	3	0	0	0
			(8)	(0)	(0)	(0)	(16)	(0)	(0)	(0)	(13)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	hyperplasia		1	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0
			(3)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	Rathke pouch		1	0	0	0	2	0	0	0	4	0	0	0	2	0	0	0
			(3)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(13)	(0)	(0)	(0)	(7)	(0)	(0)	(0)
thyroid			<37>				<31>				<32>				<30>			
	C-cell hyperplasia		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)	(3)	(0)	(0)	(0)
parathyroid			<18>				<24>				<22>				<20>			
	respiratory metaplasia:olfactory epithelium		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)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
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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				20ppm				75ppm				300ppm			
		No. of Animals on Study	39				31				32				30			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]																		
parathyroid			<18>				<24>				<22>				<20>			
	respiratory metaplasia:gland		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)
adrenal			<39>				<31>				<32>				<30>			
	deposit of amyloid		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)
	mastcell hyperplasia		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)
	spindle-cell hyperplasia		14	1	0	0	14	0	0	0	18	0	0	0	14	0	0	0
			(36)	(3)	(0)	(0)	(45)	(0)	(0)	(0)	(56)	(0)	(0)	(0)	(47)	(0)	(0)	(0)
	hyperplasia:cortical cell		3	0	0	0	3	1	0	0	2	0	0	0	0	0	0	0
			(8)	(0)	(0)	(0)	(10)	(3)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyperplasia:medulla		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)
	focal fatty change:cortex		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)
[Reproductive system]																		
testis			<39>				<31>				<32>				<30>			
	mineralization		21	0	0	0	24	0	0	0	27	0	0	0 *	25	0	0	0 *
			(54)	(0)	(0)	(0)	(77)	(0)	(0)	(0)	(84)	(0)	(0)	(0)	(83)	(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 39 1 (%)	Control 39 2 (%)	Control 39 3 (%)	Control 39 4 (%)	20ppm 31 1 (%)	20ppm 31 2 (%)	20ppm 31 3 (%)	20ppm 31 4 (%)	75ppm 32 1 (%)	75ppm 32 2 (%)	75ppm 32 3 (%)	75ppm 32 4 (%)	300ppm 30 1 (%)	300ppm 30 2 (%)	300ppm 30 3 (%)	300ppm 30 4 (%)
[Reproductive system]																		
testis			<39>				<31>				<32>				<30>			
	xanthogranuloma		0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
epididymis			<39>				<31>				<32>				<30>			
	spermatogenic granuloma		2 (5)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	2 (6)	0 (0)	0 (0)	0 (0)	1 (3)	2 (7)	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)	2 (7)	0 (0)	0 (0)	0 (0)
prep/cli gl			<39>				<31>				<32>				<30>			
	duct ectasia		0 (0)	3 (8)	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)
[Nervous system]																		
brain			<39>				<31>				<32>				<30>			
	deposit of calcium		18 (46)	0 (0)	0 (0)	0 (0)	13 (42)	0 (0)	0 (0)	0 (0)	17 (53)	0 (0)	0 (0)	0 (0)	19 (63)	0 (0)	0 (0)	0 (0)
	hyaline body		34 (87)	0 (0)	0 (0)	0 (0)	24 (77)	0 (0)	0 (0)	0 (0)	30 (94)	0 (0)	0 (0)	0 (0)	24 (80)	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				20ppm				75ppm				300ppm			
		No. of Animals on Study	39				31				32				30			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Special sense organs/appandage]																		
eye			<39>				<31>				<32>				<30>			
	keratitis		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)	(3)	(0)	(0)	(0)
	degeneration:cornea		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:cornea		1	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0
			(3)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
Harder gl			<39>				<31>				<32>				<30>			
	hyperplasia		1	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
nasolacr d			<39>				<31>				<32>				<30>			
	hyperplasia		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)
[Body cavities]																		
peritoneum			<39>				<31>				<32>				<30>			
	hemorrhage		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)

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				20ppm				75ppm				300ppm			
		No. of Animals on Study	39				31				32				30			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Body cavities]																		
adipose			<39>				<31>				<32>				<30>			
	granulation		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)

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 J 8

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOSUE : FEMALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

Organ	Findings	Group Name	Control				20ppm				75ppm				300ppm			
		No. of Animals on Study	28				25				23				26			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
nasal cavit			<28>				<25>				<23>				<26>			
	eosinophilic change:olfactory epithelium		8	0	0	0	7	0	0	0	2	0	0	0	2	0	0	0
			(29)	(0)	(0)	(0)	(28)	(0)	(0)	(0)	(9)	(0)	(0)	(0)	(8)	(0)	(0)	(0)
	eosinophilic change:respiratory epithelium		19	3	0	0	14	7	0	0	15	5	1	0	16	7	0	0
			(68)	(11)	(0)	(0)	(56)	(28)	(0)	(0)	(65)	(22)	(4)	(0)	(62)	(27)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		6	0	0	0	2	0	0	0	1	0	0	0	12	0	0	0
			(21)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(46)	(0)	(0)	(0)
	respiratory metaplasia:gland		7	0	0	0	4	0	0	0	4	0	0	0	9	0	0	0
			(25)	(0)	(0)	(0)	(16)	(0)	(0)	(0)	(17)	(0)	(0)	(0)	(35)	(0)	(0)	(0)
	atrophy:olfactory epithelium		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)	(0)	(0)	(0)	(0)
lung			<28>				<25>				<23>				<26>			
	granulation		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)	(0)	(0)	(0)	(0)
	hyperplasia		0	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(12)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Hematopoietic system]																		
bone marrow			<28>				<25>				<23>				<26>			
	increased hematopoiesis		11	0	0	0	11	0	0	0	9	0	0	0	19	0	0	0 *
			(39)	(0)	(0)	(0)	(44)	(0)	(0)	(0)	(39)	(0)	(0)	(0)	(73)	(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				20ppm				75ppm				300ppm			
		No. of Animals on Study	28				25				23				26			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
bone marrow			<28>				<25>				<23>				<26>			
	erythropoiesis:increased		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)	(12)	(0)	(0)	(0)
	granulopoiesis:increased		1	0	0	0	1	0	0	0	1	0	0	0	1	0	0	0
			(4)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	osteofibrosis		0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
lymph node			<28>				<25>				<23>				<26>			
	lymphadenitis		2	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0
			(7)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)
	follicular hyperplasia		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)
spleen			<28>				<25>				<23>				<26>			
	deposit of melanin		6	0	0	0	5	0	0	0	2	0	0	0	1	0	0	0
			(21)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(9)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	extramedullary hematopoiesis		5	1	3	0	4	2	0	0	6	1	0	0	5	4	5	2
			(18)	(4)	(11)	(0)	(16)	(8)	(0)	(0)	(26)	(4)	(0)	(0)	(19)	(15)	(19)	(8)

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				20ppm				75ppm				300ppm			
		No. of Animals on Study	28				25				23				26			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
spleen			<28>				<25>				<23>				<26>			
	follicular hyperplasia		2	0	0	0	4	0	0	0	2	0	1	0	2	1	0	0
			(7)	(0)	(0)	(0)	(16)	(0)	(0)	(0)	(9)	(0)	(4)	(0)	(8)	(4)	(0)	(0)
[Circulatory system]																		
heart			<28>				<25>				<23>				<26>			
	mineralization		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)	(0)	(0)	(0)	(0)
[Digestive system]																		
tooth			<28>				<25>				<23>				<26>			
	dysplasia		5	3	0	0	9	1	0	0	5	4	0	0	11	1	1	0
			(18)	(11)	(0)	(0)	(36)	(4)	(0)	(0)	(22)	(17)	(0)	(0)	(42)	(4)	(4)	(0)
salivary gl			<28>				<25>				<23>				<26>			
	inflammatory infiltration		2	0	0	0	2	0	0	0	4	0	0	0	0	0	1	0
			(7)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(17)	(0)	(0)	(0)	(0)	(0)	(4)	(0)
stomach			<28>				<25>				<23>				<26>			
	hyperplasia:glandular stomach		3	9	15	0	0	6	19	0	1	8	14	0	6	13	3	0 **
			(11)	(32)	(54)	(0)	(0)	(24)	(76)	(0)	(4)	(35)	(61)	(0)	(23)	(50)	(12)	(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 28 1 (%)	Control 28 2 (%)	Control 28 3 (%)	Control 28 4 (%)	20ppm 25 1 (%)	20ppm 25 2 (%)	20ppm 25 3 (%)	20ppm 25 4 (%)	75ppm 23 1 (%)	75ppm 23 2 (%)	75ppm 23 3 (%)	75ppm 23 4 (%)	300ppm 26 1 (%)	300ppm 26 2 (%)	300ppm 26 3 (%)	300ppm 26 4 (%)
[Digestive system]																		
liver			<28>				<25>				<23>				<26>			
	angiectasis		1 (4)	0 (0)	0 (0)	0 (0)	1 (4)	2 (8)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)
	hemorrhage		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)
	necrosis:focal		0 (0)	0 (0)	0 (0)	0 (0)	2 (8)	1 (4)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	5 (19)	0 (0)	0 (0)	0 * (0)
	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 (4)	0 (0)	0 (0)	0 (0)
	deposit of ceroid		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)
	granulation		18 (64)	2 (7)	0 (0)	0 (0)	11 (44)	7 (28)	0 (0)	0 (0)	9 (39)	3 (13)	0 (0)	0 (0)	5 (19)	0 (0)	0 (0)	0 ** (0)
	clear cell focus		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (13)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	acidophilic cell focus		0 (0)	0 (0)	0 (0)	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)

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				20ppm				75ppm				300ppm			
		No. of Animals on Study	28				25				23				26			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver			<28>				<25>				<23>				<26>			
	basophilic cell focus		0 (0)	0 (0)	0 (0)	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)
	biliary cyst		0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)
	hepatocellular hypertrophy:central		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)
[Urinary system]																		
kidney			<28>				<25>				<23>				<26>			
	infarct		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hyaline droplet		1 (4)	0 (0)	0 (0)	0 (0)	2 (8)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)
	basophilic change		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	2 (8)	0 (0)	0 (0)	0 (0)
	deposit of hemosiderin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	2 (8)	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	Control				20ppm				75ppm				300ppm			
		No. of Animals on Study	28				25				23				26			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																		
kidney			<28>				<25>				<23>				<26>			
	hyaline cast		2	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
			(7)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(8)	(0)	(0)	(0)
	lymphocytic infiltration		5	0	0	0	9	0	0	0	6	0	0	0	2	0	0	0
			(18)	(0)	(0)	(0)	(36)	(0)	(0)	(0)	(26)	(0)	(0)	(0)	(8)	(0)	(0)	(0)
	inflammatory polyp		2	1	1	0	0	0	0	0	1	0	0	0	0	1	0	0
			(7)	(4)	(4)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(4)	(0)	(0)
	vacuolization of proximal tubule		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)	(0)	(0)	(0)	(0)
	hydronephrosis		0	1	3	0	0	0	0	0	0	0	0	0	0	0	1	0
			(0)	(4)	(11)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)
	tubular necrosis		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)
	mineralization:papilla		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)
	glomerulosclerosis		1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(4)	(0)	(0)	(0)	(4)	(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				20ppm				75ppm				300ppm			
		No. of Animals on Study	28				25				23				26			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																		
urin bladd			<28>				<25>				<23>				<26>			
	inflammatory infiltration		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)	(0)	(0)	(0)
	lymphocytic infiltration		8	0	0	0	8	0	0	0	0	0	0	0 *	2	0	0	0
			(29)	(0)	(0)	(0)	(32)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(8)	(0)	(0)	(0)
[Endocrine system]																		
pituitary			<28>				<25>				<23>				<26>			
	angiectasis		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)
	cyst		4	0	0	0	3	0	0	0	3	0	0	0	4	0	0	0
			(14)	(0)	(0)	(0)	(12)	(0)	(0)	(0)	(13)	(0)	(0)	(0)	(15)	(0)	(0)	(0)
	hyperplasia		2	0	0	0	4	2	0	0	10	2	0	0 **	5	3	0	0
			(7)	(0)	(0)	(0)	(16)	(8)	(0)	(0)	(43)	(9)	(0)	(0)	(19)	(12)	(0)	(0)
	Rathke pouch		2	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(7)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
thyroid			<28>				<25>				<23>				<26>			
	cyst		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)

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				20ppm				75ppm				300ppm			
		No. of Animals on Study	28				25				23				26			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]																		
thyroid			<28>				<25>				<23>				<26>			
	inflammation		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)	(0)	(0)	(0)	(0)
adrenal			<28>				<25>				<23>				<26>			
	deposit of amyloid		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)	(0)	(0)	(0)	(0)
	spindle-cell hyperplasia		1	27	0	0	2	20	3	0	1	18	1	0	7	17	0	0 *
			(4)	(96)	(0)	(0)	(8)	(80)	(12)	(0)	(4)	(78)	(4)	(0)	(27)	(65)	(0)	(0)
	hyperplasia:cortical cell		0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(4)	(0)	(0)	(0)	(0)	(0)	(0)
	hyperplasia:medulla		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)	(0)	(0)	(0)	(0)
[Reproductive system]																		
ovary			<28>				<25>				<23>				<25>			
	congestion		0	0	0	0	0	0	0	0	0	1	0	0	0	2	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(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				20ppm				75ppm				300ppm			
		No. of Animals on Study	28				25				23				26			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
[Reproductive system]																		
ovary			<28>				<25>				<23>				<25>			
	thrombus		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)	(0)	(0)	(0)
	cyst		6	2	4	0	5	4	1	0	4	3	3	0	4	0	1	0
			(21)	(7)	(14)	(0)	(20)	(16)	(4)	(0)	(17)	(13)	(13)	(0)	(16)	(0)	(4)	(0)
	cystic endometrial hyperplasia		1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(4)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
uterus			<28>				<25>				<23>				<26>			
	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)
	decidual 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)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	cystic endometrial hyperplasia		14	1	1	0	7	7	1	0	11	3	2	0	15	1	2	0
			(50)	(4)	(4)	(0)	(28)	(28)	(4)	(0)	(48)	(13)	(9)	(0)	(58)	(4)	(8)	(0)
	xanthogranuloma		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)
mammary gl			<28>				<25>				<23>				<26>			
	hyperplasia		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)	(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				20ppm				75ppm				300ppm			
		No. of Animals on Study	28				25				23				26			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Reproductive system]																		
mammary gl			<28>				<25>				<23>				<26>			
	galactocele		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)
prep/cli gl			<28>				<25>				<23>				<26>			
	duct ectasia		0	1	0	0	0	0	0	0	1	0	0	0	2	0	0	0
			(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(8)	(0)	(0)	(0)
[Nervous system]																		
brain			<28>				<25>				<23>				<26>			
	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)	(4)	(0)	(0)	(0)
	deposit of calcium		18	0	0	0	12	0	0	0	14	0	0	0	7	0	0	0 *
			(64)	(0)	(0)	(0)	(48)	(0)	(0)	(0)	(61)	(0)	(0)	(0)	(27)	(0)	(0)	(0)
	hyaline body		21	0	0	0	23	0	0	0	19	0	0	0	22	0	0	0
			(75)	(0)	(0)	(0)	(92)	(0)	(0)	(0)	(83)	(0)	(0)	(0)	(85)	(0)	(0)	(0)
[Special sense organs/appandage]																		
eye			<28>				<24>				<23>				<26>			
	keratitis		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)	(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				20ppm				75ppm				300ppm			
		No. of Animals on Study	28				25				23				26			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Special sense organs/appandage]																		
eye			<28>				<24>				<23>				<26>			
	degeneration:cornea		2	0	0	0	4	0	0	0	1	0	0	0	0	0	0	0
			(7)	(0)	(0)	(0)	(17)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:cornea		1	0	0	0	2	0	0	0	5	0	0	0	4	0	0	0
			(4)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(22)	(0)	(0)	(0)	(15)	(0)	(0)	(0)
Harder gl			<28>				<24>				<23>				<26>			
	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)

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 K 1

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

RAT : MALE

STUDY NO. : 0158
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	20 ppm	75 ppm	300 ppm
0 - 52	NO. OF EXAMINED ANIMALS		0	1	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		1	2	4	3
	NO. OF ANIMALS WITH TUMORS		1	2	3	3
	NO. OF ANIMALS WITH SINGLE TUMORS		0	2	2	0
	NO. OF ANIMALS WITH MULTIPLE TUMORS		1	0	1	3
	NO. OF BENIGN TUMORS		1	2	3	6
	NO. OF MALIGNANT TUMORS		2	0	1	2
	NO. OF TOTAL TUMORS		3	2	4	8
79 - 104	NO. OF EXAMINED ANIMALS		16	13	17	29
	NO. OF ANIMALS WITH TUMORS		16	13	17	29
	NO. OF ANIMALS WITH SINGLE TUMORS		1	2	1	2
	NO. OF ANIMALS WITH MULTIPLE TUMORS		15	11	16	27
	NO. OF BENIGN TUMORS		33	18	36	68
	NO. OF MALIGNANT TUMORS		9	10	10	14
	NO. OF TOTAL TUMORS		42	28	46	82
105 - 105	NO. OF EXAMINED ANIMALS		18	20	18	10
	NO. OF ANIMALS WITH TUMORS		18	19	18	10
	NO. OF ANIMALS WITH SINGLE TUMORS		3	5	1	2
	NO. OF ANIMALS WITH MULTIPLE TUMORS		15	14	17	8
	NO. OF BENIGN TUMORS		41	38	43	25
	NO. OF MALIGNANT TUMORS		6	8	2	4
	NO. OF TOTAL TUMORS		47	46	45	29

STUDY NO. : 0158
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	20 ppm	75 ppm	300 ppm
0 - 105	NO. OF EXAMINED ANIMALS		50	50	50	50
	NO. OF ANIMALS WITH TUMORS		35	34	38	42
	NO. OF ANIMALS WITH SINGLE TUMORS		4	9	4	4
	NO. OF ANIMALS WITH MULTIPLE TUMORS		31	25	34	38
	NO. OF BENIGN TUMORS		75	58	82	99
	NO. OF MALIGNANT TUMORS		17	18	13	20
	NO. OF TOTAL TUMORS		92	76	95	119

APPENDIX K 2

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

RAT : FEMALE

STUDY NO. : 0158
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	20 ppm	75 ppm	300 ppm
0 - 52	NO. OF EXAMINED ANIMALS		0	1	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		1	1	1	1
	NO. OF ANIMALS WITH TUMORS		1	1	1	1
	NO. OF ANIMALS WITH SINGLE TUMORS		1	1	1	1
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	0	0	0
	NO. OF BENIGN TUMORS		1	0	0	0
	NO. OF MALIGNANT TUMORS		0	1	1	1
	NO. OF TOTAL TUMORS		1	1	1	1
79 - 104	NO. OF EXAMINED ANIMALS		11	14	11	13
	NO. OF ANIMALS WITH TUMORS		11	14	11	13
	NO. OF ANIMALS WITH SINGLE TUMORS		6	11	5	8
	NO. OF ANIMALS WITH MULTIPLE TUMORS		5	3	6	5
	NO. OF BENIGN TUMORS		14	9	12	16
	NO. OF MALIGNANT TUMORS		4	8	10	4
	NO. OF TOTAL TUMORS		18	17	22	20
105 - 105	NO. OF EXAMINED ANIMALS		21	17	22	20
	NO. OF ANIMALS WITH TUMORS		17	13	22	15
	NO. OF ANIMALS WITH SINGLE TUMORS		10	3	7	6
	NO. OF ANIMALS WITH MULTIPLE TUMORS		7	10	15	9
	NO. OF BENIGN TUMORS		23	24	33	26
	NO. OF MALIGNANT TUMORS		4	3	7	4
	NO. OF TOTAL TUMORS		27	27	40	30

STUDY NO. : 0158
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	20 ppm	75 ppm	300 ppm
0 - 105	NO. OF EXAMINED ANIMALS		50	50	50	50
	NO. OF ANIMALS WITH TUMORS		29	28	34	29
	NO. OF ANIMALS WITH SINGLE TUMORS		17	15	13	15
	NO. OF ANIMALS WITH MULTIPLE TUMORS		12	13	21	14
	NO. OF BENIGN TUMORS		38	33	45	42
	NO. OF MALIGNANT TUMORS		8	12	18	9
	NO. OF TOTAL TUMORS		46	45	63	51

APPENDIX K 3

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

MOUSE : MALE

STUDY NO. : 0159
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	20ppm	75ppm	300ppm
0 - 52	NO. OF EXAMINED ANIMALS		2	0	1	1
	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	2	4	4
	NO. OF ANIMALS WITH TUMORS		1	1	3	3
	NO. OF ANIMALS WITH SINGLE TUMORS		0	0	2	2
	NO. OF ANIMALS WITH MULTIPLE TUMORS		1	1	1	1
	NO. OF BENIGN TUMORS		1	1	0	0
	NO. OF MALIGNANT TUMORS		1	3	5	4
	NO. OF TOTAL TUMORS		2	4	5	4
79 - 104	NO. OF EXAMINED ANIMALS		6	16	13	14
	NO. OF ANIMALS WITH TUMORS		6	13	12	14
	NO. OF ANIMALS WITH SINGLE TUMORS		4	10	7	4
	NO. OF ANIMALS WITH MULTIPLE TUMORS		2	3	5	10
	NO. OF BENIGN TUMORS		4	4	4	4
	NO. OF MALIGNANT TUMORS		4	13	16	25
	NO. OF TOTAL TUMORS		8	17	20	29
105 - 105	NO. OF EXAMINED ANIMALS		39	31	32	30
	NO. OF ANIMALS WITH TUMORS		27	26	26	27
	NO. OF ANIMALS WITH SINGLE TUMORS		14	12	12	10
	NO. OF ANIMALS WITH MULTIPLE TUMORS		13	14	14	17
	NO. OF BENIGN TUMORS		19	14	10	17
	NO. OF MALIGNANT TUMORS		24	28	35	34
	NO. OF TOTAL TUMORS		43	42	45	51

STUDY NO. : 0159
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	20ppm	75ppm	300ppm
0 - 105	NO. OF EXAMINED ANIMALS		49	49	50	49
	NO. OF ANIMALS WITH TUMORS		34	40	41	44
	NO. OF ANIMALS WITH SINGLE TUMORS		18	22	21	16
	NO. OF ANIMALS WITH MULTIPLE TUMORS		16	18	20	28
	NO. OF BENIGN TUMORS		24	19	14	21
	NO. OF MALIGNANT TUMORS		29	44	56	63
	NO. OF TOTAL TUMORS		53	63	70	84

APPENDIX K 4

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

MOUSE: FEMALE

STUDY NO. : 0159
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	20ppm	75ppm	300ppm
0 - 52	NO. OF EXAMINED ANIMALS		3	1	1	0
	NO. OF ANIMALS WITH TUMORS		1	1	1	0
	NO. OF ANIMALS WITH SINGLE TUMORS		1	1	1	0
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	0	0	0
	NO. OF BENIGN TUMORS		0	0	0	0
	NO. OF MALIGNANT TUMORS		1	1	1	0
	NO. OF TOTAL TUMORS		1	1	1	0
53 - 78	NO. OF EXAMINED ANIMALS		6	7	4	5
	NO. OF ANIMALS WITH TUMORS		5	6	4	5
	NO. OF ANIMALS WITH SINGLE TUMORS		5	5	1	4
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	1	3	1
	NO. OF BENIGN TUMORS		1	1	1	1
	NO. OF MALIGNANT TUMORS		4	6	7	5
	NO. OF TOTAL TUMORS		5	7	8	6
79 - 104	NO. OF EXAMINED ANIMALS		13	17	21	19
	NO. OF ANIMALS WITH TUMORS		13	16	21	19
	NO. OF ANIMALS WITH SINGLE TUMORS		5	11	13	4
	NO. OF ANIMALS WITH MULTIPLE TUMORS		8	5	8	15
	NO. OF BENIGN TUMORS		2	6	7	12
	NO. OF MALIGNANT TUMORS		19	16	23	34
	NO. OF TOTAL TUMORS		21	22	30	46
105 - 105	NO. OF EXAMINED ANIMALS		28	25	23	26
	NO. OF ANIMALS WITH TUMORS		21	23	20	26
	NO. OF ANIMALS WITH SINGLE TUMORS		8	11	10	2
	NO. OF ANIMALS WITH MULTIPLE TUMORS		13	12	10	24
	NO. OF BENIGN TUMORS		15	19	15	25
	NO. OF MALIGNANT TUMORS		23	20	17	46
	NO. OF TOTAL TUMORS		38	39	32	71

STUDY NO. : 0159
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	20ppm	75ppm	300ppm
0 - 105	NO. OF EXAMINED ANIMALS		50	50	49	50
	NO. OF ANIMALS WITH TUMORS		40	46	46	50
	NO. OF ANIMALS WITH SINGLE TUMORS		19	28	25	10
	NO. OF ANIMALS WITH MULTIPLE TUMORS		21	18	21	40
	NO. OF BENIGN TUMORS		18	26	23	38
	NO. OF MALIGNANT TUMORS		47	43	48	85
	NO. OF TOTAL TUMORS		65	69	71	123

APPENDIX L 1

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS : SUMMARY

RAT : MALE :

(2-YEAR STUDY)

STUDY NO. : 0158
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control	20 ppm	75 ppm	300 ppm
		No. of animals on Study	50	50	50	50
[Integumentary system/appandage]						
skin/app			<50>	<50>	<50>	<50>
	squamous cell papilloma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
	schwannoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
	keratoacanthoma		1 (2%)	4 (8%)	0 (0%)	3 (6%)
subcutis			<50>	<50>	<50>	<50>
	fibroma		4 (8%)	3 (6%)	6 (12%)	6 (12%)
	lipoma		0 (0%)	1 (2%)	1 (2%)	0 (0%)
	fibrosarcoma		1 (2%)	1 (2%)	0 (0%)	0 (0%)
	hemangiosarcoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
[Respiratory system]						
nasal cavit			<50>	<50>	<50>	<50>
	adenoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
lung			<50>	<50>	<50>	<50>
	bronchiolar-alveolar adenoma		1 (2%)	0 (0%)	1 (2%)	1 (2%)
[Hematopoietic system]						
bone marrow			<50>	<50>	<50>	<50>
	malignant histiocytosis		1 (2%)	0 (0%)	0 (0%)	0 (0%)
spleen			<50>	<50>	<50>	<50>
	fibroma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
	hemangioma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
	sarcoma:NOS		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

STUDY NO. : 0158
ANIMAL : RAT F344
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	20 ppm 50	75 ppm 50	300 ppm 50
[Hematopoietic system]						
spleen			<50>	<50>	<50>	<50>
	mononuclear cell leukemia		9 (18%)	14 (28%)	10 (20%)	13 (26%)
	hemangiosarcoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
[Digestive system]						
oral cavity			<50>	<50>	<50>	<50>
	squamous cell papilloma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
tongue			<50>	<50>	<50>	<50>
	squamous cell papilloma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
stomach			<50>	<49>	<50>	<50>
	squamous cell papilloma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
small intes			<50>	<50>	<50>	<50>
	schwannoma:malignant		0 (0%)	1 (2%)	0 (0%)	0 (0%)
liver			<50>	<50>	<50>	<50>
	hepatocellular adenoma		1 (2%)	2 (4%)	0 (0%)	1 (2%)
	histiocytic sarcoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
[Urinary system]						
urin bladd			<50>	<50>	<50>	<50>
	transitional cell papilloma		1 (2%)	0 (0%)	1 (2%)	0 (0%)
[Endocrine system]						
pituitary			<50>	<50>	<50>	<50>
	adenoma		24 (48%)	21 (42%)	26 (52%)	23 (46%)
thyroid			<49>	<49>	<50>	<50>
	C-cell adenoma		10 (20%)	5 (10%)	8 (16%)	9 (18%)
	follicular adenoma		1 (2%)	0 (0%)	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

STUDY NO. : 0158
ANIMAL : RAT F344
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	20 ppm 50	75 ppm 50	300 ppm 50
[Endocrine system]						
thyroid			<49>	<49>	<50>	<50>
	C-cell carcinoma		4 (8%)	0 (0%)	0 (0%)	1 (2%)
	follicular adenocarcinoma		2 (4%)	1 (2%)	2 (4%)	1 (2%)
panc islet			<50>	<50>	<50>	<50>
	islet cell adenoma		6 (12%)	4 (8%)	5 (10%)	3 (6%)
adrenal			<50>	<50>	<50>	<50>
	pheochromocytoma		15 (30%)	9 (18%)	12 (24%)	16 (32%)
	cortical adenoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
[Reproductive system]						
testis			<50>	<50>	<50>	<50>
	interstitial cell tumor		44 (88%)	42 (84%)	43 (86%)	47 (94%)
mammary gl			<50>	<50>	<50>	<50>
	fibroadenoma		0 (0%)	2 (4%)	0 (0%)	0 (0%)
	adenocarcinoma		2 (4%)	1 (2%)	1 (2%)	0 (0%)
prep/cli gl			<50>	<50>	<50>	<50>
	adenoma		4 (8%)	3 (6%)	1 (2%)	6 (12%)
[Nervous system]						
brain			<50>	<50>	<50>	<50>
	glioma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
spinal cord			<50>	<50>	<50>	<50>
	glioma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
[Special sense organs/appandage]						
Zymbal gl			<50>	<50>	<50>	<50>
	carcinoma:NOS		0 (0%)	1 (2%)	0 (0%)	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	20 ppm 50	75 ppm 50	300 ppm 50
[Musculoskeletal system]						
muscle			<50>	<50>	<50>	<50>
	fibrosarcoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
	hemangiosarcoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
bone			<50>	<50>	<50>	<50>
	osteosarcoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
vertebra			<50>	<50>	<50>	<50>
	chordoma:malignant		0 (0%)	0 (0%)	1 (2%)	0 (0%)
[Body cavities]						
peritoneum			<50>	<50>	<50>	<50>
	lipoma		1 (2%)	0 (0%)	0 (0%)	1 (2%)
	mesothelioma		1 (2%)	2 (4%)	3 (6%)	1 (2%)

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

APPENDIX L 2

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE :

(2-YEAR STUDY)

Organ	Findings	Group Name	Control	20 ppm	75 ppm	300 ppm
		No. of animals on Study	50	50	50	50
[Integumentary system/appandage]						
skin/app			<50>	<50>	<50>	<50>
	schwannoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
	keratoacanthoma		2 (4%)	0 (0%)	0 (0%)	0 (0%)
subcutis			<50>	<50>	<50>	<50>
	fibroma		0 (0%)	0 (0%)	0 (0%)	2 (4%)
	fibrosarcoma		0 (0%)	2 (4%)	0 (0%)	0 (0%)
[Respiratory system]						
lung			<50>	<50>	<50>	<50>
	bronchiolar-alveolar adenoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
[Hematopoietic system]						
lymph node			<50>	<50>	<50>	<50>
	malignant lymphoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
spleen			<50>	<50>	<50>	<50>
	mononuclear cell leukemia		6 (12%)	7 (14%)	9 (18%)	7 (14%)
	hemangiosarcoma		1 (2%)	1 (2%)	0 (0%)	0 (0%)
[Digestive system]						
small intes			<50>	<50>	<50>	<50>
	schwannoma:malignant		0 (0%)	1 (2%)	0 (0%)	0 (0%)
liver			<50>	<50>	<50>	<50>
	hepatocellular adenoma		0 (0%)	1 (2%)	1 (2%)	1 (2%)
	histiocytic sarcoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
	hepatocellular carcinoma		0 (0%)	0 (0%)	1 (2%)	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	20 ppm 50	75 ppm 50	300 ppm 50
[Digestive system]						
liver	cholangiocellular carcinoma		<50> 0 (0%)	<50> 2 (4%)	<50> 0 (0%)	<50> 0 (0%)
[Urinary system]						
urin bladd	transitional cell papilloma		<50> 1 (2%)	<50> 1 (2%)	<50> 1 (2%)	<50> 0 (0%)
[Endocrine system]						
pituitary	adenoma		<50> 33 (66%)	<50> 30 (60%)	<50> 32 (64%)	<50> 28 (56%)
	adenocarcinoma		1 (2%)	0 (0%)	1 (2%)	0 (0%)
thyroid	C-cell adenoma		<47> 2 (4%)	<50> 7 (14%)	<49> 9 (18%)	<49> 6 (12%)
	C-cell carcinoma		0 (0%)	0 (0%)	1 (2%)	1 (2%)
	follicular adenocarcinoma		1 (2%)	2 (4%)	1 (2%)	0 (0%)
panc islet	islet cell adenoma		<50> 1 (2%)	<50> 1 (2%)	<50> 0 (0%)	<50> 2 (4%)
adrenal	pheochromocytoma		<50> 2 (4%)	<50> 4 (8%)	<50> 6 (12%)	<50> 5 (10%)
	cortical adenoma		1 (2%)	1 (2%)	1 (2%)	0 (0%)
[Reproductive system]						
ovary	granulosa-theca cell tumor		<50> 1 (2%)	<50> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)
uterus	adenoma		<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)	<50> 0 (0%)

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

STUDY NO. : 0158
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name / No. of animals on Study	Control 50	20 ppm 50	75 ppm 50	300 ppm 50
[Reproductive system]						
uterus			<50>	<50>	<50>	<50>
	endometrial stromal polyp		9 (18%)	1 (2%)	9 (18%)	10 (20%)
	adenocarcinoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
	leiomyosarcoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
	endometrial stromal sarcoma		0 (0%)	2 (4%)	2 (4%)	0 (0%)
vagina			<50>	<50>	<50>	<50>
	squamous cell papilloma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
mammary gl			<50>	<50>	<50>	<50>
	fibroadenoma		4 (8%)	6 (12%)	6 (12%)	8 (16%)
	adenocarcinoma		1 (2%)	0 (0%)	1 (2%)	1 (2%)
prep/cli gl			<50>	<50>	<50>	<50>
	adenoma		2 (4%)	3 (6%)	2 (4%)	4 (8%)
[Nervous system]						
brain			<50>	<50>	<50>	<50>
	glioma		0 (0%)	0 (0%)	2 (4%)	0 (0%)
[Musculoskeletal system]						
muscle			<50>	<50>	<50>	<50>
	fibroma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
	lipoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
[Body cavities]						
pleura			<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

Organ	Findings	Group Name	Control	20 ppm	75 ppm	300 ppm
		No. of animals on Study	50	50	50	50
[Body cavities]						
peritoneum			<50>	<50>	<50>	<50>
	lipoma		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 L 3

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS : SUMMARY

MOUSE: MALE

(2-YEAR STUDY)

STUDY NO. : 0159
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 49	20ppm 49	75ppm 50	300ppm 49
[Integumentary system/appandage]						
skin/app			<49>	<49>	<50>	<49>
	mastcytoma:malignant		0 (0%)	0 (0%)	0 (0%)	1 (2%)
subcutis			<49>	<49>	<50>	<49>
	lipoma		1 (2%)	0 (0%)	1 (2%)	0 (0%)
	histiocytic sarcoma		0 (0%)	0 (0%)	2 (4%)	0 (0%)
	hemangiosarcoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
[Respiratory system]						
lung			<49>	<49>	<50>	<49>
	bronchiolar-alveolar adenoma		3 (6%)	3 (6%)	3 (6%)	4 (8%)
	squamous cell carcinoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
	bronchiolar-alveolar carcinoma		4 (8%)	5 (10%)	5 (10%)	1 (2%)
[Hematopoietic system]						
bone marrow			<49>	<49>	<50>	<49>
	hemangioma		0 (0%)	1 (2%)	1 (2%)	0 (0%)
lymph node			<49>	<49>	<50>	<49>
	malignant lymphoma		4 (8%)	7 (14%)	13 (26%)	8 (16%)
spleen			<49>	<49>	<50>	<49>
	hemangioma		1 (2%)	2 (4%)	0 (0%)	0 (0%)
	malignant lymphoma		1 (2%)	1 (2%)	1 (2%)	1 (2%)
	mastcytoma:malignant		1 (2%)	1 (2%)	0 (0%)	1 (2%)
	hemangiosarcoma		1 (2%)	3 (6%)	3 (6%)	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 49	20ppm 49	75ppm 50	300ppm 49
[Digestive system]						
salivary gl			<49>	<49>	<50>	<49>
	histiocytic sarcoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
stomach			<49>	<49>	<50>	<49>
	leiomyosarcoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
small intes			<49>	<49>	<50>	<49>
	adenocarcinoma		0 (0%)	0 (0%)	1 (2%)	1 (2%)
	leiomyosarcoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
	hemangiosarcoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
large intes			<49>	<49>	<50>	<49>
	leiomyosarcoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
liver			<49>	<49>	<50>	<49>
	hemangioma		1 (2%)	0 (0%)	0 (0%)	1 (2%)
	hepatocellular adenoma		13 (27%)	9 (18%)	7 (14%)	13 (27%)
	histiocytic sarcoma		0 (0%)	3 (6%)	1 (2%)	6 (12%)
	hemangiosarcoma		5 (10%)	5 (10%)	5 (10%)	5 (10%)
	hepatocellular carcinoma		12 (24%)	17 (35%)	16 (32%)	38 (78%)
[Urinary system]						
urin bladd			<49>	<49>	<50>	<49>
	histiocytic sarcoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
[Endocrine system]						
pituitary			<49>	<49>	<50>	<49>
	adenoma		1 (2%)	1 (2%)	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 49	20ppm 49	75ppm 50	300ppm 49
[Endocrine system]						
thyroid			<47>	<49>	<50>	<49>
	C-cell adenoma		1 (2%)	1 (2%)	0 (0%)	0 (0%)
	follicular adenoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
[Reproductive system]						
epididymis			<49>	<49>	<50>	<49>
	histiocytic sarcoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
[Nervous system]						
periph nerv			<49>	<49>	<50>	<49>
	schwannoma:malignant		0 (0%)	1 (2%)	0 (0%)	0 (0%)
[Special sense organs/appandage]						
Harder gl			<49>	<49>	<50>	<49>
	adenoma		2 (4%)	2 (4%)	1 (2%)	2 (4%)
[Musculoskeletal system]						
bone			<49>	<49>	<50>	<49>
	osteogenic sarcoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
[Body cavities]						
peritoneum			<49>	<49>	<50>	<49>
	histiocytic sarcoma		0 (0%)	0 (0%)	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

APPENDIX L 4

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS : SUMMARY

MOUSE: FEMALE

(2-YEAR STUDY)

Organ	Findings	Group Name / No. of animals on Study	Control 50	20ppm 50	75ppm 49	300ppm 50
[Integumentary system/appandage]						
skin/app			<50>	<50>	<49>	<50>
	squamous cell carcinoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
subcutis			<50>	<50>	<49>	<50>
	hemangioma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
	histiocytic sarcoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
	sarcoma:NOS		0 (0%)	0 (0%)	0 (0%)	1 (2%)
[Respiratory system]						
lung			<50>	<50>	<49>	<50>
	bronchiolar-alveolar adenoma		0 (0%)	3 (6%)	1 (2%)	3 (6%)
	bronchiolar-alveolar carcinoma		1 (2%)	1 (2%)	1 (2%)	4 (8%)
[Hematopoietic system]						
bone marrow			<50>	<50>	<49>	<50>
	hemangioma		0 (0%)	1 (2%)	1 (2%)	0 (0%)
lymph node			<50>	<50>	<49>	<50>
	malignant lymphoma		21 (42%)	21 (42%)	18 (37%)	23 (46%)
spleen			<50>	<50>	<49>	<50>
	malignant lymphoma		1 (2%)	1 (2%)	2 (4%)	2 (4%)
	mastcytoma:malignant		0 (0%)	1 (2%)	0 (0%)	0 (0%)
	hemangiosarcoma		0 (0%)	1 (2%)	1 (2%)	1 (2%)
[Digestive system]						
tongue			<50>	<50>	<49>	<50>
	keratoacanthoma		0 (0%)	0 (0%)	1 (2%)	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	20ppm 50	75ppm 49	300ppm 50
[Digestive system]						
salivary gl			<50>	<50>	<49>	<50>
	histiocytic sarcoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
stomach			<50>	<50>	<49>	<50>
	squamous cell papilloma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
small intes			<50>	<50>	<49>	<50>
	adenoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
liver			<50>	<50>	<49>	<50>
	hepatocellular adenoma		2 (4%)	10 (20%)	6 (12%)	20 (40%)
	histiocytic sarcoma		2 (4%)	1 (2%)	1 (2%)	0 (0%)
	malignant lymphoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
	hemangiosarcoma		1 (2%)	3 (6%)	5 (10%)	0 (0%)
	hepatocellular carcinoma		2 (4%)	4 (8%)	2 (4%)	41 (82%)
[Urinary system]						
urin bladd			<50>	<50>	<49>	<50>
	histiocytic sarcoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
[Endocrine system]						
pituitary			<50>	<50>	<49>	<50>
	adenoma		5 (10%)	7 (14%)	9 (18%)	8 (16%)
	adenocarcinoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
adrenal			<50>	<50>	<49>	<50>
	pheochromocytoma		1 (2%)	2 (4%)	1 (2%)	0 (0%)
[Reproductive system]						
ovary			<50>	<50>	<49>	<49>
	cystadenoma		1 (2%)	0 (0%)	0 (0%)	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	20ppm 50	75ppm 49	300ppm 50
[Reproductive system]						
ovary			<50>	<50>	<49>	<49>
	hemangioma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
uterus			<50>	<50>	<49>	<50>
	endometrial stromal polyp		2 (4%)	0 (0%)	2 (4%)	0 (0%)
	fibrosarcoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
	histiocytic sarcoma		11 (22%)	6 (12%)	13 (27%)	12 (24%)
	hemangiosarcoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
vagina			<50>	<50>	<49>	<50>
	histiocytic sarcoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
mammary gl			<50>	<50>	<49>	<50>
	adenocarcinoma		1 (2%)	0 (0%)	1 (2%)	0 (0%)
[Nervous system]						
periph nerv			<50>	<50>	<49>	<50>
	schwannoma:malignant		1 (2%)	0 (0%)	0 (0%)	0 (0%)
[Special sense organs/appandage]						
Harder gl			<50>	<49>	<49>	<50>
	adenoma		6 (12%)	2 (4%)	2 (4%)	2 (4%)
[Musculoskeletal system]						
muscle			<50>	<50>	<49>	<50>
	hemangiosarcoma		1 (2%)	0 (0%)	2 (4%)	0 (0%)
[Body cavities]						
peritoneum			<50>	<50>	<49>	<50>
	hemangiosarcoma		1 (2%)	0 (0%)	1 (2%)	0 (0%)

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

STUDY NO. : 0159
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name	Control	20ppm	75ppm	300ppm
		No. of animals on Study	50	50	49	50
[Body cavities]						
retroperit			<50>	<50>	<49>	<50>
	hemangiosarcoma		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 M 1

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

RAT : MALE

(2-YEAR STUDY)

Group Name	Control	20 ppm	75 ppm	300 ppm
	SITE : skin/appendage TUMOR : keratoacanthoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	4/50(8.0)	0/50(0.0)	3/50(6.0)
Adjusted rates(b)	2.78	11.43	0.0	16.67
Terminal rates(c)	0/33(0.0)	3/34(8.8)	0/29(0.0)	3/18(16.7)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.1274			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.5658			
Fisher Exact test(e)		P = 0.1998	P = 0.4950	P = 0.3235
	SITE : subcutis TUMOR : fibroma			
Tumor rate				
Overall rates(a)	4/50(8.0)	3/50(6.0)	6/50(12.0)	6/50(12.0)
Adjusted rates(b)	12.12	8.82	20.69	10.34
Terminal rates(c)	4/33(12.1)	3/34(8.8)	6/29(20.7)	0/18(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.0106* ?			
Prevalence method(d)	P = 0.2880			
Combined analysis(d)	P = 0.0855			
Cochran-Armitage test(e)	P = 0.3810			
Fisher Exact test(e)		P = 0.4895	P = 0.3944	P = 0.3944
	SITE : subcutis TUMOR : fibroma,fibrosarcoma			
Tumor rate				
Overall rates(a)	5/50(10.0)	4/50(8.0)	6/50(12.0)	6/50(12.0)
Adjusted rates(b)	12.12	11.76	20.69	10.34
Terminal rates(c)	4/33(12.1)	4/34(11.8)	6/29(20.7)	0/18(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.0809			
Prevalence method(d)	P = 0.3316			
Combined analysis(d)	P = 0.1539			
Cochran-Armitage test(e)	P = 0.6206			
Fisher Exact test(e)		P = 0.4883	P = 0.4872	P = 0.4872

Group Name	Control	20 ppm	75 ppm	300 ppm
	SITE : spleen TUMOR : mononuclear cell leukemia			
Tumor rate				
Overall rates(a)	9/50(18.0)	14/50(28.0)	10/50(20.0)	13/50(26.0)
Adjusted rates(b)	12.77	18.92	13.16	16.67
Terminal rates(c)	4/33(12.1)	6/34(17.6)	3/29(10.3)	3/18(16.7)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.0116*			
Prevalence method(d)	P = 0.7900			
Combined analysis(d)	P = 0.0977			
Cochran-Armitage test(e)	P = 0.5855			
Fisher Exact test(e)		P = 0.2397	P = 0.4839	P = 0.2965
	SITE : pituitary gland TUMOR : adenoma			
Tumor rate				
Overall rates(a)	24/50(48.0)	21/50(42.0)	26/50(52.0)	23/50(46.0)
Adjusted rates(b)	48.48	48.65	51.43	54.29
Terminal rates(c)	16/33(48.5)	16/34(47.1)	14/29(48.3)	7/18(38.9)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8027			
Prevalence method(d)	P = 0.1767			
Combined analysis(d)	P = 0.3426			
Cochran-Armitage test(e)	P = 0.9882			
Fisher Exact test(e)		P = 0.4242	P = 0.4771	P = 0.4774
	SITE : pituitary gland TUMOR : adenoma,adenocarcinoma			
Tumor rate				
Overall rates(a)	24/50(48.0)	21/50(42.0)	26/50(52.0)	23/50(46.0)
Adjusted rates(b)	48.48	48.65	51.43	54.29
Terminal rates(c)	16/33(48.5)	16/34(47.1)	14/29(48.3)	7/18(38.9)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8027			
Prevalence method(d)	P = 0.1767			
Combined analysis(d)	P = 0.3426			
Cochran-Armitage test(e)	P = 0.9882			
Fisher Exact test(e)		P = 0.4242	P = 0.4771	P = 0.4774

Group Name	Control	20 ppm	75 ppm	300 ppm
	SITE : thyroid TUMOR : C-cell adenoma			
Tumor rate				
Overall rates(a)	10/49(20.4)	5/49(10.2)	8/50(16.0)	9/50(18.0)
Adjusted rates(b)	23.08	14.71	20.69	22.22
Terminal rates(c)	7/32(21.9)	5/34(14.7)	6/29(20.7)	4/18(22.2)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.2366			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.7331			
Fisher Exact test(e)		P = 0.1776	P = 0.4147	P = 0.5000
	SITE : thyroid TUMOR : follicular adenoma			
Tumor rate				
Overall rates(a)	1/49(2.0)	0/49(0.0)	3/50(6.0)	2/50(4.0)
Adjusted rates(b)	3.13	0.0	8.33	5.56
Terminal rates(c)	1/32(3.1)	0/34(0.0)	1/29(3.4)	1/18(5.6)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.1736			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.4313			
Fisher Exact test(e)		P = 0.4949	P = 0.3312	P = 0.4851
	SITE : thyroid TUMOR : C-cell carcinoma			
Tumor rate				
Overall rates(a)	4/49(8.2)	0/49(0.0)	0/50(0.0)	1/50(2.0)
Adjusted rates(b)	8.33	0.0	0.0	3.45
Terminal rates(c)	2/32(6.3)	0/34(0.0)	0/29(0.0)	0/18(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 1.0000 ?			
Prevalence method(d)	P = 0.5307			
Combined analysis(d)	P = 0.6543			
Cochran-Armitage test(e)	P = 0.4530			
Fisher Exact test(e)		P = 0.0689	P = 0.0662	P = 0.1936

Group Name	Control	20 ppm	75 ppm	300 ppm
	SITE : thyroid TUMOR : C-cell adenoma,C-cell carcinoma			
Tumor rate				
Overall rates(a)	13/49(26.5)	5/49(10.2)	8/50(16.0)	10/50(20.0)
Adjusted rates(b)	28.95	14.71	20.69	22.86
Terminal rates(c)	9/32(28.1)	5/34(14.7)	6/29(20.7)	4/18(22.2)
Statistical analysis				
Peto test				
Standard method(d)	P = 1.0000 ?			
Prevalence method(d)	P = 0.2476			
Combined analysis(d)	P = 0.2920			
Cochran-Armitage test(e)	P = 0.8622			
Fisher Exact test(e)		P = 0.0680	P = 0.2143	P = 0.3541
	SITE : thyroid TUMOR : follicular adenoma,follicular adenocarcinoma			
Tumor rate				
Overall rates(a)	3/49(6.1)	1/49(2.0)	5/50(10.0)	3/50(6.0)
Adjusted rates(b)	9.38	2.94	13.89	11.11
Terminal rates(c)	3/32(9.4)	1/34(2.9)	3/29(10.3)	2/18(11.1)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.2145			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.8049			
Fisher Exact test(e)		P = 0.3237	P = 0.3899	P = 0.3300
	SITE : pancreas islet TUMOR : islet cell adenoma			
Tumor rate				
Overall rates(a)	6/50(12.0)	4/50(8.0)	5/50(10.0)	3/50(6.0)
Adjusted rates(b)	15.15	9.52	14.29	6.38
Terminal rates(c)	5/33(15.2)	3/34(8.8)	2/29(6.9)	0/18(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.7604			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.3819			
Fisher Exact test(e)		P = 0.3944	P = 0.4872	P = 0.2728

Group Name	Control	20 ppm	75 ppm	300 ppm
	SITE : adrenal gland			
	TUMOR : pheochromocytoma			
Tumor rate				
Overall rates(a)	15/50(30.0)	9/50(18.0)	12/50(24.0)	16/50(32.0)
Adjusted rates(b)	31.91	23.53	31.25	47.62
Terminal rates(c)	10/33(30.3)	8/34(23.5)	7/29(24.1)	7/18(38.9)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.0581			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.3145			
Fisher Exact test(e)		P = 0.1915	P = 0.3844	P = 0.4805
	SITE : testis			
	TUMOR : interstitial cell tumor			
Tumor rate				
Overall rates(a)	44/50(88.0)	42/50(84.0)	43/50(86.0)	47/50(94.0)
Adjusted rates(b)	95.24	95.24	96.55	100.00
Terminal rates(c)	31/33(93.9)	32/34(94.1)	28/29(96.6)	18/18(100.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.0039**			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.1525			
Fisher Exact test(e)		P = 0.4956	P = 0.4728	P = 0.4671
	SITE : mammary gland			
	TUMOR : fibroadenoma,adenocarcinoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	3/50(6.0)	1/50(2.0)	0/50(0.0)
Adjusted rates(b)	3.03	8.82	3.45	0.0
Terminal rates(c)	1/33(3.0)	3/34(8.8)	1/29(3.4)	0/18(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 1.0000 ?			
Prevalence method(d)	P = 0.8428			
Combined analysis(d)	P = 0.9060			
Cochran-Armitage test(e)	P = 0.1122			
Fisher Exact test(e)		P = 0.4909	P = 0.4926	P = 0.2574

Group Name	Control	20 ppm	75 ppm	300 ppm
	SITE : preputial/clitoral gland TUMOR : adenoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	3/50(6.0)	1/50(2.0)	6/50(12.0)
Adjusted rates(b)	9.52	7.14	3.45	15.38
Terminal rates(c)	3/33(9.1)	2/34(5.9)	1/29(3.4)	2/18(11.1)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.0629			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.1997			
Fisher Exact test(e)		P = 0.4895	P = 0.1998	P = 0.3944
	SITE : peritoneum TUMOR : mesothelioma			
Tumor rate				
Overall rates(a)	1/50(2.0)	2/50(4.0)	3/50(6.0)	1/50(2.0)
Adjusted rates(b)	3.03	5.88	0.0	0.0
Terminal rates(c)	1/33(3.0)	2/34(5.9)	0/29(0.0)	0/18(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.2358			
Prevalence method(d)	P = 0.8550			
Combined analysis(d)	P = 0.4837			
Cochran-Armitage test(e)	P = 0.6841			
Fisher Exact test(e)		P = 0.4926	P = 0.3235	P = 0.2475

(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 M 2

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

RAT : FEMALE

(2-YEAR STUDY)

Group Name	Control	20 ppm	75 ppm	300 ppm
	SITE : spleen TUMOR : mononuclear cell leukemia			
Tumor rate				
Overall rates(a)	6/50(12.0)	7/50(14.0)	9/50(18.0)	7/50(14.0)
Adjusted rates(b)	9.30	5.88	7.89	13.89
Terminal rates(c)	3/38(7.9)	2/34(5.9)	3/38(7.9)	5/36(13.9)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.7701			
Prevalence method(d)	P = 0.2134			
Combined analysis(d)	P = 0.4966			
Cochran-Armitage test(e)	P = 0.9313			
Fisher Exact test(e)		P = 0.4863	P = 0.3291	P = 0.4863
	SITE : pituitary gland TUMOR : adenoma			
Tumor rate				
Overall rates(a)	33/50(66.0)	30/50(60.0)	32/50(64.0)	28/50(56.0)
Adjusted rates(b)	65.79	68.57	70.00	56.10
Terminal rates(c)	25/38(65.8)	23/34(67.6)	26/38(68.4)	19/36(52.8)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.7954			
Prevalence method(d)	P = 0.8429			
Combined analysis(d)	P = 0.9054			
Cochran-Armitage test(e)	P = 0.3637			
Fisher Exact test(e)		P = 0.4463	P = 0.4750	P = 0.3663
	SITE : pituitary gland TUMOR : adenoma,adenocarcinoma			
Tumor rate				
Overall rates(a)	34/50(68.0)	30/50(60.0)	33/50(66.0)	28/50(56.0)
Adjusted rates(b)	68.42	68.57	72.50	56.10
Terminal rates(c)	26/38(68.4)	23/34(67.6)	27/38(71.1)	19/36(52.8)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.7954			
Prevalence method(d)	P = 0.8835			
Combined analysis(d)	P = 0.9290			
Cochran-Armitage test(e)	P = 0.2879			
Fisher Exact test(e)		P = 0.4090	P = 0.4747	P = 0.3312

Group Name	Control	20 ppm	75 ppm	300 ppm
	SITE : thyroid			
	TUMOR : C-cell adenoma			
Tumor rate				
Overall rates(a)	2/47(4.3)	7/50(14.0)	9/49(18.4)	6/49(12.2)
Adjusted rates(b)	4.35	20.00	20.45	16.67
Terminal rates(c)	1/35(2.9)	6/34(17.6)	7/37(18.9)	6/36(16.7)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.3614			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.6741			
Fisher Exact test(e)		P = 0.1221	P = 0.0494*	P = 0.1757
	SITE : thyroid			
	TUMOR : C-cell adenoma,C-cell carcinoma			
Tumor rate				
Overall rates(a)	2/47(4.3)	7/50(14.0)	10/49(20.4)	7/49(14.3)
Adjusted rates(b)	4.35	20.00	22.73	18.42
Terminal rates(c)	1/35(2.9)	6/34(17.6)	8/37(21.6)	6/36(16.7)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.2631			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.4731			
Fisher Exact test(e)		P = 0.1221	P = 0.0318*	P = 0.1164
	SITE : adrenal gland			
	TUMOR : pheochromocytoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	4/50(8.0)	6/50(12.0)	5/50(10.0)
Adjusted rates(b)	4.55	11.76	15.38	12.20
Terminal rates(c)	0/38(0.0)	4/34(11.8)	5/38(13.2)	4/36(11.1)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.2686			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.4557			
Fisher Exact test(e)		P = 0.3574	P = 0.1606	P = 0.2425

Group Name	Control	20 ppm	75 ppm	300 ppm
	SITE : uterus			
	TUMOR : endometrial stromal polyp			
Tumor rate				
Overall rates(a)	9/50(18.0)	1/50(2.0)	9/50(18.0)	10/50(20.0)
Adjusted rates(b)	19.51	2.94	22.50	22.22
Terminal rates(c)	7/38(18.4)	1/34(2.9)	8/38(21.1)	7/36(19.4)
Statistical analysis				
Peto test				
Standard method(d)	P = 1.0000 ?			
Prevalence method(d)	P = 0.0932			
Combined analysis(d)	P = 0.1285			
Cochran-Armitage test(e)	P = 0.1621			
Fisher Exact test(e)		P = 0.0150*	P = 0.3993	P = 0.4839
	SITE : uterus			
	TUMOR : endometrial stromal polyp,endometrial stromal sarcoma			
Tumor rate				
Overall rates(a)	9/50(18.0)	3/50(6.0)	11/50(22.0)	10/50(20.0)
Adjusted rates(b)	19.51	2.94	22.50	22.22
Terminal rates(c)	7/38(18.4)	1/34(2.9)	8/38(21.1)	7/36(19.4)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8790			
Prevalence method(d)	P = 0.0932			
Combined analysis(d)	P = 0.2266			
Cochran-Armitage test(e)	P = 0.3177			
Fisher Exact test(e)		P = 0.0899	P = 0.4357	P = 0.4839
	SITE : mammary gland			
	TUMOR : fibroadenoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	6/50(12.0)	6/50(12.0)	8/50(16.0)
Adjusted rates(b)	10.00	14.71	15.38	19.44
Terminal rates(c)	3/38(7.9)	5/34(14.7)	5/38(13.2)	7/36(19.4)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.2418			
Prevalence method(d)	P = 0.2232			
Combined analysis(d)	P = 0.1749			
Cochran-Armitage test(e)	P = 0.2742			
Fisher Exact test(e)		P = 0.3944	P = 0.3944	P = 0.2169

Group Name	Control	20 ppm	75 ppm	300 ppm
	SITE : mammary gland TUMOR : fibroadenoma,adenocarcinoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	6/50(12.0)	7/50(14.0)	8/50(16.0)
Adjusted rates(b)	10.00	14.71	17.95	19.44
Terminal rates(c)	3/38(7.9)	5/34(14.7)	6/38(15.8)	7/36(19.4)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.2418			
Prevalence method(d)	P = 0.2409			
Combined analysis(d)	P = 0.1899			
Cochran-Armitage test(e)	P = 0.3021			
Fisher Exact test(e)		P = 0.3944	P = 0.2958	P = 0.2169
	SITE : preputial/clitoral gland TUMOR : adenoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	3/50(6.0)	2/50(4.0)	4/50(8.0)
Adjusted rates(b)	5.26	8.82	4.76	11.11
Terminal rates(c)	2/38(5.3)	3/34(8.8)	1/38(2.6)	4/36(11.1)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.2157			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.4003			
Fisher Exact test(e)		P = 0.4909	P = 0.3088	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 M 3

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

MOSUE : MALE

(2-YEAR STUDY)

Group Name	Control	20ppm	75ppm	300ppm
	SITE : lung			
	TUMOR : bronchiolar-alveolar adenoma			
Tumor rate				
Overall rates(a)	3/49(6.1)	3/49(6.1)	3/50(6.0)	4/49(8.2)
Adjusted rates(b)	7.32	9.68	8.82	12.50
Terminal rates(c)	2/39(5.1)	3/31(9.7)	2/32(6.3)	3/30(10.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.2488			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.6251			
Fisher Exact test(e)		P = 0.3391	P = 0.3300	P = 0.4893
	SITE : lung			
	TUMOR : bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	4/49(8.2)	5/49(10.2)	5/50(10.0)	1/49(2.0)
Adjusted rates(b)	10.26	11.11	15.63	3.33
Terminal rates(c)	4/39(10.3)	3/31(9.7)	5/32(15.6)	1/30(3.3)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.9308			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.1121			
Fisher Exact test(e)		P = 0.4880	P = 0.4763	P = 0.2000
	SITE : lung			
	TUMOR : bronchiolar-alveolar adenoma,bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	7/49(14.3)	8/49(16.3)	8/50(16.0)	5/49(10.2)
Adjusted rates(b)	17.07	19.44	23.53	15.63
Terminal rates(c)	6/39(15.4)	6/31(19.4)	7/32(21.9)	4/30(13.3)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.7194			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.3901			
Fisher Exact test(e)		P = 0.4851	P = 0.4706	P = 0.4066

Group Name	Control	20ppm	75ppm	300ppm
	SITE : lymph node			
	TUMOR : malignant lymphoma			
Tumor rate				
Overall rates(a)	4/49(8.2)	7/49(14.3)	13/50(26.0)	8/49(16.3)
Adjusted rates(b)	10.26	16.13	28.13	15.79
Terminal rates(c)	4/39(10.3)	5/31(16.1)	9/32(28.1)	3/30(10.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.2802			
Prevalence method(d)	P = 0.2591			
Combined analysis(d)	P = 0.2021			
Cochran-Armitage test(e)	P = 0.5606			
Fisher Exact test(e)		P = 0.2962	P = 0.0404*	P = 0.2174
	SITE : spleen			
	TUMOR : hemangiosarcoma			
Tumor rate				
Overall rates(a)	1/49(2.0)	3/49(6.1)	3/50(6.0)	0/49(0.0)
Adjusted rates(b)	2.56	2.17	4.44	0.0
Terminal rates(c)	1/39(2.6)	0/31(0.0)	0/32(0.0)	0/30(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.7683			
Prevalence method(d)	P = 0.8099			
Combined analysis(d)	P = 0.9012			
Cochran-Armitage test(e)	P = 0.1902			
Fisher Exact test(e)		P = 0.3237	P = 0.3312	P = 0.4949
	SITE : spleen			
	TUMOR : hemangioma,hemangiosarcoma			
Tumor rate				
Overall rates(a)	2/49(4.1)	5/49(10.2)	3/50(6.0)	0/49(0.0)
Adjusted rates(b)	5.13	6.52	4.44	0.0
Terminal rates(c)	2/39(5.1)	1/31(3.2)	0/32(0.0)	0/30(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.7683			
Prevalence method(d)	P = 0.9508			
Combined analysis(d)	P = 0.9711			
Cochran-Armitage test(e)	P = 0.0715			
Fisher Exact test(e)		P = 0.2428	P = 0.4816	P = 0.2576

Group Name	Control	20ppm	75ppm	300ppm
	SITE : liver			
	TUMOR : hepatocellular adenoma			
Tumor rate				
Overall rates(a)	13/49(26.5)	9/49(18.4)	7/50(14.0)	13/49(26.5)
Adjusted rates(b)	28.89	22.58	18.75	36.67
Terminal rates(c)	11/39(28.2)	7/31(22.6)	6/32(18.8)	11/30(36.7)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.1723			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.4993			
Fisher Exact test(e)		P = 0.2971	P = 0.1537	P = 0.4129
	SITE : liver			
	TUMOR : histiocytic sarcoma			
Tumor rate				
Overall rates(a)	0/49(0.0)	3/49(6.1)	1/50(2.0)	6/49(12.2)
Adjusted rates(b)	0.0	3.23	0.0	0.0
Terminal rates(c)	0/39(0.0)	1/31(3.2)	0/32(0.0)	0/30(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.0029**			
Prevalence method(d)	P = 0.4473			
Combined analysis(d)	P = 0.0072**			
Cochran-Armitage test(e)	P = 0.0097**			
Fisher Exact test(e)		P = 0.1326	P = 0.4900	P = 0.0191*
	SITE : liver			
	TUMOR : hemangiosarcoma			
Tumor rate				
Overall rates(a)	5/49(10.2)	5/49(10.2)	5/50(10.0)	5/49(10.2)
Adjusted rates(b)	10.26	9.76	9.30	10.42
Terminal rates(c)	4/39(10.3)	3/31(9.7)	1/32(3.1)	2/30(6.7)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8003			
Prevalence method(d)	P = 0.3528			
Combined analysis(d)	P = 0.5004			
Cochran-Armitage test(e)	P = 0.9962			
Fisher Exact test(e)		P = 0.3709	P = 0.3592	P = 0.3709

Group Name	Control	20ppm	75ppm	300ppm
	SITE : liver			
	TUMOR : hepatocellular carcinoma			
Tumor rate				
Overall rates(a)	12/49(24.5)	17/49(34.7)	16/50(32.0)	38/49(77.6)
Adjusted rates(b)	25.64	41.94	39.39	81.58
Terminal rates(c)	10/39(25.6)	13/31(41.9)	12/32(37.5)	23/30(76.7)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.0507			
Prevalence method(d)	P < 0.0001**?			
Combined analysis(d)	P < 0.0001**			
Cochran-Armitage test(e)	P < 0.0001**			
Fisher Exact test(e)		P = 0.2733	P = 0.3429	P = 0.0018**
	SITE : liver			
	TUMOR : hemangioma,hemangiosarcoma			
Tumor rate				
Overall rates(a)	6/49(12.2)	5/49(10.2)	5/50(10.0)	6/49(12.2)
Adjusted rates(b)	12.82	9.76	9.30	12.50
Terminal rates(c)	5/39(12.8)	3/31(9.7)	1/32(3.1)	3/30(10.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8003			
Prevalence method(d)	P = 0.2914			
Combined analysis(d)	P = 0.4294			
Cochran-Armitage test(e)	P = 0.8417			
Fisher Exact test(e)		P = 0.4870	P = 0.5000	P = 0.3805

Group Name	Control	20ppm	75ppm	300ppm
	SITE : liver			
	TUMOR : hepatocellular adenoma,hepatocellular carcinoma			
Tumor rate				
Overall rates(a)	20/49(40.8)	21/49(42.9)	18/50(36.0)	41/49(83.7)
Adjusted rates(b)	43.59	51.61	42.42	89.47
Terminal rates(c)	17/39(43.6)	16/31(51.6)	13/32(40.6)	26/30(86.7)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.0507			
Prevalence method(d)	P < 0.0001**			
Combined analysis(d)	P < 0.0001**			
Cochran-Armitage test(e)	P < 0.0001**			
Fisher Exact test(e)		P = 0.4781	P = 0.4453	P = 0.0242*

(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

Group Name	Control	20ppm	75ppm	300ppm
	SITE : ALL SITE TUMOR : hemangioma			
Tumor rate				
Overall rates(a)	2/49(4.1)	3/49(6.1)	1/50(2.0)	1/49(2.0)
Adjusted rates(b)	5.13	6.25	2.27	3.33
Terminal rates(c)	2/39(5.1)	1/31(3.2)	0/32(0.0)	1/30(3.3)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.7665			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.4092			
Fisher Exact test(e)		P = 0.4907	P = 0.5000	P = 0.4925
	SITE : ALL SITE TUMOR : histiocytic sarcoma			
Tumor rate				
Overall rates(a)	0/49(0.0)	3/49(6.1)	8/50(16.0)	6/49(12.2)
Adjusted rates(b)	0.0	3.23	12.50	0.0
Terminal rates(c)	0/39(0.0)	1/31(3.2)	4/32(12.5)	0/30(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.0113*			
Prevalence method(d)	P = 0.6657			
Combined analysis(d)	P = 0.0433*			
Cochran-Armitage test(e)	P = 0.0952			
Fisher Exact test(e)		P = 0.1326	P = 0.0059**	P = 0.0191*
	SITE : ALL SITE TUMOR : malignant lymphoma			
Tumor rate				
Overall rates(a)	5/49(10.2)	8/49(16.3)	14/50(28.0)	8/49(16.3)
Adjusted rates(b)	12.82	19.35	31.25	15.79
Terminal rates(c)	5/39(12.8)	6/31(19.4)	10/32(31.3)	3/30(10.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.2802			
Prevalence method(d)	P = 0.3782			
Combined analysis(d)	P = 0.2934			
Cochran-Armitage test(e)	P = 0.8047			
Fisher Exact test(e)		P = 0.3145	P = 0.0524	P = 0.3145

Group Name	Control	20ppm	75ppm	300ppm
	SITE : ALL SITE			
	TUMOR : hemangiosarcoma			
Tumor rate				
Overall rates(a)	6/49(12.2)	8/49(16.3)	6/50(12.0)	6/49(12.2)
Adjusted rates(b)	12.82	12.90	9.09	12.50
Terminal rates(c)	5/39(12.8)	4/31(12.9)	1/32(3.1)	3/30(10.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.0001			
Prevalence method(d)	P = 0.3653			
Combined analysis(d)	P = 0.6164			
Cochran-Armitage test(e)	P = 0.7850			
Fisher Exact test(e)		P = 0.4161	P = 0.3679	P = 0.3805

(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 M 4

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

MOSUE :FEMALE

(2-YEAR STUDY)

Group Name	Control	20ppm	75ppm	300ppm
	SITE : lung			
	TUMOR : bronchiolar-alveolar adenoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	3/50(6.0)	1/49(2.0)	3/50(6.0)
Adjusted rates(b)	0.0	10.34	3.33	7.69
Terminal rates(c)	0/28(0.0)	2/25(8.0)	0/23(0.0)	2/26(7.7)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.1595			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.2702			
Fisher Exact test(e)		P = 0.1325	P = 0.5000	P = 0.1325
	SITE : lung			
	TUMOR : bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	1/50(2.0)	1/49(2.0)	4/50(8.0)
Adjusted rates(b)	3.57	4.00	4.35	10.53
Terminal rates(c)	1/28(3.6)	1/25(4.0)	1/23(4.3)	2/26(7.7)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.0377*			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.0526			
Fisher Exact test(e)		P = 0.2475	P = 0.2525	P = 0.1998
	SITE : lung			
	TUMOR : bronchiolar-alveolar adenoma,bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	4/50(8.0)	2/49(4.1)	7/50(14.0)
Adjusted rates(b)	3.57	13.79	6.67	17.50
Terminal rates(c)	1/28(3.6)	3/25(12.0)	1/23(4.3)	4/26(15.4)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.0237*			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.0285*			
Fisher Exact test(e)		P = 0.1998	P = 0.5000	P = 0.0430*

Group Name	Control	20ppm	75ppm	300ppm
	SITE : lymph node			
	TUMOR : malignant lymphoma			
Tumor rate				
Overall rates(a)	21/50(42.0)	21/50(42.0)	18/49(36.7)	23/50(46.0)
Adjusted rates(b)	41.38	38.46	34.78	50.00
Terminal rates(c)	11/28(39.3)	9/25(36.0)	8/23(34.8)	13/26(50.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.6230			
Prevalence method(d)	P = 0.1665			
Combined analysis(d)	P = 0.3415			
Cochran-Armitage test(e)	P = 0.5774			
Fisher Exact test(e)		P = 0.4271	P = 0.4351	P = 0.4721
	SITE : liver			
	TUMOR : hepatocellular adenoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	10/50(20.0)	6/49(12.2)	20/50(40.0)
Adjusted rates(b)	4.76	36.00	21.74	50.00
Terminal rates(c)	1/28(3.6)	9/25(36.0)	5/23(21.7)	13/26(50.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P < 0.0001**			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P < 0.0001**			
Fisher Exact test(e)		P = 0.0270*	P = 0.1540	P = 0.0003**
	SITE : liver			
	TUMOR : hemangiosarcoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	3/50(6.0)	5/49(10.2)	0/50(0.0)
Adjusted rates(b)	3.57	11.54	8.70	0.0
Terminal rates(c)	1/28(3.6)	2/25(8.0)	2/23(8.7)	0/26(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5299			
Prevalence method(d)	P = 0.9065			
Combined analysis(d)	P = 0.9021			
Cochran-Armitage test(e)	P = 0.1948			
Fisher Exact test(e)		P = 0.3235	P = 0.1163	P = 0.4950

Group Name	Control	20ppm	75ppm	300ppm
	SITE : liver			
	TUMOR : hepatocellular carcinoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	4/50(8.0)	2/49(4.1)	41/50(82.0)
Adjusted rates(b)	7.14	12.00	8.33	100.00
Terminal rates(c)	2/28(7.1)	3/25(12.0)	1/23(4.3)	26/26(100.0)
Statistical analysis				
Peto test				
Standard method(d)	P < 0.0001**			
Prevalence method(d)	P < 0.0001**?			
Combined analysis(d)	P < 0.0001**?			
Cochran-Armitage test(e)	P < 0.0001**			
Fisher Exact test(e)		P = 0.3574	P = 0.3162	P < 0.0001**
	SITE : liver			
	TUMOR : hepatocellular adenoma,hepatocellular carcinoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	13/50(26.0)	7/49(14.3)	45/50(90.0)
Adjusted rates(b)	10.71	44.00	25.00	100.00
Terminal rates(c)	3/28(10.7)	11/25(44.0)	5/23(21.7)	26/26(100.0)
Statistical analysis				
Peto test				
Standard method(d)	P < 0.0001**			
Prevalence method(d)	P < 0.0001**?			
Combined analysis(d)	P < 0.0001**?			
Cochran-Armitage test(e)	P < 0.0001**			
Fisher Exact test(e)		P = 0.0371*	P = 0.2850	P < 0.0001**
	SITE : pituitary gland			
	TUMOR : adenoma			
Tumor rate				
Overall rates(a)	5/50(10.0)	7/50(14.0)	9/49(18.4)	8/50(16.0)
Adjusted rates(b)	17.86	24.00	25.93	23.33
Terminal rates(c)	5/28(17.9)	6/25(24.0)	4/23(17.4)	6/26(23.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.6912			
Prevalence method(d)	P = 0.2069			
Combined analysis(d)	P = 0.2911			
Cochran-Armitage test(e)	P = 0.5593			
Fisher Exact test(e)		P = 0.4062	P = 0.2273	P = 0.3141

Group Name	Control	20ppm	75ppm	300ppm
	SITE : pituitary gland			
	TUMOR : adenoma,adenocarcinoma			
Tumor rate				
Overall rates(a)	6/50(12.0)	7/50(14.0)	9/49(18.4)	8/50(16.0)
Adjusted rates(b)	17.86	24.00	25.93	23.33
Terminal rates(c)	5/28(17.9)	6/25(24.0)	4/23(17.4)	6/26(23.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8170			
Prevalence method(d)	P = 0.2173			
Combined analysis(d)	P = 0.3637			
Cochran-Armitage test(e)	P = 0.6803			
Fisher Exact test(e)		P = 0.4863	P = 0.3161	P = 0.4157
	SITE : ovary			
	TUMOR : cystadenoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	0/50(0.0)	0/49(0.0)	3/49(6.1)
Adjusted rates(b)	3.57	0.0	0.0	8.00
Terminal rates(c)	1/28(3.6)	0/25(0.0)	0/23(0.0)	2/25(8.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.0285*			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.0310*			
Fisher Exact test(e)		P = 0.4950	P = 0.4900	P = 0.3162
	SITE : uterus			
	TUMOR : histiocytic sarcoma			
Tumor rate				
Overall rates(a)	11/50(22.0)	6/50(12.0)	13/49(26.5)	12/50(24.0)
Adjusted rates(b)	8.11	8.00	10.81	15.15
Terminal rates(c)	1/28(3.6)	2/25(8.0)	2/23(8.7)	3/26(11.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.4512			
Prevalence method(d)	P = 0.1527			
Combined analysis(d)	P = 0.2515			
Cochran-Armitage test(e)	P = 0.4310			
Fisher Exact test(e)		P = 0.1955	P = 0.4277	P = 0.4826

Group Name	Control	20ppm	75ppm	300ppm
	SITE : Harderian gland TUMOR : adenoma			
Tumor rate				
Overall rates(a)	6/50(12.0)	2/49(4.1)	2/49(4.1)	2/50(4.0)
Adjusted rates(b)	16.67	5.41	8.70	6.06
Terminal rates(c)	4/28(14.3)	1/24(4.2)	2/23(8.7)	1/26(3.8)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.8328			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.3187			
Fisher Exact test(e)		P = 0.1677	P = 0.1677	P = 0.1606

(HPT360A)

BAIS2

(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

Group Name	Control	20ppm	75ppm	300ppm
	SITE : ALL SITE TUMOR : histiocytic sarcoma			
Tumor rate				
Overall rates(a)	15/50(30.0)	8/50(16.0)	14/49(28.6)	13/50(26.0)
Adjusted rates(b)	16.67	12.00	11.11	18.18
Terminal rates(c)	4/28(14.3)	3/25(12.0)	2/23(8.7)	3/26(11.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5763			
Prevalence method(d)	P = 0.2963			
Combined analysis(d)	P = 0.4401			
Cochran-Armitage test(e)	P = 0.8201			
Fisher Exact test(e)		P = 0.1384	P = 0.4617	P = 0.4525
	SITE : ALL SITE TUMOR : malignant lymphoma			
Tumor rate				
Overall rates(a)	23/50(46.0)	22/50(44.0)	20/49(40.8)	25/50(50.0)
Adjusted rates(b)	48.28	38.46	41.67	53.85
Terminal rates(c)	13/28(46.4)	9/25(36.0)	9/23(39.1)	14/26(53.8)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.6629			
Prevalence method(d)	P = 0.1448			
Combined analysis(d)	P = 0.3461			
Cochran-Armitage test(e)	P = 0.5191			
Fisher Exact test(e)		P = 0.4777	P = 0.4430	P = 0.4755

Group Name	Control	20ppm	75ppm	300ppm
	SITE : ALL SITE			
	TUMOR : hemangiosarcoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	5/50(10.0)	8/49(16.3)	1/50(2.0)
Adjusted rates(b)	9.68	15.38	14.29	3.23
Terminal rates(c)	2/28(7.1)	3/25(12.0)	3/23(13.0)	0/26(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5860			
Prevalence method(d)	P = 0.9459			
Combined analysis(d)	P = 0.9461			
Cochran-Armitage test(e)	P = 0.1491			
Fisher Exact test(e)		P = 0.3790	P = 0.1257	P = 0.3235

(HPT360A)

BAIS2

(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 N 1

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

RAT: MALE : DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0158
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	20 ppm	75 ppm	300 ppm
			17	16	21	32
[Respiratory system]						
larynx			<17>	<16>	<21>	<32>
	metastasis:thyroid tumor		1	0	0	0
lung			<17>	<16>	<21>	<32>
	leukemic cell infiltration		2	7	6	9
	metastasis:zymbal gland tumor		0	1	0	0
	metastasis:vertebra tumor		0	0	1	0
[Hematopoietic system]						
bone marrow			<17>	<16>	<21>	<32>
	leukemic cell infiltration		0	3	2	4
lymph node			<17>	<16>	<21>	<32>
	leukemic cell infiltration		2	3	0	8
spleen			<17>	<16>	<21>	<32>
	metastasis:bone marrow tumor		1	0	0	0
[Circulatory system]						
heart			<17>	<16>	<21>	<32>
	leukemic cell infiltration		0	2	1	0
[Digestive system]						
liver			<17>	<16>	<21>	<32>
	leukemic cell infiltration		1	6	4	5
	metastasis:bone marrow tumor		1	1	0	0

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

STUDY NO. : 0158
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control	20 ppm	75 ppm	300 ppm
		No. of Animals on Study	17	16	21	32
[Digestive system]						
pancreas			<17>	<16>	<21>	<32>
	leukemic cell infiltration		0	2	0	0
[Urinary system]						
kidney			<17>	<16>	<21>	<32>
	leukemic cell infiltration		1	2	0	2
urin bladd			<17>	<16>	<21>	<32>
	leukemic cell infiltration		1	.0	0	0
[Endocrine system]						
thyroid			<17>	<16>	<21>	<32>
	leukemic cell infiltration		0	1	0	0
adrenal			<17>	<16>	<21>	<32>
	leukemic cell infiltration		0	0	0	2
[Reproductive system]						
testis			<17>	<16>	<21>	<32>
	metastasis:zymbal gland tumor		0	1	0	0
semin ves			<17>	<16>	<21>	<32>
	leukemic cell infiltration		1	0	0	0
[Nervous system]						
brain			<17>	<16>	<21>	<32>
	leukemic cell infiltration		1	3	2	3

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

STUDY NO. : 0158
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	20 ppm	75 ppm	300 ppm
			17	16	21	32
[Nervous system]						
spinal cord			<17>	<16>	<21>	<32>
	leukemic cell infiltration		1	1	1	1
[Special sense organs/appandage]						
Harder gl			<17>	<16>	<21>	<32>
	leukemic cell infiltration		0	0	0	1

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

APPENDIX N 2

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

RAT: FEMALE : DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

Organ	Findings	Control	20 ppm	75 ppm	300 ppm
	Group Name	Control	20 ppm	75 ppm	300 ppm
	No. of Animals on Study	12	16	12	14
[Respiratory system]					
lung		<12>	<16>	<12>	<14>
	leukemic cell infiltration	2	5	5	2
	metastasis:pleura tumor	0	0	0	1
[Hematopoietic system]					
bone marrow		<12>	<16>	<12>	<14>
	leukemic cell infiltration	0	1	0	0
lymph node		<12>	<16>	<12>	<14>
	leukemic cell infiltration	0	3	2	1
[Circulatory system]					
heart		<12>	<16>	<12>	<14>
	leukemic cell infiltration	0	1	1	1
[Digestive system]					
salivary gl		<12>	<16>	<12>	<14>
	leukemic cell infiltration	0	1	0	0
liver		<12>	<16>	<12>	<14>
	leukemic cell infiltration	2	4	6	1
pancreas		<12>	<16>	<12>	<14>
	leukemic cell infiltration	0	0	1	1
[Urinary system]					
kidney		<12>	<16>	<12>	<14>
	leukemic cell infiltration	0	2	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	20 ppm	75 ppm	300 ppm
			12	16	12	14
[Urinary system]						
urin bladd			<12>	<16>	<12>	<14>
	leukemic cell infiltration		0	2	1	0
	metastasis:uterus tumor		0	0	1	0
[Endocrine system]						
pituitary			<12>	<16>	<12>	<14>
	leukemic cell infiltration		0	0	1	0
thyroid			<12>	<16>	<12>	<14>
	leukemic cell infiltration		0	1	0	0
adrenal			<12>	<16>	<12>	<14>
	leukemic cell infiltration		0	1	1	0
[Reproductive system]						
ovary			<12>	<16>	<12>	<14>
	leukemic cell infiltration		0	1	0	0
uterus			<12>	<16>	<12>	<14>
	leukemic cell infiltration		0	2	1	0
vagina			<12>	<16>	<12>	<14>
	leukemic cell infiltration		0	3	1	0
	metastasis:uterus tumor		0	1	0	0
[Nervous system]						
brain			<12>	<16>	<12>	<14>
	leukemic cell infiltration		0	4	2	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	20 ppm	75 ppm	300 ppm
			12	16	12	14
[Nervous system]						
brain			<12>	<16>	<12>	<14>
	metastasis:pituitary tumor		0	0	2	1
spinal cord			<12>	<16>	<12>	<14>
	leukemic cell infiltration		0	2	0	0
[Special sense organs/appandage]						
Harder gl			<12>	<16>	<12>	<14>
	leukemic cell infiltration		0	1	1	0
[Musculoskeletal system]						
muscle			<12>	<16>	<12>	<14>
	leukemic cell infiltration		0	1	0	0
[Body cavities]						
mediastinum			<12>	<16>	<12>	<14>
	leukemic cell infiltration		0	1	0	0

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

APPENDIX N 3

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

RAT: MALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0158
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control	20 ppm	75 ppm	300 ppm
		No. of Animals on Study	33	34	29	18
[Integumentary system/appandage]						
subcutis			<33>	<34>	<29>	<18>
	metastasis:peritoneum tumor		0	1	0	0
[Respiratory system]						
lung			<33>	<34>	<29>	<18>
	leukemic cell infiltration		0	4	1	2
[Hematopoietic system]						
lymph node			<33>	<34>	<29>	<18>
	leukemic cell infiltration		0	1	0	0
[Digestive system]						
liver			<33>	<34>	<29>	<18>
	leukemic cell infiltration		0	2	1	0
	metastasis:bone marrow tumor		2	0	0	0
[Urinary system]						
kidney			<33>	<34>	<29>	<18>
	leukemic cell infiltration		1	1	0	0
[Endocrine system]						
adrenal			<33>	<34>	<29>	<18>
	leukemic cell infiltration		0	0	1	0

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

APPENDIX N 4

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

RAT: FEMALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0158
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name / No. of Animals on Study	Control	20 ppm	75 ppm	300 ppm
			38	34	38	36
[Respiratory system]						
lung			<38>	<34>	<38>	<36>
	leukemic cell infiltration		1	0	1	5
	metastasis:liver tumor		0	0	1	0
[Hematopoietic system]						
bone marrow			<38>	<34>	<38>	<36>
	leukemic cell infiltration		0	0	0	1
lymph node			<38>	<34>	<38>	<36>
	leukemic cell infiltration		1	0	0	2
[Digestive system]						
liver			<38>	<34>	<38>	<36>
	leukemic cell infiltration		1	1	2	5
[Reproductive system]						
vagina			<38>	<34>	<38>	<36>
	metastasis:uterus tumor		1	0	0	0
	metastasis:subcutis tumor		0	1	0	0
[Nervous system]						
brain			<38>	<34>	<38>	<36>
	leukemic cell infiltration		0	0	0	2
	metastasis:pituitary tumor		1	0	1	0

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

APPENDIX N 5

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

MOUSE: MALE : DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0159
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	20ppm	75ppm	300ppm
			10	18	18	19
[Respiratory system]						
nasal cavit			<10>	<18>	<18>	<19>
	leukemic cell infiltration		0	0	1	0
	metastasis:uterus tumor		0	0	0	1
lung			<10>	<18>	<18>	<19>
	leukemic cell infiltration		0	0	1	1
	metastasis:liver tumor		0	3	1	2
[Hematopoietic system]						
bone marrow			<10>	<18>	<18>	<19>
	metastasis:liver tumor		0	1	1	0
lymph node			<10>	<18>	<18>	<19>
	metastasis:stomach tumor		1	0	0	0
thymus			<10>	<18>	<18>	<19>
	leukemic cell infiltration		0	0	0	1
spleen			<10>	<18>	<18>	<19>
	leukemic cell infiltration		0	2	2	1
[Circulatory system]						
heart			<10>	<18>	<18>	<19>
	leukemic cell infiltration		0	0	0	1
[Digestive system]						
salivary gl			<10>	<18>	<18>	<19>
	leukemic cell infiltration		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 10	20ppm 18	75ppm 18	300ppm 19
[Digestive system]						
stomach			<10>	<18>	<18>	<19>
	leukemic cell infiltration		0	0	0	2
small intes			<10>	<18>	<18>	<19>
	leukemic cell infiltration		0	0	1	0
	metastasis:peritoneum tumor		0	0	1	0
liver			<10>	<18>	<18>	<19>
	leukemic cell infiltration		1	1	1	1
	metastasis:peritoneum tumor		0	0	1	0
	metastasis:subcutis tumor		0	0	1	0
	metastasis:stomach tumor		1	0	0	0
pancreas			<10>	<18>	<18>	<19>
	leukemic cell infiltration		0	1	0	1
	metastasis:liver tumor		0	0	0	1
	metastasis:peritoneum tumor		0	0	1	0
[Urinary system]						
kidney			<10>	<18>	<18>	<19>
	leukemic cell infiltration		1	1	2	2
	metastasis:liver tumor		0	0	0	2
urin bladd			<10>	<18>	<18>	<19>
	leukemic cell infiltration		0	0	1	1
	metastasis:liver tumor		0	0	0	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 10	20ppm 18	75ppm 18	300ppm 19
[Urinary system]						
urethra			<10>	<18>	<18>	<19>
	metastasis:liver tumor		0	0	0	1
[Endocrine system]						
pituitary			<10>	<18>	<18>	<19>
	leukemic cell infiltration		0	1	0	0
adrenal			<10>	<18>	<18>	<19>
	leukemic cell infiltration		0	1	0	1
	metastasis:liver tumor		0	0	0	1
[Reproductive system]						
epididymis			<10>	<18>	<18>	<19>
	leukemic cell infiltration		0	0	0	1
	metastasis:liver tumor		0	0	0	1
	metastasis:peritoneum tumor		0	0	1	0
	metastasis:subcutis tumor		0	1	0	0
semin ves			<10>	<18>	<18>	<19>
	leukemic cell infiltration		0	0	0	1
	metastasis:stomach tumor		1	0	0	0
prostate			<10>	<18>	<18>	<19>
	leukemic cell infiltration		0	0	1	3
	metastasis:liver tumor		0	0	0	1

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

STUDY NO. : 0159
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control	20ppm	75ppm	300ppm
		No. of Animals on Study	10	18	18	19
[Reproductive system]						
prostate			<10>	<18>	<18>	<19>
	metastasis:peritoneum tumor		0	0	1	0
[Nervous system]						
brain			<10>	<18>	<18>	<19>
	leukemic cell infiltration		0	1	0	0
	metastasis:liver tumor		0	0	0	1
	metastasis:periferal nerve tumor		0	1	0	0
[Musculoskeletal system]						
muscle			<10>	<18>	<18>	<19>
	leukemic cell infiltration		0	0	1	0
[Body cavities]						
peritoneum			<10>	<18>	<18>	<19>
	metastasis:liver tumor		0	0	0	2
	metastasis:stomach tumor		1	0	0	0
retroperit			<10>	<18>	<18>	<19>
	metastasis:stomach tumor		1	0	0	0

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

APPENDIX N 6

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

MOUSE: FEMALE : DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0159
ANIMAL : MOUSE BDF1
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	20ppm	75ppm	300ppm
			22	25	26	24
[Integumentary system/appandage]						
skin/app			<22>	<25>	<26>	<24>
	leukemic cell infiltration		2	3	0	1
subcutis			<22>	<25>	<26>	<24>
	leukemic cell infiltration		1	1	2	1
	metastasis:uterus tumor		0	0	0	1
[Respiratory system]						
nasal cavit			<22>	<25>	<26>	<24>
	leukemic cell infiltration		1	0	0	0
	metastasis:uterus tumor		0	1	1	2
lung			<22>	<25>	<26>	<24>
	leukemic cell infiltration		3	5	5	5
	metastasis:liver tumor		0	1	0	2
	metastasis:uterus tumor		3	2	3	2
[Hematopoietic system]						
bone marrow			<22>	<25>	<26>	<24>
	leukemic cell infiltration		3	5	3	4
	metastasis:liver tumor		0	1	0	1
	metastasis:uterus tumor		1	1	3	2
	metastasis:subcutis tumor		0	0	0	1
lymph node			<22>	<25>	<26>	<24>
	leukemic cell infiltration		0	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 22	20ppm 25	75ppm 26	300ppm 24
[Hematopoietic system]						
lymph node			<22>	<25>	<26>	<24>
	metastasis:uterus tumor		3	1	1	1
spleen			<22>	<25>	<26>	<24>
	leukemic cell infiltration		4	8	7	7
	metastasis:liver tumor		0	1	0	0
	metastasis:uterus tumor		0	1	1	0
[Circulatory system]						
heart			<22>	<25>	<26>	<24>
	leukemic cell infiltration		2	5	3	2
	metastasis:uterus tumor		0	0	0	1
[Digestive system]						
tongue			<22>	<25>	<26>	<24>
	leukemic cell infiltration		2	1	1	2
salivary gl			<22>	<25>	<26>	<24>
	leukemic cell infiltration		2	4	4	4
stomach			<22>	<25>	<26>	<24>
	leukemic cell infiltration		5	5	1	1
	metastasis:uterus tumor		1	0	0	2
small intes			<22>	<25>	<26>	<24>
	leukemic cell infiltration		1	0	0	0
	metastasis:uterus tumor		0	0	0	1

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

STUDY NO. : 0159
ANIMAL : MOUSE BDF1
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 22	20ppm 25	75ppm 26	300ppm 24
[Digestive system]						
large intes			<22>	<25>	<26>	<24>
	leukemic cell infiltration		2	0	0	0
	metastasis:uterus tumor		0	0	0	1
liver			<22>	<25>	<26>	<24>
	leukemic cell infiltration		5	7	6	4
	metastasis:uterus tumor		6	4	9	5
pancreas			<22>	<25>	<26>	<24>
	leukemic cell infiltration		5	3	5	1
	metastasis:uterus tumor		2	1	1	4
[Urinary system]						
kidney			<22>	<25>	<26>	<24>
	leukemic cell infiltration		3	4	6	6
	metastasis:liver tumor		1	1	0	0
	metastasis:uterus tumor		2	1	5	5
urin bladd			<22>	<25>	<26>	<24>
	leukemic cell infiltration		2	6	3	6
	metastasis:uterus tumor		1	1	2	0
[Endocrine system]						
pituitary			<22>	<25>	<26>	<24>
	metastasis:uterus tumor		2	1	0	0

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

STUDY NO. : 0159
ANIMAL : MOUSE BDF1
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 22	20ppm 25	75ppm 26	300ppm 24
[Endocrine system]						
thyroid			<22>	<25>	<26>	<24>
	leukemic cell infiltration		1	0	0	1
adrenal			<22>	<25>	<26>	<24>
	leukemic cell infiltration		4	1	2	5
	metastasis:uterus tumor		1	0	0	1
[Reproductive system]						
ovary			<22>	<25>	<26>	<24>
	leukemic cell infiltration		7	5	6	9
	metastasis:liver tumor		1	1	0	0
	metastasis:uterus tumor		5	5	10	6
uterus			<22>	<25>	<26>	<24>
	leukemic cell infiltration		3	5	1	3
vagina			<22>	<25>	<26>	<24>
	leukemic cell infiltration		0	4	2	3
	metastasis:uterus tumor		1	1	1	0
mammary gl			<22>	<25>	<26>	<24>
	leukemic cell infiltration		1	1	1	0
[Nervous system]						
brain			<22>	<25>	<26>	<24>
	leukemic cell infiltration		1	2	0	4
	metastasis:liver tumor		0	1	0	0

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

STUDY NO. : 0159
ANIMAL : MOUSE BDF1
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 22	20ppm 25	75ppm 26	300ppm 24
[Nervous system]						
brain						
	metastasis:uterus tumor	<22>	1	0	0	0
spinal cord						
	leukemic cell infiltration	<22>	1	0	1	2
[Special sense organs/appandage]						
Harder gl						
	leukemic cell infiltration	<22>	1	5	1	3
[Musculoskeletal system]						
muscle						
	leukemic cell infiltration	<22>	1	2	0	3
[Body cavities]						
mediastinum						
	metastasis:uterus tumor	<22>	0	0	1	0
peritoneum						
	leukemic cell infiltration	<22>	0	1	0	0
	metastasis:liver tumor		0	0	1	0
	metastasis:uterus tumor		0	2	3	0

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

APPENDIX N 7

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

MOUSE: MALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0159
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	20ppm	75ppm	300ppm
			39	31	32	30
[Integumentary system/appandage]						
skin/app			<39>	<31>	<32>	<30>
	leukemic cell infiltration		0	0	1	0
[Respiratory system]						
lung			<39>	<31>	<32>	<30>
	leukemic cell infiltration		1	0	1	0
	metastasis:liver tumor		2	0	0	2
[Hematopoietic system]						
bone marrow			<39>	<31>	<32>	<30>
	leukemic cell infiltration		0	0	1	0
lymph node			<39>	<31>	<32>	<30>
	leukemic cell infiltration		0	0	0	1
spleen			<39>	<31>	<32>	<30>
	leukemic cell infiltration		1	4	5	1
[Circulatory system]						
heart			<39>	<31>	<32>	<30>
	leukemic cell infiltration		0	0	1	0
[Digestive system]						
tongue			<39>	<31>	<32>	<30>
	leukemic cell infiltration		0	0	1	0
salivary gl			<39>	<31>	<32>	<30>
	leukemic cell infiltration		0	1	2	0

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

STUDY NO. : 0159
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 39	20ppm 31	75ppm 32	300ppm 30
[Digestive system]						
stomach			<39>	<31>	<32>	<30>
	leukemic cell infiltration		1	0	1	2
small intes			<39>	<31>	<32>	<30>
	leukemic cell infiltration		0	1	1	0
large intes			<39>	<31>	<32>	<30>
	leukemic cell infiltration		0	0	1	0
liver			<39>	<31>	<32>	<30>
	leukemic cell infiltration		2	1	2	1
pancreas			<39>	<31>	<32>	<30>
	leukemic cell infiltration		1	2	1	0
[Urinary system]						
kidney			<39>	<31>	<32>	<30>
	leukemic cell infiltration		1	1	2	1
	metastasis:liver tumor		0	0	1	0
urin bladd			<39>	<31>	<32>	<30>
	leukemic cell infiltration		1	0	0	0
[Endocrine system]						
adrenal			<39>	<31>	<32>	<30>
	leukemic cell infiltration		1	0	0	0
[Reproductive system]						
epididymis			<39>	<31>	<32>	<30>
	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	20ppm	75ppm	300ppm
			39	31	32	30
[Reproductive system]						
epididymis			<39>	<31>	<32>	<30>
	metastasis:liver tumor		1	0	0	0
[Special sense organs/appandage]						
Harder gl			<39>	<31>	<32>	<30>
	leukemic cell infiltration		0	0	1	0

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

APPENDIX N 8

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

MOUSE: FEMALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0159
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 28	20ppm 25	75ppm 23	300ppm 26
[Integumentary system/appandage]						
subcutis			<28>	<25>	<23>	<26>
	leukemic cell infiltration		0	0	2	1
[Respiratory system]						
nasal cavit			<28>	<25>	<23>	<26>
	metastasis:uterus tumor		0	0	0	1
lung			<28>	<25>	<23>	<26>
	leukemic cell infiltration		3	1	3	5
	metastasis:liver tumor		0	0	0	2
	metastasis:uterus tumor		0	0	0	1
[Hematopoietic system]						
bone marrow			<28>	<25>	<23>	<26>
	leukemic cell infiltration		3	1	4	6
spleen			<28>	<25>	<23>	<26>
	leukemic cell infiltration		4	3	4	4
[Circulatory system]						
heart			<28>	<25>	<23>	<26>
	leukemic cell infiltration		1	1	2	0
[Digestive system]						
tongue			<28>	<25>	<23>	<26>
	leukemic cell infiltration		0	1	3	0

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

STUDY NO. : 0159
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 28	20ppm 25	75ppm 23	300ppm 26
[Digestive system]						
salivary gl			<28>	<25>	<23>	<26>
	leukemic cell infiltration		2	1	6	0
stomach			<28>	<25>	<23>	<26>
	leukemic cell infiltration		3	2	0	3
liver			<28>	<25>	<23>	<26>
	leukemic cell infiltration		3	4	8	7
	metastasis:uterus tumor		0	0	0	1
	metastasis:stomach tumor		1	0	0	0
pancreas			<28>	<25>	<23>	<26>
	leukemic cell infiltration		3	2	1	1
[Urinary system]						
kidney			<28>	<25>	<23>	<26>
	leukemic cell infiltration		9	6	6	11
	metastasis:uterus tumor		0	0	1	1
urin bladd			<28>	<25>	<23>	<26>
	leukemic cell infiltration		2	3	3	3
[Endocrine system]						
pituitary			<28>	<25>	<23>	<26>
	leukemic cell infiltration		1	0	0	0
	metastasis:periferal nerve tumor		1	0	0	0
adrenal			<28>	<25>	<23>	<26>
	leukemic cell infiltration		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 28	20ppm 25	75ppm 23	300ppm 26
[Reproductive system]						
ovary			<28>	<25>	<23>	<26>
	leukemic cell infiltration		1	1	2	1
	metastasis:uterus tumor		0	0	1	1
uterus			<28>	<25>	<23>	<26>
	leukemic cell infiltration		0	0	0	2
vagina			<28>	<25>	<23>	<26>
	leukemic cell infiltration		0	1	2	1
mammary gl			<28>	<25>	<23>	<26>
	leukemic cell infiltration		0	0	1	0
[Nervous system]						
brain			<28>	<25>	<23>	<26>
	leukemic cell infiltration		2	0	0	0
spinal cord			<28>	<25>	<23>	<26>
	leukemic cell infiltration		0	0	0	1
[Special sense organs/appandage]						
Harder gl			<28>	<25>	<23>	<26>
	leukemic cell infiltration		1	1	3	0
[Body cavities]						
peritoneum			<28>	<25>	<23>	<26>
	leukemic cell infiltration		0	0	1	0

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

APPENDIX O 1

IDENTITY OF p-DICHLOROBENZENE

(2-YEAR STUDY)

IDENTITY OF p-DICHLOROBENZENE(TWO-YEAR STUDIES)

A. Lot no. CTJ0580

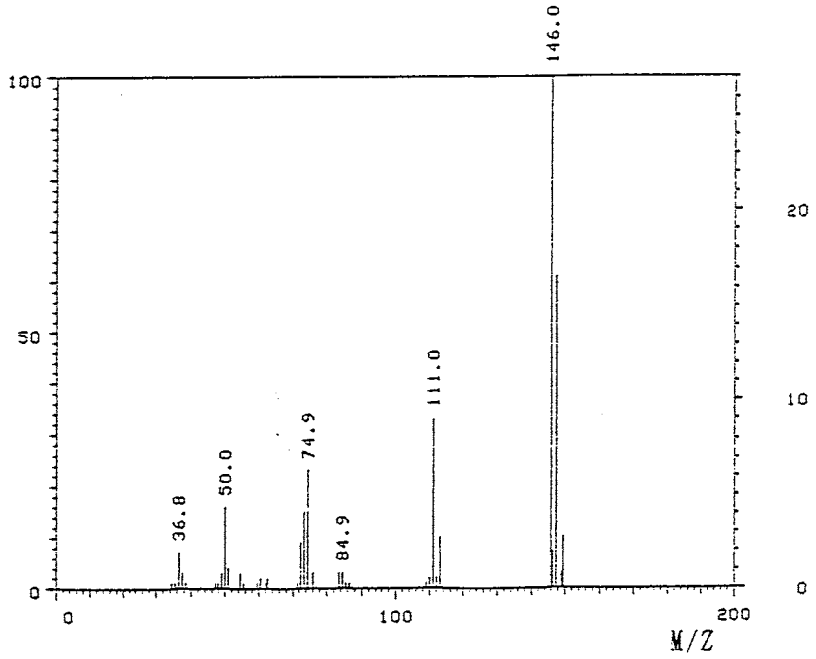
1. Spectral data

(1) Mass Spectrometry

Instrument: Hitachi M-80B Mass Spectrometer

Ionization: EI(Electron Ionization)

Ionization Voltage: 70eV



Mass Spectrum of Test Substance

Result:

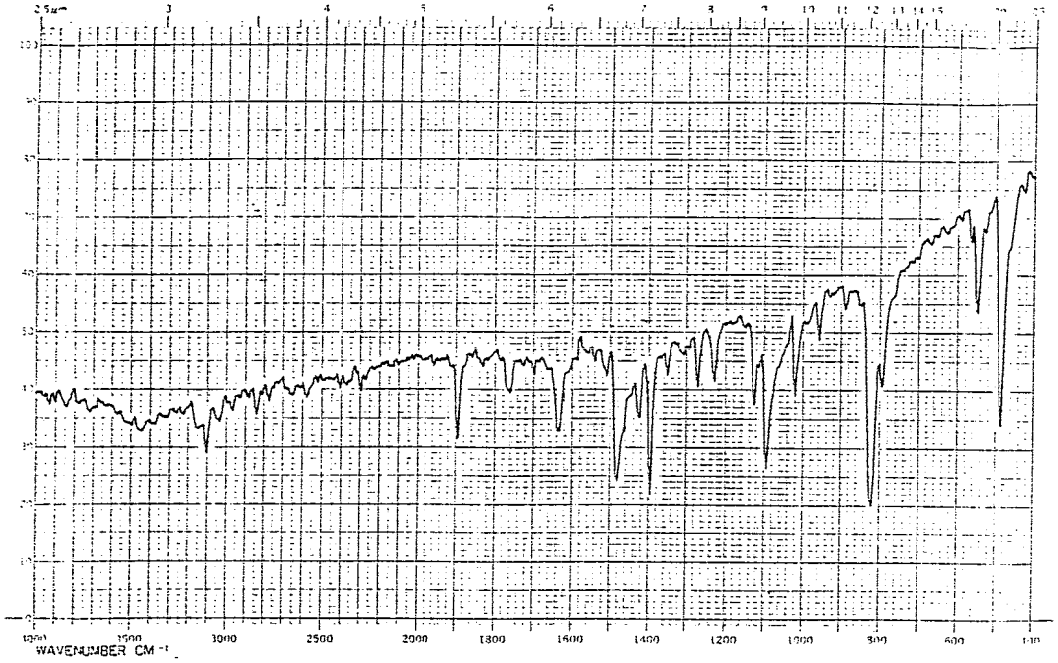
	Molecule Weight
Calculated Value (calculated as Cl=35.0)	146.0
Determined	146.0

(2) Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium



Infrared Spectrum of Test Substance

Results

Determines Wave Number(cm^{-1})	Literature Values* Wave Number(cm^{-1})
460～ 520	470～ 510
540～ 580	530～ 570
800～ 860	800～ 840
1010～1050	1000～1050
1080～1130	1070～1130
1390～1430	1380～1420
1460～1510	1450～1500
1630～1670	1620～1660
1760～1800	1750～1780
1890～1930	1870～1920
3100～3150	3080～3150

(*Sadtler Handbook by Sadtler Research Laboratories, Inc.)

2. Gas Chromatography

Instrument: Hewlett Packard 5890A Gass Chromatograph

Column: Methyl Silicone(0.2mmϕ × 38m)

Column Temperature: 200°C

Flow Rate: 1 ml/min

Detector: FID(Flame Ionization Detector)

Injection Volume: 1 μl

Results: Only major peak

Peak No.	Retention Time(min)	Retention Time Relative to Major Peak	AREA (percent of major peak)
1	2.517(Solvent peak)		
2	2.955	1.00	100

3. Conclusions: The result of the mass spectrum agreed with the calculated value and the infrared spectrum agreed with the literature values. Chromtogram indicated only the major peak without solvent peak. Consequently, the test substance was identified as p-dichlorobenzene.

B. Lot no. SAJ0701

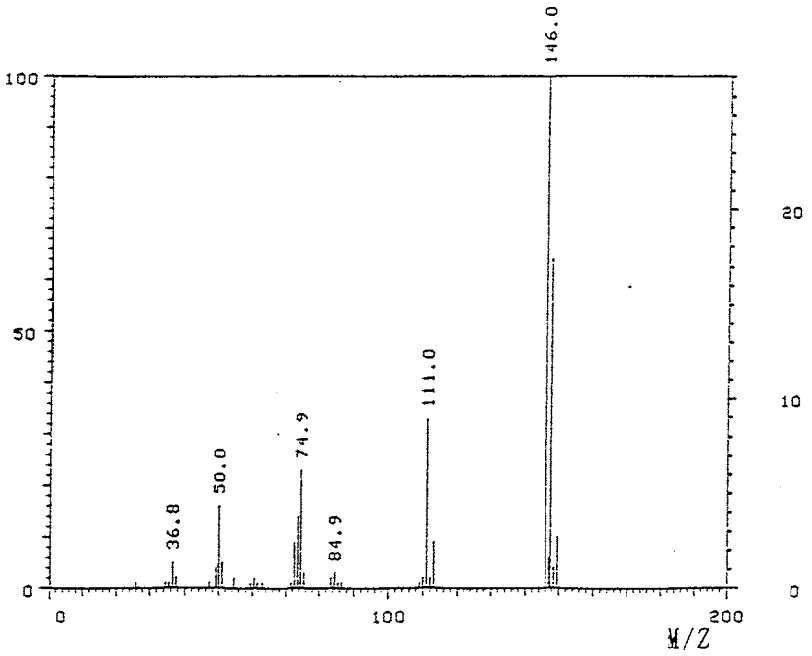
1. Spectral data

(1) Mass Spectrometry

Instrument: Hitachi M-80B Mass Spectrometer

Ionization: EI(Electron Ionization)

Ionization Voltage: 70eV



Mass Spectrum of Test Substance

Result:

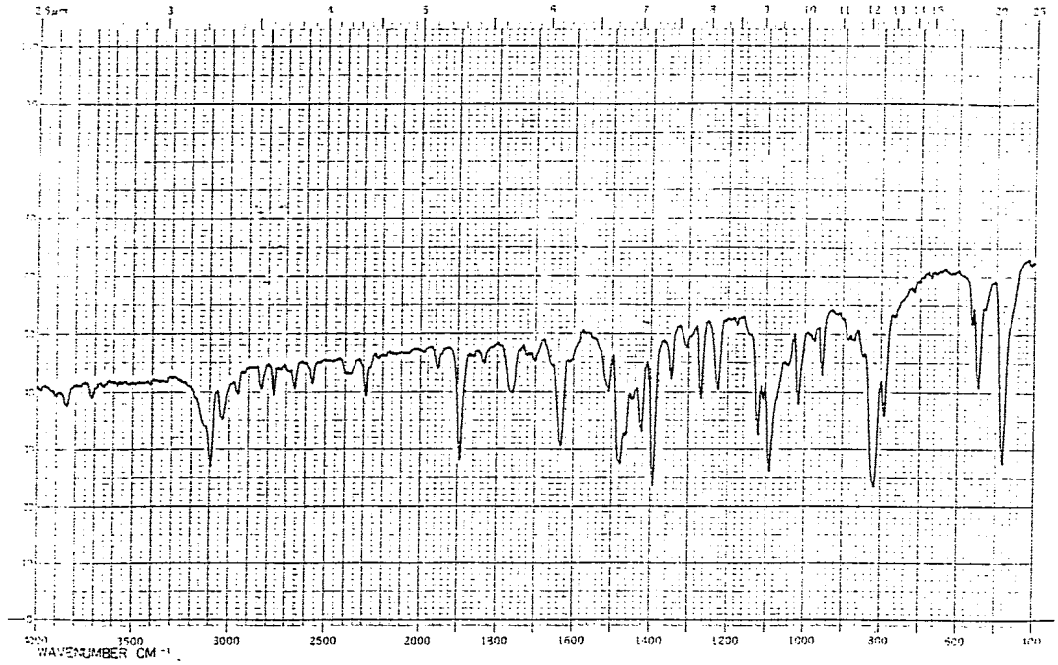
	Molecule Weight
Calculated Value (calculated as Cl=35.0)	146.0
Determined	146.0

(2) Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium



Infrared Spectrum of Test Substance

Results

Determines Wave Number(cm^{-1})	Literature Values* Wave Number(cm^{-1})
460～ 520	470～ 510
540～ 580	530～ 570
800～ 860	800～ 840
1010～1050	1000～1050
1080～1130	1070～1130
1390～1430	1380～1420
1460～1510	1450～1500
1630～1670	1620～1660
1760～1800	1750～1780
1890～1930	1870～1920
3100～3150	3080～3150

(*Sadtler Handbook by Sadtler Research Laboratories, Inc.)

2. Gas Chromatography

Instrument: Hewlett Packard 5890A Gass Chromatograph

Column: Methyl Silicone(0.2mmϕ × 38m)

Column Temperature: 200°C

Flow Rate: 1 ml/min

Detector: FID(Flame Ionization Detector)

Injection Volume: 1 μl

Results: Only major peak

Peak No.	Retention Time(min)	Retention Time Relative to Major Peak	AREA (percent of major peak)
1	2.517(Solvent peak)		
2	2.957	1.00	100

3. Conclusions: The result of the mass spectrum agreed with the calculated value and the infrared spectrum agreed with the literature values. Chromtogram indicated only the major peak without solvent peak. Consequently, the test substance was identified as p-dichlorobenzene.

C. Lot no. SAE1630

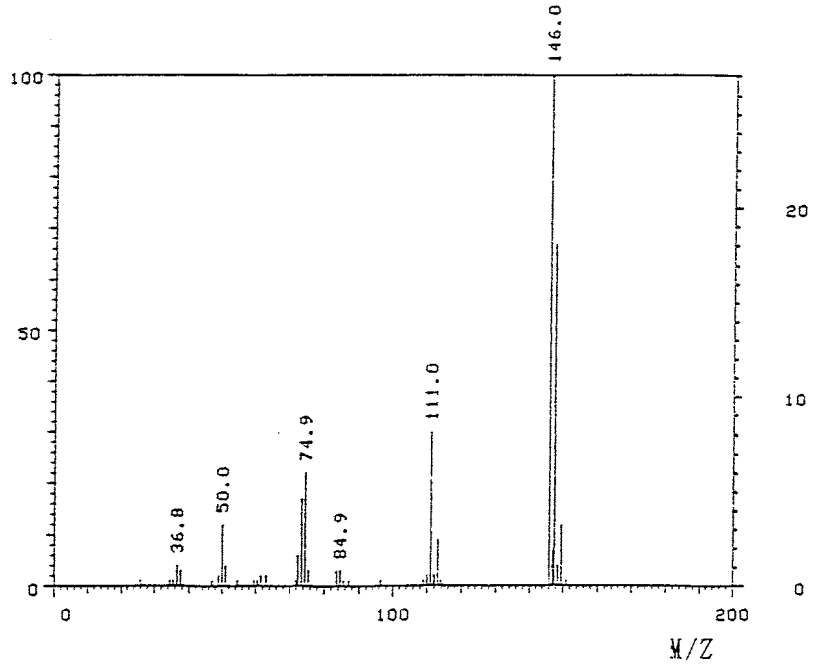
1. Spectral data

(1) Mass Spectrometry

Instrument: Hitachi M-80B Mass Spectrometer

Ionization: EI(Electron Ionization)

Ionization Voltage: 70eV



Mass Spectrum of Test Substance

Result:

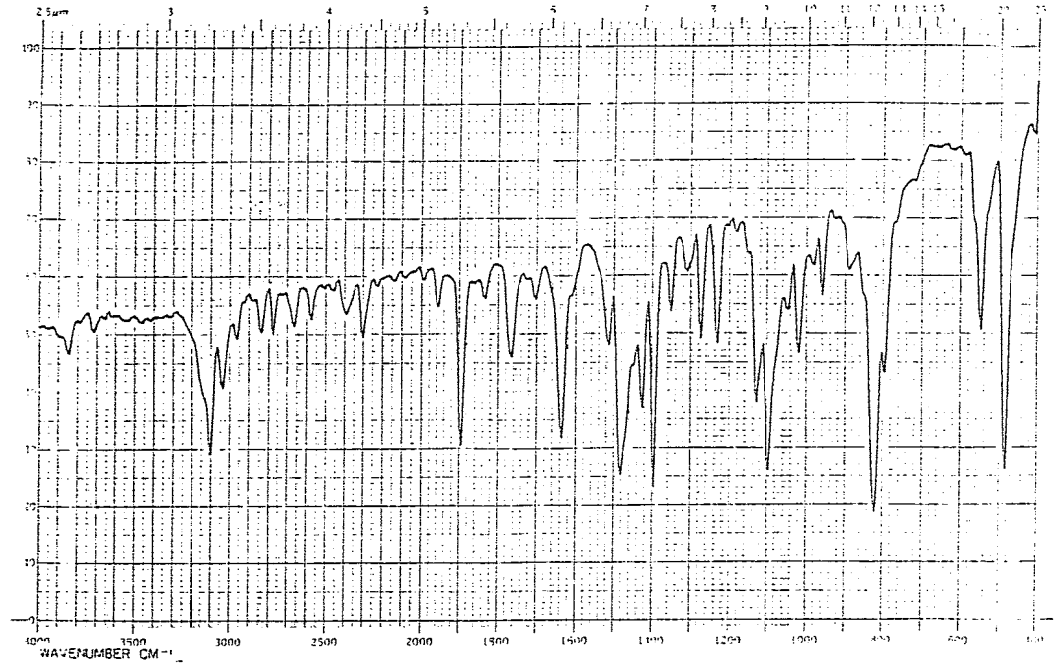
	Molecule Weight
Calculated Value (calculated as Cl=35.0)	146.0
Determined	146.0

(2) Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium



Infrared Spectrum of Test Substance

Results

Determines Wave Number(cm^{-1})	Literature Values* Wave Number(cm^{-1})
460～ 520	470～ 510
540～ 580	530～ 570
800～ 860	800～ 840
1010～1050	1000～1050
1080～1130	1070～1130
1390～1430	1380～1420
1460～1510	1450～1500
1630～1670	1620～1660
1760～1800	1750～1780
1890～1930	1870～1920
3100～3150	3080～3150

(*Sadtler Handbook by Sadtler Research Laboratories, Inc.)

2. Gas Chromatography

Instrument: Hewlett Packard 5890A Gass Chromatograph

Column: Methyl Silicone(0.2mmϕ × 38m)

Column Temperature: 200°C

Flow Rate: 1 ml/min

Detector: FID(Flame Ionization Detector)

Injection Volume: 1 μl

Results: Only major peak

Peak No.	Retention Time(min)	Retention Time Relative to Major Peak	AREA (percent of major peak)
1	2.517(Solvent peak)		
2	2.957	1.00	100

3. Conclusions: The result of the mass spectrum agreed with the calculated value and the infrared spectrum agreed with the literature values. Chromtogram indicated only the major peak without solvent peak. Consequently, the test substance was identified as p-dichlorobenzene.

D. Lot no. LKP0057

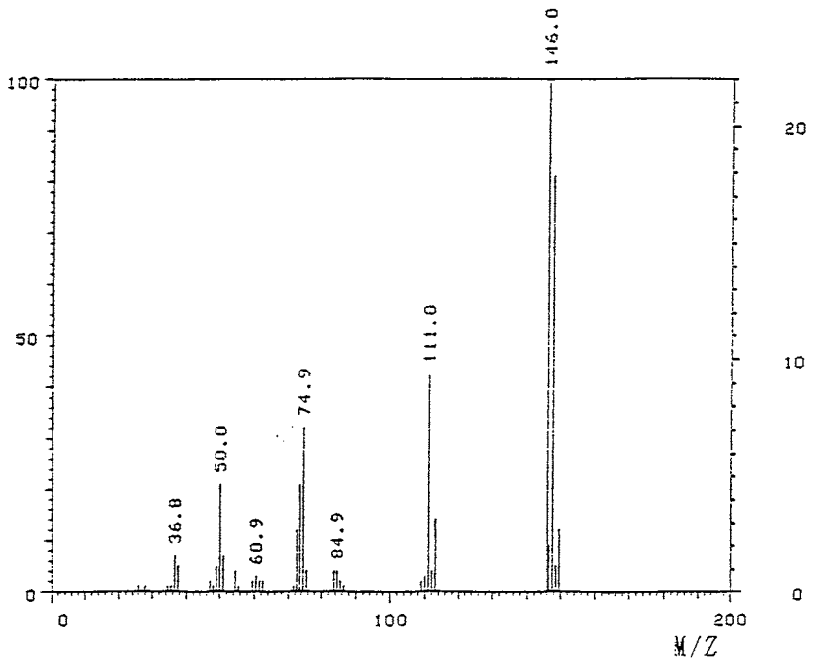
1. Spectral data

(1) Mass Spectrometry

Instrument: Hitachi M-80B Mass Spectrometer

Ionization: EI(Electron Ionization)

Ionization Voltage: 70eV



Mass Spectrum of Test Substance

Result:

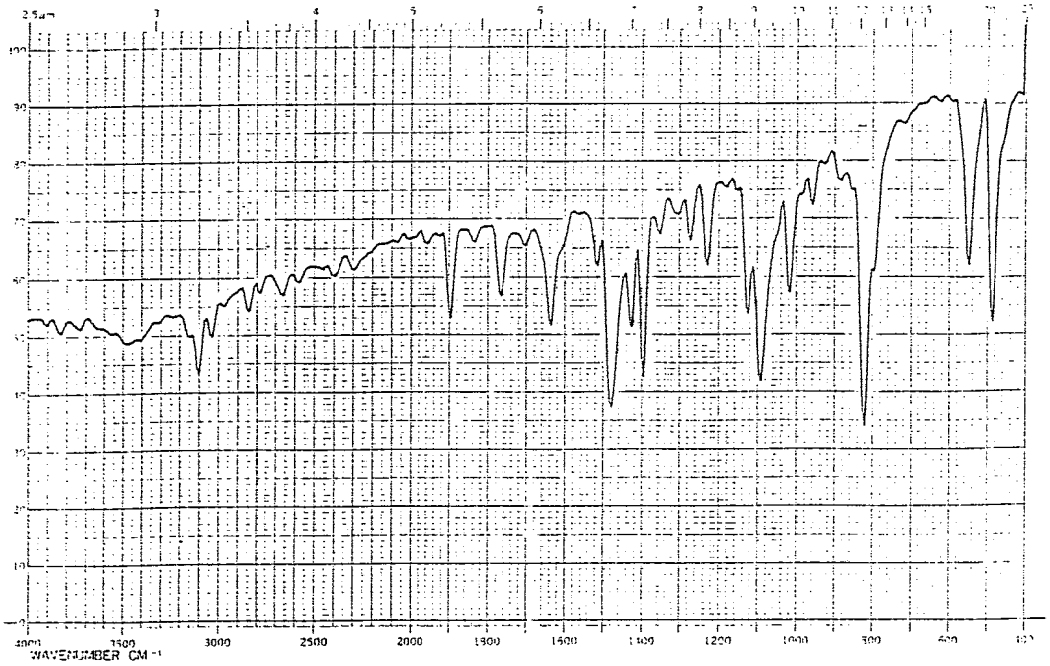
	Molecule Weight
Calculated Value (calculated as Cl=35.0)	146.0
Determined	146.0

(2) Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium



Infrared Spectrum of Test Substance

Results

Determines Wave Number(cm^{-1})	Literature Values* Wave Number(cm^{-1})
460～ 520	470～ 510
540～ 580	530～ 570
800～ 860	800～ 840
1010～1050	1000～1050
1080～1130	1070～1130
1390～1430	1380～1420
1460～1510	1450～1500
1630～1670	1620～1660
1760～1800	1750～1780
1890～1930	1870～1920
3100～3150	3080～3150

(*Sadtler Handbook by Sadtler Research Laboratories, Inc.)

2. Gas Chromatography

Instrument: Hewlett Packard 5890A Gass Chromatograph

Column: Methyl Silicone(0.2mmϕ × 38m)

Column Temperature: 200°C

Flow Rate: 1 ml/min

Detector: FID(Flame Ionization Detector)

Injection Volume: 1 μl

Results: Only major peak

Peak No.	Retention Time(min)	Retention Time Relative to Major Peak	AREA (percent of major peak)
1	2.515(Solvent peak)		
2	2.955	1.00	100

3. Conclusions: The result of the mass spectrum agreed with the calculated value and the infrared spectrum agreed with the literature values. Chromtogram indicated only the major peak without solvent peak. Consequently, the test substance was identified as p-dichlorobenzene.

E. Lot no. LKL0656

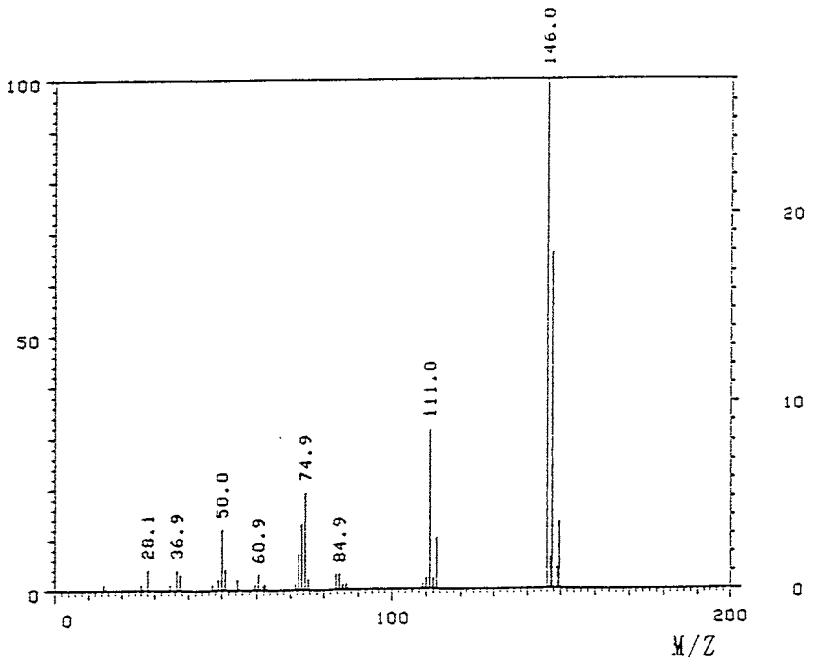
1. Spectral data

(1) Mass Spectrometry

Instrument: Hitachi M-80B Mass Spectrometer

Ionization: EI(Electron Ionization)

Ionization Voltage: 70eV



Mass Spectrum of Test Substance

Result:

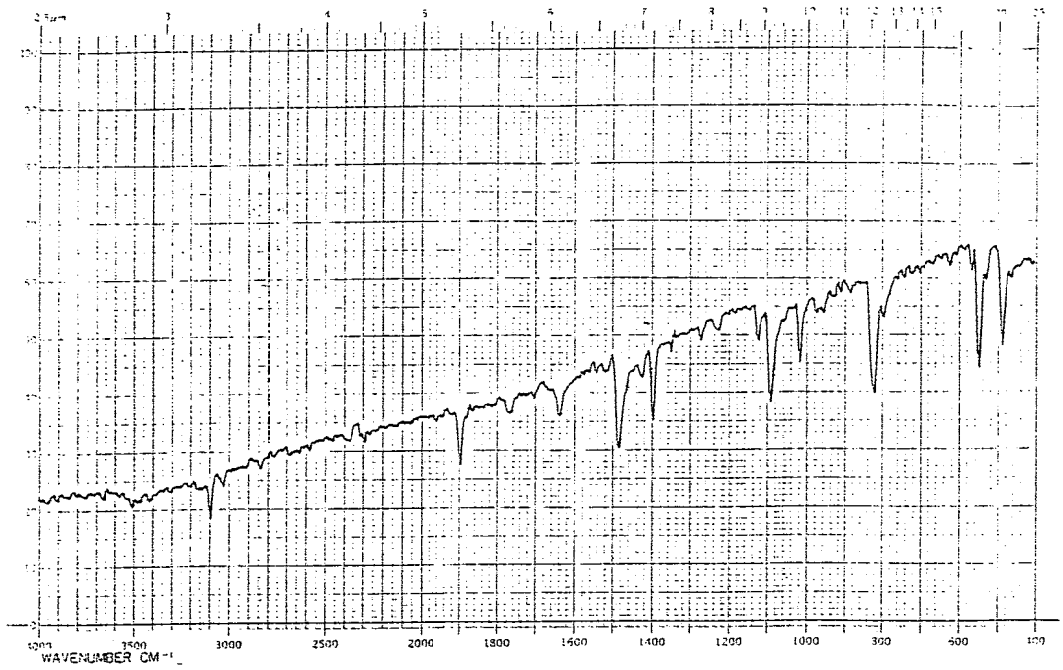
	Molecule Weight
Calculated Value (calculated as Cl=35.0)	146.0
Determined	146.0

(2) Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium



Infrared Spectrum of Test Substance

Results

Determines Wave Number(cm^{-1})	Literature Values* Wave Number(cm^{-1})
460～ 520	470～ 510
540～ 580	530～ 570
800～ 860	800～ 840
1010～1050	1000～1050
1080～1130	1070～1130
1390～1430	1380～1420
1460～1510	1450～1500
1630～1670	1620～1660
1760～1800	1750～1780
1890～1930	1870～1920
3100～3150	3080～3150

(*Sadtler Handbook by Sadtler Research Laboratories, Inc.)

2. Gas Chromatography

Instrument: Hewlett Packard 5890A Gass Chromatograph

Column: Methyl Silicone(0.2mmϕ × 38m)

Column Temperature: 200°C

Flow Rate: 1 ml/min

Detector: FID(Flame Ionization Detector)

Injection Volume: 1 μl

Results: Only major peak

Peak No.	Retention Time(min)	Retention Time Relative to Major Peak	AREA (percent of major peak)
1	2.517(Solvent peak)		
2	2.957	1.00	100

3. Conclusions: The result of the mass spectrum agreed with the calculated value and the infrared spectrum agreed with the literature values. Chromtogram indicated only the major peak without solvent peak. Consequently, the test substance was identified as p-dichlorobenzene.

F. Lot no. LKF1795

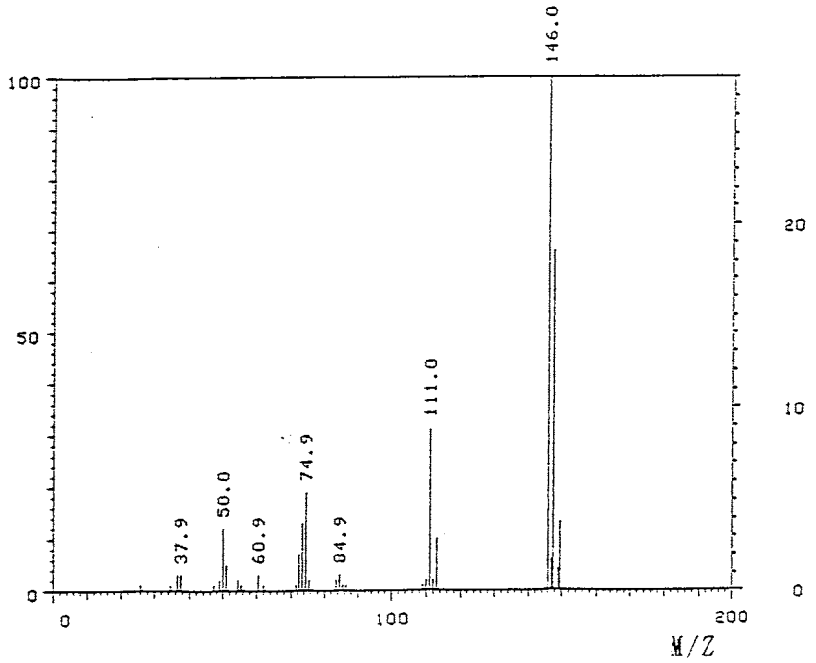
1. Spectral data

(1) Mass Spectrometry

Instrument: Hitachi M-80B Mass Spectrometer

Ionization: EI(Electron Ionization)

Ionization Voltage: 70eV



Mass Spectrum of Test Substance

Result:

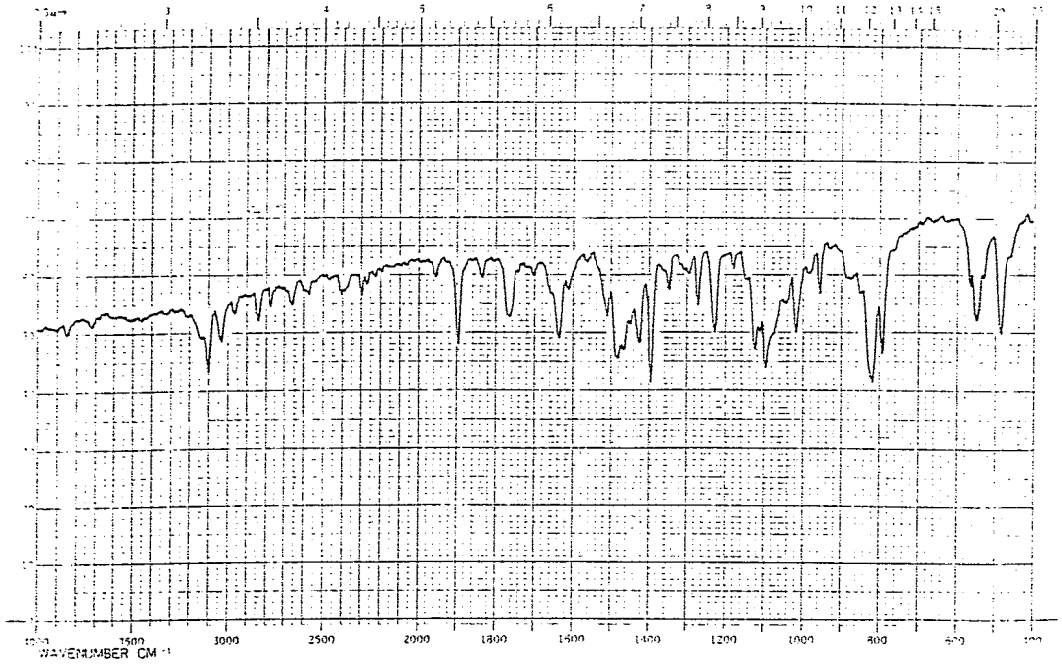
	Molecule Weight
Calculated Value (calculated as Cl=35.0)	146.0
Determined	146.0

(2) Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium



Infrared Spectrum of Test Substance

Results	Determines Wave Number(cm^{-1})	Literature Values* Wave Number(cm^{-1})
	460～ 520	470～ 510
	540～ 580	530～ 570
	800～ 860	800～ 840
	1010～1050	1000～1050
	1080～1130	1070～1130
	1390～1430	1380～1420
	1460～1510	1450～1500
	1630～1670	1620～1660
	1760～1800	1750～1780
	1890～1930	1870～1920
	3100～3150	3080～3150

(*Sadtler Handbook by Sadtler Research Laboratories, Inc.)

2. Gas Chromatography

Instrument: Hewlett Packard 5890A Gass Chromatograph

Column: Methyl Silicone(0.2mmϕ × 38m)

Column Temperature: 200°C

Flow Rate: 1 ml/min

Detector: FID(Flame Ionization Detector)

Injection Volume: 1 μl

Results: Only major peak

Peak No.	Retention Time(min)	Retention Time Relative to Major Peak	AREA (percent of major peak)
1	2.517(Solvent peak)		
2	2.958	1.00	100

3. Conclusions: The result of the mass spectrum agreed with the calculated value and the infrared spectrum agreed with the literature values. Chromtogram indicated only the major peak without solvent peak. Consequently, the test substance was identified as p-dichlorobenzene.

G. Lot no. WDQ0426

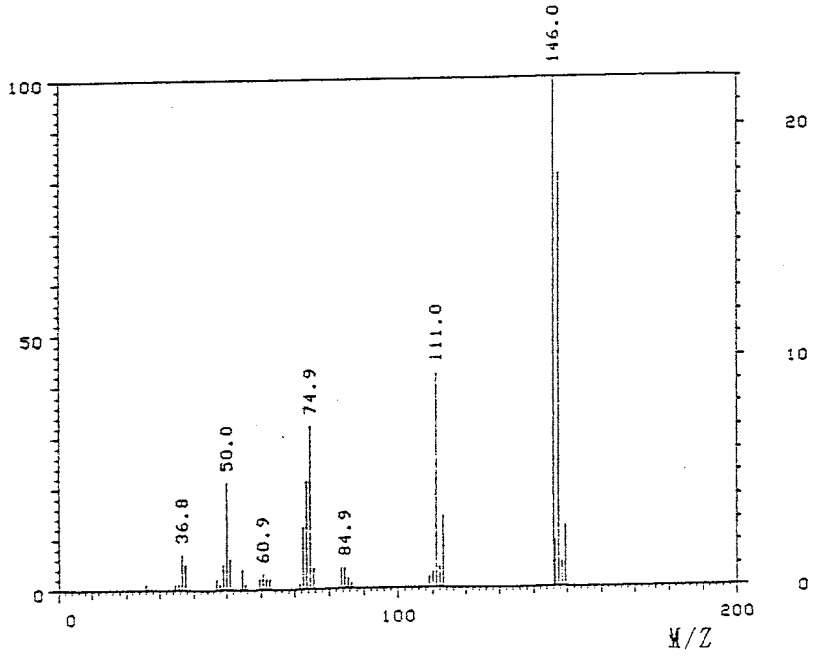
1. Spectral data

(1) Mass Spectrometry

Instrument: Hitachi M-80B Mass Spectrometer

Ionization: EI(Electron Ionization)

Ionization Voltage: 70eV



Mass Spectrum of Test Substance

Result:

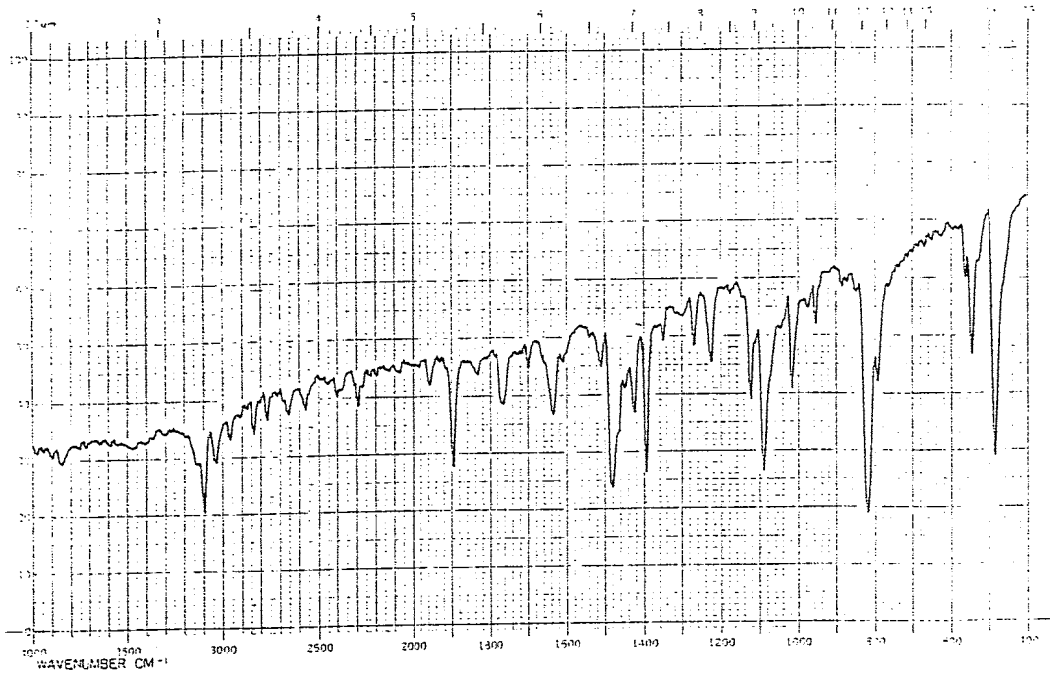
	Molecule Weight
Calculated Value (calculated as Cl=35.0)	146.0
Determined	146.0

(2) Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium



Infrared Spectrum of Test Substance

Results

Determines Wave Number(cm^{-1})	Literature Values* Wave Number(cm^{-1})
460～ 520	470～ 510
540～ 580	530～ 570
800～ 860	800～ 840
1010～1050	1000～1050
1080～1130	1070～1130
1390～1430	1380～1420
1460～1510	1450～1500
1630～1670	1620～1660
1760～1800	1750～1780
1890～1930	1870～1920
3100～3150	3080～3150

(*Sadtler Handbook by Sadtler Research Laboratories, Inc.)

2. Gas Chromatography

Instrument: Hewlett Packard 5890A Gass Chromatograph

Column: Methyl Silicone(0.2mmϕ × 38m)

Column Temperature: 200°C

Flow Rate: 1 ml/min

Detector: FID(Flame Ionization Detector)

Injection Volume: 1 μl

Results: Only major peak

Peak No.	Retention Time(min)	Retention Time Relative to Major Peak	AREA (percent of major peak)
1	2.517(Solvent peak)		
2	2.957	1.00	100

3. Conclusions: The result of the mass spectrum agreed with the calculated value and the infrared spectrum agreed with the literature values. Chromtogram indicated only the major peak without solvent peak. Consequently, the test substance was identified as p-dichlorobenzene.

H. Lot no. WDK0052

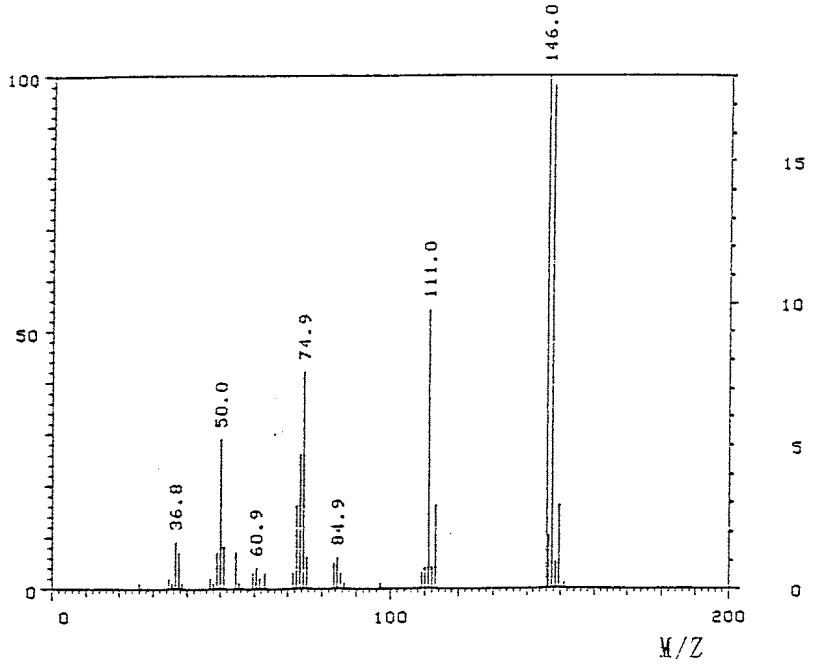
1. Spectral data

(1) Mass Spectrometry

Instrument: Hitachi M-80B Mass Spectrometer

Ionization: EI(Electron Ionization)

Ionization Voltage: 70eV



Mass Spectrum of Test Substance

Result:

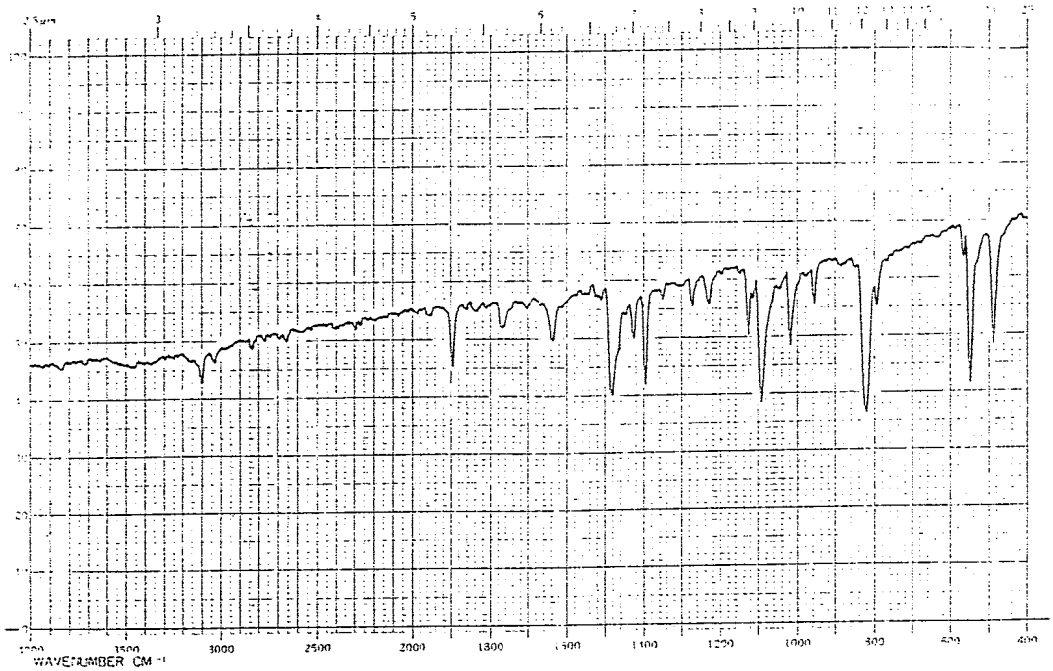
	Molecule Weight
Calculated Value (calculated as Cl=35.0)	146.0
Determined	146.0

(2) Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium



Infrared Spectrum of Test Substance

Results

Determines Wave Number(cm^{-1})	Literature Values* Wave Number(cm^{-1})
460～ 520	470～ 510
540～ 580	530～ 570
800～ 860	800～ 840
1010～1050	1000～1050
1080～1130	1070～1130
1390～1430	1380～1420
1460～1510	1450～1500
1630～1670	1620～1660
1760～1800	1750～1780
1890～1930	1870～1920
3100～3150	3080～3150

(*Sadtler Handbook by Sadtler Research Laboratories, Inc.)

2. Gas Chromatography

Instrument:	Hewlett Packard 5890A Gass Chromatograph
Column:	Methyl Silicone(0.2mmϕ × 38m)
Column Temperature:	200°C
Flow Rate:	1 ml/min
Detector:	FID(Flame Ionization Detector)
Injection Volume:	1 μl

Results: Only major peak

Peak No.	Retention Time(min)	Retention Time Relative to Major Peak	AREA (percent of major peak)
1	2.48(Solvent peak)		
2	2.927	1.00	100

3. Conclusions: The result of the mass spectrum agreed with the calculated value and the infrared spectrum agreed with the literature values. Chromtogram indicated only the major peak without solvent peak. Consequently, the test substance was identified as p-dichlorobenzene.

APPENDIX O 2

STABILITY OF p-DICHLOROBENZENE

(2-YEAR STUDY)

STABILITY OF p-DICHLOROBENZENE(TWO-YEAR STUDIES)

A. Lot no. CTJ0580

1. Sample storage: This lot was used from 1990.11.22 to 1990.12.19. Test substance was stored at 5°C.

2. Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium

Results

1990.11.19(date analyzed) Wave Number(cm^{-1})	1991.01.08(date analyzed) Wave Number(cm^{-1})
460～ 520	460～ 520
540～ 580	540～ 580
800～ 860	800～ 860
1010～1050	1010～1050
1080～1130	1080～1130
1390～1430	1390～1430
1460～1510	1460～1510
1630～1670	1630～1670
1760～1800	1760～1800
1890～1930	1890～1930
3100～3150	3100～3150

3. Gas Chromatography

Instrument: Hewlett Packard 5890A Gass Chromatograph

Column: Methyl Silicone(0.2mmϕ × 38m)

Column Temperature: 200°C

Flow Rate: 1 ml/min

Detector: FID(Flame Ionization Detector)

Injection Volume: 1 μl

Results: Chromatogram indicated one major peak(peak No. 2) and solvent peak(peak No. 1) analyzed at 1990. 11. 19 and one major peak(peak No. 2) and solvent peak(peak No. 1) analyzed at 1991. 1. 8. The new treace impurity peak in the test substance analyzed at 1991. 1. 8 was not detected.

Date	Peak No.	Retention Time(min)	Retention Time Relative to Major Peak	Area (percent of Major peak)
1990. 11. 19	1	2. 517(Solvent peak)		
(date analyzed)	2	2. 955	1. 00	100
1991. 01. 08	1	2. 515(Solvent peak)		
(date analyzed)	2	2. 955	1. 00	100

3. Conclusions: The results indicated that the test sabstance did not change when stored in the dark at 5°C during this period(for about 2 months).

B. Lot no. SAJ0701

1. Sample storage: This lot was used from 1990.12.19 to 1991.2.13. Test substance was stored at 5°C.

2. Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium

Results

1990.11.19(date analyzed) Wave Number(cm^{-1})	1991.02.14(date analyzed) Wave Number(cm^{-1})
460～ 520	460～ 520
540～ 580	540～ 580
800～ 860	800～ 860
1010～1050	1010～1050
1080～1130	1080～1130
1390～1430	1390～1430
1460～1510	1460～1510
1630～1670	1630～1670
1760～1800	1760～1800
1890～1930	1890～1930
3100～3150	3100～3150

3. Gas Chromatography

Instrument: Hewlett Packard 5890A Gass Chromatograph

Column: Methyl Silicone(0.2mmϕ × 38m)

Column Temperature: 200°C

Flow Rate: 1 ml/min

Detector: FID(Flame Ionization Detector)

Injection Volume: 1 μl

Results: Chromatogram indicated one major peak(peak No. 2) and solvent peak(peak No. 1) analyzed at 1990. 11. 19 and one major peak(peak No. 2) and solvent peak(peak No. 1) analyzed at 1991. 2. 14. The new treace impurity peak in the test substance analyzed at 1991. 2. 14 was not detected.

Date	Peak No.	Retention Time(min)	Retention Time Relative to Major Peak	Area (percent of Major peak)
1990. 11. 19	1	2. 517(Solvent peak)		
(date analyzed)	2	2. 957	1. 00	100
1990. 02. 1	1	2. 515(Solvent peak)		
(date analyzed)	2	2. 955	1. 00	100

3. Conclusions: The results indicated that the test sabstance did not change when stored in the dark at 5°C during this period(for about 3 months).

C. Lot no. SAE1630

1. Sample storage: This lot was used from 1991.2.13 to 1991.5.1. Test substance was stored at 5°C.

2. Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium

Results

1991.01.31(date analyzed) Wave Number(cm^{-1})	1991.05.01(date analyzed) Wave Number(cm^{-1})
460～ 520	460～ 520
540～ 580	540～ 580
800～ 860	800～ 860
1010～1050	1010～1050
1080～1130	1080～1130
1390～1430	1390～1430
1460～1510	1460～1510
1630～1670	1630～1670
1760～1800	1760～1800
1890～1930	1890～1930
3100～3150	3100～3150

3. Gas Chromatography

Instrument: Hewlett Packard 5890A Gass Chromatograph

Column: Methyl Silicone(0.2mmϕ × 38m)

Column Temperature: 200°C

Flow Rate: 1 ml/min

Detector: FID(Flame Ionization Detector)

Injection Volume: 1 μl

Results: Chromatogram indicated one major peak(peak No. 2) and solvent peak(peak No. 1) analyzed at 1991. 1. 31 and one major peak(peak No. 2) and solvent peak(peak No. 1) analyzed at 1991. 5. 1. The new treace impurity peak in the test substance analyzed at 1991. 5. 1 was not detected.

Date	Peak No.	Retention Time(min)	Retention Time Relative to Major Peak	Area (percent of Major peak)
1991. 01. 31	1	2. 517(Solvent peak)		
(date analyzed)	2	2. 957	1. 00	100
1991. 05. 01	1	2. 515(Solvent peak)		
(date analyzed)	2	2. 955	1. 00	100

3. Conclusions: The results indicated that the test sabstance did not change when stored in the dark at 5°C during this period(for about 2 months).

D. Lot no. LKP0057

1. Sample storage: This lot was used from 1991.5.1 to 1991.8.30. Test substance was stored at 5°C.

2. Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium

Results

1991.04.02(date analyzed) Wave Number(cm^{-1})	1991.09.04(date analyzed) Wave Number(cm^{-1})
460～ 520	460～ 520
540～ 580	540～ 580
800～ 860	800～ 860
1010～1050	1010～1050
1080～1130	1080～1130
1390～1430	1390～1430
1460～1510	1460～1510
1630～1670	1630～1670
1760～1800	1760～1800
1890～1930	1890～1930
3100～3150	3100～3150

3. Gas Chromatography

Instrument: Hewlett Packard 5890A Gass Chromatograph

Column: Methyl Silicone(0.2mmϕ × 38m)

Column Temperature: 200°C

Flow Rate: 1 ml/min

Detector: FID(Flame Ionization Detector)

Injection Volume: 1 μl

Results: Chromatogram indicated one major peak(peak No. 2) and solvent peak(peak No. 1) analyzed at 1991. 4. 2 and one major peak(peak No. 2) and solvent peak(peak No. 1) analyzed at 1991. 9. 4. The new treace impurity peak in the test substance analyzed at 1991. 9. 4 was not detected.

Date	Peak No.	Retention Time(min)	Retention Time Relative to Major Peak	Area (percent of Major peak)
1991. 04. 02	1	2. 515(Solvent peak)		
(date analyzed)	2	2. 955	1. 00	100
1991. 09. 04	1	2. 515(Solvent peak)		
(date analyzed)	2	2. 955	1. 00	100

3. Conclusions: The results indicated that the test sabstance did not change when stored in the dark at 5°C during this period(for about 5 months).

E. Lot no. LKL0656

1. Sample storage: This lot was used from 1991.8.30 to 1991.12.28. Test substance was stored at 5°C.

2. Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium

Results

1991.08.20(date analyzed) Wave Number(cm^{-1})	1992.01.07(date analyzed) Wave Number(cm^{-1})
460～ 520	460～ 520
540～ 580	540～ 580
800～ 860	800～ 860
1010～1050	1010～1050
1080～1130	1080～1130
1390～1430	1390～1430
1460～1510	1460～1510
1630～1670	1630～1670
1760～1800	1760～1800
1890～1930	1890～1930
3100～3150	3100～3150

3. Gas Chromatography

Instrument: Hewlett Packard 5890A Gass Chromatograph

Column: Methyl Silicone(0.2mmϕ × 38m)

Column Temperature: 200°C

Flow Rate: 1 ml/min

Detector: FID(Flame Ionization Detector)

Injection Volume: 1 μl

Results: Chromatogram indicated one major peak(peak No. 2) and solvent peak(peak No. 1) analyzed at 1991. 8. 20 and one major peak(peak No. 2) and solvent peak(peak No. 1) analyzed at 1992. 1. 7. The new treace impurity peak in the test substance analyzed at 1992. 1. 7 was not detected.

Date	Peak No.	Retention Time(min)	Retention Time Relative to Major Peak	Area (percent of Major peak)
1991. 08. 20	1	2. 517(Solvent peak)		
(date analyzed)	2	2. 957	1. 00	100
1992. 01. 07	1	2. 517(Solvent peak)		
(date analyzed)	2	2. 957	1. 00	100

3. Conclusions: The results indicated that the test sabstance did not change when stored in the dark at 5°C during this period(for about 5 months).

F. Lot no. LKF1795

1. Sample storage: This lot was used from 1991. 12. 28 to 1992. 5. 20. Test substance was stored at 5°C.

2. Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium

Results

1991. 12. 25(date analyzed) Wave Number(cm^{-1})	1992. 05. 20(date analyzed) Wave Number(cm^{-1})
460～ 520	460～ 520
540～ 580	540～ 580
800～ 860	800～ 860
1010～1050	1010～1050
1080～1130	1080～1130
1390～1430	1390～1430
1460～1510	1460～1510
1630～1670	1630～1670
1760～1800	1760～1800
1890～1930	1890～1930
3100～3150	3100～3150

3. Gas Chromatography

Instrument: Hewlett Packard 5890A Gass Chromatograph

Column: Methyl Silicone(0. 2mmϕ × 38m)

Column Temperature: 200°C

Flow Rate: 1 ml/min

Detector: FID(Flame Ionization Detector)

Injection Volume: 1 μl

Results: Chromatogram indicated one major peak(peak No. 2) and solvent peak(peak No. 1) analyzed at 1991. 12. 25 and one major peak(peak No. 2) and solvent peak(peak No. 1) analyzed at 1992. 5. 20. The new treace impurity peak in the test substance analyzed at 1992. 5. 20 was not detected.

Date	Peak No.	Retention Time(min)	Retention Time Relative to Major Peak	Area (percent of Major peak)
1991. 12. 25	1	2. 517(Solvent peak)		
(date analyzed)	2	2. 958	1. 00	100
1992. 05. 20	1	2. 517(Solvent peak)		
(date analyzed)	2	2. 958	1. 00	100

3. Conclusions: The results indicated that the test sabstance did not change when stored in the dark at 5°C during this period(for about 5 months).

G. Lot no. WDQ0426

1. Sample storage: This lot was used from 1992.5.20 to 1992.9.16. Test substance was stored at 5°C.

2. Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium

Results

1992.05.11(date analyzed) Wave Number(cm^{-1})	1992.09.17(date analyzed) Wave Number(cm^{-1})
460～ 520	460～ 520
540～ 580	540～ 580
800～ 860	800～ 860
1010～1050	1010～1050
1080～1130	1080～1130
1390～1430	1390～1430
1460～1510	1460～1510
1630～1670	1630～1670
1760～1800	1760～1800
1890～1930	1890～1930
3100～3150	3100～3150

3. Gas Chromatography

Instrument: Hewlett Packard 5890A Gass Chromatograph

Column: Methyl Silicone(0.2mmϕ × 38m)

Column Temperature: 200°C

Flow Rate: 1 ml/min

Detector: FID(Flame Ionization Detector)

Injection Volume: 1 μl

Results:Chromatogram indicated one major peak(peak No.2) and solvent peak(peak No.1) analyzed at 1992.5.11 and one major peak(peak No.2) and solvent peak(peak No.1) analyzed at 1992.9.17. The new treace impurity peak in the test substance analyzed at 1992.9.17 was not detected.

Date	Peak No.	Retention Time(min)	Retention Time Relative to Major Peak	Area (percent of Major peak)
1992.05.11	1	2.517(Solvent peak)		
(date analyzed)	2	2.957	1.00	100
1992.09.17	1	2.517(Solvent peak)		
(date analyzed)	2	2.958	1.00	100

3. Conclusions:The results indicated that the test sabstance did not change when stored in the dark at 5°C during this period(for about 4 months).

H. Lot no. WDK0052

1. Sample storage: This lot was used from 1992.9.16 to 1992.12.10. Test substance was stored at 5°C.

2. Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium

Results

1992.09.11(date analyzed) Wave Number(cm^{-1})	1992.12.10(date analyzed) Wave Number(cm^{-1})
460～ 520	460～ 520
540～ 580	540～ 580
800～ 860	800～ 860
1010～1050	1010～1050
1080～1130	1080～1130
1390～1430	1390～1430
1460～1510	1460～1510
1630～1670	1630～1670
1760～1800	1760～1800
1890～1930	1890～1930
3100～3150	3100～3150

3. Gas Chromatography

Instrument: Hewlett Packard 5890A Gass Chromatograph

Column: Methyl Silicone(0.2mmϕ × 38m)

Column Temperature: 200°C

Flow Rate: 1 ml/min

Detector: FID(Flame Ionization Detector)

Injection Volume: 1 μl

Results: Chromatogram indicated one major peak(peak No. 2) and solvent peak(peak No. 1) analyzed at 1992. 9. 11 and one major peak(peak No. 2) and solvent peak(peak No. 1) analyzed at 1992. 12. 10. The new treace impurity peak in the test substance analyzed at 1992. 12. 10 was not detected.

Date	Peak No.	Retention Time(min)	Retention Time Relative to Major Peak	Area (percent of Major peak)
1992. 09. 11	1	2. 48(Solvent peak)		
(date analyzed)	2	2. 927	1. 00	100
1992. 12. 10	1	2. 48(Solvent peak)		
(date analyzed)	2	2. 928	1. 00	100

3. Conclusions: The results indicated that the test sabstance did not change when stored in the dark at 5°C during this period(for about 3 months).

APPENDIX P 1

CONDETRATION OF p-DICHLOROBENZENE IN INHALATION CHAMBER

(2-YEAR STUDY)

CONCENTRATION OF p-DICHLOROBENZENE IN INHALTION CHAMBER
(RAT : TWO-YEAR STUDY)

Group Name	Concentration (ppm) Mean ± S.D.
Control	0.0 ± 0.0
20ppm	19.8 ± 0.4
75ppm	74.8 ± 1.0
300ppm	298.4 ± 4.0

CONCENTRATION OF p-DICHLOROBENZENE IN INHALTION CHAMBER
(MOUSE : TWO-YEAR STUDY)

Group Name	Concentration (ppm) Mean ± S.D.
Control	0.0 ± 0.0
20ppm	19.9 ± 0.4
75ppm	74.8 ± 0.8
300ppm	298.3 ± 2.8

APPENDIX P 2

ENVIRONMET OF INHALATION CHAMBER

(2-YEAR STUDY)

ENVIRONMENT OF INHALATION CHAMBER (RAT : TWO-YEAR STUDY)

Group Name	Temperature(℃) Mean ± S.D.	Humidity(%) Mean ± S.D.	Ventilation Rate(L/min) Mean ± S.D.	Room Air Change(time/h) Mean
Control	23.0 ± 0.3	55.2 ± 4.4	1524.7 ± 29.0	12.0
20ppm	23.0 ± 0.2	53.8 ± 1.7	1523.1 ± 11.2	12.0
75ppm	23.6 ± 0.4	50.5 ± 4.3	1513.3 ± 10.9	11.9
300ppm	23.6 ± 0.5	56.7 ± 3.6	1523.9 ± 11.4	12.0

ENVIRONMENT OF INHALATION CHAMBER (MOUSE : TWO-YEAR STUDY)

Group Name	Temperature(℃) Mean ± S.D.	Humidity(%) Mean ± S.D.	Ventilation Rate(L/min) Mean ± S.D.	Room Air Change(time/h) Mean
Control	23.0 ± 0.3	50.5 ± 2.9	743.5 ± 5.1	12.1
20ppm	23.1 ± 0.3	48.9 ± 1.8	746.9 ± 6.3	12.1
75ppm	23.0 ± 0.2	50.0 ± 1.8	743.8 ± 5.8	12.1
300ppm	23.5 ± 0.4	49.2 ± 3.0	741.1 ± 6.8	12.0

APPENDIX Q 1

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS

METHODS FOR HEMATOLOGY,BIOCHEMISTRY AND URINALYSIS

Item	Method	Unit
Hematology		
Red blood cell	Light scattering method [1]	$\times 10^6 / \mu L$
Hemoglobin	Cyanmethemoglobin method [1]	g/dL
Hematocrit	Calculated as RBC × MCV/10 [1]	%
Mean corpuscular volume (MCV)	Light scattering method [1]	fL
Mean corpuscular hemoglobin (MCH)	Calculated as Hgb/RBC × 10 [1]	pg
Mean corpuscular hemoglobin concentration (MCHC)	Calculated as Hgb/Hct × 10 [1]	g/dL
Platelet	Light scattering method [1]	$\times 10^3 / \mu L$
White blood cell (WBC)	Light scattering method [1]	$\times 10^3 / \mu L$
Differential WBC	Pattern recognition method [2] (May−Grunwald−Giemsa staining)	%
Biochemistry		
Total protein	Biuret method [3]	g/dL
Albumin	BCG method [3]	g/dL
A/G ratio	Calculated as Alb/(TP−Alb) [3]	
T−bilirubin	Michaelson method [3]	mg/dL
Glucose	Enzymatic method (HK·G−6−PDH) [3]	mg/dL
T−cholesterol	Enzymatic method (CEH·COD·POD) [3]	mg/dL
Triglyceride	Enzymatic method (GK·GPO·POD) [3]	mg/dL
Phospholipid	Enzymatic method (PLD·COD·POD) [3]	mg/dL
Glutamic oxaloacetic transaminase (GOT)	Karmen method [3]	IU/L
Glutamic pyruvic transaminase(GPT)	Karmen method [3]	IU/L
Lactate dehydrogenase (LDH)	Wroblewski−LaDue method [3]	IU/L
Alkaline phosphatase (ALP)	GSCC method [3]	IU/L
γ −Glutamyl transpeptidase (G−GTP)	L− γ −Glutamyl−p−nitroanilide substrate method [3]	IU/L
Creatine phosphokinase (CPK)	GSCC method [3]	IU/L
Urea nitrogen	Enzymatic method (Urease ·GLDH) [3]	mg/dL
Creatinine	Jaffe metod [3]	mg/dL
Sodium	Flame photometry [4]	mEq/L
Potassium	Flame photometry [4]	mEq/L
Chloride	Coulometric titration [4]	mEq/L
Calcium	OCPC method 3)	mg/dL
Inorganic phosphorus	Enzymatic method (SPL·PGM·G−6−PDH) [3]	mg/dL
Urinalysis		
pH,Protein,Glucose,Ketone body, Bilirubin, Occult Blood,Urobilinogen	Urinalysis reagent paper metod [5]	

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 705 : Hitachi ,Ltd.,Japan)
4) Flame photometer (Hitachi 750 : Hitachi ,Ltd.,Japan)
5) Ames reagent strips for urinalysis (Multistix,Uro−Labstix : Miles Sankyo Co.,Ltd.,Japan)

APPENDIX Q 2

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

	TEST ITEM	DECIMAL PLACE	UNIT
HEMATOLOGY	Red blood cell	2	$\times 10^6/\mu L$
	Hemoglobin	1	g/dL
	Hematocrit	1	%
	MCV	1	fL
	MCH	1	pg
	MCHC	1	g/dL
	Platelet	0	$\times 10^3/\mu L$
	White blood cell	2	$\times 10^3/\mu L$
	Differential WBC	0	%
BIOCHEMISTRY	Total protein	1	g/dL
	Albumin	1	g/dL
	A/G ratio	1	—
	T-bilirubin	2	mg/dL
	Glucose	0	mg/dL
	T-cholesterol	0	mg/dL
	Triglyceride	0	mg/dL
	Phospholipid	0	mg/dL
	GOT	0	IU/L
	GPT	0	IU/L
	LDH	0	IU/L
	ALP	0	IU/L
	G-GTP	0	IU/L
	CPK	0	IU/L
	Urea nitrogen	1	mg/dL
	Creatinine	1	mg/dL
	Sodium	0	mEq/L
	Potassium	1	mEq/L
	Chloride	0	mEq/L
	Calcium	1	mg/dL
	Inorganic phosphorus	1	mg/dL