酢酸ビニルのラット及びマウスを用いた
経口投与によるがん原性試験(混水試験)報告書

APPENDIX

(L1～R2)
がん原性：ラット/0162；マウス/0163

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIX L 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0162
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				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	6				10				14				11			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Integumentary system/appandage]																		
skin/app			<6>				<10>				<14>				<11>			
	scar:dermis		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Respiratory system]																		
nasal cavit			<6>				<10>				<14>				<11>			
	eosinophilic change:olfactory epithelium		1	0	0	0	6	0	0	0	4	1	0	0	0	0	0	0
			(17)	(0)	(0)	(0)	(60)	(0)	(0)	(0)	(29)	(7)	(0)	(0)	(0)	(0)	(0)	(0)
	eosinophilic change:respiratory epithelium		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	inflammation:foreign body		0	2	0	0	0	0	0	0	2	0	0	0	0	0	1	0
			(0)	(33)	(0)	(0)	(0)	(0)	(0)	(0)	(14)	(0)	(0)	(0)	(0)	(0)	(9)	(0)
	respiratory metaplasia: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)	(7)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	respiratory metaplasia:gland		1	1	0	0	5	0	0	0	8	1	0	0	3	1	0	0
			(17)	(17)	(0)	(0)	(50)	(0)	(0)	(0)	(57)	(7)	(0)	(0)	(27)	(9)	(0)	(0)
lung			<6>				<10>				<14>				<11>			
	congestion		0	1	0	0	0	1	0	0	1	0	0	0	0	1	0	0
			(0)	(17)	(0)	(0)	(0)	(10)	(0)	(0)	(7)	(0)	(0)	(0)	(0)	(9)	(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				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	6				10				14				11			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Hematopoietic system]																		
spleen			< 6>				<10>				<14>				<11>			
	atrophy		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (14)	0 (0)	0 (0)	0 (0)	2 (18)	1 (9)	0 (0)
	deposit of hemosiderin		0 (0)	2 (33)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	1 (9)	0 (0)	0 (0)	0 (0)
	extramedullary hematopoiesis		0 (0)	0 (0)	1 (17)	0 (0)	0 (0)	1 (10)	1 (10)	0 (0)	0 (0)	2 (14)	1 (7)	0 (0)	0 (0)	0 (0)	2 (18)	0 (0)
[Circulatory system]																		
heart			< 6>				<10>				<14>				<11>			
	thrombus		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (9)	0 (0)
	mineralization		0 (0)	0 (0)	1 (17)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hypertrophy		0 (0)	1 (17)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	myocardial fibrosis		3 (50)	0 (0)	1 (17)	0 (0)	5 (50)	0 (0)	0 (0)	0 (0)	10 (71)	0 (0)	0 (0)	0 (0)	6 (55)	0 (0)	0 (0)	0 (0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 6				400 ppm 10				2000 ppm 14				10000 ppm 11			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Circulatory system]																		
artery/aort			<6>				<10>				<14>				<11>			
	mineralization		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(17)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]																		
tooth			<6>				<10>				<14>				<11>			
	inflammation		0	0	0	0	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)	(9)	(0)	(0)
tongue			<6>				<10>				<14>				<10>			
	mineralization		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(17)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	arteritis		0	0	0	0	2	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
stomach			<6>				<10>				<14>				<11>			
	mineralization		0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(17)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(0)	(0)	(0)
	erosion:forestomach		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 6				400 ppm 10				2000 ppm 14				10000 ppm 11			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
stomach			<6>				<10>				<14>				<11>			
	ulcer:forestomach		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyperplasia:forestomach		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	erosion:glandular stomach		0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(9)	(0)	(0)	(0)
	ulcer:glandular stomach		0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(9)	(0)	(0)	(0)
liver			<6>				<10>				<14>				<11>			
	necrosis:central		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	fatty change		1	0	0	0	0	1	0	0	1	3	0	0	0	0	0	0
			(17)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(7)	(21)	(0)	(0)	(0)	(0)	(0)	(0)
	inflammatory infiltration		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	granulation		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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Organ	Findings	Group Name	Control				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	6				10				14				11			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver			< 6>				<10>				<14>				<11>			
	vacuolated cell focus		1 (17)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (18)	0 (0)	0 (0)
	spongiosis hepatis		2 (33)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (14)	0 (0)	0 (0)	0 (0)	1 (9)	0 (0)	0 (0)	0 (0)
	bile duct hyperplasia		1 (17)	3 (50)	1 (17)	0 (0)	0 (0)	6 (60)	3 (30)	0 (0)	3 (21)	8 (57)	1 (7)	0 (0)	1 (9)	4 (36)	4 (36)	0 (0)
pancreas			< 6>				<10>				<14>				<11>			
	atrophy		0 (0)	0 (0)	0 (0)	0 (0)	4 (40)	0 (0)	0 (0)	0 (0)	2 (14)	4 (29)	0 (0)	0 (0)	1 (9)	0 (0)	1 (9)	0 (0)
[Urinary system]																		
kidney			< 6>				<10>				<14>				<11>			
	hyaline droplet		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (14)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	deposit of hemosiderin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (14)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

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Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 6				400 ppm 10				2000 ppm 14				10000 ppm 11			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Urinary system]																		
kidney			<6>				<10>				<14>				<11>			
	chronic nephropathy		0 (0)	1 (17)	1 (17)	2 (33)	1 (10)	3 (30)	3 (30)	0 (0)	2 (14)	2 (14)	1 (7)	3 (21)	2 (18)	0 (0)	2 (18)	0 (0)
	hydronephrosis		1 (17)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	tubular necrosis		0 (0)	0 (0)	1 (17)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	2 (14)	0 (0)	1 (9)	2 (18)	4 (36)	0 (0)
[Endocrine system]																		
pituitary			<6>				<10>				<14>				<11>			
	angiectasis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (9)	0 (0)	0 (0)	0 (0)
	cyst		0 (0)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	3 (21)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
thyroid			<6>				< 9>				<14>				<10>			
	C-cell hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	1 (11)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)

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		No. of Animals on Study	6				10				14				11			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]																		
parathyroid			<6>				<10>				<14>				<11>			
	hyperplasia		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(17)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
adrenal			<6>				<10>				<14>				<11>			
	hyperplasia:medulla		4	0	0	0	1	0	0	0	1	1	0	0 *	0	0	0	0 *
			(67)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(7)	(7)	(0)	(0)	(0)	(0)	(0)	(0)
	focal fatty change:cortex		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(17)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Reproductive system]																		
testis			<6>				<10>				<14>				<11>			
	atrophy		0	1	0	0	1	2	0	0	0	1	0	0	0	2	3	0
			(0)	(17)	(0)	(0)	(10)	(20)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(18)	(27)	(0)
	mineralization		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	arteritis		0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(17)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(0)	(0)	(0)

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Organ	Findings	Group Name	Control				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	6				10				14				11			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Reproductive system]																		
testis			<6>				<10>				<14>				<11>			
	interstitial cell hyperplasia		1	0	0	0	3	0	0	0	1	0	0	0	0	0	0	0
			(17)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
epididymis			<6>				<10>				<14>				<11>			
	degeneration		0	0	0	0	2	0	0	0	3	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(21)	(0)	(0)	(0)	(27)	(0)	(0)	(0)
prostate			<6>				<10>				<14>				<11>			
	inflammation		1	0	0	0	1	0	0	0	1	0	0	0	1	1	0	0
			(17)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(9)	(9)	(0)	(0)
mammary gl			<6>				<10>				<14>				<11>			
	galactocele		1	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(17)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Nervous system]																		
brain			<6>				<10>				<14>				<11>			
	hemorrhage		1	0	0	0	1	0	0	0	0	1	0	0	0	1	0	0
			(17)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(9)	(0)	(0)
spinal cord			<6>				<10>				<14>				<11>			
	hemorrhage		0	1	0	0	0	1	0	0	0	1	0	0	0	1	0	0
			(0)	(17)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(9)	(0)	(0)

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			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Special sense organs/appandage]																		
eye			< 6>				<10>				<14>				<11>			
	cataract		1 (17)	0 (0)	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)
	retinal atrophy		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	1 (10)	0 (0)	1 (7)	1 (7)	1 (7)	0 (0)	0 (0)	0 (0)	1 (9)	0 (0)
	keratitis		0 (0)	1 (17)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	degeneration:cornea		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)	0 (0)	0 (0)	0 (0)
Harder gl			< 6>				<10>				<14>				<11>			
	degeneration		1 (17)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	inflammation		0 (0)	0 (0)	0 (0)	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)
	inflammatory infiltration		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)	0 (0)	0 (0)	0 (0)
nasolacr d			< 6>				<10>				<14>				<11>			
	inflammation		0 (0)	0 (0)	0 (0)	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)

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				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	6				10				14				11			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Musculoskeletal system]																		
bone			< 6>				<10>				<14>				<11>			
	ostitis fibrosa		0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(17)	(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

APPENDIX L 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

Organ	Findings	Group Name	Control				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	9				10				9				13			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
[Respiratory system]																		
nasal cavit			< 9>				<10>				< 9>				<13>			
	inflammation		0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(22)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	eosinophilic change:olfactory epithelium		5	1	0	0	3	1	0	0	5	2	0	0	1	5	0	0 *
			(56)	(11)	(0)	(0)	(30)	(10)	(0)	(0)	(56)	(22)	(0)	(0)	(8)	(38)	(0)	(0)
	inflammation:foreign body		1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(11)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(8)	(0)	(0)
	respiratory metaplasia:gland		3	0	0	0	6	0	0	0	6	0	0	0	5	0	0	0
			(33)	(0)	(0)	(0)	(60)	(0)	(0)	(0)	(67)	(0)	(0)	(0)	(38)	(0)	(0)	(0)
trachea			< 9>				<10>				< 9>				<13>			
	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)	(11)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lung			< 9>				<10>				< 9>				<13>			
	congestion		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	inflammatory infiltration		1	0	0	0	0	0	0	0	1	0	0	0	3	0	0	0
			(11)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(23)	(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				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	9				10				9				13			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
bone marrow			<9>				<10>				<9>				<13>			
	angiectasis		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)	(8)	(0)	(0)	(0)
	fibrosis		1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(11)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(8)	(0)	(0)	(0)
	increased hematopoiesis		2	0	0	0	1	0	0	0	3	0	0	0	1	0	0	0
			(22)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(33)	(0)	(0)	(0)	(8)	(0)	(0)	(0)
spleen			<9>				<10>				<9>				<13>			
	atrophy		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(11)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	deposit of hemosiderin		1	0	0	0	1	1	1	0	0	0	0	0	3	0	0	0
			(11)	(0)	(0)	(0)	(10)	(10)	(10)	(0)	(0)	(0)	(0)	(0)	(23)	(0)	(0)	(0)
	fibrosis		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)	(8)	(0)	(0)
	extramedullary hematopoiesis		2	0	2	0	1	1	0	0	0	0	5	0	0	0	2	0
			(22)	(0)	(22)	(0)	(10)	(10)	(0)	(0)	(0)	(0)	(56)	(0)	(0)	(0)	(15)	(0)
[Circulatory system]																		
heart			<9>				<10>				<9>				<13>			
	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)	(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				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	9				10				9				13			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Circulatory system]																		
heart			<9>				<10>				<9>				<13>			
	mineralization		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(11)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	myocardial fibrosis		3	0	0	0	3	0	0	0	3	1	0	0	4	0	0	0
			(33)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(33)	(11)	(0)	(0)	(31)	(0)	(0)	(0)
[Digestive system]																		
oral cavity			<9>				<10>				<9>				<13>			
	inflammation		0	0	0	0	0	0	0	0	1	1	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(11)	(11)	(0)	(0)	(0)	(8)	(0)	(0)
	fibrosis		0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(8)	(0)
esophagus			<9>				<10>				<9>				<13>			
	squamous cell 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)	(8)	(0)	(0)
stomach			<9>				<10>				<9>				<13>			
	mineralization		0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(11)	(0)	(0)	(0)	(0)	(0)	(11)	(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 9				400 ppm 10				2000 ppm 9				10000 ppm 13			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
stomach			< 9>				<10>				< 9>				<13>			
	ulcer:forestomach		0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	erosion:glandular stomach		0	0	0	0	1	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(8)	(0)	(0)	(0)
	ulcer:glandular stomach		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
liver			< 9>				<10>				< 9>				<13>			
	herniation		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:central		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)	(8)	(8)	(0)	(0)
	necrosis:focal		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(11)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	fatty change		0	2	0	0	2	0	0	0	0	1	0	0	0	0	0	0
			(0)	(22)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(0)	(0)	(0)
	granulation		0	1	0	0	0	0	1	0	1	0	0	0	2	0	0	0
			(0)	(11)	(0)	(0)	(0)	(0)	(10)	(0)	(11)	(0)	(0)	(0)	(15)	(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				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	9				10				9				13			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
liver			< 9>				<10>				< 9>				<13>			
	basophilic cell focus		2	1	0	0	1	1	0	0	1	0	0	0	1	0	0	0
			(22)	(11)	(0)	(0)	(10)	(10)	(0)	(0)	(11)	(0)	(0)	(0)	(8)	(0)	(0)	(0)
	vacuolated cell focus		1	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0
			(11)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(8)	(0)	(0)	(0)
	spongiosis hepatis		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	bile duct hyperplasia		1	1	0	0	3	1	0	0	0	1	0	0	0	0	0	0
			(11)	(11)	(0)	(0)	(30)	(10)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(0)	(0)	(0)
pancreas			< 9>				<10>				< 9>				<13>			
	atrophy		0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Urinary system]																		
kidney			< 9>				<10>				< 9>				<13>			
	hyperplasia:tubular epithelial cell		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(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				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	9				10				9				13			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Urinary system]																		
kidney			< 9>				<10>				< 9>				<13>			
	infarct		0 (0)	0 (0)	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)
	hyaline droplet		0 (0)	0 (0)	1 (11)	0 (0)	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 hemosiderin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (11)	1 (11)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	inflammatory infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (11)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	chronic nephropathy		0 (0)	0 (0)	0 (0)	0 (0)	2 (20)	2 (20)	1 (10)	0 (0)	2 (22)	0 (0)	1 (11)	0 (0)	3 (23)	1 (8)	0 (0)	1 (8)
	hydronephrosis		0 (0)	1 (11)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (11)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	tubular necrosis		0 (0)	1 (11)	2 (22)	0 (0)	1 (10)	1 (10)	1 (10)	0 (0)	0 (0)	0 (0)	3 (33)	0 (0)	0 (0)	2 (15)	3 (23)	0 (0)
	mineralization:cortico-medullary junction		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (11)	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				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	9				10				9				13			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																		
kidney			< 9>				<10>				< 9>				<13>			
	mineralization:papilla		1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(11)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(8)	(0)	(0)	(0)
	mineralization:pelvis		1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(11)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Endocrine system]																		
pituitary			< 9>				<10>				< 9>				<13>			
	angiectasis		0	0	0	0	1	0	0	0	2	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(22)	(0)	(0)	(0)	(8)	(0)	(0)	(0)
	cyst		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)	(15)	(0)	(0)	(0)
	hyperplasia		0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(11)	(0)	(0)	(8)	(0)	(0)	(0)
thyroid			< 9>				<10>				< 9>				<13>			
	ultimibranchial body remanet		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(11)	(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				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	9				10				9				13			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]																		
thyroid			< 9>				<10>				< 9>				<13>			
	C-cell hyperplasia		0	0	0	0	0	0	0	0	1	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(15)	(0)	(0)	(0)
adrenal			< 9>				<10>				< 9>				<13>			
	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)	(8)	(0)	(0)	(0)
	peliosis-like lesion		1	1	0	0	1	0	0	0	1	0	0	0	1	0	0	0
			(11)	(11)	(0)	(0)	(10)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(8)	(0)	(0)	(0)
	necrosis		0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(8)	(0)	(0)	(0)
	hyperplasia:cortical cell		0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(11)	(0)	(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)	(11)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	focal fatty change:cortex		0	0	0	0	1	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(8)	(0)	(0)	(0)
[Reproductive system]																		
uterus			< 9>				<10>				< 9>				<13>			
	cystic endometrial hyperplasia		1	0	0	0	1	0	0	0	1	0	0	0	1	0	0	0
			(11)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(8)	(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				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	9				10				9				13			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Reproductive system]																		
mammary gl			< 9>				<10>				< 9>				<13>			
	hyperplasia		0	0	0	0	2	0	0	0	2	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(22)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	galactocele		0	0	0	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)	(8)	(0)	(0)	(0)
[Nervous system]																		
brain			< 9>				<10>				< 9>				<13>			
	hemorrhage		0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spinal cord			< 9>				<10>				< 9>				<13>			
	hemorrhage		0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Special sense organs/appandage]																		
eye			< 9>				<10>				< 9>				<13>			
	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)	(8)	(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 9				400 ppm 10				2000 ppm 9				10000 ppm 13			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Special sense organs/appandage]																		
eye			< 9>				<10>				< 9>				<13>			
	retinal atrophy		0	0	0	0	1	0	1	0	2	2	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(10)	(0)	(22)	(22)	(0)	(0)	(0)	(0)	(0)	(0)
	keratitis		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(11)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	iritis		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(11)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
Harder gl			< 9>				<10>				< 9>				<13>			
	degeneration		0	1	0	0	1	0	0	0	1	0	0	0	1	1	0	0
			(0)	(11)	(0)	(0)	(10)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(8)	(8)	(0)	(0)
nasolacr d			< 9>				<10>				< 9>				<13>			
	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)	(11)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Musculoskeletal system]																		
bone			< 9>				<10>				< 9>				<13>			
	osteosclerosis		1	0	0	0	1	0	0	0	1	0	0	0	1	0	0	0
			(11)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(8)	(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 9				400 ppm 10				2000 ppm 9				10000 ppm 13			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Body cavities]																		
retroperit			< 9>				<10>				< 9>				<13>			
	inflammation		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)	(11)	(0)	(0)	(0)	(0)

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

APPENDIX L 3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0162
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 44				400 ppm 40				2000 ppm 36				10000 ppm 39			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Integumentary system/appandage]																		
skin/app			<44>				<40>				<36>				<39>			
	hyperplasia:epithelium		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)
	hyperplasia:epidermis		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)
	duct ectasia:sebaceous gland		0 (0)	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)
[Respiratory system]																		
nasal cavit			<44>				<40>				<36>				<39>			
	eosinophilic change:olfactory epithelium		24 (55)	2 (5)	1 (2)	0 (0)	22 (55)	3 (8)	1 (3)	0 (0)	20 (56)	3 (8)	0 (0)	0 (0)	17 (44)	0 (0)	0 (0)	0 (0)
	eosinophilic change:respiratory epithelium		3 (7)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)
	inflammation:foreign body		5 (11)	2 (5)	0 (0)	0 (0)	6 (15)	0 (0)	0 (0)	0 (0)	5 (14)	1 (3)	0 (0)	0 (0)	1 (3)	1 (3)	0 (0)	0 (0)
	respiratory metaplasia:olfactory epithelium		3 (7)	0 (0)	0 (0)	0 (0)	5 (13)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

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

Organ	Findings	Group Name	Control				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	44				40				36				39			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
nasal cavit			<44>				<40>				<36>				<39>			
	respiratory metaplasia:gland		21	7	0	0	24	3	0	0	22	0	0	0 *	23	5	0	0
			(48)	(16)	(0)	(0)	(60)	(8)	(0)	(0)	(61)	(0)	(0)	(0)	(59)	(13)	(0)	(0)
lung			<44>				<40>				<36>				<39>			
	accumulation of foamy cells		2	0	0	0	2	0	0	0	1	1	0	0	2	0	0	0
			(5)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(3)	(3)	(0)	(0)	(5)	(0)	(0)	(0)
	bronchiolar-alveolar cell hyperplasia		4	2	0	0	0	0	0	0	2	0	0	0	0	0	0	0
			(9)	(5)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Hematopoietic system]																		
bone marrow			<44>				<40>				<36>				<39>			
	granulation		1	0	0	0	3	1	0	0	1	1	0	0	3	3	0	0
			(2)	(0)	(0)	(0)	(8)	(3)	(0)	(0)	(3)	(3)	(0)	(0)	(8)	(8)	(0)	(0)
	fibrosis		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)
	increased hematopoiesis		0	0	0	0	0	0	0	0	2	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(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				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	44				40				36				39			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
lymph node			<44>				<40>				<36>				<39>			
	ectasia of sinus		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)	(5)	(0)	(0)	(0)
spleen			<44>				<40>				<35>				<39>			
	deposit of hemosiderin		3	0	0	0	0	0	0	0	0	1	0	0	2	0	0	0
			(7)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(5)	(0)	(0)	(0)
	fibrosis		0	1	0	0	1	0	1	0	0	3	0	0	0	1	0	0
			(0)	(2)	(0)	(0)	(3)	(0)	(3)	(0)	(0)	(9)	(0)	(0)	(0)	(3)	(0)	(0)
	extramedullary hematopoiesis		0	1	0	0	1	0	0	0	1	1	0	0	2	0	0	0
			(0)	(2)	(0)	(0)	(3)	(0)	(0)	(0)	(3)	(3)	(0)	(0)	(5)	(0)	(0)	(0)
	lymphoid 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)	(3)	(0)	(0)
[Circulatory system]																		
heart			<44>				<40>				<36>				<39>			
	myocardial fibrosis		21	2	0	0	19	4	0	0	23	0	0	0	17	1	0	0
			(48)	(5)	(0)	(0)	(48)	(10)	(0)	(0)	(64)	(0)	(0)	(0)	(44)	(3)	(0)	(0)

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

Organ	Findings	Group Name	Control				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	44				40				36				39			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Circulatory system]																		
artery/aort			<44>				<40>				<36>				<39>			
	arteritis		1	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]																		
oral cavity			<44>				<40>				<36>				<39>			
	inflammation		4	2	0	0	2	3	0	0	0	4	0	0	5	3	0	0
			(9)	(5)	(0)	(0)	(5)	(8)	(0)	(0)	(0)	(11)	(0)	(0)	(13)	(8)	(0)	(0)
	basal cell activation		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)	(5)	(0)	(0)	(0)
tooth			<44>				<40>				<36>				<39>			
	inflammation		0	1	0	0	1	2	0	0	1	1	0	0	3	0	0	0
			(0)	(2)	(0)	(0)	(3)	(5)	(0)	(0)	(3)	(3)	(0)	(0)	(8)	(0)	(0)	(0)
tongue			<44>				<40>				<36>				<39>			
	inflammation		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)	(5)	(0)	(0)	(0)
	arteritis		0	0	0	0	1	0	0	0	4	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(11)	(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				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	44				40				36				39			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
salivary gl			<44>				<40>				<36>				<39>			
	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)
esophagus			<44>				<40>				<36>				<39>			
	squamous 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)
stomach			<44>				<40>				<36>				<39>			
	basal cell activation		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)	(5)	(0)	(0)	(0)
	erosion:forestomach		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)
	ulcer:forestomach		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)
	hyperplasia:forestomach		1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(2)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	erosion:glandular stomach		0	0	0	0	1	0	0	0	3	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(8)	(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				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	44				40				36				39			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
stomach			<44>				<40>				<36>				<39>			
	ulcer:glandular stomach		0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	lymph node with epithelial 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)
liver			<44>				<40>				<36>				<39>			
	herniation		3 (7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (8)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)
	fatty change		2 (5)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	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)
	granulation		9 (20)	2 (5)	2 (5)	0 (0)	10 (25)	1 (3)	1 (3)	0 (0)	3 (8)	5 (14)	2 (6)	0 (0)	12 (31)	4 (10)	6 (15)	0 (0)
	hyperplasia		0 (0)	0 (0)	1 (2)	0 (0)	1 (3)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	clear cell focus		6 (14)	1 (2)	0 (0)	0 (0)	9 (23)	1 (3)	0 (0)	0 (0)	7 (19)	1 (3)	0 (0)	0 (0)	3 (8)	2 (5)	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 44				400 ppm 40				2000 ppm 36				10000 ppm 39			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver			<44>				<40>				<36>				<39>			
	acidophilic cell focus		1 (2)	1 (2)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	3 (8)	0 (0)	0 (0)	0 (0)
	basophilic cell focus		4 (9)	0 (0)	0 (0)	0 (0)	3 (8)	0 (0)	0 (0)	0 (0)	7 (19)	1 (3)	0 (0)	0 (0)	4 (10)	2 (5)	0 (0)	0 (0)
	vacuolated cell focus		2 (5)	0 (0)	0 (0)	0 (0)	6 (15)	0 (0)	0 (0)	0 (0)	3 (8)	0 (0)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)
	spongiosis hepatis		9 (20)	2 (5)	0 (0)	0 (0)	9 (23)	1 (3)	0 (0)	0 (0)	4 (11)	2 (6)	0 (0)	0 (0)	11 (28)	0 (0)	0 (0)	0 (0)
	bile duct hyperplasia		3 (7)	27 (61)	14 (32)	0 (0)	0 (0)	28 (70)	12 (30)	0 (0)	2 (6)	28 (78)	6 (17)	0 (0)	0 (0)	33 (85)	7 (18)	0 (0)
	biliary cyst		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
pancreas			<44>				<40>				<36>				<39>			
	atrophy		14 (32)	5 (11)	0 (0)	0 (0)	11 (28)	5 (13)	1 (3)	1 (3)	14 (39)	9 (25)	2 (6)	0 * (0)	9 (23)	4 (10)	1 (3)	0 (0)
	arteritis		0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

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				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	44				40				36				39			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
pancreas			<44>				<40>				<36>				<39>			
	hyperplasia:acinar cell		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			<44>				<40>				<36>				<39>			
	infarct		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)	(5)	(0)	(0)	(0)
	inflammatory infiltration		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)	(0)
	chronic nephropathy		2	7	19	15	0	7	10	23	1	11	12	10	10	9	14	6 *
			(5)	(16)	(43)	(34)	(0)	(18)	(25)	(58)	(3)	(31)	(33)	(28)	(26)	(23)	(36)	(15)
	mineralization:pelvis		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Endocrine system]																		
pituitary			<44>				<40>				<36>				<39>			
	angiectasis		1	0	0	0	1	1	0	0	3	0	0	0	0	1	0	0
			(2)	(0)	(0)	(0)	(3)	(3)	(0)	(0)	(8)	(0)	(0)	(0)	(0)	(3)	(0)	(0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 44				400 ppm 40				2000 ppm 36				10000 ppm 39			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Endocrine system]																		
pituitary			<44>				<40>				<36>				<39>			
	cyst		3 (7)	0 (0)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)	2 (6)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)
	hyperplasia		11 (25)	0 (0)	0 (0)	0 (0)	7 (18)	3 (8)	0 (0)	0 (0)	6 (17)	2 (6)	0 (0)	0 (0)	5 (13)	1 (3)	0 (0)	0 (0)
	Rathke pouch		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)
thyroid			<44>				<40>				<35>				<39>			
	cyst		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)
	ultimibranchial body remanet		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)
	C-cell hyperplasia		8 (18)	0 (0)	0 (0)	0 (0)	2 (5)	1 (3)	0 (0)	0 (0)	4 (11)	0 (0)	0 (0)	0 (0)	5 (13)	0 (0)	0 (0)	0 (0)
panc islet			<44>				<40>				<36>				<39>			
	islet cell hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 44				400 ppm 40				2000 ppm 36				10000 ppm 39			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Endocrine system]																		
adrenal			<44>				<40>				<36>				<39>			
	thrombus		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyperplasia:cortical cell		0	0	0	0	2	0	0	0	2	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyperplasia:medulla		11	2	0	0	10	2	0	0	6	1	0	0	4	1	0	0
			(25)	(5)	(0)	(0)	(25)	(5)	(0)	(0)	(17)	(3)	(0)	(0)	(10)	(3)	(0)	(0)
	focal fatty change:cortex		0	0	0	0	2	0	0	0	1	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(8)	(0)	(0)	(0)
[Reproductive system]																		
testis			<44>				<40>				<36>				<39>			
	atrophy		1	2	0	0	2	0	0	0	0	0	0	0	0	1	1	0
			(2)	(5)	(0)	(0)	(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(3)	(0)
	mineralization		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	arteritis		1	4	0	0	1	3	0	0	0	2	0	0	0	1	0	0
			(2)	(9)	(0)	(0)	(3)	(8)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(3)	(0)	(0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 44 1 (%)	2 (%)	3 (%)	4 (%)	400 ppm 40 1 (%)	2 (%)	3 (%)	4 (%)	2000 ppm 36 1 (%)	2 (%)	3 (%)	4 (%)	10000 ppm 39 1 (%)	2 (%)	3 (%)	4 (%)
[Reproductive system]																		
testis			<44>				<40>				<36>				<39>			
	interstitial cell hyperplasia		2 (5)	1 (2)	0 (0)	0 (0)	8 (20)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	4 (10)	0 (0)	0 (0)	0 (0)
epididymis			<44>				<40>				<36>				<39>			
	degeneration		6 (14)	0 (0)	0 (0)	0 (0)	7 (18)	0 (0)	0 (0)	0 (0)	12 (33)	0 (0)	0 (0)	0 (0)	8 (21)	0 (0)	0 (0)	0 (0)
prostate			<44>				<40>				<35>				<39>			
	inflammation		4 (9)	0 (0)	0 (0)	0 (0)	5 (13)	0 (0)	0 (0)	0 (0)	3 (9)	0 (0)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)
	hyperplasia		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)	0 (0)	0 (0)	0 (0)
mammary gl			<44>				<40>				<36>				<39>			
	inflammation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	galactocele		0 (0)	2 (5)	0 (0)	0 (0)	1 (3)	1 (3)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)
[Nervous system]																		
brain			<44>				<40>				<36>				<39>			
	mineralization		2 (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 / No. of Animals on Study / Grade	Control 44				400 ppm 40				2000 ppm 36				10000 ppm 39			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Special sense organs/appandage]																		
eye			<44>				<40>				<36>				<39>			
	hemorrhage		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	cataract		2 (5)	0 (0)	0 (0)	0 (0)	7 (18)	0 (0)	0 (0)	0 (0)	4 (11)	0 (0)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)
	retinal atrophy		5 (11)	4 (9)	1 (2)	0 (0)	5 (13)	10 (25)	7 (18)	0 ** (0)	4 (11)	7 (19)	3 (8)	0 (0)	9 (23)	5 (13)	2 (5)	0 (0)
	degeneration:cornea		2 (5)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Harder gl			<44>				<40>				<36>				<39>			
	degeneration		0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4 (11)	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)
	hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

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

APPENDIX L 4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 41				400 ppm 40				2000 ppm 41				10000 ppm 37			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Integumentary system/appandage]																		
skin/app			<41>				<40>				<41>				<37>			
	inflammation		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)
	duct ectasia:sebaceous gland		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)
[Respiratory system]																		
nasal cavit			<41>				<40>				<41>				<37>			
	inflammation		2 (5)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	eosinophilic change:olfactory epithelium		14 (34)	12 (29)	3 (7)	0 (0)	12 (30)	7 (18)	2 (5)	0 (0)	15 (37)	13 (32)	3 (7)	0 (0)	15 (41)	11 (30)	5 (14)	0 (0)
	eosinophilic change:respiratory epithelium		3 (7)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	inflammation:foreign body		1 (2)	0 (0)	0 (0)	0 (0)	1 (3)	1 (3)	0 (0)	0 (0)	2 (5)	1 (2)	0 (0)	0 (0)	1 (3)	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)	1 (2)	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 41				400 ppm 40				2000 ppm 41				10000 ppm 37			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
nasal cavit			<41>				<40>				<41>				<37>			
	respiratory metaplasia:gland		30	1	0	0	29	1	0	0	28	1	0	0	25	2	0	0
			(73)	(2)	(0)	(0)	(73)	(3)	(0)	(0)	(68)	(2)	(0)	(0)	(68)	(5)	(0)	(0)
lung			<41>				<40>				<41>				<37>			
	hemorrhage		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	inflammatory infiltration		2	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
			(5)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
	accumulation of foamy cells		1	0	0	0	0	0	0	0	2	0	0	0	1	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
[Hematopoietic system]																		
bone marrow			<41>				<40>				<41>				<37>			
	granulation		7	2	0	0	5	0	0	0	5	1	1	0	7	3	0	0
			(17)	(5)	(0)	(0)	(13)	(0)	(0)	(0)	(12)	(2)	(2)	(0)	(19)	(8)	(0)	(0)
	increased hematopoiesis		2	0	0	0	0	0	0	0	1	0	0	0	3	0	0	0
			(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(8)	(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 41				400 ppm 40				2000 ppm 41				10000 ppm 37			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Hematopoietic system]																		
bone marrow			<41>				<40>				<41>				<37>			
	reticulosis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
spleen			<41>				<40>				<41>				<37>			
	atrophy		0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)
	deposit of hemosiderin		8 (20)	0 (0)	0 (0)	0 (0)	9 (23)	0 (0)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	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)	0 (0)	1 (3)	0 (0)	0 (0)
	extramedullary hematopoiesis		4 (10)	3 (7)	0 (0)	0 (0)	4 (10)	4 (10)	0 (0)	0 (0)	3 (7)	0 (0)	1 (2)	0 (0)	2 (5)	2 (5)	1 (3)	0 (0)
[Circulatory system]																		
heart			<41>				<40>				<41>				<37>			
	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)	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 41				400 ppm 40				2000 ppm 41				10000 ppm 37			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Circulatory system]																		
heart			<41>				<40>				<41>				<37>			
	myocardial fibrosis		8 (20)	0 (0)	0 (0)	0 (0)	10 (25)	1 (3)	0 (0)	0 (0)	13 (32)	0 (0)	0 (0)	0 (0)	9 (24)	1 (3)	0 (0)	0 (0)
	endothelial cell hyperplasia		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
artery/aort			<41>				<40>				<41>				<37>			
	arteritis		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)
[Digestive system]																		
oral cavity			<41>				<40>				<41>				<37>			
	inflammation		3 (7)	7 (17)	0 (0)	0 (0)	3 (8)	6 (15)	0 (0)	0 (0)	4 (10)	6 (15)	0 (0)	0 (0)	3 (8)	3 (8)	0 (0)	0 (0)
	basal cell activation		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)
	epithelial dysplasia		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 / No. of Animals on Study / Grade	Control 41				400 ppm 40				2000 ppm 41				10000 ppm 37			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
tooth		<41>	1	0	0	0	0	1	0	0	1	0	0	0	0	1	0	0
	inflammation		(2)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(3)	(0)	(0)
tongue		<41>	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	lymphocytic infiltration		(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	arteritis		2	0	0	0	2	0	0	0	3	0	0	0	1	0	0	0
			(5)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
esophagus		<41>	0	0	0	0	0	0	0	0	0	0	0	0	4	0	0	0
	basal cell activation		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(11)	(0)	(0)	(0)
stomach		<41>	0	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0 *
	basal cell activation		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(14)	(0)	(0)	(0)
liver		<41>	2	0	0	0	2	0	0	0	0	0	0	0	2	0	0	0
	herniation		(5)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)	(0)
	peliosis-like lesion		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	41				40				41				37			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
liver			<41>				<40>				<41>				<37>			
	necrosis:focal		0	0	0	0	2	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
	fatty change		0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	inflammatory infiltration		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	lymphocytic infiltration		1	2	0	0	0	1	0	0	0	0	0	0	1	0	0	0
			(2)	(5)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
	granulation		11	11	6	0	11	4	4	0	15	5	4	0	14	4	3	0
			(27)	(27)	(15)	(0)	(28)	(10)	(10)	(0)	(37)	(12)	(10)	(0)	(38)	(11)	(8)	(0)
	clear cell focus		5	1	0	0	0	0	0	0 *	1	0	0	0	4	1	0	0
			(12)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(11)	(3)	(0)	(0)
	basophilic cell focus		11	2	0	0	18	2	0	0	19	2	0	0	14	1	0	0
			(27)	(5)	(0)	(0)	(45)	(5)	(0)	(0)	(46)	(5)	(0)	(0)	(38)	(3)	(0)	(0)
	vacuolated cell focus		2	0	0	0	3	0	0	0	3	0	0	0	1	0	0	0
			(5)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(7)	(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 41 1 (%)	2 (%)	3 (%)	4 (%)	400 ppm 40 1 (%)	2 (%)	3 (%)	4 (%)	2000 ppm 41 1 (%)	2 (%)	3 (%)	4 (%)	10000 ppm 37 1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver																		
	bile duct hyperplasia	<a>	41				40				41				37			
		b	2	4	0	0	5	0	0	0	5	1	0	0	6	0	0	0 *
		(c)	(5)	(10)	(0)	(0)	(13)	(0)	(0)	(0)	(12)	(2)	(0)	(0)	(16)	(0)	(0)	(0)
pancreas																		
	atrophy	<a>	41				40				41				37			
		b	3	2	0	0	8	1	0	0	2	4	2	0	5	4	0	0
		(c)	(7)	(5)	(0)	(0)	(20)	(3)	(0)	(0)	(5)	(10)	(5)	(0)	(14)	(11)	(0)	(0)
[Urinary system]																		
kidney																		
	infarct	<a>	41				40				41				37			
		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)
	chronic nephropathy	b	16	7	4	3	15	8	8	1	19	10	4	4	12	9	4	2
		(c)	(39)	(17)	(10)	(7)	(38)	(20)	(20)	(3)	(46)	(24)	(10)	(10)	(32)	(24)	(11)	(5)
	mineralization:cortico-medullary junction	b	5	0	0	0	3	0	0	0	3	0	0	0	1	0	0	0
		(c)	(12)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
	mineralization:papilla	b	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
		(c)	(2)	(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 41				400 ppm 40				2000 ppm 41				10000 ppm 37			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Urinary system]																		
kidney			<41>				<40>				<41>				<37>			
	mineralization:pelvis		1 (2)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Endocrine system]																		
pituitary			<41>				<40>				<41>				<37>			
	angiectasis		6 (15)	1 (2)	0 (0)	0 (0)	5 (13)	1 (3)	0 (0)	0 (0)	5 (12)	1 (2)	0 (0)	0 (0)	1 (3)	1 (3)	0 (0)	0 (0)
	cyst		8 (20)	0 (0)	0 (0)	0 (0)	3 (8)	1 (3)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)	6 (16)	0 (0)	0 (0)	0 (0)
	hyperplasia		5 (12)	1 (2)	0 (0)	0 (0)	10 (25)	2 (5)	0 (0)	0 (0)	6 (15)	5 (12)	0 (0)	0 (0)	2 (5)	1 (3)	0 (0)	0 (0)
	Rathke pouch		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)
thyroid			<41>				<40>				<41>				<37>			
	ultimibranchial body remanet		3 (7)	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)

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				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	41				40				41				37			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Endocrine system]																		
thyroid			<41>				<40>				<41>				<37>			
	follicular hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)
	C-cell hyperplasia		7 (17)	0 (0)	0 (0)	0 (0)	5 (13)	1 (3)	0 (0)	0 (0)	7 (17)	0 (0)	0 (0)	0 (0)	6 (16)	1 (3)	0 (0)	0 (0)
adrenal			<41>				<40>				<41>				<37>			
	peliosis-like lesion		7 (17)	1 (2)	0 (0)	0 (0)	11 (28)	2 (5)	0 (0)	0 (0)	7 (17)	0 (0)	0 (0)	0 (0)	8 (22)	0 (0)	0 (0)	0 (0)
	hyperplasia:cortical cell		1 (2)	0 (0)	0 (0)	0 (0)	3 (8)	0 (0)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)
	hyperplasia:medulla		3 (7)	0 (0)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)	3 (7)	0 (0)	0 (0)	0 (0)	3 (8)	0 (0)	0 (0)	0 (0)
	focal fatty change:cortex		1 (2)	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)
[Reproductive system]																		
ovary			<41>				<40>				<41>				<37>			
	cyst		2 (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)	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 41				400 ppm 40				2000 ppm 41				10000 ppm 37			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Reproductive system]																		
uterus			<41>				<40>				<41>				<37>			
	hyperplasia:gland		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	mucous plug		0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	cystic endometrial hyperplasia		6 (15)	1 (2)	0 (0)	0 (0)	7 (18)	0 (0)	0 (0)	0 (0)	3 (7)	2 (5)	0 (0)	0 (0)	2 (5)	5 (14)	0 (0)	0 (0)
mammary gl			<41>				<40>				<41>				<37>			
	inflammation		0 (0)	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)
	hyperplàsia		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)
	atypical hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	galactocele		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)
[Nervous system]																		
brain			<41>				<40>				<41>				<37>			
	mineralization		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)

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 41 1 (%)	2 (%)	3 (%)	4 (%)	400 ppm 40 1 (%)	2 (%)	3 (%)	4 (%)	2000 ppm 41 1 (%)	2 (%)	3 (%)	4 (%)	10000 ppm 37 1 (%)	2 (%)	3 (%)	4 (%)
[Special sense organs/appandage]																		
eye			<41>				<40>				<41>				<37>			
	hemorrhage		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	cataract		4 (10)	0 (0)	0 (0)	0 (0)	5 (13)	0 (0)	0 (0)	0 (0)	6 (15)	0 (0)	0 (0)	0 (0)	4 (11)	0 (0)	0 (0)	0 (0)
	retinal atrophy		4 (10)	6 (15)	5 (12)	0 (0)	7 (18)	3 (8)	7 (18)	0 (0)	10 (24)	6 (15)	9 (22)	0 (0)	4 (11)	1 (3)	7 (19)	0 (0)
	keratitis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Harder gl			<41>				<40>				<41>				<37>			
	degeneration		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)
	inflammation		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)
	lymphocytic infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hyperplasia		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

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 1 (%)	Control 2 (%)	Control 3 (%)	Control 4 (%)	400 ppm 1 (%)	400 ppm 2 (%)	400 ppm 3 (%)	400 ppm 4 (%)	2000 ppm 1 (%)	2000 ppm 2 (%)	2000 ppm 3 (%)	2000 ppm 4 (%)	10000 ppm 1 (%)	10000 ppm 2 (%)	10000 ppm 3 (%)	10000 ppm 4 (%)
		Group Name	Control				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	41				40				41				37			
[Special sense organs/appandage]																		
nasolacr d			<41>				<40>				<41>				<37>			
	inflammation		0	0	0	0	1	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(3)	(0)	(0)	(0)
[Musculoskeletal system]																		
bone			<41>				<40>				<41>				<37>			
	osteosclerosis		7	2	4	0	6	1	6	0	12	3	1	0	8	4	2	0
			(17)	(5)	(10)	(0)	(15)	(3)	(15)	(0)	(29)	(7)	(2)	(0)	(22)	(11)	(5)	(0)

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

APPENDIX L 5

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOSUE : MALE : DEAD AND MORIBUND ANIMALS

MOSUE (2-YEAR STUDY)

STUDY NO. : 0163
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 15				400 ppm 8				2000 ppm 12				10000 ppm 17			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Integumentary system/appandage]																		
skin/app			<15>				< 8>				<12>				<17>			
	ulcer		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(7)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	inflammation		0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(0)	(7)	(0)	(0)	(0)	(13)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Respiratory system]																		
nasal cavit			<15>				< 8>				<12>				<17>			
	inflammation		0	0	0	0	1	0	0	0	0	0	0	0	0	2	0	0
			(0)	(0)	(0)	(0)	(13)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(12)	(0)	(0)
	eosinophilic change:olfactory epithelium		2	1	0	0	4	0	0	0	0	0	0	0	7	0	0	0
			(13)	(7)	(0)	(0)	(50)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(41)	(0)	(0)	(0)
	eosinophilic change:respiratory epithelium		2	3	1	0	1	0	0	0	2	1	0	0	3	0	0	0
			(13)	(20)	(7)	(0)	(13)	(0)	(0)	(0)	(17)	(8)	(0)	(0)	(18)	(0)	(0)	(0)
	inflammation:foreign body		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)	(8)	(0)	(0)	(0)	(0)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		1	0	0	0	2	0	0	0	0	0	0	0	1	0	0	0
			(7)	(0)	(0)	(0)	(25)	(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	Grade	Control 15				400 ppm 8				2000 ppm 12				10000 ppm 17			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
nasal cavit			<15>				< 8>				<12>				<17>			
	respiratory metaplasia:gland		2 (13)	3 (20)	0 (0)	0 (0)	1 (13)	1 (13)	0 (0)	0 (0)	3 (25)	2 (17)	0 (0)	0 (0)	3 (18)	1 (6)	0 (0)	0 (0)
larynx			<15>				< 8>				<12>				<17>			
	basal cell activation		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 (6)	0 (0)	0 (0)	0 (0)
	epithelial dysplasia		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 (6)	0 (0)	0 (0)	0 (0)
lung			<15>				< 8>				<12>				<17>			
	congestion		0 (0)	1 (7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (8)	1 (8)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)
	inflammatory infiltration		2 (13)	0 (0)	0 (0)	0 (0)	1 (13)	1 (13)	0 (0)	0 (0)	2 (17)	0 (0)	0 (0)	0 (0)	3 (18)	0 (0)	0 (0)	0 (0)
	bronchiolar-alveolar cell hyperplasia		1 (7)	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			<15>				< 8>				<12>				<17>			
	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 (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 / No. of Animals on Study / Grade	Control 15				400 ppm 8				2000 ppm 12				10000 ppm 17			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Hematopoietic system]																		
spleen			<15>				< 8>				<12>				<17>			
	atrophy		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)	(8)	(0)	(0)	(0)	(0)	(0)
	deposit of melanin		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)
	extramedullary hematopoiesis		3	1	0	0	2	1	0	0	1	2	0	0	1	3	1	0
			(20)	(7)	(0)	(0)	(25)	(13)	(0)	(0)	(8)	(17)	(0)	(0)	(6)	(18)	(6)	(0)
[Circulatory system]																		
heart			<15>				< 8>				<12>				<17>			
	mineralization		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(13)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	myocardial fibrosis		1	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0
			(7)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(6)	(0)	(0)
[Digestive system]																		
oral cavity			<15>				< 8>				<12>				<17>			
	squamous 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)	(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 15				400 ppm 8				2000 ppm 12				10000 ppm 17			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
oral cavity			<15>				< 8>				<12>				<17>			
	basal cell activation		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)
	epithelial dysplasia		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)	(18)	(0)	(0)	(0)
tooth			<15>				< 8>				<12>				<17>			
	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)	(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	dysplasia		2	1	0	0	1	0	0	0	2	0	1	0	4	0	1	0
			(13)	(7)	(0)	(0)	(13)	(0)	(0)	(0)	(17)	(0)	(8)	(0)	(24)	(0)	(6)	(0)
salivary gl			<15>				< 8>				<12>				<17>			
	atrophy		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)	(24)	(0)	(0)
esophagus			<15>				< 8>				<12>				<17>			
	squamous cell hyperplasia		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)	(12)	(0)	(0)	(0)
	basal cell activation		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				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	15				8				12				17			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
esophagus			<15>				< 8>				<12>				<17>			
	epithelial dysplasia		0 (0)	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 (6)	0 (0)	0 (0)
stomach			<15>				< 8>				<12>				<17>			
	erosion:forestomach		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 (6)	0 (0)	0 (0)	0 (0)
	erosion:glandular stomach		0 (0)	0 (0)	0 (0)	0 (0)	1 (13)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	1 (6)	0 (0)	0 (0)
	hyperplasia:glandular stomach		1 (7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (8)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)
liver			<15>				< 8>				<12>				<17>			
	necrosis:focal		0 (0)	1 (7)	0 (0)	0 (0)	0 (0)	1 (13)	0 (0)	0 (0)	2 (17)	2 (17)	0 (0)	0 (0)	2 (12)	0 (0)	0 (0)	0 (0)
	fatty change		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)
	fatty change: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 (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				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	15				8				12				17			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
[Digestive system]																		
liver			<15>				< 8>				<12>				<17>			
	granulation		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)	(12)	(0)	(0)	(0)
	basophilic cell focus		1	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(7)	(13)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
gall bladd			<15>				< 8>				<12>				<17>			
	granulation		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)	(8)	(0)	(0)	(0)	(0)	(0)	(0)
[Urinary system]																		
kidney			<15>				< 8>				<12>				<17>			
	hyaline droplet		0	0	0	0	2	0	0	0	0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(25)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(12)	(0)	(0)	(0)
	basophilic change		3	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	deposit of hemosiderin		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(7)	(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
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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 15				400 ppm 8				2000 ppm 12				10000 ppm 17			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Urinary system]																		
kidney			<15>				< 8>				<12>				<17>			
	lymphocytic infiltration		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(7)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	inflammatory polyp		0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(13)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	vacuolization of proximal tubule		4	0	0	0	2	0	0	0	5	0	0	0	6	0	0	0
			(27)	(0)	(0)	(0)	(25)	(0)	(0)	(0)	(42)	(0)	(0)	(0)	(35)	(0)	(0)	(0)
	hydronephrosis		0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	1
			(0)	(0)	(13)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)
	tubular necrosis		0	1	0	0	0	1	0	0	0	1	0	0	0	0	0	0
			(0)	(7)	(0)	(0)	(0)	(13)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:cortico-medullary junction		0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(13)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
	mineralization:pelvis		0	0	0	0	2	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(25)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:cortex		7	0	0	0	4	0	0	0	9	0	0	0	12	0	0	0
			(47)	(0)	(0)	(0)	(50)	(0)	(0)	(0)	(75)	(0)	(0)	(0)	(71)	(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 15				400 ppm 8				2000 ppm 12				10000 ppm 17			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Endocrine system]																		
pituitary			<15>				< 8>				<12>				<17>			
	Rathke pouch		0 (0)	0 (0)	0 (0)	0 (0)	1 (13)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
adrenal			<15>				< 8>				<12>				<17>			
	hyperplasia:cortical cell		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)
[Reproductive system]																		
testis			<15>				< 8>				<12>				<17>			
	atrophy		1 (7)	0 (0)	0 (0)	0 (0)	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		0 (0)	2 (13)	0 (0)	0 (0)	1 (13)	0 (0)	0 (0)	0 (0)	1 (8)	0 (0)	0 (0)	0 (0)	2 (12)	1 (6)	0 (0)	0 (0)
epididymis			<15>				< 8>				<12>				<17>			
	spermatogenic granuloma		1 (7)	0 (0)	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)
prostate			<15>				< 8>				<12>				<17>			
	inflammation		1 (7)	1 (7)	0 (0)	0 (0)	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 15				400 ppm 8				2000 ppm 12				10000 ppm 17			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Reproductive system]																		
prep/cli gl			<15>				< 8>				<12>				<17>			
	duct ectasia		0	1	0	0	0	0	0	0	0	1	0	0	0	3	0	0
			(0)	(7)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(18)	(0)	(0)
[Nervous system]																		
brain			<15>				< 8>				<12>				<17>			
	mineralization		3	0	0	0	2	0	0	0	3	0	0	0	5	0	0	0
			(20)	(0)	(0)	(0)	(25)	(0)	(0)	(0)	(25)	(0)	(0)	(0)	(29)	(0)	(0)	(0)
[Special sense organs/appandage]																		
Harder gl			<15>				< 8>				<12>				<17>			
	degeneration		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(7)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
nasolacr d			<15>				< 8>				<12>				<17>			
	inflammation		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)
[Musculoskeletal system]																		
muscle			<15>				< 8>				<12>				<17>			
	degeneration		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)	(8)	(0)	(0)	(0)	(0)	(0)	(0)

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

APPENDIX L 6

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOSUE : FEMALE : DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

Organ	Findings	Group Name	Control				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	24				23				25				26			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
nasal cavit			<24>				<23>				<25>				<26>			
	inflammation		2 (8)	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)
	squamous cell metaplasia		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)	0 (0)	0 (0)	0 (0)
	epidermal cyst		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)
	eosinophilic change:olfactory epithelium		1 (4)	2 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (12)	0 (0)	0 (0)	0 (0)	3 (12)	0 (0)	0 (0)	0 (0)
	eosinophilic change:respiratory epithelium		6 (25)	3 (13)	0 (0)	0 (0)	6 (26)	3 (13)	0 (0)	0 (0)	9 (36)	5 (20)	1 (4)	0 (0)	7 (27)	3 (12)	0 (0)	1 (4)
	respiratory metaplasia:olfactory epithelium		1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:gland		1 (4)	0 (0)	0 (0)	0 (0)	2 (9)	0 (0)	0 (0)	0 (0)	2 (8)	1 (4)	0 (0)	0 (0)	2 (8)	0 (0)	0 (0)	0 (0)
	arteritis		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				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	24				23				25				26			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
larynx			<24>				<23>				<25>				<26>			
	basal cell activation		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)
lung			<24>				<23>				<25>				<26>			
	congestion		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	3 (12)	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)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)
	edema		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)	0 (0)	0 (0)	0 (0)
	inflammatory infiltration		2 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	4 (15)	2 (8)	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)	0 (0)	1 (4)	0 (0)	0 (0)
	bronchiolar-alveolar cell hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)
	infiltration:alveolar macrophage		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				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	24				23				25				26			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Hematopoietic system]																		
bone marrow			<24>				<23>				<25>				<26>			
	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)	(4)	(0)	(0)
Lymph node			<24>				<23>				<25>				<26>			
	lymphadenitis		0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(0)	(0)
spleen			<24>				<23>				<25>				<26>			
	deposit of melanin		1	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(4)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	extramedullary hematopoiesis		4	9	0	0	1	8	0	0	3	4	0	0	1	5	0	0
			(17)	(38)	(0)	(0)	(4)	(35)	(0)	(0)	(12)	(16)	(0)	(0)	(4)	(19)	(0)	(0)
[Circulatory system]																		
heart			<24>				<23>				<25>				<26>			
	thrombus		0	1	0	0	0	0	0	0	2	0	0	0	0	0	0	0
			(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization		1	1	0	0	0	0	0	0	1	1	0	0	0	0	0	0
			(4)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(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 24				400 ppm 23				2000 ppm 25				10000 ppm 26			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Circulatory system]																		
heart			<24>				<23>				<25>				<26>			
	myocardial fibrosis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	2 (8)	0 (0)	0 (0)	0 (0)
	arteritis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)
artery/aort			<24>				<23>				<25>				<26>			
	arteritis		0 (0)	0 (0)	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)
[Digestive system]																		
oral cavity			<24>				<23>				<25>				<26>			
	squamous cell hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)
	basal cell activation		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 (12)	1 (4)	0 (0)	0 (0)
	epithelial dysplasia		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)	1 (4)	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 24				400 ppm 23				2000 ppm 25				10000 ppm 26			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
tooth			<24>				<23>				<25>				<26>			
	inflammation		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)
	dysplasia		1 (4)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	2 (8)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)
tongue			<24>				<23>				<25>				<26>			
	erosion		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)
	inflammation		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)
	arteritis		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)	0 (0)	0 (0)	0 (0)
salivary gl			<24>				<23>				<25>				<26>			
	atrophy		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)
esophagus			<24>				<23>				<25>				<26>			
	squamous cell hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (8)	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 24				400 ppm 23				2000 ppm 25				10000 ppm 26			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
esophagus			<24>				<23>				<25>				<26>			
	basal cell activation		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 (19)	1 (4)	0 (0)	0 * (0)
	epithelial dysplasia		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)
stomach			<24>				<23>				<25>				<26>			
	erosion:forestomach		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)
	hyperplasia:forestomach		0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (8)	0 (0)	0 (0)	0 (0)
	hyperplasia:glandular stomach		3 (13)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (12)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
liver			<24>				<23>				<25>				<26>			
	angiectasis		1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	necrosis:focal		1 (4)	0 (0)	0 (0)	0 (0)	2 (9)	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 24				400 ppm 23				2000 ppm 25				10000 ppm 26			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver			<24>				<23>				<25>				<26>			
	fatty change:central		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)	0 (0)	0 (0)	0 (0)
	degeneration:central		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)	0 (0)	0 (0)	0 (0)
	inflammatory infiltration		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)	1 (4)	0 (0)	0 (0)
	granulation		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)	0 (0)	0 (0)
	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)	1 (4)	0 (0)	0 (0)	0 (0)
pancreas			<24>				<23>				<25>				<26>			
	atrophy		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)
[Urinary system]																		
kidney			<24>				<23>				<25>				<26>			
	infarct		1 (4)	0 (0)	0 (0)	0 (0)	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				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	24				23				25				26			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Urinary system]																		
kidney			<24>				<23>				<25>				<26>			
	hyaline droplet		2 (8)	4 (17)	0 (0)	0 (0)	2 (9)	6 (26)	1 (4)	0 (0)	1 (4)	6 (24)	0 (0)	0 (0)	1 (4)	4 (15)	0 (0)	0 (0)
	basophilic change		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	deposit of hemosiderin		2 (8)	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	inflammatory polyp		0 (0)	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)
	hydronephrosis		0 (0)	1 (4)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (8)	0 (0)	0 (0)	1 (4)	3 (12)	0 (0)
	tubular necrosis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (9)	0 (0)	0 (0)	0 (0)	2 (8)	0 (0)	0 (0)	0 (0)	2 (8)	1 (4)	0 (0)
	mineralization:cortico-medullary junction		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)
	mineralization:papilla		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				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	24				23				25				26			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Endocrine system]																		
pituitary			<24>				<22>				<25>				<26>			
	angiectasis		0 (0)	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	cyst		0 (0)	0 (0)	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)
	hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	2 (9)	0 (0)	0 (0)	0 (0)	2 (8)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)
[Reproductive system]																		
ovary			<24>				<23>				<25>				<26>			
	hemorrhage		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)	0 (0)	0 (0)	0 (0)
	thrombus		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)
	cyst		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)
uterus			<24>				<23>				<25>				<25>			
	cystic endometrial hyperplasia		2 (8)	2 (8)	0 (0)	0 (0)	3 (13)	2 (9)	0 (0)	0 (0)	3 (12)	5 (20)	0 (0)	0 (0)	4 (16)	5 (20)	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				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	24				23				25				26			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Reproductive system]																		
mammary gl			<24>				<23>				<25>				<26>			
	hyperplasia		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)	1 (4)	0 (0)	0 (0)
	galactocele		0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)
prep/cli gl			<24>				<23>				<25>				<26>			
	duct ectasia		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)	0 (0)	0 (0)
[Nervous system]																		
brain			<24>				<23>				<25>				<26>			
	hemorrhage		1 (4)	0 (0)	0 (0)	0 (0)	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		8 (33)	0 (0)	0 (0)	0 (0)	5 (22)	0 (0)	0 (0)	0 (0)	6 (24)	0 (0)	0 (0)	0 (0)	7 (27)	0 (0)	0 (0)	0 (0)
[Special sense organs/appandage]																		
eye			<24>				<23>				<25>				<26>			
	retinal atrophy		1 (4)	0 (0)	0 (0)	0 (0)	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				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	24				23				25				26			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Special sense organs/appandage]																		
Harder gl			<24>				<23>				<25>				<26>			
	inflammatory infiltration		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		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)
[Musculoskeletal system]																		
muscle			<24>				<23>				<25>				<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)

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

APPENDIX L 7

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOSUE : MALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0163
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	35				42				38				33			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Integumentary system/appandage]																		
skin/app			<35>				<42>				<38>				<33>			
	ulcer		0	0	0	0	0	3	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)
	inflammation		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	epidermal cyst		0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Respiratory system]																		
nasal cavit			<35>				<42>				<38>				<33>			
	eosinophilic change:olfactory epithelium		11	0	0	0	22	0	0	0	12	0	0	0	15	0	0	0
			(31)	(0)	(0)	(0)	(52)	(0)	(0)	(0)	(32)	(0)	(0)	(0)	(45)	(0)	(0)	(0)
	eosinophilic change:respiratory epithelium		12	6	1	0	11	2	0	0	14	4	0	0	7	1	1	0
			(34)	(17)	(3)	(0)	(26)	(5)	(0)	(0)	(37)	(11)	(0)	(0)	(21)	(3)	(3)	(0)
	respiratory metaplasia:olfactory epithelium		3	0	0	0	11	0	0	0	4	0	0	0	3	0	0	0
			(9)	(0)	(0)	(0)	(26)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(9)	(0)	(0)	(0)
	respiratory metaplasia:gland		10	14	2	0	13	14	1	0	15	10	1	0	9	3	0	0 **
			(29)	(40)	(6)	(0)	(31)	(33)	(2)	(0)	(39)	(26)	(3)	(0)	(27)	(9)	(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 35				400 ppm 42				2000 ppm 38				10000 ppm 33			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
larynx			<35>				<42>				<38>				<33>			
	squamous cell hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)
	basal cell activation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (6)	0 (0)	0 (0)	0 (0)
	epithelial dysplasia		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)
lung			<35>				<42>				<38>				<33>			
	inflammation		0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	inflammatory infiltration		0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (6)	0 (0)	0 (0)	0 (0)
	bronchiolar-alveolar cell hyperplasia		3 (9)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	infiltration:alveolar macrophage		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)
[Hematopoietic system]																		
lymph node			<35>				<42>				<38>				<33>			
	lymphadenitis		0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	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	Grade	Control (35) 1 (%)	2 (%)	3 (%)	4 (%)	400 ppm (42) 1 (%)	2 (%)	3 (%)	4 (%)	2000 ppm (38) 1 (%)	2 (%)	3 (%)	4 (%)	10000 ppm (33) 1 (%)	2 (%)	3 (%)	4 (%)
[Hematopoietic system]																		
spleen			<35>				<42>				<38>				<33>			
	deposit of melanin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	1 (3)	1 (3)	0 (0)	0 (0)
	extramedullary hematopoiesis		3 (9)	0 (0)	0 (0)	0 (0)	2 (5)	4 (10)	0 (0)	0 (0)	2 (5)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	follicular hyperplasia		1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)	3 (9)	0 (0)	0 (0)	0 (0)
[Circulatory system]																		
heart			<35>				<42>				<38>				<33>			
	mineralization		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)
	myocardial fibrosis		1 (3)	0 (0)	0 (0)	0 (0)	2 (5)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
artery/aort			<35>				<42>				<38>				<33>			
	mineralization		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 35				400 ppm 42				2000 ppm 38				10000 ppm 33			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Circulatory system]																		
artery/aort			<35>				<42>				<38>				<33>			
	arteritis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Digestive system]																		
oral cavity			<35>				<42>				<38>				<33>			
	inflammation		0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)
	squamous 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)	7 (21)	5 (15)	0 (0)	0 (0) **
	basal cell activation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	12 (36)	5 (15)	0 (0)	0 (0) **
	epithelial dysplasia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	18 (55)	3 (9)	0 (0)	0 (0) **
tooth			<35>				<42>				<38>				<33>			
	cyst		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 35				400 ppm 42				2000 ppm 38				10000 ppm 33			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
tooth			<35>				<42>				<38>				<33>			
	inflammation		5	0	0	0	4	0	0	0	1	0	0	0	2	0	0	0
			(14)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
	dysplasia		8	1	0	0	7	2	1	0	11	0	5	1	3	0	1	1
			(23)	(3)	(0)	(0)	(17)	(5)	(2)	(0)	(29)	(0)	(13)	(3)	(9)	(0)	(3)	(3)
tongue			<35>				<42>				<38>				<33>			
	epithelial dysplasia		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)
	arteritis		1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(3)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
salivary gl			<35>				<42>				<38>				<33>			
	atrophy		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)
	mineralization		0	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)
esophagus			<35>				<42>				<38>				<33>			
	basal cell activation		0	0	0	0	0	0	0	0	0	0	0	0	7	1	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(21)	(3)	(0)	(0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 35				400 ppm 42				2000 ppm 38				10000 ppm 33			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
esophagus			<35>				<42>				<38>				<33>			
	epithelial dysplasia		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)
stomach			<35>				<42>				<38>				<33>			
	basal cell activation		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)
	epithelial dysplasia		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:forestomach		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hyperplasia:forestomach		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)
	erosion:glandular stomach		1 (3)	0 (0)	0 (0)	0 (0)	3 (7)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)
	hyperplasia:glandular stomach		10 (29)	13 (37)	2 (6)	0 (0)	19 (45)	11 (26)	1 (2)	0 (0)	13 (34)	12 (32)	1 (3)	0 (0)	7 (21)	4 (12)	0 (0)	0 (0) **
large intes			<35>				<42>				<38>				<33>			
	inflammatory 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)	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 35				400 ppm 42				2000 ppm 38				10000 ppm 33			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver			<35>				<42>				<38>				<33>			
	angiectasis		0 (0)	0 (0)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)
	necrosis:focal		0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	2 (5)	0 (0)	1 (3)	0 (0)	1 (3)	0 (0)	0 (0)	1 (3)	1 (3)	0 (0)
	fatty change		0 (0)	0 (0)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	inflammatory infiltration		0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	granulation		3 (9)	0 (0)	0 (0)	0 (0)	1 (2)	2 (5)	0 (0)	0 (0)	4 (11)	3 (8)	0 (0)	0 (0)	2 (6)	1 (3)	0 (0)	0 (0)
	hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	clear cell focus		0 (0)	2 (6)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	4 (11)	0 (0)	0 (0)	0 (0)	2 (6)	0 (0)	0 (0)	0 (0)
	basophilic cell focus		1 (3)	1 (3)	0 (0)	0 (0)	3 (7)	0 (0)	0 (0)	0 (0)	4 (11)	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

STUDY NO. : 0163
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 35				400 ppm 42				2000 ppm 38				10000 ppm 33			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver			<35>				<42>				<38>				<33>			
	vacuolated cell focus		0	1	0	0	2	1	0	0	2	0	0	0	0	1	0	0
			(0)	(3)	(0)	(0)	(5)	(2)	(0)	(0)	(5)	(0)	(0)	(0)	(0)	(3)	(0)	(0)
	mixed cell focus		2	1	0	0	0	0	0	0	2	0	0	0	0	0	0	0
			(6)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	biliary cyst		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)
[Urinary system]																		
kidney			<35>				<42>				<38>				<33>			
	cyst		1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(3)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	basophilic change		17	0	0	0	8	2	0	0 *	11	1	0	0	11	0	0	0
			(49)	(0)	(0)	(0)	(19)	(5)	(0)	(0)	(29)	(3)	(0)	(0)	(33)	(0)	(0)	(0)
	inflammatory infiltration		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	lymphocytic infiltration		2	0	0	0	2	0	0	0	2	0	0	0	0	0	0	0
			(6)	(0)	(0)	(0)	(5)	(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 / No. of Animals on Study / Grade	Control 35				400 ppm 42				2000 ppm 38				10000 ppm 33			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Urinary system]																		
kidney			<35>				<42>				<38>				<33>			
	osseous metaplasia		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)
	vacuolization of proximal tubule		23 (66)	0 (0)	0 (0)	0 (0)	30 (71)	0 (0)	0 (0)	0 (0)	36 (95)	0 (0)	0 (0)	0 ** (0)	22 (67)	0 (0)	0 (0)	0 (0)
	mineralization:cortico-medullary junction		3 (9)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	mineralization:papilla		0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	3 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	mineralization:pelvis		2 (6)	0 (0)	0 (0)	0 (0)	3 (7)	0 (0)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)	3 (9)	0 (0)	0 (0)	0 (0)
	mineralization:cortex		26 (74)	0 (0)	0 (0)	0 (0)	37 (88)	0 (0)	0 (0)	0 (0)	29 (76)	0 (0)	0 (0)	0 (0)	30 (91)	0 (0)	0 (0)	0 (0)
	glomerulosclerosis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)
urin bladd			<35>				<42>				<38>				<33>			
	inflammation		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)

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 (35)				400 ppm (42)				2000 ppm (38)				10000 ppm (33)			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Endocrine system]																		
pituitary			<34>				<42>				<38>				<33>			
	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)
	cyst		0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
adrenal			<35>				<42>				<38>				<33>			
	hyperplasia:cortical cell		2 (6)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Reproductive system]																		
testis			<35>				<42>				<38>				<33>			
	atrophy		2 (6)	2 (6)	0 (0)	0 (0)	5 (12)	5 (12)	0 (0)	0 (0)	3 (8)	4 (11)	1 (3)	0 (0)	0 (0)	6 (18)	0 (0)	0 (0)
	mineralization		2 (6)	1 (3)	0 (0)	0 (0)	9 (21)	6 (14)	0 (0)	0 * (0)	3 (8)	9 (24)	1 (3)	0 * (0)	6 (18)	1 (3)	0 (0)	0 (0)
	xanthogranuloma		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

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				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	35				42				38				33			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Reproductive system]																		
epididymis			<35>				<42>				<38>				<33>			
	lymphocytic infiltration		0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	spermatogenic granuloma		2 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)
semin ves			<35>				<42>				<38>				<33>			
	mineralization		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)
	inflammatory infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
prep/cli gl			<35>				<42>				<38>				<33>			
	duct ectasia		3 (9)	12 (34)	0 (0)	0 (0)	1 (2)	11 (26)	1 (2)	0 (0)	1 (3)	16 (42)	0 (0)	0 (0)	0 (0)	9 (27)	0 (0)	0 (0)
[Nervous system]																		
brain			<35>				<42>				<38>				<33>			
	mineralization		8 (23)	0 (0)	0 (0)	0 (0)	17 (40)	0 (0)	0 (0)	0 (0)	16 (42)	0 (0)	0 (0)	0 (0)	19 (58)	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				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	35				42				38				33			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Special sense organs/appandage]																		
Harder gl			<35>				<42>				<38>				<33>			
	hyperplasia		0	1	0	0	1	0	0	0	2	0	0	0	0	0	0	0
			(0)	(3)	(0)	(0)	(2)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Musculoskeletal system]																		
bone			<35>				<42>				<38>				<32>			
	osteosclerosis		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

APPENDIX L 8

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOSUE : FEMALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 26				400 ppm 27				2000 ppm 25				10000 ppm 23			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Integumentary system/appandage]																		
skin/app			<26>				<27>				<25>				<23>			
	squamous cell hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	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)	0 (0)	1 (4)	0 (0)	0 (0)
[Respiratory system]																		
nasal cavit			<26>				<27>				<25>				<23>			
	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		0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	5 (20)	0 (0)	0 (0)	0 * (0)	2 (9)	2 (9)	0 (0)	0 (0)
	eosinophilic change:respiratory epithelium		12 (46)	5 (19)	0 (0)	0 (0)	16 (59)	2 (7)	0 (0)	0 (0)	8 (32)	9 (36)	0 (0)	0 (0)	11 (48)	4 (17)	1 (4)	0 (0)
	respiratory metaplasia:olfactory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	3 (13)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:gland		5 (19)	1 (4)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	9 (36)	0 (0)	0 (0)	0 (0)	1 (4)	1 (4)	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 26				400 ppm 27				2000 ppm 25				10000 ppm 23			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
larynx			<26>				<27>				<25>				<23>			
	basal cell activation		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 (22)	0 (0)	0 (0)	0 * (0)
	epithelial dysplasia		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 (9)	1 (4)	0 (0)	0 (0)
lung			<26>				<27>				<25>				<23>			
	lymphocytic infiltration		0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	2 (7)	0 (0)	0 (0)	2 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	bronchiolar-alveolar cell hyperplasia		1 (4)	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)
[Hematopoietic system]																		
bone marrow			<25>				<27>				<25>				<23>			
	myelofibrosis		1 (4)	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)
lymph node			<26>				<27>				<25>				<23>			
	lymphadenitis		1 (4)	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				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	26				27				25				23			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Hematopoietic system]																		
spleen			<26>				<27>				<25>				<23>			
	atrophy		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)
	angiectasis		2 (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 melanin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (9)	1 (4)	0 (0)	0 (0)
	extramedullary hematopoiesis		0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	2 (8)	0 (0)	0 (0)	0 (0)	0 (0)	4 (17)	0 (0)	0 (0)
	hyperplasia:vascular		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)
	follicular hyperplasia		1 (4)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	2 (8)	0 (0)	0 (0)	0 (0)	1 (4)	1 (4)	0 (0)	0 (0)
[Digestive system]																		
oral cavity			<26>				<27>				<25>				<23>			
	squamous cell hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	5 (22)	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 26				400 ppm 27				2000 ppm 25				10000 ppm 23			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
oral cavity			<26>				<27>				<25>				<23>			
	basal cell activation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	11 (48)	2 (9)	0 (0)	0 (0) **
	epithelial dysplasia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	14 (61)	0 (0)	0 (0)	0 (0) **
	epithelial dysplasia:incisive duct		0 (0)	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)
tooth			<26>				<27>				<25>				<23>			
	inflammation		1 (4)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	6 (24)	0 (0)	0 (0)	0 (0)	2 (9)	0 (0)	0 (0)	0 (0)
	dysplasia		1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	1 (4)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)
tongue			<26>				<27>				<25>				<23>			
	epithelial dysplasia		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)
	arteritis		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)

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 26				400 ppm 27				2000 ppm 25				10000 ppm 23			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
salivary gl			<26>				<27>				<25>				<23>			
	atrophy		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (13)	0 (0)	0 (0)
	lymphocytic infiltration		1 (4)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (9)	0 (0)	0 (0)	0 (0)
esophagus			<26>				<27>				<25>				<23>			
	basal cell activation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	7 (30)	2 (9)	0 (0)	0 (0) **
	epithelial dysplasia		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 (13)	0 (0)	1 (4)	2 (9)
stomach			<26>				<27>				<25>				<23>			
	lymphocytic infiltration		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)
	basal cell activation		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)
	erosion:forestomach		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 26				400 ppm 27				2000 ppm 25				10000 ppm 23			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
stomach			<26>				<27>				<25>				<23>			
	hyperplasia:forestomach		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 (9)	0 (0)	0 (0)	0 (0)
	erosion:glandular stomach		1 (4)	0 (0)	0 (0)	0 (0)	2 (7)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)
	hyperplasia:glandular stomach		6 (23)	1 (4)	0 (0)	0 (0)	8 (30)	4 (15)	0 (0)	0 (0)	10 (40)	1 (4)	0 (0)	0 (0)	4 (17)	0 (0)	0 (0)	0 (0)
liver			<26>				<27>				<25>				<23>			
	angiectasis		2 (8)	1 (4)	0 (0)	0 (0)	2 (7)	0 (0)	0 (0)	0 (0)	1 (4)	1 (4)	0 (0)	0 (0)	2 (9)	2 (9)	0 (0)	0 (0)
	necrosis:focal		0 (0)	0 (0)	1 (4)	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)
	lymphocytic infiltration		1 (4)	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)
	granulation		11 (42)	4 (15)	0 (0)	0 (0)	8 (30)	5 (19)	0 (0)	0 (0)	7 (28)	1 (4)	0 (0)	0 (0)	5 (22)	1 (4)	0 (0)	0 (0)
	clear cell focus		0 (0)	0 (0)	0 (0)	0 (0)	2 (7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 26				400 ppm 27				2000 ppm 25				10000 ppm 23			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver			<26>				<27>				<25>				<23>			
	basophilic cell focus		1 (4)	0 (0)	0 (0)	0 (0)	1 (4)	1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)
	vacuolated cell focus		1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	mixed cell focus		0 (0)	0 (0)	0 (0)	0 (0)	2 (7)	0 (0)	0 (0)	0 (0)	3 (12)	0 (0)	0 (0)	0 (0)	1 (4)	0 (0)	0 (0)	0 (0)
	biliary cyst		0 (0)	0 (0)	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)
[Urinary system]																		
kidney			<26>				<27>				<25>				<23>			
	cyst		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		1 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (9)	1 (4)	0 (0)	0 (0)
	basophilic change		1 (4)	0 (0)	0 (0)	0 (0)	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				400 ppm				2000 ppm				10000 ppm			
		No. of Animals on Study	26				27				25				23			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																		
kidney			<26>				<27>				<25>				<23>			
	lymphocytic infiltration		1	0	0	0	2	1	0	0	1	0	0	0	0	0	0	0
			(4)	(0)	(0)	(0)	(7)	(4)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	polyp		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hydronephrosis		0	0	0	0	0	1	0	0	0	2	0	0	0	2	0	0
			(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(9)	(0)	(0)
	mineralization:cortico-medullary junction		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	mineralization:papilla		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)
	mineralization:pelvis		0	0	0	0	0	0	0	0	2	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(0)	(4)	(0)	(0)
	mineralization:cortex		1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
[Endocrine system]																		
pituitary			<26>				<27>				<24>				<23>			
	angiectasis		2	0	0	0	2	0	0	0	3	0	0	0	1	0	0	0
			(8)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(13)	(0)	(0)	(0)	(4)	(0)	(0)	(0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 26				400 ppm 27				2000 ppm 25				10000 ppm 23			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Endocrine system]																		
pituitary		<a>	<26>				<27>				<24>				<23>			
	cyst	a	2	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
		b	(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyperplasia	a	1	0	0	0	4	0	0	0	1	0	0	0	1	0	0	0
		b	(4)	(0)	(0)	(0)	(15)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
thyroid		<a>	<26>				<27>				<25>				<23>			
	ectopic thymic tissue	a	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
		b	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Reproductive system]																		
ovary		<a>	<26>				<27>				<25>				<23>			
	thrombus	a	1	0	0	0	0	1	0	0	0	1	0	0	0	1	0	0
		b	(4)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(0)	(0)
	cyst	a	3	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
		b	(12)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	inflammatory infiltration	a	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
		b	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(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 / No. of Animals on Study / Grade	Control 26				400 ppm 27				2000 ppm 25				10000 ppm 23			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Reproductive system]																		
uterus		<26> / <27> / <25> / <23>	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)
	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)	(4)	(0)	(0)	(0)
	cystic endometrial hyperplasia		9	10	0	0	2	14	0	0 *	5	12	0	0	9	9	0	0
			(35)	(38)	(0)	(0)	(7)	(52)	(0)	(0)	(20)	(48)	(0)	(0)	(39)	(39)	(0)	(0)
mammary gl		<26> / <27> / <25> / <23>	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)
	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)
	atypical hyperplasia		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)	(0)	(0)	(0)	(0)
	galactocele		0	0	0	0	1	0	0	0	1	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(4)	(0)	(0)	(0)	(0)	(0)	(0)
[Nervous system]																		
brain		<26> / <27> / <25> / <23>	10	0	0	0	9	0	0	0	5	0	0	0	9	0	0	0
			(38)	(0)	(0)	(0)	(33)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(39)	(0)	(0)	(0)
	mineralization		10	0	0	0	9	0	0	0	5	0	0	0	9	0	0	0
			(38)	(0)	(0)	(0)	(33)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(39)	(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 26				400 ppm 27				2000 ppm 25				10000 ppm 23			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Special sense organs/appandage]																		
Harder gl			<26>				<27>				<25>				<23>			
	hyperplasia		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)
[Body cavities]																		
peritoneum			<26>				<27>				<25>				<23>			
	inflammation		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)
adipose			<26>				<27>				<25>				<23>			
	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)	(4)	(0)	(0)	(0)

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

APPENDIX M 1

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

RAT : MALE

STUDY NO. : 0162
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	400 ppm	2000 ppm	10000 ppm
0 - 52	NO. OF EXAMINED ANIMALS		0	0	0	0
	NO. OF ANIMALS WITH TUMORS		0	0	0	0
	NO. OF ANIMALS WITH SINGLE TUMORS		0	0	0	0
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	0	0	0
	NO. OF BENIGN TUMORS		0	0	0	0
	NO. OF MALIGNANT TUMORS		0	0	0	0
	NO. OF TOTAL TUMORS		0	0	0	0
53 - 78	NO. OF EXAMINED ANIMALS		1	2	1	0
	NO. OF ANIMALS WITH TUMORS		0	2	1	0
	NO. OF ANIMALS WITH SINGLE TUMORS		0	1	0	0
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	1	1	0
	NO. OF BENIGN TUMORS		0	1	1	0
	NO. OF MALIGNANT TUMORS		0	2	1	0
	NO. OF TOTAL TUMORS		0	3	2	0
79 - 104	NO. OF EXAMINED ANIMALS		5	8	13	11
	NO. OF ANIMALS WITH TUMORS		5	8	13	11
	NO. OF ANIMALS WITH SINGLE TUMORS		1	4	2	2
	NO. OF ANIMALS WITH MULTIPLE TUMORS		4	4	11	9
	NO. OF BENIGN TUMORS		9	11	19	16
	NO. OF MALIGNANT TUMORS		2	5	13	8
	NO. OF TOTAL TUMORS		11	16	32	24
105 - 105	NO. OF EXAMINED ANIMALS		44	40	36	39
	NO. OF ANIMALS WITH TUMORS		43	40	36	39
	NO. OF ANIMALS WITH SINGLE TUMORS		14	10	9	14
	NO. OF ANIMALS WITH MULTIPLE TUMORS		29	30	27	25
	NO. OF BENIGN TUMORS		90	75	80	73
	NO. OF MALIGNANT TUMORS		5	7	7	11
	NO. OF TOTAL TUMORS		95	82	87	84

STUDY NO. : 0162
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	400 ppm	2000 ppm	10000 ppm
0 - 105	NO. OF EXAMINED ANIMALS		50	50	50	50
	NO. OF ANIMALS WITH TUMORS		48	50	50	50
	NO. OF ANIMALS WITH SINGLE TUMORS		15	15	11	16
	NO. OF ANIMALS WITH MULTIPLE TUMORS		33	35	39	34
	NO. OF BENIGN TUMORS		99	87	100	89
	NO. OF MALIGNANT TUMORS		7	14	21	19
	NO. OF TOTAL TUMORS		106	101	121	108

APPENDIX M 2

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

RAT : FEMALE

STUDY NO. : 0162
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	400 ppm	2000 ppm	10000 ppm
0 - 52	NO. OF EXAMINED ANIMALS		1	0	0	0
	NO. OF ANIMALS WITH TUMORS		1	0	0	0
	NO. OF ANIMALS WITH SINGLE TUMORS		1	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		1	0	0	0
	NO. OF TOTAL TUMORS		1	0	0	0
53 - 78	NO. OF EXAMINED ANIMALS		0	1	2	2
	NO. OF ANIMALS WITH TUMORS		0	1	2	2
	NO. OF ANIMALS WITH SINGLE TUMORS		0	1	1	2
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	0	1	0
	NO. OF BENIGN TUMORS		0	1	1	1
	NO. OF MALIGNANT TUMORS		0	0	2	1
	NO. OF TOTAL TUMORS		0	1	3	2
79 - 104	NO. OF EXAMINED ANIMALS		8	9	7	11
	NO. OF ANIMALS WITH TUMORS		8	9	7	10
	NO. OF ANIMALS WITH SINGLE TUMORS		7	3	2	7
	NO. OF ANIMALS WITH MULTIPLE TUMORS		1	6	5	3
	NO. OF BENIGN TUMORS		3	12	10	10
	NO. OF MALIGNANT TUMORS		6	6	4	8
	NO. OF TOTAL TUMORS		9	18	14	18
105 - 105	NO. OF EXAMINED ANIMALS		41	40	41	37
	NO. OF ANIMALS WITH TUMORS		25	24	29	28
	NO. OF ANIMALS WITH SINGLE TUMORS		15	14	17	17
	NO. OF ANIMALS WITH MULTIPLE TUMORS		10	10	12	11
	NO. OF BENIGN TUMORS		31	31	34	30
	NO. OF MALIGNANT TUMORS		4	4	11	11
	NO. OF TOTAL TUMORS		35	35	45	41

STUDY NO. : 0162
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	400 ppm	2000 ppm	10000 ppm
0 - 105	NO. OF EXAMINED ANIMALS		50	50	50	50
	NO. OF ANIMALS WITH TUMORS		34	34	38	40
	NO. OF ANIMALS WITH SINGLE TUMORS		23	18	20	26
	NO. OF ANIMALS WITH MULTIPLE TUMORS		11	16	18	14
	NO. OF BENIGN TUMORS		34	44	45	41
	NO. OF MALIGNANT TUMORS		11	10	17	20
	NO. OF TOTAL TUMORS		45	54	62	61

APPENDIX M 3

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

MOUSE : MALE

STUDY NO. : 0163
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	400 ppm	2000 ppm	10000 ppm
0 - 52	NO. OF EXAMINED ANIMALS		2	0	1	1
	NO. OF ANIMALS WITH TUMORS		0	0	0	1
	NO. OF ANIMALS WITH SINGLE TUMORS		0	0	0	1
	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	1
	NO. OF TOTAL TUMORS		0	0	0	1
53 - 78	NO. OF EXAMINED ANIMALS		6	2	1	2
	NO. OF ANIMALS WITH TUMORS		4	2	1	2
	NO. OF ANIMALS WITH SINGLE TUMORS		3	2	1	2
	NO. OF ANIMALS WITH MULTIPLE TUMORS		1	0	0	0
	NO. OF BENIGN TUMORS		2	0	0	0
	NO. OF MALIGNANT TUMORS		6	2	1	2
	NO. OF TOTAL TUMORS		8	2	1	2
79 - 104	NO. OF EXAMINED ANIMALS		7	6	10	14
	NO. OF ANIMALS WITH TUMORS		6	6	10	12
	NO. OF ANIMALS WITH SINGLE TUMORS		3	3	5	7
	NO. OF ANIMALS WITH MULTIPLE TUMORS		3	3	5	5
	NO. OF BENIGN TUMORS		3	2	3	3
	NO. OF MALIGNANT TUMORS		7	7	13	17
	NO. OF TOTAL TUMORS		10	9	16	20
105 - 105	NO. OF EXAMINED ANIMALS		35	42	38	33
	NO. OF ANIMALS WITH TUMORS		24	24	27	25
	NO. OF ANIMALS WITH SINGLE TUMORS		15	16	18	13
	NO. OF ANIMALS WITH MULTIPLE TUMORS		9	8	9	12
	NO. OF BENIGN TUMORS		10	14	17	15
	NO. OF MALIGNANT TUMORS		27	24	21	26
	NO. OF TOTAL TUMORS		37	38	38	41

STUDY NO. : 0163
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	400 ppm	2000 ppm	10000 ppm
0 - 105	NO. OF EXAMINED ANIMALS		50	50	50	50
	NO. OF ANIMALS WITH TUMORS		34	32	38	40
	NO. OF ANIMALS WITH SINGLE TUMORS		21	21	24	23
	NO. OF ANIMALS WITH MULTIPLE TUMORS		13	11	14	17
	NO. OF BENIGN TUMORS		15	16	20	18
	NO. OF MALIGNANT TUMORS		40	33	35	46
	NO. OF TOTAL TUMORS		55	49	55	64

APPENDIX M 4

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

MOUSE: FEMALE

STUDY NO. : 0163
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	400 ppm	2000 ppm	10000 ppm
0 - 52	NO. OF EXAMINED ANIMALS		0	2	0	2
	NO. OF ANIMALS WITH TUMORS		0	1	0	1
	NO. OF ANIMALS WITH SINGLE TUMORS		0	1	0	1
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	0	0	0
	NO. OF BENIGN TUMORS		0	0	0	0
	NO. OF MALIGNANT TUMORS		0	1	0	1
	NO. OF TOTAL TUMORS		0	1	0	1
53 - 78	NO. OF EXAMINED ANIMALS		7	7	4	6
	NO. OF ANIMALS WITH TUMORS		6	6	2	5
	NO. OF ANIMALS WITH SINGLE TUMORS		4	6	2	5
	NO. OF ANIMALS WITH MULTIPLE TUMORS		2	0	0	0
	NO. OF BENIGN TUMORS		1	1	0	0
	NO. OF MALIGNANT TUMORS		7	5	2	5
	NO. OF TOTAL TUMORS		8	6	2	5
79 - 104	NO. OF EXAMINED ANIMALS		17	14	21	18
	NO. OF ANIMALS WITH TUMORS		17	14	19	17
	NO. OF ANIMALS WITH SINGLE TUMORS		13	10	14	11
	NO. OF ANIMALS WITH MULTIPLE TUMORS		4	4	5	6
	NO. OF BENIGN TUMORS		6	3	3	1
	NO. OF MALIGNANT TUMORS		16	20	22	23
	NO. OF TOTAL TUMORS		22	23	25	24
105 - 105	NO. OF EXAMINED ANIMALS		26	27	25	23
	NO. OF ANIMALS WITH TUMORS		15	18	17	20
	NO. OF ANIMALS WITH SINGLE TUMORS		8	11	9	9
	NO. OF ANIMALS WITH MULTIPLE TUMORS		7	7	8	11
	NO. OF BENIGN TUMORS		11	16	19	18
	NO. OF MALIGNANT TUMORS		14	12	11	22
	NO. OF TOTAL TUMORS		25	28	30	40

STUDY NO. : 0163
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	400 ppm	2000 ppm	10000 ppm
0 - 105	NO. OF EXAMINED ANIMALS		50	50	50	49
	NO. OF ANIMALS WITH TUMORS		38	39	38	43
	NO. OF ANIMALS WITH SINGLE TUMORS		25	28	25	26
	NO. OF ANIMALS WITH MULTIPLE TUMORS		13	11	13	17
	NO. OF BENIGN TUMORS		18	20	22	19
	NO. OF MALIGNANT TUMORS		37	38	35	51
	NO. OF TOTAL TUMORS		55	58	57	70

APPENDIX N 1

NEOPLASTIC LESIONS - INCIDENCE AND TUMOR OCCURRENCE

RAT : MALE :

(2-YEAR STUDY)

STUDY NO. : 0162
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	400 ppm 50	2000 ppm 50	10000 ppm 50
[Integumentary system/appandage]						
skin/app			<50>	<50>	<50>	<50>
	squamous cell papilloma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
	trichoepithelioma		1 (2%)	0 (0%)	1 (2%)	1 (2%)
	keratoacanthoma		3 (6%)	2 (4%)	4 (8%)	1 (2%)
	calcifying epithelioma		0 (0%)	0 (0%)	0 (0%)	2 (4%)
	sebaceous adenoma		0 (0%)	1 (2%)	0 (0%)	1 (2%)
	schwannoma:malignant		0 (0%)	1 (2%)	0 (0%)	1 (2%)
subcutis			<50>	<50>	<50>	<50>
	fibroma		3 (6%)	4 (8%)	8 (16%)	3 (6%)
	lipoma		1 (2%)	0 (0%)	3 (6%)	0 (0%)
	fibrosarcoma		0 (0%)	1 (2%)	1 (2%)	2 (4%)
	schwannoma:malignant		0 (0%)	1 (2%)	0 (0%)	0 (0%)
	histiocytic sarcoma		0 (0%)	0 (0%)	2 (4%)	0 (0%)
	tumor:malignant:NOS		1 (2%)	0 (0%)	0 (0%)	0 (0%)
	sarcoma:NOS		0 (0%)	0 (0%)	0 (0%)	1 (2%)
[Respiratory system]						
larynx			<50>	<50>	<50>	<50>
	squamous cell carcinoma		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 / No. of animals on Study	Control 50	400 ppm 50	2000 ppm 50	10000 ppm 50
[Respiratory system]						
lung			<50>	<50>	<50>	<50>
	bronchiolar-alveolar adenoma		3 (6%)	1 (2%)	3 (6%)	1 (2%)
[Hematopoietic system]						
lymph node			<50>	<50>	<50>	<50>
	malignant lymphoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
spleen			<50>	<50>	<49>	<50>
	mononuclear cell leukemia		3 (6%)	5 (10%)	7 (14%)	4 (8%)
	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%)	2 (4%)
	squamous cell carcinoma		0 (0%)	0 (0%)	0 (0%)	5 (10%)
tongue			<50>	<50>	<50>	<49>
	osteosarcoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
stomach			<50>	<50>	<50>	<50>
	squamous cell papilloma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
	keratoacanthoma		2 (4%)	0 (0%)	0 (0%)	1 (2%)
	squamous cell carcinoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
small intes			<50>	<50>	<50>	<50>
	adenocarcinoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
large intes			<50>	<50>	<50>	<50>
	neuroendocrine cell tumor:benign		0 (0%)	0 (0%)	1 (2%)	0 (0%)
liver			<50>	<50>	<50>	<50>
	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

Organ	Findings	Group Name / No. of animals on Study	Control 50	400 ppm 50	2000 ppm 50	10000 ppm 50
[Digestive system]						
liver			<50>	<50>	<50>	<50>
	hepatocellular carcinoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
[Endocrine system]						
pituitary			<50>	<50>	<50>	<50>
	adenoma		19 (38%)	16 (32%)	14 (28%)	11 (22%)
	adenocarcinoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
thyroid			<50>	<49>	<49>	<49>
	C-cell adenoma		7 (14%)	9 (18%)	3 (6%)	7 (14%)
	follicular adenoma		0 (0%)	1 (2%)	0 (0%)	1 (2%)
	C-cell carcinoma		1 (2%)	2 (4%)	2 (4%)	0 (0%)
	follicular adenocarcinoma		0 (0%)	2 (4%)	0 (0%)	0 (0%)
panc islet			<50>	<50>	<50>	<50>
	islet cell adenoma		6 (12%)	5 (10%)	4 (8%)	3 (6%)
adrenal			<50>	<50>	<50>	<50>
	pheochromocytoma		8 (16%)	4 (8%)	9 (18%)	7 (14%)
	cortical adenoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
	pheochromocytoma:malignant		1 (2%)	0 (0%)	1 (2%)	0 (0%)
[Reproductive system]						
testis			<50>	<50>	<50>	<50>
	interstitial cell tumor		42 (84%)	40 (80%)	44 (88%)	47 (94%)
mammary gl			<50>	<50>	<50>	<50>
	adenoma		1 (2%)	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

Organ	Findings	Group Name / No. of animals on Study	Control 50	400 ppm 50	2000 ppm 50	10000 ppm 50
[Reproductive system]						
mammary gl			<50>	<50>	<50>	<50>
	fibroadenoma		1 (2%)	0 (0%)	2 (4%)	0 (0%)
prep/cli gl			<50>	<50>	<50>	<50>
	adenoma		1 (2%)	2 (4%)	2 (4%)	0 (0%)
[Nervous system]						
brain			<50>	<50>	<50>	<50>
	meningioma:benign		0 (0%)	1 (2%)	0 (0%)	0 (0%)
	malignant reticulosis		1 (2%)	0 (0%)	0 (0%)	0 (0%)
	glioma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
[Special sense organs/appandage]						
Zymbal gl			<50>	<50>	<50>	<50>
	sebaceous adenoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
[Musculoskeletal system]						
muscle			<50>	<50>	<50>	<50>
	sarcoma:NOS		0 (0%)	1 (2%)	0 (0%)	0 (0%)
bone			<50>	<50>	<50>	<50>
	osteosarcoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
vertebra			<50>	<50>	<50>	<50>
	sarcoma:NOS		0 (0%)	0 (0%)	1 (2%)	0 (0%)
[Body cavities]						
peritoneum			<50>	<50>	<50>	<50>
	mesothelioma		0 (0%)	0 (0%)	1 (2%)	1 (2%)

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

APPENDIX N 2

NEOPLASTIC LESIONS - INCIDENCE AND TUMOR OCCURRENCE

RAT : FEMALE :

(2-YEAR STUDY)

Organ	Findings	Group Name / No. of animals on Study	Control 50	400 ppm 50	2000 ppm 50	10000 ppm 50
[Integumentary system/appandage]						
skin/app			<50>	<50>	<50>	<50>
	trichoepithelioma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
	keratoacanthoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
	schwannoma:malignant		0 (0%)	0 (0%)	1 (2%)	0 (0%)
subcutis			<50>	<50>	<50>	<50>
	fibroma		1 (2%)	2 (4%)	0 (0%)	1 (2%)
	fibrosarcoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
	histiocytic sarcoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
	sarcoma:NOS		1 (2%)	0 (0%)	0 (0%)	1 (2%)
[Respiratory system]						
lung			<50>	<50>	<50>	<50>
	bronchiolar-alveolar adenoma		1 (2%)	1 (2%)	1 (2%)	1 (2%)
	squamous cell carcinoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
[Hematopoietic system]						
bone marrow			<50>	<50>	<50>	<50>
	malignant histiocytosis		0 (0%)	0 (0%)	1 (2%)	0 (0%)
spleen			<50>	<50>	<50>	<50>
	fibrosarcoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
	mononuclear cell leukemia		4 (8%)	5 (10%)	8 (16%)	7 (14%)
[Digestive system]						
oral cavity			<50>	<50>	<50>	<50>
	squamous cell carcinoma		0 (0%)	1 (2%)	1 (2%)	3 (6%)

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

Organ	Findings	Group Name / No. of animals on Study	Control 50	400 ppm 50	2000 ppm 50	10000 ppm 50
[Digestive system]						
esophagus			<50>	<50>	<50>	<50>
	squamous cell carcinoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
stomach			<50>	<50>	<50>	<50>
	neuroendocrine cell tumor:malignant		0 (0%)	0 (0%)	1 (2%)	0 (0%)
liver			<50>	<50>	<50>	<50>
	histiocytic sarcoma		0 (0%)	1 (2%)	0 (0%)	1 (2%)
[Endocrine system]						
pituitary			<50>	<50>	<50>	<50>
	adenoma		8 (16%)	11 (22%)	9 (18%)	14 (28%)
	adenocarcinoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
thyroid			<50>	<50>	<50>	<50>
	C-cell adenoma		2 (4%)	7 (14%)	8 (16%)	5 (10%)
	C-cell carcinoma		0 (0%)	0 (0%)	1 (2%)	2 (4%)
panc islet			<50>	<50>	<50>	<50>
	islet cell adenoma		0 (0%)	1 (2%)	3 (6%)	1 (2%)
adrenal			<50>	<50>	<50>	<50>
	pheochromocytoma		4 (8%)	1 (2%)	1 (2%)	2 (4%)
	cortical adenoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
	cortical adenocarcinoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
[Reproductive system]						
ovary			<50>	<50>	<50>	<50>
	granulosa-theca cell tumor		1 (2%)	0 (0%)	0 (0%)	1 (2%)
uterus			<50>	<50>	<50>	<50>
	hemangioma		0 (0%)	1 (2%)	0 (0%)	1 (2%)

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

Organ	Findings	Group Name / No. of animals on Study	Control 50	400 ppm 50	2000 ppm 50	10000 ppm 50
[Reproductive system]						
uterus			<50>	<50>	<50>	<50>
	endometrial stromal polyp		5 (10%)	5 (10%)	10 (20%)	4 (8%)
	adenocarcinoma		1 (2%)	0 (0%)	1 (2%)	0 (0%)
	leiomyosarcoma		1 (2%)	1 (2%)	0 (0%)	0 (0%)
	endometrial stromal sarcoma		1 (2%)	0 (0%)	1 (2%)	0 (0%)
vagina			<50>	<50>	<50>	<50>
	squamous cell papilloma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
mammary gl			<50>	<50>	<50>	<50>
	adenoma		1 (2%)	3 (6%)	0 (0%)	1 (2%)
	fibroadenoma		9 (18%)	10 (20%)	8 (16%)	9 (18%)
	adenocarcinoma		0 (0%)	0 (0%)	0 (0%)	3 (6%)
prep/cli gl			<50>	<50>	<50>	<50>
	adenoma		2 (4%)	0 (0%)	3 (6%)	1 (2%)
[Nervous system]						
brain			<50>	<50>	<50>	<50>
	glioma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
[Special sense organs/appandage]						
Zymbal gl			<50>	<50>	<50>	<50>
	squamous cell carcinoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
[Body cavities]						
retroperit			<50>	<50>	<50>	<50>
	sarcoma:NOS		0 (0%)	0 (0%)	0 (0%)	1 (2%)

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

APPENDIX N 3

NEOPLASTIC LESIONS - INCIDENCE AND TUMOR OCCURRENCE

MOUSE: MALE

(2-YEAR STUDY)

Organ	Findings	Group Name / No. of animals on Study	Control 50	400 ppm 50	2000 ppm 50	10000 ppm 50
[Integumentary system/appandage]						
subcutis	xanthoma		<50> 2 (4%)	<50> 1 (2%)	<50> 1 (2%)	<50> 0 (0%)
	mastcytoma:benign		0 (0%)	0 (0%)	0 (0%)	1 (2%)
	hemangioma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
	hemangiosarcoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
[Respiratory system]						
larynx	squamous cell carcinoma		<50> 0 (0%)	<50> 0 (0%)	<50> 0 (0%)	<50> 2 (4%)
lung	bronchiolar-alveolar adenoma		<50> 3 (6%)	<50> 3 (6%)	<50> 4 (8%)	<50> 3 (6%)
	bronchiolar-alveolar carcinoma		7 (14%)	3 (6%)	5 (10%)	2 (4%)
[Hematopoietic system]						
bone marrow	hemangioma		<50> 2 (4%)	<50> 0 (0%)	<50> 0 (0%)	<49> 0 (0%)
lymph node	malignant lymphoma		<50> 5 (10%)	<50> 6 (12%)	<50> 6 (12%)	<50> 3 (6%)
	mastcytoma:malignant		0 (0%)	1 (2%)	0 (0%)	1 (2%)
spleen	hemangioma		<50> 1 (2%)	<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)
	malignant lymphoma		1 (2%)	1 (2%)	2 (4%)	0 (0%)
	hemangiosarcoma		2 (4%)	1 (2%)	4 (8%)	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	400 ppm 50	2000 ppm 50	10000 ppm 50
[Circulatory system]						
heart			<50>	<50>	<50>	<50>
	hemangioma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
[Digestive system]						
oral cavity			<50>	<50>	<50>	<50>
	squamous cell papilloma		0 (0%)	0 (0%)	0 (0%)	4 (8%)
	squamous cell carcinoma		0 (0%)	0 (0%)	0 (0%)	13 (26%)
esophagus			<50>	<50>	<50>	<50>
	squamous cell carcinoma		0 (0%)	0 (0%)	0 (0%)	7 (14%)
stomach			<50>	<50>	<50>	<50>
	squamous cell papilloma		0 (0%)	0 (0%)	0 (0%)	2 (4%)
	adenoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
	squamous cell carcinoma		1 (2%)	0 (0%)	0 (0%)	7 (14%)
	mastcytoma:malignant		0 (0%)	0 (0%)	0 (0%)	1 (2%)
liver			<50>	<50>	<50>	<50>
	hepatocellular adenoma		2 (4%)	6 (12%)	4 (8%)	3 (6%)
	angiomyolipoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
	histiocytic sarcoma		0 (0%)	2 (4%)	0 (0%)	1 (2%)
	hemangiosarcoma		4 (8%)	5 (10%)	5 (10%)	4 (8%)
	hepatocellular carcinoma		13 (26%)	10 (20%)	9 (18%)	4 (8%)
[Urinary system]						
urin bladd			<50>	<50>	<50>	<50>
	histiocytic sarcoma		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	400 ppm 50	2000 ppm 50	10000 ppm 50
[Endocrine system]						
pituitary			<49>	<50>	<50>	<50>
	adenoma		1 (2%)	0 (0%)	0 (0%)	1 (2%)
	adenocarcinoma		1 (2%)	1 (2%)	0 (0%)	0 (0%)
thyroid			<50>	<50>	<50>	<50>
	follicular adenoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
adrenal			<50>	<50>	<50>	<50>
	cortical adenoma		0 (0%)	1 (2%)	1 (2%)	0 (0%)
[Reproductive system]						
epididymis			<50>	<50>	<50>	<50>
	histiocytic sarcoma		1 (2%)	1 (2%)	0 (0%)	1 (2%)
semin ves			<50>	<50>	<50>	<50>
	fibrosarcoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
prostate			<50>	<50>	<50>	<50>
	adenoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
[Nervous system]						
periph nerv			<50>	<50>	<50>	<50>
	histiocytic sarcoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
[Special sense organs/appandage]						
Harder gl			<50>	<50>	<50>	<50>
	adenoma		3 (6%)	4 (8%)	6 (12%)	2 (4%)
	adenocarcinoma		1 (2%)	1 (2%)	0 (0%)	0 (0%)
[Musculoskeletal system]						
muscle			<50>	<50>	<50>	<50>
	hemangiosarcoma		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	400 ppm 50	2000 ppm 50	10000 ppm 50
[Musculoskeletal system]						
bone			<50>	<50>	<50>	<49>
	osteoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
[Body cavities]						
mediastinum			<50>	<50>	<50>	<50>
	hemangiosarcoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
peritoneum			<50>	<50>	<50>	<50>
	hemangiosarcoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
retroperit			<50>	<50>	<50>	<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

APPENDIX N 4

NEOPLASTIC LESIONS - INCIDENCE AND TUMOR OCCURRENCE

MOUSE: FEMALE

(2-YEAR STUDY)

Organ	Findings	Group Name / No. of animals on Study	Control 50	400 ppm 50	2000 ppm 50	10000 ppm 49
[Integumentary system/appandage]						
skin/app			<50>	<50>	<50>	<49>
	squamous cell carcinoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
subcutis			<50>	<50>	<50>	<49>
	xanthoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
	hemangiosarcoma		1 (2%)	1 (2%)	0 (0%)	0 (0%)
[Respiratory system]						
nasal cavit			<50>	<50>	<50>	<49>
	histiocytic sarcoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
larynx			<50>	<50>	<50>	<49>
	squamous cell carcinoma		0 (0%)	0 (0%)	1 (2%)	1 (2%)
lung			<50>	<50>	<50>	<49>
	bronchiolar-alveolar adenoma		1 (2%)	3 (6%)	1 (2%)	2 (4%)
	bronchiolar-alveolar carcinoma		2 (4%)	3 (6%)	1 (2%)	1 (2%)
[Hematopoietic system]						
bone marrow			<49>	<50>	<50>	<49>
	hemangioma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
	mastcytoma:malignant		0 (0%)	0 (0%)	0 (0%)	1 (2%)
	hemangiosarcoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
lymph node			<50>	<50>	<50>	<49>
	mastcytoma:benign		0 (0%)	0 (0%)	0 (0%)	1 (2%)
	malignant lymphoma		11 (22%)	10 (20%)	17 (34%)	10 (20%)
	mastcytoma:malignant		1 (2%)	0 (0%)	0 (0%)	0 (0%)

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

Organ	Findings	Group Name / No. of animals on Study	Control 50	400 ppm 50	2000 ppm 50	10000 ppm 49
[Hematopoietic system]						
thymus			<50>	<50>	<50>	<49>
	malignant lymphoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
spleen			<50>	<50>	<50>	<49>
	malignant lymphoma		0 (0%)	5 (10%)	1 (2%)	1 (2%)
	hemangiosarcoma		1 (2%)	1 (2%)	1 (2%)	0 (0%)
[Digestive system]						
oral cavity			<50>	<50>	<50>	<49>
	squamous cell papilloma		0 (0%)	0 (0%)	0 (0%)	3 (6%)
	squamous cell carcinoma		0 (0%)	0 (0%)	0 (0%)	15 (31%)
tongue			<50>	<50>	<50>	<49>
	squamous cell papilloma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
	squamous cell carcinoma		2 (4%)	0 (0%)	0 (0%)	1 (2%)
salivary gl			<50>	<50>	<50>	<49>
	adenocarcinoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
esophagus			<50>	<50>	<50>	<49>
	squamous cell papilloma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
	squamous cell carcinoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
stomach			<50>	<50>	<50>	<49>
	squamous cell papilloma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
	mastcytoma:benign		1 (2%)	0 (0%)	0 (0%)	0 (0%)
	squamous cell carcinoma		0 (0%)	0 (0%)	0 (0%)	3 (6%)
small intes			<50>	<50>	<50>	<49>
	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

Organ	Findings	Group Name / No. of animals on Study	Control 50	400 ppm 50	2000 ppm 50	10000 ppm 49
[Digestive system]						
liver			<50>	<50>	<50>	<49>
	hemangioma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
	hepatocellular adenoma		3 (6%)	1 (2%)	4 (8%)	0 (0%)
	histiocytic sarcoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
	hemangiosarcoma		3 (6%)	3 (6%)	0 (0%)	1 (2%)
	hepatocellular carcinoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
[Endocrine system]						
pituitary			<50>	<49>	<49>	<49>
	adenoma		10 (20%)	6 (12%)	8 (16%)	7 (14%)
	adenocarcinoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
adrenal			<50>	<50>	<50>	<49>
	pheochromocytoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
	cortical adenoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
[Reproductive system]						
ovary			<50>	<50>	<50>	<49>
	cystadenoma		2 (4%)	0 (0%)	2 (4%)	0 (0%)
	hemangioma		1 (2%)	0 (0%)	1 (2%)	1 (2%)
	cystadenocarcinoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
uterus			<50>	<50>	<50>	<48>
	fibroma		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

Organ	Findings	Group Name / No. of animals on Study	Control 50	400 ppm 50	2000 ppm 50	10000 ppm 49
[Reproductive system]						
uterus			<50>	<50>	<50>	<48>
	endometrial stromal polyp		0 (0%)	1 (2%)	0 (0%)	0 (0%)
	leiomyosarcoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
	histiocytic sarcoma		10 (20%)	11 (22%)	8 (16%)	10 (21%)
	hemangioendothelioma		1 (2%)	0 (0%)	0 (0%)	1 (2%)
mammary gl			<50>	<50>	<50>	<49>
	adenoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
	adenocarcinoma		2 (4%)	1 (2%)	2 (4%)	0 (0%)
[Nervous system]						
periph nerv			<50>	<50>	<50>	<49>
	histiocytic sarcoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
[Special sense organs/appandage]						
Harder gl			<50>	<50>	<50>	<49>
	adenoma		0 (0%)	4 (8%)	3 (6%)	0 (0%)
	adenocarcinoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
[Musculoskeletal system]						
muscle			<50>	<50>	<50>	<49>
	hemangiosarcoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
bone			<49>	<50>	<50>	<49>
	osteoma		0 (0%)	1 (2%)	0 (0%)	1 (2%)
	osteosarcoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)

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

Organ	Findings	Group Name / No. of animals on Study	Control 50	400 ppm 50	2000 ppm 50	10000 ppm 49
[Body cavities]						
peritoneum			<50>	<50>	<50>	<49>
	hemangioma		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 O 1

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

RAT : MALE

(2-YEAR STUDY)

Group Name	Control	400 ppm	2000 ppm	10000 ppm
	SITE : skin/appendage TUMOR : keratoacanthoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	2/50(4.0)	4/50(8.0)	1/50(2.0)
Adjusted rates(b)	6.82	5.00	10.53	2.56
Terminal rates(c)	3/44(6.8)	2/40(5.0)	3/36(8.3)	1/39(2.6)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.8230			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.3288			
Fisher Exact test(e)		P = 0.4909	P = 0.4895	P = 0.3235
	SITE : subcutis TUMOR : fibroma			
Tumor rate				
Overall rates(a)	3/50(6.0)	4/50(8.0)	8/50(16.0)	3/50(6.0)
Adjusted rates(b)	6.82	10.00	19.44	5.13
Terminal rates(c)	3/44(6.8)	4/40(10.0)	7/36(19.4)	2/39(5.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1883			
Prevalence method(d)	P = 0.7841			
Combined analysis(d)	P = 0.6457			
Cochran-Armitage test(e)	P = 0.6172			
Fisher Exact test(e)		P = 0.4895	P = 0.1322	P = 0.3392
	SITE : subcutis TUMOR : lipoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	0/50(0.0)	3/50(6.0)	0/50(0.0)
Adjusted rates(b)	2.27	0.0	8.33	0.0
Terminal rates(c)	1/44(2.3)	0/40(0.0)	3/36(8.3)	0/39(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.7438			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.4252			
Fisher Exact test(e)		P = 0.4950	P = 0.3235	P = 0.4950

Group Name	Control	400 ppm	2000 ppm	10000 ppm
	SITE : subcutis TUMOR : fibroma,fibrosarcoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	5/50(10.0)	9/50(18.0)	5/50(10.0)
Adjusted rates(b)	6.82	10.00	22.22	10.26
Terminal rates(c)	3/44(6.8)	4/40(10.0)	8/36(22.2)	4/39(10.3)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3122			
Prevalence method(d)	P = 0.4746			
Combined analysis(d)	P = 0.4113			
Cochran-Armitage test(e)	P = 0.9201			
Fisher Exact test(e)		P = 0.3790	P = 0.0899	P = 0.3790
	SITE : lung TUMOR : bronchiolar-alveolar adenoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	1/50(2.0)	3/50(6.0)	1/50(2.0)
Adjusted rates(b)	6.82	2.50	6.82	2.56
Terminal rates(c)	3/44(6.8)	1/40(2.5)	2/36(5.6)	1/39(2.6)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.7670			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.4546			
Fisher Exact test(e)		P = 0.3235	P = 0.3392	P = 0.3235
	SITE : spleen TUMOR : mononuclear cell leukemia			
Tumor rate				
Overall rates(a)	3/50(6.0)	5/50(10.0)	7/49(14.3)	4/50(8.0)
Adjusted rates(b)	4.55	7.50	11.43	2.56
Terminal rates(c)	2/44(4.5)	3/40(7.5)	4/35(11.4)	1/39(2.6)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.2447			
Prevalence method(d)	P = 0.8011			
Combined analysis(d)	P = 0.5418			
Cochran-Armitage test(e)	P = 0.8584			
Fisher Exact test(e)		P = 0.3790	P = 0.1836	P = 0.4895

Group Name	Control	400 ppm	2000 ppm	10000 ppm
	SITE : oral cavity TUMOR : squamous cell carcinoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	0/50(0.0)	0/50(0.0)	5/50(10.0)
Adjusted rates(b)	0.0	0.0	0.0	7.69
Terminal rates(c)	0/44(0.0)	0/40(0.0)	0/36(0.0)	3/39(7.7)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.0161* ?			
Prevalence method(d)	P = 0.0019**?			
Combined analysis(d)	P = 0.0001**?			
Cochran-Armitage test(e)	P = 0.0001**			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.0360*
	SITE : oral cavity TUMOR : squamous cell papilloma,squamous cell carcinoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	0/50(0.0)	0/50(0.0)	7/50(14.0)
Adjusted rates(b)	0.0	0.0	0.0	12.82
Terminal rates(c)	0/44(0.0)	0/40(0.0)	0/36(0.0)	5/39(12.8)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.0161* ?			
Prevalence method(d)	P < 0.0001**?			
Combined analysis(d)	P < 0.0001**?			
Cochran-Armitage test(e)	P < 0.0001**			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.0101*
	SITE : pituitary gland TUMOR : adenoma			
Tumor rate				
Overall rates(a)	19/50(38.0)	16/50(32.0)	14/50(28.0)	11/50(22.0)
Adjusted rates(b)	36.36	30.95	27.78	23.26
Terminal rates(c)	16/44(36.4)	12/40(30.0)	10/36(27.8)	8/39(20.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8020			
Prevalence method(d)	P = 0.9032			
Combined analysis(d)	P = 0.9418			
Cochran-Armitage test(e)	P = 0.1133			
Fisher Exact test(e)		P = 0.4055	P = 0.2902	P = 0.1411

Group Name	Control	400 ppm	2000 ppm	10000 ppm
	SITE : pituitary gland			
	TUMOR : adenoma,adenocarcinoma			
Tumor rate				
Overall rates(a)	19/50(38.0)	16/50(32.0)	15/50(30.0)	11/50(22.0)
Adjusted rates(b)	36.36	30.95	29.73	23.26
Terminal rates(c)	16/44(36.4)	12/40(30.0)	10/36(27.8)	8/39(20.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8020			
Prevalence method(d)	P = 0.9091			
Combined analysis(d)	P = 0.9453			
Cochran-Armitage test(e)	P = 0.1057			
Fisher Exact test(e)		P = 0.4055	P = 0.3472	P = 0.1411
	SITE : thyroid			
	TUMOR : C-cell adenoma			
Tumor rate				
Overall rates(a)	7/50(14.0)	9/49(18.4)	3/49(6.1)	7/49(14.3)
Adjusted rates(b)	15.22	22.50	8.33	17.95
Terminal rates(c)	6/44(13.6)	9/40(22.5)	2/35(5.7)	7/39(17.9)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.4844			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.9755			
Fisher Exact test(e)		P = 0.4089	P = 0.2004	P = 0.4019
	SITE : thyroid			
	TUMOR : C-cell adenoma,C-cell carcinoma			
Tumor rate				
Overall rates(a)	8/50(16.0)	11/49(22.4)	5/49(10.2)	7/49(14.3)
Adjusted rates(b)	17.39	27.50	11.90	17.95
Terminal rates(c)	7/44(15.9)	11/40(27.5)	3/35(8.6)	7/39(17.9)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.7025			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.5880			
Fisher Exact test(e)		P = 0.3379	P = 0.3267	P = 0.4706

Group Name	Control	400 ppm	2000 ppm	10000 ppm
	SITE : thyroid			
	TUMOR : follicular adenoma,follicular adenocarcinoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	3/49(6.1)	0/49(0.0)	1/49(2.0)
Adjusted rates(b)	0.0	6.38	0.0	2.56
Terminal rates(c)	0/44(0.0)	2/40(5.0)	0/35(0.0)	1/39(2.6)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.5241			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.8872			
Fisher Exact test(e)		P = 0.1287	P = 0.5000	P = 0.5000
	SITE : pancreas islet			
	TUMOR : islet cell adenoma			
Tumor rate				
Overall rates(a)	6/50(12.0)	5/50(10.0)	4/50(8.0)	3/50(6.0)
Adjusted rates(b)	13.04	12.50	11.11	6.12
Terminal rates(c)	5/44(11.4)	5/40(12.5)	4/36(11.1)	2/39(5.1)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.8427			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.3355			
Fisher Exact test(e)		P = 0.4872	P = 0.3944	P = 0.2728
	SITE : adrenal gland			
	TUMOR : pheochromocytoma			
Tumor rate				
Overall rates(a)	8/50(16.0)	4/50(8.0)	9/50(18.0)	7/50(14.0)
Adjusted rates(b)	17.78	10.00	23.68	15.38
Terminal rates(c)	7/44(15.9)	4/40(10.0)	8/36(22.2)	6/39(15.4)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.4493			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.8881			
Fisher Exact test(e)		P = 0.2169	P = 0.4846	P = 0.4854

Group Name	Control	400 ppm	2000 ppm	10000 ppm
	SITE : adrenal gland			
	TUMOR : pheochromocytoma,pheochromocytoma:malignant			
Tumor rate				
Overall rates(a)	9/50(18.0)	4/50(8.0)	10/50(20.0)	7/50(14.0)
Adjusted rates(b)	20.00	10.00	23.81	15.38
Terminal rates(c)	8/44(18.2)	4/40(10.0)	8/36(22.2)	6/39(15.4)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.5452			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.9455			
Fisher Exact test(e)		P = 0.1562	P = 0.4839	P = 0.4234
	SITE : testis			
	TUMOR : interstitial cell tumor			
Tumor rate				
Overall rates(a)	42/50(84.0)	40/50(80.0)	44/50(88.0)	47/50(94.0)
Adjusted rates(b)	88.89	86.05	94.59	100.00
Terminal rates(c)	39/44(88.6)	34/40(85.0)	34/36(94.4)	39/39(100.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.0188*			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.0543			
Fisher Exact test(e)		P = 0.4942	P = 0.4956	P = 0.4053

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

APPENDIX O 2

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

RAT : FEMALE

(2-YEAR STUDY)

Group Name	Control	400 ppm	2000 ppm	10000 ppm
	SITE : spleen TUMOR : mononuclear cell leukemia			
Tumor rate				
Overall rates(a)	4/50(8.0)	5/50(10.0)	8/50(16.0)	7/50(14.0)
Adjusted rates(b)	4.88	6.98	12.20	8.11
Terminal rates(c)	2/41(4.9)	2/40(5.0)	5/41(12.2)	3/37(8.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1657			
Prevalence method(d)	P = 0.4001			
Combined analysis(d)	P = 0.2003			
Cochran-Armitage test(e)	P = 0.4653			
Fisher Exact test(e)		P = 0.4883	P = 0.2169	P = 0.2958
	SITE : oral cavity TUMOR : squamous cell carcinoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	1/50(2.0)	1/50(2.0)	3/50(6.0)
Adjusted rates(b)	0.0	2.50	2.44	8.11
Terminal rates(c)	0/41(0.0)	1/40(2.5)	1/41(2.4)	3/37(8.1)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.0342*			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.0590			
Fisher Exact test(e)		P = 0.4950	P = 0.4950	P = 0.1325
	SITE : oral cavity TUMOR : squamous cell papilloma,squamous cell carcinoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	1/50(2.0)	1/50(2.0)	3/50(6.0)
Adjusted rates(b)	0.0	2.50	2.44	8.11
Terminal rates(c)	0/41(0.0)	1/40(2.5)	1/41(2.4)	3/37(8.1)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.0342*			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.0590			
Fisher Exact test(e)		P = 0.4950	P = 0.4950	P = 0.1325

Group Name	Control	400 ppm	2000 ppm	10000 ppm
	SITE : pituitary gland TUMOR : adenoma			
Tumor rate				
Overall rates(a)	8/50(16.0)	11/50(22.0)	9/50(18.0)	14/50(28.0)
Adjusted rates(b)	17.07	12.50	17.39	27.50
Terminal rates(c)	7/41(17.1)	5/40(12.5)	7/41(17.1)	10/37(27.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.4575			
Prevalence method(d)	P = 0.0586			
Combined analysis(d)	P = 0.0890			
Cochran-Armitage test(e)	P = 0.1679			
Fisher Exact test(e)		P = 0.3526	P = 0.4846	P = 0.1781
	SITE : pituitary gland TUMOR : adenoma,adenocarcinoma			
Tumor rate				
Overall rates(a)	8/50(16.0)	12/50(24.0)	9/50(18.0)	14/50(28.0)
Adjusted rates(b)	17.07	15.00	17.39	27.50
Terminal rates(c)	7/41(17.1)	6/40(15.0)	7/41(17.1)	10/37(27.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.4575			
Prevalence method(d)	P = 0.0766			
Combined analysis(d)	P = 0.1086			
Cochran-Armitage test(e)	P = 0.2103			
Fisher Exact test(e)		P = 0.2846	P = 0.4846	P = 0.1781
	SITE : thyroid TUMOR : C-cell adenoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	7/50(14.0)	8/50(16.0)	5/50(10.0)
Adjusted rates(b)	4.88	15.00	18.18	12.82
Terminal rates(c)	2/41(4.9)	6/40(15.0)	7/41(17.1)	4/37(10.8)
Statistical analysis				
Peto test				
Standard method(d)	P = -------			
Prevalence method(d)	P = 0.4601			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.9733			
Fisher Exact test(e)		P = 0.1045	P = 0.0671	P = 0.2425

Group Name	Control	400 ppm	2000 ppm	10000 ppm
	SITE : thyroid			
	TUMOR : C-cell adenoma,C-cell carcinoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	7/50(14.0)	9/50(18.0)	6/50(12.0)
Adjusted rates(b)	4.88	15.00	20.45	15.38
Terminal rates(c)	2/41(4.9)	6/40(15.0)	8/41(19.5)	5/37(13.5)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.3422			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.7312			
Fisher Exact test(e)		P = 0.1045	P = 0.0427*	P = 0.1606
	SITE : pancreas islet			
	TUMOR : islet cell adenoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	1/50(2.0)	3/50(6.0)	1/50(2.0)
Adjusted rates(b)	0.0	2.50	6.82	2.70
Terminal rates(c)	0/41(0.0)	1/40(2.5)	2/41(4.9)	1/37(2.7)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.4189			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.9199			
Fisher Exact test(e)		P = 0.4950	P = 0.1325	P = 0.4950
	SITE : adrenal gland			
	TUMOR : phenchromocytoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	1/50(2.0)	1/50(2.0)	2/50(4.0)
Adjusted rates(b)	9.76	2.50	2.44	5.13
Terminal rates(c)	4/41(9.8)	1/40(2.5)	1/41(2.4)	1/37(2.7)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.5314			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.8308			
Fisher Exact test(e)		P = 0.1998	P = 0.1998	P = 0.3574

Group Name	Control	400 ppm	2000 ppm	10000 ppm
	SITE : adrenal gland TUMOR : pheochromocytoma,pheochromocytoma:malignant			
Tumor rate				
Overall rates(a)	4/50(8.0)	1/50(2.0)	1/50(2.0)	2/50(4.0)
Adjusted rates(b)	9.76	2.50	2.44	5.13
Terminal rates(c)	4/41(9.8)	1/40(2.5)	1/41(2.4)	1/37(2.7)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.5314			
Combined analysis(d)	P = -------			
Cochran-Armitage test(e)	P = 0.8308			
Fisher Exact test(e)		P = 0.1998	P = 0.1998	P = 0.3574
	SITE : uterus TUMOR : endometrial stromal polyp			
Tumor rate				
Overall rates(a)	5/50(10.0)	5/50(10.0)	10/50(20.0)	4/50(8.0)
Adjusted rates(b)	10.64	10.64	20.45	9.76
Terminal rates(c)	4/41(9.8)	3/40(7.5)	7/41(17.1)	1/37(2.7)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3209			
Prevalence method(d)	P = 0.7098			
Combined analysis(d)	P = 0.7255			
Cochran-Armitage test(e)	P = 0.5056			
Fisher Exact test(e)		P = 0.3710	P = 0.1771	P = 0.4883
	SITE : uterus TUMOR : endometrial stromal polyp,endometrial stromal sarcoma			
Tumor rate				
Overall rates(a)	6/50(12.0)	5/50(10.0)	11/50(22.0)	4/50(8.0)
Adjusted rates(b)	10.87	10.64	20.45	9.76
Terminal rates(c)	4/41(9.8)	3/40(7.5)	7/41(17.1)	1/37(2.7)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.7320			
Prevalence method(d)	P = 0.7167			
Combined analysis(d)	P = 0.7912			
Cochran-Armitage test(e)	P = 0.3892			
Fisher Exact test(e)		P = 0.4872	P = 0.1955	P = 0.3944

Group Name	Control	400 ppm	2000 ppm	10000 ppm
	SITE : mammary gland TUMOR : adenoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	3/50(6.0)	0/50(0.0)	1/50(2.0)
Adjusted rates(b)	2.44	6.67	0.0	2.70
Terminal rates(c)	1/41(2.4)	2/40(5.0)	0/41(0.0)	1/37(2.7)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.6475			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.6309			
Fisher Exact test(e)		P = 0.3235	P = 0.4950	P = 0.2475
	SITE : mammary gland TUMOR : fibroadenoma			
Tumor rate				
Overall rates(a)	9/50(18.0)	10/50(20.0)	8/50(16.0)	9/50(18.0)
Adjusted rates(b)	19.51	25.00	18.18	21.62
Terminal rates(c)	8/41(19.5)	10/40(25.0)	7/41(17.1)	8/37(21.6)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.2456			
Prevalence method(d)	P = 0.5360			
Combined analysis(d)	P = 0.4628			
Cochran-Armitage test(e)	P = 0.9421			
Fisher Exact test(e)		P = 0.4839	P = 0.4846	P = 0.3993
	SITE : mammary gland TUMOR : adenocarcinoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	0/50(0.0)	0/50(0.0)	3/50(6.0)
Adjusted rates(b)	0.0	0.0	0.0	5.41
Terminal rates(c)	0/41(0.0)	0/40(0.0)	0/41(0.0)	2/37(5.4)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1723			
Prevalence method(d)	P = 0.0117* ?			
Combined analysis(d)	P = 0.0017**?			
Cochran-Armitage test(e)	P = 0.0030**			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.1325

Group Name	Control	400 ppm	2000 ppm	10000 ppm
	SITE : mammary gland TUMOR : adenoma,fibroadenoma			
Tumor rate				
Overall rates(a)	10/50(20.0)	12/50(24.0)	8/50(16.0)	10/50(20.0)
Adjusted rates(b)	21.95	27.50	18.18	24.32
Terminal rates(c)	9/41(22.0)	11/40(27.5)	7/41(17.1)	9/37(24.3)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.2456			
Prevalence method(d)	P = 0.5619			
Combined analysis(d)	P = 0.4912			
Cochran-Armitage test(e)	P = 0.8890			
Fisher Exact test(e)		P = 0.4406	P = 0.4300	P = 0.4035
	SITE : mammary gland TUMOR : adenoma,adenocarcinoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	3/50(6.0)	0/50(0.0)	4/50(8.0)
Adjusted rates(b)	2.44	6.67	0.0	8.11
Terminal rates(c)	1/41(2.4)	2/40(5.0)	0/41(0.0)	3/37(8.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1723			
Prevalence method(d)	P = 0.1852			
Combined analysis(d)	P = 0.0832			
Cochran-Armitage test(e)	P = 0.1443			
Fisher Exact test(e)		P = 0.3235	P = 0.4950	P = 0.1998
	SITE : mammary gland TUMOR : adenoma,adenocarcinoma,fibroadenoma			
Tumor rate				
Overall rates(a)	10/50(20.0)	12/50(24.0)	8/50(16.0)	13/50(26.0)
Adjusted rates(b)	21.95	27.50	18.18	29.73
Terminal rates(c)	9/41(22.0)	11/40(27.5)	7/41(17.1)	11/37(29.7)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.0860			
Prevalence method(d)	P = 0.3179			
Combined analysis(d)	P = 0.1829			
Cochran-Armitage test(e)	P = 0.4574			
Fisher Exact test(e)		P = 0.4406	P = 0.4300	P = 0.3703

Group Name	Control	400 ppm	2000 ppm	10000 ppm
	SITE : preputial/clitoral gland TUMOR : adenoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	0/50(0.0)	3/50(6.0)	1/50(2.0)
Adjusted rates(b)	4.88	0.0	2.44	2.70
Terminal rates(c)	2/41(4.9)	0/40(0.0)	1/41(2.4)	1/37(2.7)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5477			
Prevalence method(d)	P = 0.4433			
Combined analysis(d)	P = 0.5405			
Cochran-Armitage test(e)	P = 0.7903			
Fisher Exact test(e)		P = 0.2574	P = 0.4909	P = 0.4926

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

APPENDIX O 3

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

MOSUE : MALE

(2-YEAR STUDY)

Group Name	Control	400 ppm	2000 ppm	10000 ppm
	SITE : lung			
	TUMOR : bronchiolar-alveolar adenoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	3/50(6.0)	4/50(8.0)	3/50(6.0)
Adjusted rates(b)	8.57	6.38	10.53	8.82
Terminal rates(c)	3/35(8.6)	2/42(4.8)	4/38(10.5)	2/33(6.1)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.4681			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.9380			
Fisher Exact test(e)		P = 0.3392	P = 0.4895	P = 0.3392
	SITE : lung			
	TUMOR : bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	7/50(14.0)	3/50(6.0)	5/50(10.0)	2/50(4.0)
Adjusted rates(b)	17.14	7.14	7.89	3.03
Terminal rates(c)	6/35(17.1)	3/42(7.1)	3/38(7.9)	1/33(3.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3806			
Prevalence method(d)	P = 0.9399			
Combined analysis(d)	P = 0.8794			
Cochran-Armitage test(e)	P = 0.1787			
Fisher Exact test(e)		P = 0.1917	P = 0.4062	P = 0.1045
	SITE : lung			
	TUMOR : bronchiolar-alveolar adenoma,bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	10/50(20.0)	6/50(12.0)	9/50(18.0)	5/50(10.0)
Adjusted rates(b)	25.71	12.77	18.42	11.76
Terminal rates(c)	9/35(25.7)	5/42(11.9)	7/38(18.4)	3/33(9.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3806			
Prevalence method(d)	P = 0.8587			
Combined analysis(d)	P = 0.8134			
Cochran-Armitage test(e)	P = 0.2695			
Fisher Exact test(e)		P = 0.2557	P = 0.4839	P = 0.1771

Group Name	Control	400 ppm	2000 ppm	10000 ppm
	SITE : lymph node TUMOR : malignant lymphoma			
Tumor rate				
Overall rates(a)	5/50(10.0)	6/50(12.0)	6/50(12.0)	3/50(6.0)
Adjusted rates(b)	11.43	7.14	7.89	6.06
Terminal rates(c)	4/35(11.4)	3/42(7.1)	3/38(7.9)	2/33(6.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.7299			
Prevalence method(d)	P = 0.6891			
Combined analysis(d)	P = 0.7977			
Cochran-Armitage test(e)	P = 0.3061			
Fisher Exact test(e)		P = 0.4872	P = 0.4872	P = 0.3790
	SITE : spleen TUMOR : hemangiosarcoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	1/50(2.0)	4/50(8.0)	0/50(0.0)
Adjusted rates(b)	0.0	2.38	6.52	0.0
Terminal rates(c)	0/35(0.0)	1/42(2.4)	1/38(2.6)	0/33(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8477			
Prevalence method(d)	P = 0.7584			
Combined analysis(d)	P = 0.9070			
Cochran-Armitage test(e)	P = 0.2068			
Fisher Exact test(e)		P = 0.4926	P = 0.3574	P = 0.2574
	SITE : spleen TUMOR : hemangioma,hemangiosarcoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	1/50(2.0)	5/50(10.0)	0/50(0.0)
Adjusted rates(b)	2.86	2.38	8.70	0.0
Terminal rates(c)	1/35(2.9)	1/42(2.4)	2/38(5.3)	0/33(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8477			
Prevalence method(d)	P = 0.8614			
Combined analysis(d)	P = 0.9439			
Cochran-Armitage test(e)	P = 0.1408			
Fisher Exact test(e)		P = 0.3235	P = 0.3790	P = 0.1325

Group Name	Control	400 ppm	2000 ppm	10000 ppm
	SITE : oral cavity TUMOR : squamous cell papilloma			
Tumor rate				
Overall rates(a)	0/50(0.0)	0/50(0.0)	0/50(0.0)	4/50(8.0)
Adjusted rates(b)	0.0	0.0	0.0	9.76
Terminal rates(c)	0/35(0.0)	0/42(0.0)	0/38(0.0)	3/33(9.1)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.0003**?			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.0006**			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.0688
	SITE : oral cavity TUMOR : squamous cell carcinoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	0/50(0.0)	0/50(0.0)	13/50(26.0)
Adjusted rates(b)	0.0	0.0	0.0	17.07
Terminal rates(c)	0/35(0.0)	0/42(0.0)	0/38(0.0)	4/33(12.1)
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 = 0.5000	P = 0.5000	P = 0.0003**
	SITE : oral cavity TUMOR : squamous cell papilloma,squamous cell carcinoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	0/50(0.0)	0/50(0.0)	16/50(32.0)
Adjusted rates(b)	0.0	0.0	0.0	24.39
Terminal rates(c)	0/35(0.0)	0/42(0.0)	0/38(0.0)	7/33(21.2)
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 = 0.5000	P = 0.5000	P < 0.0001**

Group Name	Control	400 ppm	2000 ppm	10000 ppm
	SITE : esophagus TUMOR : squamous cell carcinoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	0/50(0.0)	0/50(0.0)	7/50(14.0)
Adjusted rates(b)	0.0	0.0	0.0	15.15
Terminal rates(c)	0/35(0.0)	0/42(0.0)	0/38(0.0)	5/33(15.2)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1801			
Prevalence method(d)	P < 0.0001**?			
Combined analysis(d)	P < 0.0001**?			
Cochran-Armitage test(e)	P < 0.0001**			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.0101*
	SITE : stomach TUMOR : squamous cell carcinoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	0/50(0.0)	0/50(0.0)	7/50(14.0)
Adjusted rates(b)	2.86	0.0	0.0	18.18
Terminal rates(c)	1/35(2.9)	0/42(0.0)	0/38(0.0)	6/33(18.2)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1821			
Prevalence method(d)	P = 0.0001**			
Combined analysis(d)	P < 0.0001**			
Cochran-Armitage test(e)	P = 0.0001**			
Fisher Exact test(e)		P = 0.4950	P = 0.4950	P = 0.0430*
	SITE : stomach TUMOR : squamous cell papilloma,squamous cell carcinoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	0/50(0.0)	0/50(0.0)	9/50(18.0)
Adjusted rates(b)	2.86	0.0	0.0	24.24
Terminal rates(c)	1/35(2.9)	0/42(0.0)	0/38(0.0)	8/33(24.2)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1821			
Prevalence method(d)	P < 0.0001**			
Combined analysis(d)	P < 0.0001**			
Cochran-Armitage test(e)	P < 0.0001**			
Fisher Exact test(e)		P = 0.4950	P = 0.4950	P = 0.0150*

Group Name	Control	400 ppm	2000 ppm	10000 ppm
	SITE : liver TUMOR : hepatocellular adenoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	6/50(12.0)	4/50(8.0)	3/50(6.0)
Adjusted rates(b)	5.56	14.29	10.00	6.06
Terminal rates(c)	1/35(2.9)	6/42(14.3)	3/38(7.9)	2/33(6.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1705			
Prevalence method(d)	P = 0.7427			
Combined analysis(d)	P = 0.5537			
Cochran-Armitage test(e)	P = 0.6862			
Fisher Exact test(e)		P = 0.1606	P = 0.3574	P = 0.4909
	SITE : liver TUMOR : hemangiosarcoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	5/50(10.0)	5/50(10.0)	4/50(8.0)
Adjusted rates(b)	9.09	9.52	7.89	9.09
Terminal rates(c)	2/35(5.7)	4/42(9.5)	3/38(7.9)	3/33(9.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3769			
Prevalence method(d)	P = 0.6249			
Combined analysis(d)	P = 0.5650			
Cochran-Armitage test(e)	P = 0.8168			
Fisher Exact test(e)		P = 0.4883	P = 0.4883	P = 0.3579
	SITE : liver TUMOR : hepatocellular carcinoma			
Tumor rate				
Overall rates(a)	13/50(26.0)	10/50(20.0)	9/50(18.0)	4/50(8.0)
Adjusted rates(b)	31.43	23.26	23.68	11.76
Terminal rates(c)	11/35(31.4)	9/42(21.4)	9/38(23.7)	3/33(9.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 1.0000 ?			
Prevalence method(d)	P = 0.9783			
Combined analysis(d)	P = 0.9837			
Cochran-Armitage test(e)	P = 0.0243*			
Fisher Exact test(e)		P = 0.3703	P = 0.2965	P = 0.0371*

Group Name	Control	400 ppm	2000 ppm	10000 ppm
	SITE : liver			
	TUMOR : hemangioma,hemangiosarcoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	5/50(10.0)	5/50(10.0)	4/50(8.0)
Adjusted rates(b)	9.09	9.52	7.89	9.09
Terminal rates(c)	2/35(5.7)	4/42(9.5)	3/38(7.9)	3/33(9.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3769			
Prevalence method(d)	P = 0.6249			
Combined analysis(d)	P = 0.5650			
Cochran-Armitage test(e)	P = 0.8168			
Fisher Exact test(e)		P = 0.4883	P = 0.4883	P = 0.3579
	SITE : liver			
	TUMOR : hepatocellular adenoma,hepatocellular carcinoma			
Tumor rate				
Overall rates(a)	14/50(28.0)	13/50(26.0)	13/50(26.0)	7/50(14.0)
Adjusted rates(b)	34.29	30.23	32.50	17.65
Terminal rates(c)	12/35(34.3)	12/42(28.6)	12/38(31.6)	5/33(15.2)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.2361			
Prevalence method(d)	P = 0.9639			
Combined analysis(d)	P = 0.9400			
Cochran-Armitage test(e)	P = 0.0671			
Fisher Exact test(e)		P = 0.4815	P = 0.4815	P = 0.1246
	SITE : Harderian gland			
	TUMOR : adenoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	4/50(8.0)	6/50(12.0)	2/50(4.0)
Adjusted rates(b)	8.57	8.51	14.29	6.06
Terminal rates(c)	3/35(8.6)	3/42(7.1)	4/38(10.5)	2/33(6.1)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.7794			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.3929			
Fisher Exact test(e)		P = 0.4895	P = 0.2728	P = 0.4909

Group Name	Control	400 ppm	2000 ppm	10000 ppm
	SITE : Harderian gland			
	TUMOR : adenoma,adenocarcinoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	5/50(10.0)	6/50(12.0)	2/50(4.0)
Adjusted rates(b)	11.43	10.64	14.29	6.06
Terminal rates(c)	4/35(11.4)	3/42(7.1)	4/38(10.5)	2/33(6.1)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.8679			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.2421			
Fisher Exact test(e)		P = 0.4883	P = 0.3944	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

Group Name	Control	400 ppm	2000 ppm	10000 ppm
	SITE : ALL SITE TUMOR : hemangioma			
Tumor rate				
Overall rates(a)	3/50(6.0)	0/50(0.0)	2/50(4.0)	0/50(0.0)
Adjusted rates(b)	6.82	0.0	5.26	0.0
Terminal rates(c)	1/35(2.9)	0/42(0.0)	2/38(5.3)	0/33(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.9182			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.1988			
Fisher Exact test(e)		P = 0.1325	P = 0.4909	P = 0.1325
	SITE : ALL SITE TUMOR : malignant lymphoma			
Tumor rate				
Overall rates(a)	6/50(12.0)	7/50(14.0)	8/50(16.0)	3/50(6.0)
Adjusted rates(b)	14.29	9.52	13.16	6.06
Terminal rates(c)	5/35(14.3)	4/42(9.5)	5/38(13.2)	2/33(6.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.7299			
Prevalence method(d)	P = 0.8266			
Combined analysis(d)	P = 0.8800			
Cochran-Armitage test(e)	P = 0.1694			
Fisher Exact test(e)		P = 0.4863	P = 0.4157	P = 0.2728

Group Name	Control	400 ppm	2000 ppm	10000 ppm
	SITE : ALL SITE TUMOR : hemangiosarcoma			
Tumor rate				
Overall rates(a)	6/50(12.0)	7/50(14.0)	7/50(14.0)	4/50(8.0)
Adjusted rates(b)	8.57	11.90	7.89	9.09
Terminal rates(c)	3/35(8.6)	5/42(11.9)	3/38(7.9)	3/33(9.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8258			
Prevalence method(d)	P = 0.5365			
Combined analysis(d)	P = 0.7672			
Cochran-Armitage test(e)	P = 0.3448			
Fisher Exact test(e)		P = 0.4863	P = 0.4863	P = 0.3944

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

APPENDIX O 4

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

MOSUE :FEMALE

(2-YEAR STUDY)

Group Name	Control	400 ppm	2000 ppm	10000 ppm
	SITE : lung TUMOR : bronchiolar-alveolar adenoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	3/50(6.0)	1/50(2.0)	2/49(4.1)
Adjusted rates(b)	2.56	11.11	4.00	8.70
Terminal rates(c)	0/26(0.0)	3/27(11.1)	1/25(4.0)	2/23(8.7)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.3856			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.8680			
Fisher Exact test(e)		P = 0.3235	P = 0.2475	P = 0.5000
	SITE : lung TUMOR : bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	3/50(6.0)	1/50(2.0)	1/49(2.0)
Adjusted rates(b)	4.26	5.41	4.00	4.35
Terminal rates(c)	1/26(3.8)	1/27(3.7)	1/25(4.0)	1/23(4.3)
Statistical analysis				
Peto test				
Standard method(d)	P = 1.0000 ?			
Prevalence method(d)	P = 0.6925			
Combined analysis(d)	P = 0.7720			
Cochran-Armitage test(e)	P = 0.4309			
Fisher Exact test(e)		P = 0.4909	P = 0.4926	P = 0.4851
	SITE : lung TUMOR : bronchiolar-alveolar adenoma,bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	6/50(12.0)	2/50(4.0)	3/49(6.1)
Adjusted rates(b)	6.38	14.81	8.00	13.04
Terminal rates(c)	1/26(3.8)	4/27(14.8)	2/25(8.0)	3/23(13.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 1.0000 ?			
Prevalence method(d)	P = 0.5740			
Combined analysis(d)	P = 0.6444			
Cochran-Armitage test(e)	P = 0.6544			
Fisher Exact test(e)		P = 0.2728	P = 0.4909	P = 0.3483

Group Name	Control	400 ppm	2000 ppm	10000 ppm
	SITE : lymph node TUMOR : malignant lymphoma			
Tumor rate				
Overall rates(a)	11/50(22.0)	10/50(20.0)	17/50(34.0)	10/49(20.4)
Adjusted rates(b)	15.38	16.67	24.00	8.70
Terminal rates(c)	4/26(15.4)	4/27(14.8)	6/25(24.0)	2/23(8.7)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3556			
Prevalence method(d)	P = 0.8661			
Combined analysis(d)	P = 0.6221			
Cochran-Armitage test(e)	P = 0.7075			
Fisher Exact test(e)		P = 0.4833	P = 0.2154	P = 0.4662
	SITE : spleen TUMOR : malignant lymphoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	5/50(10.0)	1/50(2.0)	1/49(2.0)
Adjusted rates(b)	0.0	7.41	4.00	4.35
Terminal rates(c)	0/26(0.0)	2/27(7.4)	1/25(4.0)	1/23(4.3)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8889			
Prevalence method(d)	P = 0.3952			
Combined analysis(d)	P = 0.7198			
Cochran-Armitage test(e)	P = 0.4769			
Fisher Exact test(e)		P = 0.0360*	P = 0.4950	P = 0.5000
	SITE : oral cavity TUMOR : squamous cell papilloma			
Tumor rate				
Overall rates(a)	0/50(0.0)	0/50(0.0)	0/50(0.0)	3/49(6.1)
Adjusted rates(b)	0.0	0.0	0.0	12.50
Terminal rates(c)	0/26(0.0)	0/27(0.0)	0/25(0.0)	2/23(8.7)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.0014**?			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.0027**			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.1287

Group Name	Control	400 ppm	2000 ppm	10000 ppm
	SITE : oral cavity TUMOR : squamous cell carcinoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	0/50(0.0)	0/50(0.0)	15/49(30.6)
Adjusted rates(b)	0.0	0.0	0.0	35.48
Terminal rates(c)	0/26(0.0)	0/27(0.0)	0/25(0.0)	8/23(34.8)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.0004**?			
Prevalence method(d)	P < 0.0001**?			
Combined analysis(d)	P < 0.0001**?			
Cochran-Armitage test(e)	P < 0.0001**			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.0001**
	SITE : oral cavity TUMOR : squamous cell papilloma,squamous cell carcinoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	0/50(0.0)	0/50(0.0)	18/49(36.7)
Adjusted rates(b)	0.0	0.0	0.0	45.83
Terminal rates(c)	0/26(0.0)	0/27(0.0)	0/25(0.0)	10/23(43.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.0004**?			
Prevalence method(d)	P < 0.0001**?			
Combined analysis(d)	P < 0.0001**?			
Cochran-Armitage test(e)	P < 0.0001**			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P < 0.0001**
	SITE : stomach TUMOR : squamous cell carcinoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	0/50(0.0)	0/50(0.0)	3/49(6.1)
Adjusted rates(b)	0.0	0.0	0.0	4.35
Terminal rates(c)	0/26(0.0)	0/27(0.0)	0/25(0.0)	1/23(4.3)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.0146* ?			
Prevalence method(d)	P = 0.1561			
Combined analysis(d)	P = 0.0019**?			
Cochran-Armitage test(e)	P = 0.0027**			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.1287

Group Name	Control	400 ppm	2000 ppm	10000 ppm
	SITE : stomach			
	TUMOR : squamous cell papilloma,squamous cell carcinoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	0/50(0.0)	0/50(0.0)	4/49(8.2)
Adjusted rates(b)	0.0	0.0	0.0	8.70
Terminal rates(c)	0/26(0.0)	0/27(0.0)	0/25(0.0)	2/23(8.7)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.0146* ?			
Prevalence method(d)	P = 0.0103* ?			
Combined analysis(d)	P = 0.0002**?			
Cochran-Armitage test(e)	P = 0.0005**			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.0662
	SITE : liver			
	TUMOR : hepatocellular adenoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	1/50(2.0)	4/50(8.0)	0/49(0.0)
Adjusted rates(b)	11.54	3.70	15.38	0.0
Terminal rates(c)	3/26(11.5)	1/27(3.7)	3/25(12.0)	0/23(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.9402			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.1492			
Fisher Exact test(e)		P = 0.3235	P = 0.4895	P = 0.1364
	SITE : liver			
	TUMOR : hemangiosarcoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	3/50(6.0)	0/50(0.0)	1/49(2.0)
Adjusted rates(b)	9.38	6.45	0.0	3.23
Terminal rates(c)	2/26(7.7)	1/27(3.7)	0/25(0.0)	0/23(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 1.0000 ?			
Prevalence method(d)	P = 0.7676			
Combined analysis(d)	P = 0.8309			
Cochran-Armitage test(e)	P = 0.3279			
Fisher Exact test(e)		P = 0.3392	P = 0.1325	P = 0.3312

Group Name	Control	400 ppm	2000 ppm	10000 ppm
	SITE : liver TUMOR : hemangioma,hemangiosarcoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	3/50(6.0)	0/50(0.0)	2/49(4.1)
Adjusted rates(b)	9.38	6.45	0.0	6.45
Terminal rates(c)	2/26(7.7)	1/27(3.7)	0/25(0.0)	1/23(4.3)
Statistical analysis				
Peto test				
Standard method(d)	P = 1.0000 ?			
Prevalence method(d)	P = 0.4983			
Combined analysis(d)	P = 0.5906			
Cochran-Armitage test(e)	P = 0.7663			
Fisher Exact test(e)		P = 0.3392	P = 0.1325	P = 0.4816
	SITE : liver TUMOR : hepatocellular adenoma,hepatocellular carcinoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	1/50(2.0)	4/50(8.0)	0/49(0.0)
Adjusted rates(b)	15.38	3.70	15.38	0.0
Terminal rates(c)	4/26(15.4)	1/27(3.7)	3/25(12.0)	0/23(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.9635			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.1047			
Fisher Exact test(e)		P = 0.1998	P = 0.3579	P = 0.0715
	SITE : pituitary gland TUMOR : adenoma			
Tumor rate				
Overall rates(a)	10/50(20.0)	6/49(12.2)	8/49(16.3)	7/49(14.3)
Adjusted rates(b)	22.86	18.52	29.17	30.43
Terminal rates(c)	5/26(19.2)	5/27(18.5)	7/24(29.2)	7/23(30.4)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8435			
Prevalence method(d)	P = 0.4523			
Combined analysis(d)	P = 0.5960			
Cochran-Armitage test(e)	P = 0.7275			
Fisher Exact test(e)		P = 0.2683	P = 0.4459	P = 0.3564

Group Name	Control	400 ppm	2000 ppm	10000 ppm
	SITE : pituitary gland TUMOR : adenoma,adenocarcinoma			
Tumor rate				
Overall rates(a)	10/50(20.0)	6/49(12.2)	8/49(16.3)	8/49(16.3)
Adjusted rates(b)	22.86	18.52	29.17	30.43
Terminal rates(c)	5/26(19.2)	5/27(18.5)	7/24(29.2)	7/23(30.4)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.4700			
Prevalence method(d)	P = 0.4523			
Combined analysis(d)	P = 0.4612			
Cochran-Armitage test(e)	P = 0.9887			
Fisher Exact test(e)		P = 0.2683	P = 0.4459	P = 0.4459
	SITE : uterus TUMOR : histiocytic sarcoma			
Tumor rate				
Overall rates(a)	10/50(20.0)	11/50(22.0)	8/50(16.0)	10/48(20.8)
Adjusted rates(b)	7.69	10.81	4.00	23.08
Terminal rates(c)	2/26(7.7)	2/27(7.4)	1/25(4.0)	5/23(21.7)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8738			
Prevalence method(d)	P = 0.0656			
Combined analysis(d)	P = 0.5100			
Cochran-Armitage test(e)	P = 0.9213			
Fisher Exact test(e)		P = 0.4833	P = 0.4300	P = 0.4361
	SITE : mammary gland TUMOR : adenoma,adenocarcinoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	1/50(2.0)	3/50(6.0)	0/49(0.0)
Adjusted rates(b)	3.85	0.0	8.00	0.0
Terminal rates(c)	1/26(3.8)	0/27(0.0)	2/25(8.0)	0/23(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8447			
Prevalence method(d)	P = 0.7509			
Combined analysis(d)	P = 0.8959			
Cochran-Armitage test(e)	P = 0.2178			
Fisher Exact test(e)		P = 0.4926	P = 0.4909	P = 0.2626

Group Name	Control	400 ppm	2000 ppm	10000 ppm
	SITE : Harderian gland TUMOR : adenoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	4/50(8.0)	3/50(6.0)	0/49(0.0)
Adjusted rates(b)	0.0	12.90	12.00	0.0
Terminal rates(c)	0/26(0.0)	3/27(11.1)	3/25(12.0)	0/23(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.9268			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.1862			
Fisher Exact test(e)		P = 0.0688	P = 0.1325	P = 0.5000
	SITE : Harderian gland TUMOR : adenoma,adenocarcinoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	4/50(8.0)	3/50(6.0)	1/49(2.0)
Adjusted rates(b)	0.0	12.90	12.00	4.35
Terminal rates(c)	0/26(0.0)	3/27(11.1)	3/25(12.0)	1/23(4.3)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.7267			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.5357			
Fisher Exact test(e)		P = 0.0688	P = 0.1325	P = 0.5000

(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	400 ppm	2000 ppm	10000 ppm
	SITE : ALL SITE TUMOR : malignant lymphoma			
Tumor rate				
Overall rates(a)	11/50(22.0)	16/50(32.0)	18/50(36.0)	11/49(22.4)
Adjusted rates(b)	15.38	24.14	28.00	13.04
Terminal rates(c)	4/26(15.4)	6/27(22.2)	7/25(28.0)	3/23(13.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5370			
Prevalence method(d)	P = 0.8304			
Combined analysis(d)	P = 0.7371			
Cochran-Armitage test(e)	P = 0.4517			
Fisher Exact test(e)		P = 0.2625	P = 0.1751	P = 0.4239
	SITE : ALL SITE TUMOR : hemangiosarcoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	5/50(10.0)	1/50(2.0)	1/49(2.0)
Adjusted rates(b)	12.50	9.68	0.0	3.23
Terminal rates(c)	2/26(7.7)	2/27(7.4)	0/25(0.0)	0/23(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.7972			
Prevalence method(d)	P = 0.8907			
Combined analysis(d)	P = 0.9444			
Cochran-Armitage test(e)	P = 0.1294			
Fisher Exact test(e)		P = 0.4883	P = 0.1998	P = 0.2063

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

APPENDIX P 1

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

RAT: MALE : DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0162
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 6	400 ppm 10	2000 ppm 14	10000 ppm 11
[Respiratory system]						
nasal cavit			< 6>	<10>	<14>	<11>
	leukemic cell infiltration		0	0	0	2
lung			< 6>	<10>	<14>	<11>
	leukemic cell infiltration		1	3	3	3
	metastasis:liver tumor		0	0	1	0
	metastasis:subcutis tumor		1	1	0	1
	metastasis:skin/appendage tumor		0	1	0	0
[Hematopoietic system]						
bone marrow			< 6>	<10>	<14>	<11>
	leukemic cell infiltration		0	2	2	3
	metastasis:liver tumor		0	0	1	0
lymph node			< 6>	<10>	<14>	<11>
	leukemic cell infiltration		1	0	0	1
	metastasis:liver tumor		0	0	1	0
	metastasis:skin/appendage tumor		0	1	0	0
spleen			< 6>	<10>	<14>	<11>
	metastasis:liver tumor		0	0	1	0
[Circulatory system]						
heart			< 6>	<10>	<14>	<11>
	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	Control	400 ppm	2000 ppm	10000 ppm
		No. of Animals on Study	6	10	14	11
[Digestive system]						
tongue			< 6>	<10>	<14>	<10>
	leukemic cell infiltration		0	0	0	1
	metastasis:oral cavity tumor		0	0	0	1
stomach			< 6>	<10>	<14>	<11>
	leukemic cell infiltration		0	1	0	0
large intes			< 6>	<10>	<14>	<11>
	leukemic cell infiltration		0	1	0	0
liver			< 6>	<10>	<14>	<11>
	leukemic cell infiltration		1	3	3	3
	metastasis:subcutis tumor		0	1	0	0
pancreas			< 6>	<10>	<14>	<11>
	leukemic cell infiltration		1	1	0	1
	metastasis:liver tumor		0	0	1	0
[Urinary system]						
kidney			< 6>	<10>	<14>	<11>
	leukemic cell infiltration		0	0	3	3
	metastasis:liver tumor		0	0	1	0
[Endocrine system]						
pituitary			< 6>	<10>	<14>	<11>
	leukemic cell infiltration		1	0	0	0
adrenal			< 6>	<10>	<14>	<11>
	leukemic cell infiltration		1	1	2	2

< 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	400 ppm	2000 ppm	10000 ppm
			6	10	14	11
[Endocrine system]						
adrenal			< 6>	<10>	<14>	<11>
	metastasis:liver tumor		0	0	1	0
[Reproductive system]						
epididymis			< 6>	<10>	<14>	<11>
	leukemic cell infiltration		0	0	0	1
semin ves			< 6>	<10>	<14>	<11>
	leukemic cell infiltration		0	1	0	0
prostate			< 6>	<10>	<14>	<11>
	leukemic cell infiltration		0	1	0	1
[Special sense organs/appandage]						
eye			< 6>	<10>	<14>	<11>
	leukemic cell infiltration		0	0	0	1
Harder gl			< 6>	<10>	<14>	<11>
	leukemic cell infiltration		0	0	0	1
[Musculoskeletal system]						
muscle			< 6>	<10>	<14>	<11>
	metastasis:liver tumor		0	0	1	0
[Body cavities]						
pleura			< 6>	<10>	<14>	<11>
	metastasis:liver tumor		0	0	1	0

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

STUDY NO. : 0162
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 6	400 ppm 10	2000 ppm 14	10000 ppm 11
[Body cavities]						
mediastinum			< 6>	<10>	<14>	<11>
	metastasis:liver tumor		0	0	1	0
peritoneum			< 6>	<10>	<14>	<11>
	metastasis:liver tumor		0	0	1	0

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

APPENDIX P 2

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

RAT: FEMALE : DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

Organ	Findings	Group Name / No. of Animals on Study	Control 9	400 ppm 10	2000 ppm 9	10000 ppm 13
[Integumentary system/appandage]						
skin/app			< 9>	<10>	< 9>	<13>
	leukemic cell infiltration		1	0	0	0
	metastasis:subcutis tumor		1	0	0	0
subcutis			< 9>	<10>	< 9>	<13>
	leukemic cell infiltration		1	0	0	0
[Respiratory system]						
nasal cavit			< 9>	<10>	< 9>	<13>
	leukemic cell infiltration		1	0	0	0
trachea			< 9>	<10>	< 9>	<13>
	metastasis:subcutis tumor		1	0	0	0
lung			< 9>	<10>	< 9>	<13>
	leukemic cell infiltration		2	3	3	4
	metastasis:liver tumor		0	1	0	1
	metastasis:uterus tumor		0	0	1	0
[Hematopoietic system]						
bone marrow			< 9>	<10>	< 9>	<13>
	leukemic cell infiltration		1	2	2	1
	metastasis:liver tumor		0	0	0	1
lymph node			< 9>	<10>	< 9>	<13>
	leukemic cell infiltration		2	1	1	3
	metastasis:subcutis tumor		1	0	0	0

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

Organ	Findings	Group Name / No. of Animals on Study	Control 9	400 ppm 10	2000 ppm 9	10000 ppm 13
[Hematopoietic system]						
lymph node		< 9>	<10>	< 9>	<13>	
	metastasis:bone marrow tumor	0	0	1	0	
spleen		< 9>	<10>	< 9>	<13>	
	metastasis:liver tumor	0	0	0	1	
	metastasis:bone marrow tumor	0	0	1	0	
[Circulatory system]						
heart		< 9>	<10>	< 9>	<13>	
	leukemic cell infiltration	0	0	0	1	
	metastasis:liver tumor	0	1	0	0	
[Digestive system]						
salivary gl		< 9>	<10>	< 9>	<13>	
	leukemic cell infiltration	1	0	0	0	
stomach		< 9>	<10>	< 9>	<13>	
	leukemic cell infiltration	1	0	0	0	
	metastasis:subcutis tumor	1	0	0	0	
liver		< 9>	<10>	< 9>	<13>	
	leukemic cell infiltration	2	3	3	4	
	metastasis:uterus tumor	0	0	1	0	
	metastasis:bone marrow tumor	0	0	1	0	
pancreas		< 9>	<10>	< 9>	<13>	
	leukemic cell infiltration	1	2	0	0	

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

STUDY NO. : 0162
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name / No. of Animals on Study	Control	400 ppm	2000 ppm	10000 ppm
			9	10	9	13
[Digestive system]						
pancreas			< 9>	<10>	< 9>	<13>
	metastasis:uterus tumor		0	0	1	0
	metastasis:subcutis tumor		1	0	0	0
[Urinary system]						
kidney			< 9>	<10>	< 9>	<13>
	leukemic cell infiltration		1	1	0	3
	metastasis:uterus tumor		0	0	1	0
urin bladd			< 9>	<10>	< 9>	<13>
	leukemic cell infiltration		0	0	0	1
[Endocrine system]						
adrenal			< 9>	<10>	< 9>	<13>
	leukemic cell infiltration		1	0	1	0
[Reproductive system]						
ovary			< 9>	<10>	< 9>	<13>
	leukemic cell infiltration		1	1	1	0
	metastasis:uterus tumor		0	1	0	0
uterus			< 9>	<10>	< 9>	<13>
	leukemic cell infiltration		1	0	0	1
vagina			< 9>	<10>	< 9>	<13>
	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	400 ppm	2000 ppm	10000 ppm
			9	10	9	13
[Special sense organs/appandage]						
eye			< 9>	<10>	< 9>	<13>
	leukemic cell infiltration		1	0	0	0
Harder gl			< 9>	<10>	< 9>	<13>
	leukemic cell infiltration		1	1	0	0
[Musculoskeletal system]						
muscle			< 9>	<10>	< 9>	<13>
	leukemic cell infiltration		1	0	0	0
[Body cavities]						
peritoneum			< 9>	<10>	< 9>	<13>
	metastasis:uterus tumor		1	0	0	0
	metastasis:subcutis tumor		1	0	0	0
retroperit			< 9>	<10>	< 9>	<13>
	metastasis:uterus tumor		0	0	1	0
mesenterium			< 9>	<10>	< 9>	<13>
	metastasis:uterus tumor		1	0	0	0

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

APPENDIX P 3

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

RAT: MALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

Organ	Findings	Group Name / No. of Animals on Study	Control	400 ppm	2000 ppm	10000 ppm
			41	40	41	37
[Respiratory system]						
lung			<41>	<40>	<41>	<37>
	leukemic cell infiltration		1	0	0	0
	metastasis:adrenal tumor		0	0	0	1
	metastasis:thyroid tumor		0	0	1	0
[Hematopoietic system]						
lymph node			<41>	<40>	<41>	<37>
	metastasis:zymbal gland tumor		0	0	1	0
spleen			<41>	<40>	<41>	<37>
	metastasis:bone marrow tumor		1	0	0	0
[Digestive system]						
salivary gl			<41>	<40>	<41>	<37>
	metastasis:zymbal gland tumor		0	0	1	0
liver			<41>	<40>	<41>	<37>
	leukemic cell infiltration		2	1	5	2
[Urinary system]						
kidney			<41>	<40>	<41>	<37>
	leukemic cell infiltration		0	0	2	0
[Nervous system]						
brain			<41>	<40>	<41>	<37>
	metastasis:pituitary tumor		0	1	0	0

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

APPENDIX P 4

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

RAT: FEMALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0162
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control	400 ppm	2000 ppm	10000 ppm
		No. of Animals on Study	44	40	36	39
[Respiratory system]						
trachea			<44>	<40>	<36>	<39>
	metastasis:thyroid tumor		1	0	0	0
lung			<44>	<40>	<36>	<39>
	leukemic cell infiltration		1	2	1	1
	metastasis:thyroid tumor		1	0	0	0
	metastasis:skin/appendage tumor		0	0	0	1
[Hematopoietic system]						
bone marrow			<44>	<40>	<36>	<39>
	leukemic cell infiltration		0	0	0	1
lymph node			<44>	<40>	<36>	<39>
	leukemic cell infiltration		0	1	1	0
	metastasis:thyroid tumor		1	0	0	0
[Digestive system]						
liver			<44>	<40>	<36>	<39>
	leukemic cell infiltration		1	2	4	1
[Urinary system]						
kidney			<44>	<40>	<36>	<39>
	leukemic cell infiltration		0	0	2	1
	metastasis:skin/appendage tumor		0	0	0	1
[Endocrine system]						
adrenal			<44>	<40>	<36>	<39>
	leukemic cell infiltration		0	1	0	0

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

APPENDIX P 5

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

MOUSE: MALE : DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

Organ	Findings	Group Name	Control	400 ppm	2000 ppm	10000 ppm
		No. of Animals on Study	15	8	12	17
[Respiratory system]						
nasal cavit			<15>	< 8>	<12>	<17>
	metastasis:periferal nerve tumor		1	0	0	0
lung			<15>	< 8>	<12>	<17>
	leukemic cell infiltration		0	2	2	0
	metastasis:liver tumor		0	1	0	1
	metastasis:spleen tumor		0	0	1	0
	metastasis:oral cavity tumor		0	0	0	2
	metastasis:esophagus tumor		0	0	0	1
[Hematopoietic system]						
bone marrow			<15>	< 8>	<12>	<17>
	metastasis:liver tumor		0	0	0	1
lymph node			<15>	< 8>	<12>	<17>
	metastasis:liver tumor		0	1	0	0
	metastasis:oral cavity tumor		0	0	0	2
	metastasis:epididymis tumor		0	1	0	0
spleen			<15>	< 8>	<12>	<17>
	leukemic cell infiltration		1	2	3	1
	metastasis:liver tumor		0	1	0	0
[Circulatory system]						
heart			<15>	< 8>	<12>	<17>
	leukemic cell infiltration		1	0	1	0

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

Organ	Findings	Group Name / No. of Animals on Study	Control 15	400 ppm 8	2000 ppm 12	10000 ppm 17
[Circulatory system]						
heart			<15>	< 8>	<12>	<17>
	metastasis:liver tumor		0	0	0	1
[Digestive system]						
oral cavity			<15>	< 8>	<12>	<17>
	leukemic cell infiltration		0	0	1	0
tongue			<15>	< 8>	<12>	<17>
	leukemic cell infiltration		0	0	1	0
salivary gl			<15>	< 8>	<12>	<17>
	leukemic cell infiltration		0	0	2	0
stomach			<15>	< 8>	<12>	<17>
	leukemic cell infiltration		0	1	2	0
	metastasis:epididymis tumor		0	1	0	0
	metastasis:seminal vesicle tumor		0	0	1	0
small intes			<15>	< 8>	<12>	<17>
	metastasis:epididymis tumor		0	1	0	0
large intes			<15>	< 8>	<12>	<17>
	leukemic cell infiltration		0	0	1	0
liver			<15>	< 8>	<12>	<17>
	leukemic cell infiltration		0	2	3	0
	metastasis:epididymis tumor		0	1	0	0
gall bladd			<15>	< 8>	<12>	<17>
	leukemic cell infiltration		0	1	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	400 ppm	2000 ppm	10000 ppm
			15	8	12	17
[Digestive system]						
pancreas			<15>	< 8>	<12>	<17>
	leukemic cell infiltration		0	1	2	0
	metastasis:epididymis tumor		0	1	0	0
[Urinary system]						
kidney			<15>	< 8>	<12>	<17>
	leukemic cell infiltration		0	1	2	0
	metastasis:liver tumor		0	0	0	1
	metastasis:lung tumor		0	0	1	0
urin bladd			<15>	< 8>	<12>	<17>
	leukemic cell infiltration		0	2	1	0
	metastasis:epididymis tumor		1	1	0	0
[Endocrine system]						
pituitary			<15>	< 8>	<12>	<17>
	metastasis:periferal nerve tumor		1	0	0	0
adrenal			<15>	< 8>	<12>	<17>
	leukemic cell infiltration		0	0	1	0
[Reproductive system]						
testis			<15>	< 8>	<12>	<17>
	leukemic cell infiltration		0	1	0	0
epididymis			<15>	< 8>	<12>	<17>
	leukemic cell infiltration		0	1	1	0

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

Organ	Findings	Group Name / No. of Animals on Study	Control	400 ppm	2000 ppm	10000 ppm
			15	8	12	17
[Reproductive system]						
semin ves			<15>	< 8>	<12>	<17>
	leukemic cell infiltration		0	2	0	0
	metastasis:epididymis tumor		0	1	0	0
prostate			<15>	< 8>	<12>	<17>
	leukemic cell infiltration		0	1	2	0
	metastasis:epididymis tumor		1	1	0	1
[Nervous system]						
brain			<15>	< 8>	<12>	<17>
	leukemic cell infiltration		0	0	1	0
	metastasis:pituitary tumor		1	0	0	0
[Special sense organs/appandage]						
Harder gl			<15>	< 8>	<12>	<17>
	leukemic cell infiltration		0	0	2	0
	metastasis:pituitary tumor		1	0	0	0
[Musculoskeletal system]						
muscle			<15>	< 8>	<12>	<17>
	leukemic cell infiltration		0	0	1	0
	metastasis:epididymis tumor		0	1	0	0
[Body cavities]						
mediastinum			<15>	< 8>	<12>	<17>
	metastasis:liver tumor		0	0	0	1

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

Organ	Findings	Group Name / No. of Animals on Study	Control	400 ppm	2000 ppm	10000 ppm
			15	8	12	17
[Body cavities]						
peritoneum			<15>	< 8>	<12>	<17>
	metastasis:seminal vesicle tumor		0	0	1	0

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

APPENDIX P 6

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

MOUSE: FEMALE : DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

Organ	Findings	Control	400 ppm	2000 ppm	10000 ppm
Group Name		Control	400 ppm	2000 ppm	10000 ppm
No. of Animals on Study		24	23	25	26
[Integumentary system/appandage]					
skin/app		<24>	<23>	<25>	<26>
	leukemic cell infiltration	0	1	0	0
subcutis		<24>	<23>	<25>	<26>
	leukemic cell infiltration	0	2	0	0
[Respiratory system]					
nasal cavit		<24>	<23>	<25>	<26>
	leukemic cell infiltration	1	1	1	1
	metastasis:uterus tumor	3	2	1	0
larynx		<24>	<23>	<25>	<26>
	leukemic cell infiltration	0	0	1	0
trachea		<24>	<23>	<25>	<26>
	leukemic cell infiltration	0	0	0	1
lung		<24>	<23>	<25>	<26>
	leukemic cell infiltration	6	6	8	6
	metastasis:liver tumor	0	0	1	0
	metastasis:uterus tumor	6	6	2	3
	metastasis:oral cavity tumor	0	0	0	2
[Hematopoietic system]					
bone marrow		<24>	<23>	<25>	<26>
	leukemic cell infiltration	2	5	3	1
	metastasis:uterus tumor	1	1	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	400 ppm	2000 ppm	10000 ppm
			24	23	25	26
[Hematopoietic system]						
lymph node			<24>	<23>	<25>	<26>
	leukemic cell infiltration		0	2	0	0
	metastasis:liver tumor		0	0	1	0
	metastasis:uterus tumor		1	2	2	0
	metastasis:stomach tumor		0	0	0	1
	metastasis:oral cavity tumor		0	0	0	2
spleen			<24>	<23>	<25>	<26>
	leukemic cell infiltration		6	6	6	7
	metastasis:liver tumor		0	0	1	0
	metastasis:uterus tumor		1	1	0	0
[Circulatory system]						
heart			<24>	<23>	<25>	<26>
	leukemic cell infiltration		2	5	0	3
	metastasis:uterus tumor		1	0	0	0
[Digestive system]						
oral cavity			<24>	<23>	<25>	<26>
	leukemic cell infiltration		1	4	0	1
	metastasis:uterus tumor		0	1	2	0
tongue			<24>	<23>	<25>	<26>
	leukemic cell infiltration		0	3	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	400 ppm	2000 ppm	10000 ppm
			24	23	25	26
[Digestive system]						
salivary gl			<24>	<23>	<25>	<26>
	leukemic cell infiltration		3	6	5	4
	metastasis:oral cavity tumor		0	0	0	1
stomach			<24>	<23>	<25>	<26>
	leukemic cell infiltration		3	4	2	2
	metastasis:uterus tumor		1	0	2	0
small intes			<24>	<23>	<25>	<26>
	metastasis:uterus tumor		0	1	1	0
liver			<24>	<23>	<25>	<26>
	leukemic cell infiltration		7	8	8	8
	metastasis:uterus tumor		7	7	6	5
	metastasis:subcutis tumor		0	1	0	0
	metastasis:stomach tumor		0	0	0	1
pancreas			<24>	<23>	<25>	<26>
	leukemic cell infiltration		2	3	5	6
	metastasis:uterus tumor		2	0	2	0
	metastasis:stomach tumor		0	0	0	1
[Urinary system]						
kidney			<24>	<23>	<25>	<26>
	leukemic cell infiltration		5	5	2	6
	metastasis:uterus tumor		1	2	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 24	400 ppm 23	2000 ppm 25	10000 ppm 26
[Urinary system]						
kidney			<24>	<23>	<25>	<26>
	metastasis:stomach tumor		0	0	0	1
urin bladd			<24>	<23>	<25>	<25>
	leukemic cell infiltration		4	6	5	2
	metastasis:uterus tumor		1	0	1	0
[Endocrine system]						
pituitary			<24>	<23>	<25>	<26>
	leukemic cell infiltration		1	1	1	0
thyroid			<24>	<23>	<25>	<26>
	leukemic cell infiltration		0	2	0	0
adrenal			<24>	<23>	<25>	<26>
	leukemic cell infiltration		4	4	2	1
	metastasis:uterus tumor		1	0	0	1
[Reproductive system]						
ovary			<24>	<23>	<25>	<26>
	leukemic cell infiltration		6	7	7	5
	metastasis:uterus tumor		6	5	6	5
uterus			<24>	<23>	<25>	<26>
	leukemic cell infiltration		4	6	4	4
vagina			<24>	<23>	<25>	<26>
	leukemic cell infiltration		2	0	0	1

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

Organ	Findings	Control	400 ppm	2000 ppm	10000 ppm
	Group Name	Control	400 ppm	2000 ppm	10000 ppm
	No. of Animals on Study	24	23	25	26
[Reproductive system]					
mammary gl		<24>	<23>	<25>	<26>
	leukemic cell infiltration	1	2	3	2
[Nervous system]					
brain		<24>	<23>	<25>	<26>
	leukemic cell infiltration	1	0	1	1
spinal cord		<24>	<23>	<25>	<26>
	leukemic cell infiltration	1	0	0	1
[Special sense organs/appandage]					
eye		<24>	<23>	<25>	<26>
	leukemic cell infiltration	0	1	1	3
Harder gl		<24>	<23>	<25>	<26>
	leukemic cell infiltration	3	3	2	2
[Musculoskelotal system]					
muscle		<24>	<23>	<25>	<26>
	leukemic cell infiltration	0	3	0	3
[Body cavities]					
peritoneum		<24>	<23>	<25>	<26>
	leukemic cell infiltration	0	1	1	0
	metastasis:uterus tumor	1	2	3	0

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

APPENDIX P 7

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

MOUSE: MALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0163
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control	400 ppm	2000 ppm	10000 ppm
		No. of Animals on Study	35	42	38	33
[Integumentary system/appandage]						
subcutis			<35>	<42>	<38>	<33>
	leukemic cell infiltration		0	1	0	0
[Respiratory system]						
nasal cavit			<35>	<42>	<38>	<33>
	leukemic cell infiltration		1	0	1	0
lung			<35>	<42>	<38>	<33>
	leukemic cell infiltration		0	1	2	0
	metastasis:liver tumor		1	0	3	0
[Hematopoietic system]						
bone marrow			<35>	<42>	<38>	<32>
	leukemic cell infiltration		0	0	2	0
lymph node			<35>	<42>	<38>	<33>
	leukemic cell infiltration		1	0	0	0
spleen			<35>	<42>	<38>	<33>
	leukemic cell infiltration		3	2	2	3
[Circulatory system]						
heart			<35>	<42>	<38>	<33>
	leukemic cell infiltration		0	0	1	0
[Digestive system]						
oral cavity			<35>	<42>	<38>	<33>
	leukemic cell infiltration		0	0	1	0

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

STUDY NO. : 0163
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control	400 ppm	2000 ppm	10000 ppm
		No. of Animals on Study	35	42	38	33
[Digestive system]						
salivary gl			<35>	<42>	<38>	<33>
	leukemic cell infiltration		0	0	2	0
stomach			<35>	<42>	<38>	<33>
	leukemic cell infiltration		0	0	2	0
liver			<35>	<42>	<38>	<33>
	leukemic cell infiltration		1	0	3	1
	metastasis:stomach tumor		0	0	0	1
pancreas			<35>	<42>	<38>	<33>
	leukemic cell infiltration		1	1	2	1
[Urinary system]						
kidney			<35>	<42>	<38>	<33>
	leukemic cell infiltration		1	0	2	0
urin bladd			<35>	<42>	<38>	<33>
	leukemic cell infiltration		0	0	2	0
[Reproductive system]						
epididymis			<35>	<42>	<38>	<33>
	leukemic cell infiltration		0	0	2	0
semin ves			<35>	<42>	<38>	<33>
	leukemic cell infiltration		0	0	1	0
prostate			<35>	<42>	<38>	<33>
	leukemic cell infiltration		0	0	2	0
[Musculoskeletal system]						
muscle			<35>	<42>	<38>	<33>
	leukemic cell infiltration		0	0	1	0

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

APPENDIX P 8

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

MOUSE: FEMALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0163
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 26	400 ppm 27	2000 ppm 25	10000 ppm 23
[Integumentary system/appandage]						
skin/app			<26>	<27>	<25>	<23>
	leukemic cell infiltration		0	0	1	0
[Respiratory system]						
nasal cavit			<26>	<27>	<25>	<23>
	leukemic cell infiltration		0	1	0	0
	metastasis:uterus tumor		0	0	0	1
lung			<26>	<27>	<25>	<23>
	leukemic cell infiltration		1	4	1	1
	metastasis:liver tumor		0	1	0	0
[Hematopoietic system]						
bone marrow			<26>	<27>	<25>	<23>
	leukemic cell infiltration		1	2	1	0
lymph node			<26>	<27>	<25>	<23>
	metastasis:uterus tumor		0	0	0	1
spleen			<26>	<27>	<25>	<23>
	leukemic cell infiltration		4	3	3	2
[Circulatory system]						
heart			<26>	<27>	<25>	<23>
	leukemic cell infiltration		0	2	1	0
[Digestive system]						
oral cavity			<26>	<27>	<25>	<23>
	leukemic cell infiltration		0	2	2	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 26	400 ppm 27	2000 ppm 25	10000 ppm 23
[Digestive system]						
tongue			<26>	<27>	<25>	<23>
	leukemic cell infiltration		0	1	1	0
salivary gl			<26>	<27>	<25>	<23>
	leukemic cell infiltration		0	3	0	0
stomach			<26>	<27>	<25>	<23>
	leukemic cell infiltration		0	1	1	0
small intes			<26>	<27>	<25>	<23>
	leukemic cell infiltration		0	1	0	0
liver			<26>	<27>	<25>	<23>
	leukemic cell infiltration		1	3	2	0
	metastasis:uterus tumor		1	1	0	2
pancreas			<26>	<27>	<25>	<23>
	leukemic cell infiltration		0	2	0	0
	metastasis:uterus tumor		1	0	0	0
[Urinary system]						
kidney			<26>	<27>	<25>	<23>
	leukemic cell infiltration		2	1	1	0
urin bladd			<26>	<27>	<25>	<23>
	leukemic cell infiltration		1	2	1	0
[Endocrine system]						
adrenal			<26>	<27>	<25>	<23>
	leukemic cell infiltration		0	1	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 26	400 ppm 27	2000 ppm 25	10000 ppm 23
[Reproductive system]						
ovary			<26>	<27>	<25>	<23>
	leukemic cell infiltration		1	3	2	0
	metastasis:uterus tumor		1	0	0	2
uterus			<26>	<27>	<25>	<23>
	leukemic cell infiltration		0	2	0	0
mammary gl			<26>	<27>	<25>	<23>
	leukemic cell infiltration		0	0	1	0
[Special sense organs/appandage]						
eye			<26>	<27>	<25>	<23>
	leukemic cell infiltration		0	1	1	0
Harder gl			<26>	<27>	<25>	<23>
	leukemic cell infiltration		0	1	1	0
[Musculoskeletal system]						
muscle			<26>	<27>	<25>	<23>
	leukemic cell infiltration		0	2	1	0
[Body cavities]						
mediastinum			<26>	<27>	<25>	<23>
	leukemic cell infiltration		0	1	0	0
peritoneum			<26>	<27>	<25>	<23>
	metastasis:uterus tumor		1	0	0	1

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

APPENDIX Q 1

IDENTITY OF VINYL ACETATE

(2-YEAR STUDY)

IDENTITY OF VINYL ACETATE(TWO-YEAR STUDIES)

A. Test Substance Lot No. SAG5318

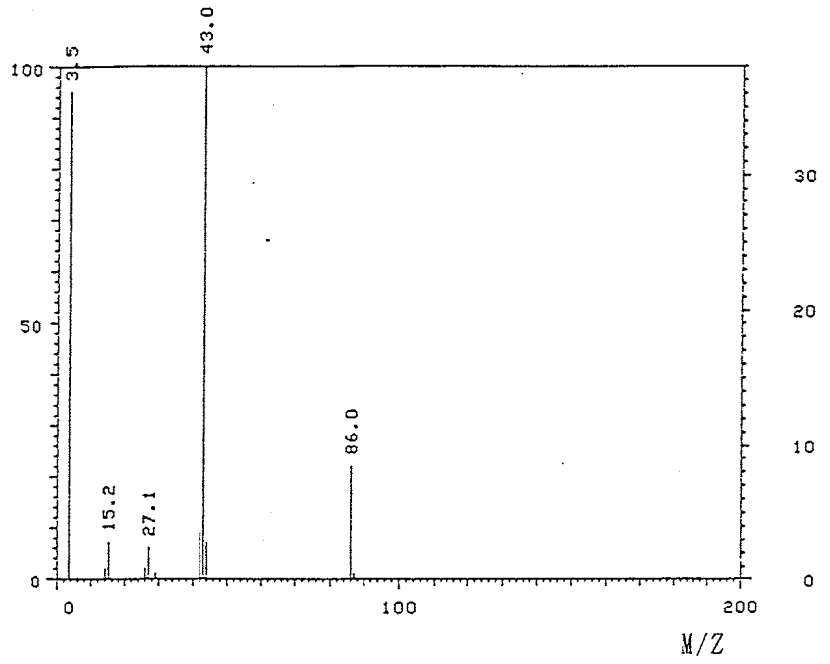
1. Spectral data

(1) Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI(Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Results:

Determined Molecular and Fragment Peak(M/Z)	Literature Value* Molecular and Fragment Peak(M/Z)
86.0	86
43.0	43
27.1	27
15.2	15

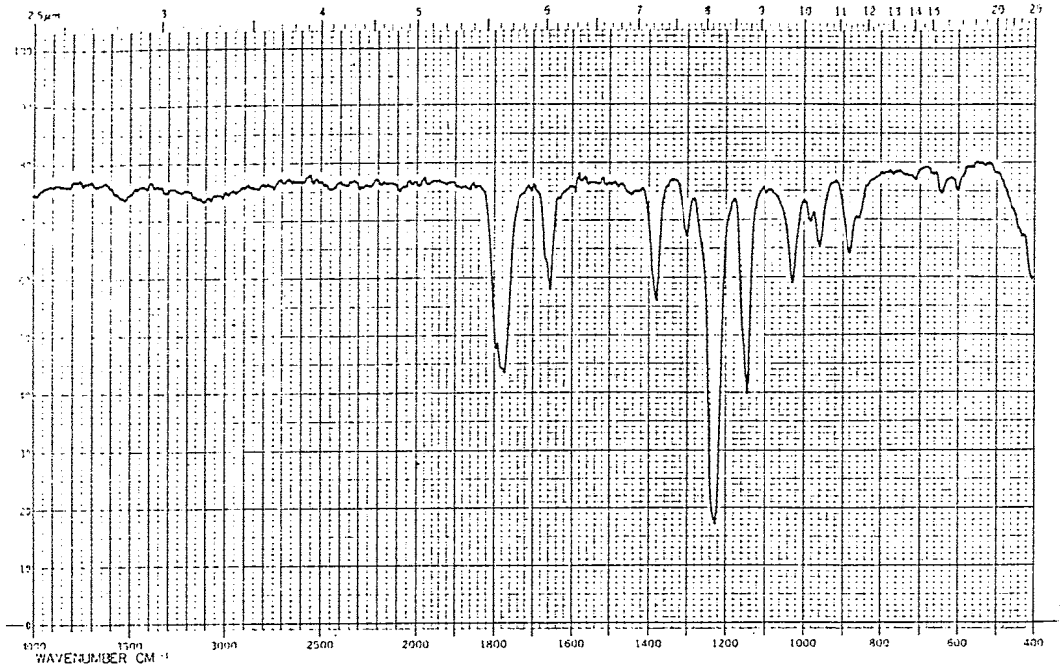
(*EPA/NIH Mass Spectral Data Base (1978) V. 1, p. 41.)

(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})
	840～ 920	830～ 910
	940～1000	930～ 990
	1000～1060	1000～1060
	1120～1180	1110～1170
	1200～1260	1180～1260
	1280～1320	1280～1320
	1360～1410	1340～1400
	1630～1690	1630～1680
	1740～1820	1730～1820

(*Performed by WAKO PURE CHEMICAL INSUSTRIES, LTD.)

2. Conclusions: The result of the mass spectrum and the infrared spectrum agreed with the literature values.
Consequently, the test substance was identified as Vinyl acetate.

B. Test Substance Lot No. LKP4386

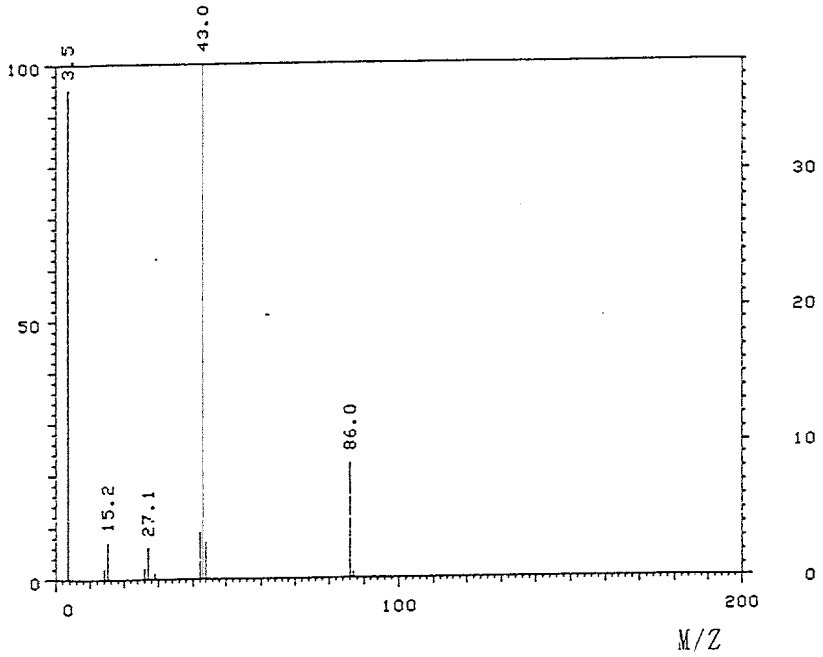
1. Spectral data

(1) Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI(Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

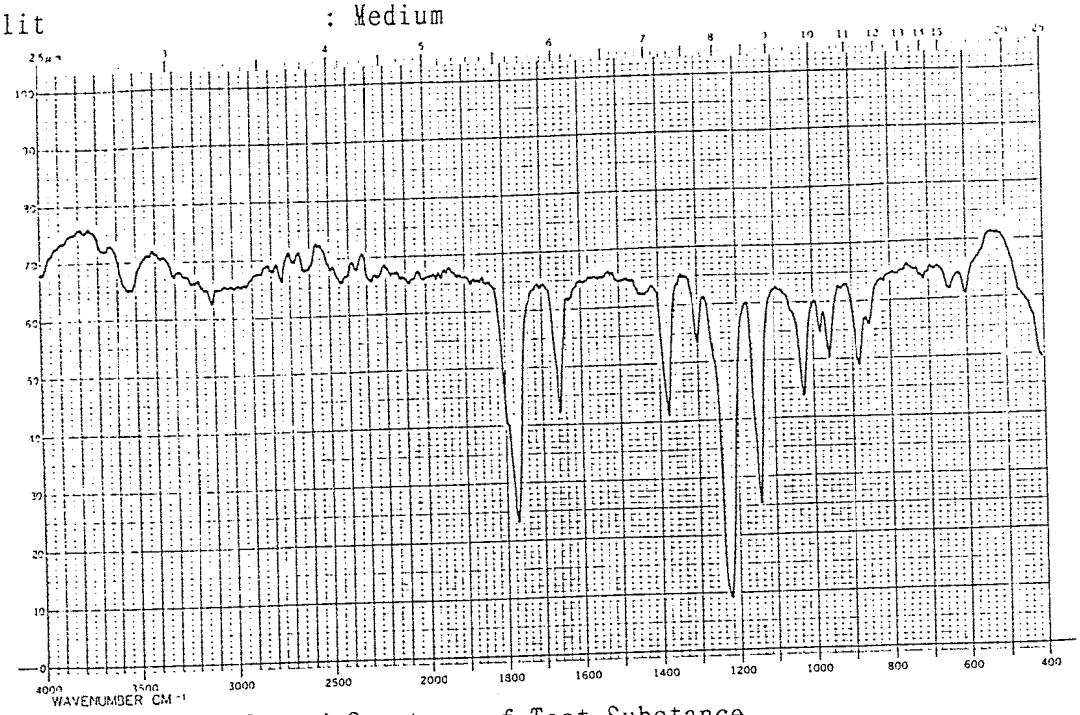
Results:	Determined Molecular and Fragment Peak(M/Z)	Literature Value* Molecular and Fragment Peak(M/Z)
	86.0	86
	43.0	43
	27.1	27
	15.2	15
		(*EPA/NIH Mass Spectral Data Base (1978) V. 1, p. 41.)

(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})
	840～ 920	830～ 910
	940～1000	930～ 990
	1000～1060	1000～1060
	1120～1180	1110～1170
	1200～1260	1180～1260
	1280～1320	1280～1320
	1360～1410	1340～1400
	1630～1690	1630～1680
	1740～1820	1730～1820

(*Performed by WAKO PURE CHEMICAL INSUSTRIES, LTD.)

2. Conclusions: The result of the mass spectrum and the infrared spectrum agreed with the literature values.
Consequently, the test substance was identified as Vinyl acetate.

C. Test Substance Lot No. WDP4895

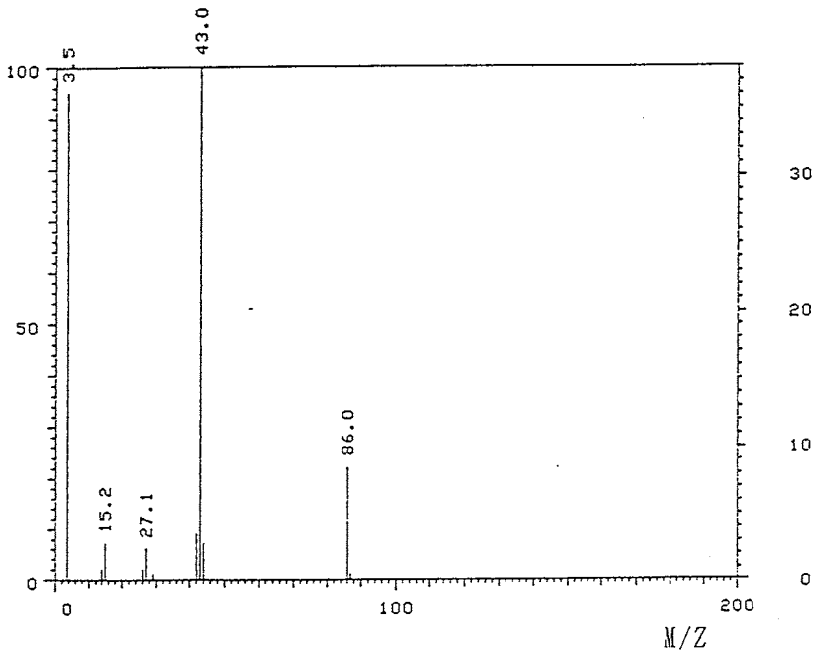
I. Spectral data

(1) Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI(Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

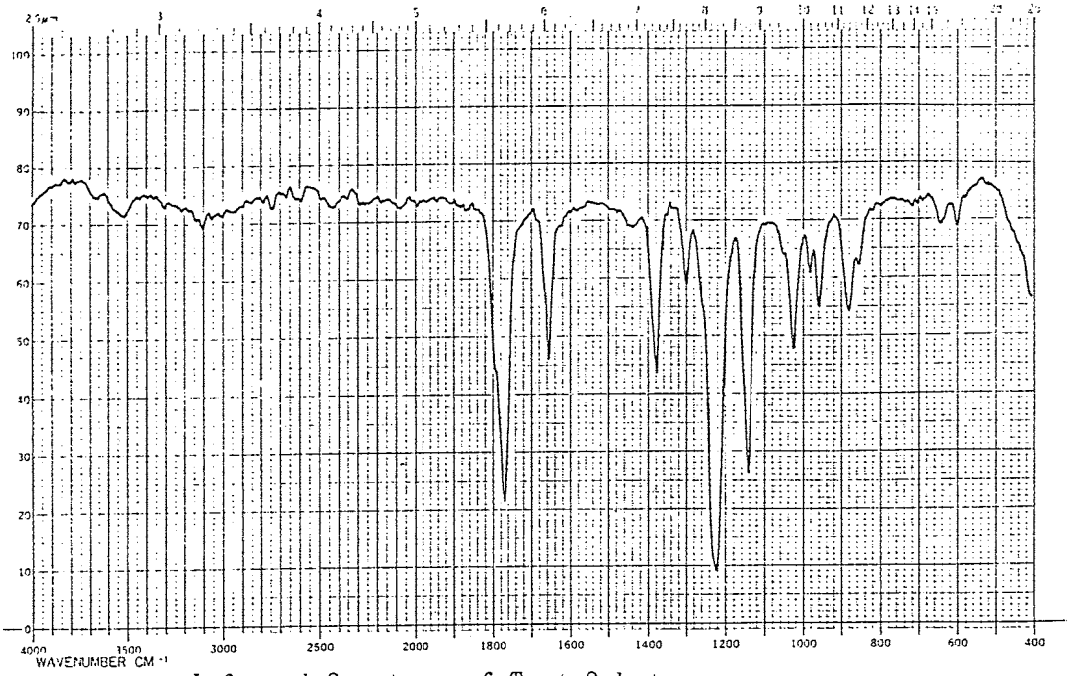
Results:	Determined Molecular and Fragment Peak(M/Z)	Literature Value* Molecular and Fragment Peak(M/Z)
	86.0	86
	43.0	43
	27.1	27
	15.2	15
		(*EPA/NIH Mass Spectral Data Base (1978) V. 1, p. 41.)

(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})
840～ 920	830～ 910
940～1000	930～ 990
1000～1060	1000～1060
1120～1180	1110～1170
1200～1260	1180～1260
1280～1320	1280～1320
1360～1410	1340～1400
1630～1690	1630～1680
1740～1820	1730～1820

(*Performed by WAKO PURE CHEMICAL INSUSTRIES, LTD.)

2. Conclusions: The result of the mass spectrum and the infrared spectrum agreed with the literature values.
Consequently, the test substance was identified as Vinyl acetate.

D. Test Substance Lot No. WDP4894

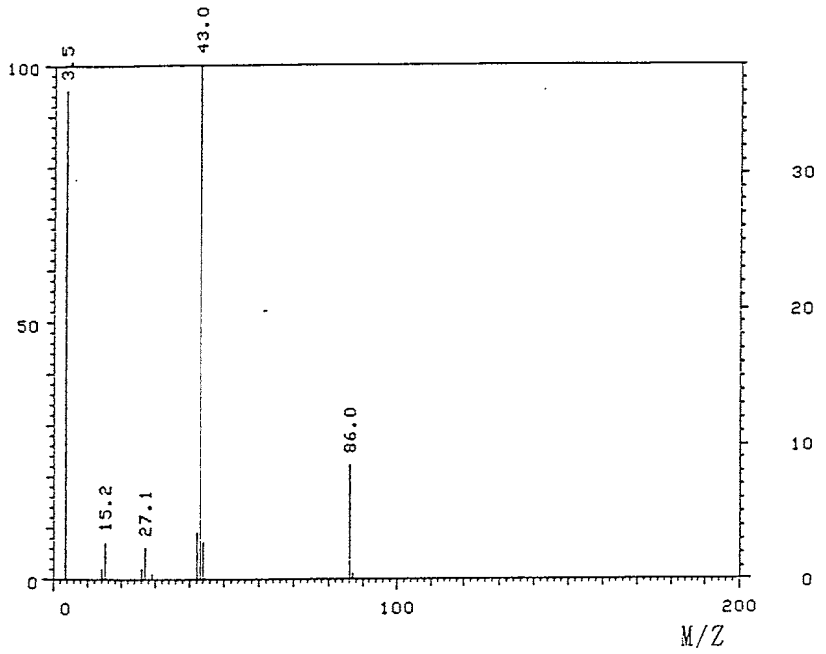
1. Spectral data

(1) Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI(Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

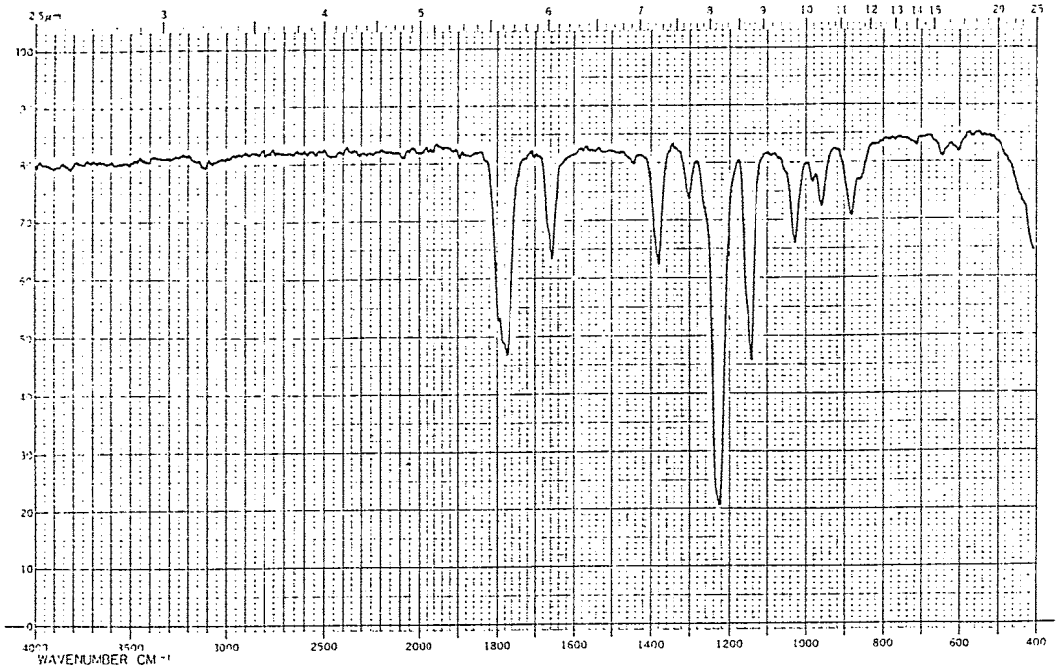
Results: Determined Molecular and Fragment Peak(M/Z)	Literature Value* Molecular and Fragment Peak(M/Z)
86.0	86
43.0	43
27.1	27
15.2	15
	(*EPA/NIH Mass Spectral Data Base (1978) V. 1, p. 41.)

(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})
	840～ 920	830～ 910
	940～1000	930～ 990
	1000～1060	1000～1060
	1120～1180	1110～1170
	1200～1260	1180～1260
	1280～1320	1280～1320
	1360～1410	1340～1400
	1630～1690	1630～1680
	1740～1820	1730～1820

(*Performed by WAKO PURE CHEMICAL INSUSTRIES, LTD.)

2. Conclusions: The result of the mass spectrum and the infrared spectrum agreed with the literature values.
Consequently, the test substance was identified as Vinyl acetate.

E. Test Substance Lot No. WDP4895

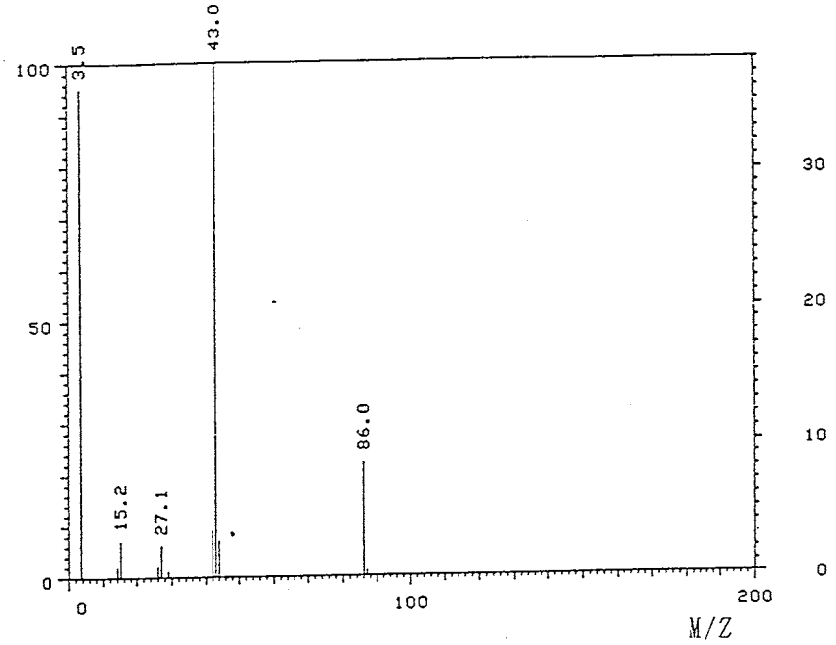
1. Spectral data

(1) Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI(Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Results: Determined Molecular and Fragment Peak(M/Z)	Literature Value* Molecular and Fragment Peak(M/Z)
86.0	86
43.0	43
27.1	27
15.2	15
	(*EPA/NIH Mass Spectral Data Base (1978) V. 1, p. 41.)

(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})
840～ 920	830～ 910
940～1000	930～ 990
1000～1060	1000～1060
1120～1180	1110～1170
1200～1260	1180～1260
1280～1320	1280～1320
1360～1410	1340～1400
1630～1690	1630～1680
1740～1820	1730～1820

(*Performed by WAKO PURE CHEMICAL INSUSTRIES, LTD.)

2. Conclusions: The result of the mass spectrum and the infrared spectrum agreed with the literature values.
Consequently, the test substance was identified as Vinyl acetate.

F. Test Substance Lot No. WDM5220

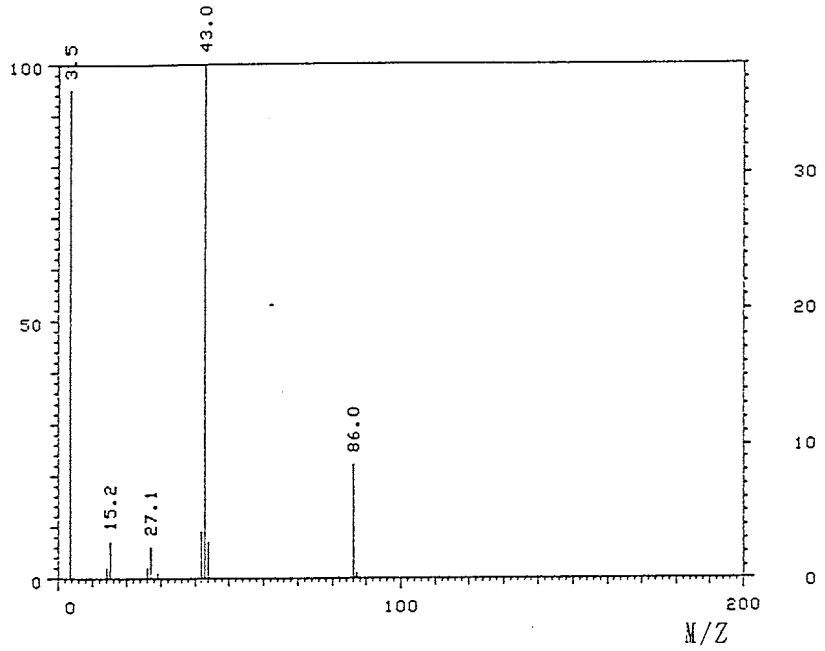
1. Spectral data

(1) Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI(Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

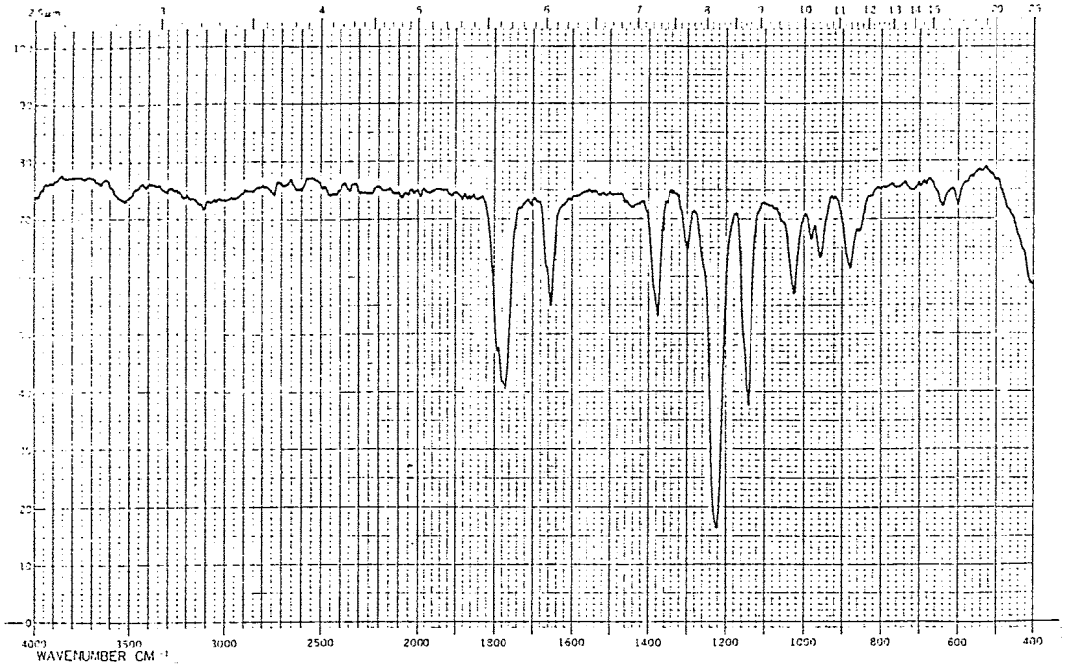
Results:	Determined Molecular and Fragment Peak(M/Z)	Literature Value* Molecular and Fragment Peak(M/Z)
	86.0	86
	43.0	43
	27.1	27
	15.2	15
		(*EPA/NIH Mass Spectral Data Base (1978) V. 1, p. 41.)

(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})
	840～ 920	830～ 910
	940～1000	930～ 990
	1000～1060	1000～1060
	1120～1180	1110～1170
	1200～1260	1180～1260
	1280～1320	1280～1320
	1360～1410	1340～1400
	1630～1690	1630～1680
	1740～1820	1730～1820

(*Performed by WAKO PURE CHEMICAL INSUSTRIES, LTD.)

2. Conclusions: The result of the mass spectrum and the infrared spectrum agreed with the literature values.
Consequently, the test substance was identified as Vinyl acetate.

APPENDIX Q 2

STABILITY OF VINYL ACETATE IN DRIKING WATER

(2-YEAR STUDY)

STABILITY OF VINYL ACETATE(TWO-YEAR STUDIES)

A. Test Substance Lot No. SAG5318

1. Sample storage: This lot was used from 1991. 3. 26 to 1991. 7. 19. Test substance was stored in the dark at 5°C.

2. Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium

Results : The result of the infrared spectrum did not change when before and after studies.

1991. 02. 15(date analyzed) Wave Number(cm^{-1})	1991. 07. 19(date analyzed) Wave Number(cm^{-1})
840～ 920	840～ 920
940～1000	940～1000
1000～1060	1000～1060
1120～1180	1120～1180
1200～1260	1200～1260
1280～1320	1280～1320
1360～1410	1360～1410
1630～1690	1630～1690
1740～1820	1740～1820

3. Gas Chromatography

Instrument : Hewlett Packard 5890A Gass Chromatograph

Column : Methyl Silicone(0.2mmϕ × 38m)

Column Temperature : 40°C

Flow Rate : 1 ml/min

Detector : FID(Flame Ionization Detector)

Injection Volume : 1 μl

Results: Chromatogram indicated one major peak analyzed at 1991.2.15 and one major peak analyzed at 1991.7.19. The new trace impurity peak in the test substance analyzed at 1991.7.19 was not detected.

Date	Retention Time(min)	AREA
1991.02.15 (date analyzed)	3.308	227600
1991.07.19 (date analyzed)	3.307	224462

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

B. Test Substance Lot No. LKP4386

1. Sample storage: This lot was used from 1991.7.19 to 1992.3.31. Test substance was stored in the dark at 5°C.

2. Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium

Results : The result of the infrared spectrum did not change when before and after studies.

1991.07.19(date analyzed) Wave Number(cm^{-1})	1992.03.31(date analyzed) Wave Number(cm^{-1})
840～ 920	840～ 920
940～1000	940～1000
1000～1060	1000～1060
1120～1180	1120～1180
1200～1260	1200～1260
1280～1320	1280～1320
1360～1410	1360～1410
1630～1690	1630～1690
1740～1820	1740～1820

3. Gas Chromatography

Instrument : Hewlett Packard 5890A Gass Chromatograph

Column : Methyl Silicone(0.2mmϕ × 38m)

Column Temperature : 40°C

Flow Rate : 1 ml/min

Detector : FID(Flame Ionization Detector)

Injection Volume : 1 μl

Results: Chromatogram indicated one major peak analyzed at 1991.7.19 and one major peak analyzed at 1992.3.31. The new trace impurity peak in the test substance analyzed at 1992.3.31 was not detected.

Date	Retention Time(min)	AREA
1991.07.19 (date analyzed)	3.3	227380
1992.03.31 (date analyzed)	3.3	227349

4. Conclusions: The results indicated that the test substance did not change when stored in the dark at 5°C during this period(for about 9 months).

C. Test Substance Lot No. WDP4895

1. Sample storage: This lot was used from 1992.3.31 to 1992.9.15. Test substance was stored in the dark at 5°C.

2. Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium

Results : The result of the infrared spectrum did not change when before and after studies.

1992.03.27(date analyzed) Wave Number(cm^{-1})	1992.09.15(date analyzed) Wave Number(cm^{-1})
840～ 920	840～ 920
940～1000	940～1000
1000～1060	1000～1060
1120～1180	1120～1180
1200～1260	1200～1260
1280～1320	1280～1320
1360～1410	1360～1410
1630～1690	1630～1690
1740～1820	1740～1820

3. Gas Chromatography

Instrument : Hewlett Packard 5890A Gass Chromatograph

Column : Methyl Silicone(0.2mmϕ × 38m)

Column Temperature : 40°C

Flow Rate : 1 ml/min

Detector : FID(Flame Ionization Detector)

Injection Volume : 1 μl

Results: Chromatogram indicated one major peak analyzed at 1992.3.27 and one major peak analyzed at 1992.9.15. The new trace impurity peak in the test substance analyzed at 1992.9.15 was not detected.

Date	Retention Time(min)	AREA
1992.03.27 (date analyzed)	3.305	230886
1992.09.15 (date analyzed)	3.307	230247

4. Conclusions: The results indicated that the test substance did not change when stored in the dark at 5°C during this period(for about 6 months).

D. Test Substance Lot No. WDP4894

1. Sample storage: This lot was used from 1992.9.15 to 1992.12.22. Test substance was stored in the dark at 5°C.

2. Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium

Results : The result of the infrared spectrum did not change when before and after studies.

1992.09.01(date analyzed) Wave Number(cm^{-1})	1992.12.22(date analyzed) Wave Number(cm^{-1})
840～ 920	840～ 920
940～1000	940～1000
1000～1060	1000～1060
1120～1180	1120～1180
1200～1260	1200～1260
1280～1320	1280～1320
1360～1410	1360～1410
1630～1690	1630～1690
1740～1820	1740～1820

3. Gas Chromatography

Instrument : Hewlett Packard 5890A Gass Chromatograph

Column : Methyl Silicone(0.2mmϕ × 38m)

Column Temperature : 40°C

Flow Rate : 1 ml/min

Detector : FID(Flame Ionization Detector)

Injection Volume : 1 μl

Results: Chromatogram indicated one major peak analyzed at 1992.9.1 and one major peak analyzed at 1992.12.22. The new trace impurity peak in the test substance analyzed at 1992.12.22 was not detected.

Date	Retention Time(min)	AREA
1992.09.01 (date analyzed)	3.3	230304
1992.12.22 (date analyzed)	3.3	229084

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

E. Test Substance Lot No. WDP4895

1. Sample storage: This lot was used from 1992.12.22 to 1993.4.6. Test substance was stored in the dark at 5°C.

2. Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium

Results : The result of the infrared spectrum did not change when before and after studies.

1992.09.15(date analyzed) Wave Number(cm^{-1})	1993.04.06(date analyzed) Wave Number(cm^{-1})
840～ 920	840～ 920
940～1000	940～1000
1000～1060	1000～1060
1120～1180	1120～1180
1200～1260	1200～1260
1280～1320	1280～1320
1360～1410	1360～1410
1630～1690	1630～1690
1740～1820	1740～1820

3. Gas Chromatography

Instrument : Hewlett Packard 5890A Gass Chromatograph

Column : Methyl Silicone(0.2mmϕ × 38m)

Column Temperature : 40°C

Flow Rate : 1 ml/min

Detector : FID(Flame Ionization Detector)

Injection Volume : 1 μl

Results: Chromatogram indicated one major peak analyzed at 1992.9.1 and one major peak analyzed at 1993.4.6. The new trace impurity peak in the test substance analyzed at 1993.4.6 was not detected.

Date	Retention Time(min)	AREA
1992.09.01 (date analyzed)	3.3	230613
1993.04.06 (date analyzed)	3.3	230757

4. Conclusions: The results indicated that the test substance did not change when stored in the dark at 5°C during this period(for about 7 months).

F. Test Substance Lot No. WDM5220

1. Sample storage: This lot was used from 1993.4.6 to 1993.4.16. Test substance was stored in the dark at 5°C.

2. Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium

Results : The result of the infrared spectrum did not change when before and after studies.

1993.03.01(date analyzed) Wave Number(cm^{-1})	1993.04.16(date analyzed) Wave Number(cm^{-1})
840～ 920	840～ 920
940～1000	940～1000
1000～1060	1000～1060
1120～1180	1120～1180
1200～1260	1200～1260
1280～1320	1280～1320
1360～1410	1360～1410
1630～1690	1630～1690
1740～1820	1740～1820

3. Gas Chromatography

Instrument : Hewlett Packard 5890A Gass Chromatograph

Column : Methyl Silicone(0.2mmϕ × 38m)

Column Temperature : 40°C

Flow Rate : 1 ml/min

Detector : FID(Flame Ionization Detector)

Injection Volume : 1 μl

Results: Chromatogram indicated one major peak analyzed at 1993.3.1 and one major peak analyzed at 1993.4.16. The new trace impurity peak in the test substance analyzed at 1993.4.16 was not detected.

Date	Retention Time(min)	AREA
1993.03.01 (date analyzed)	3.307	232010
1993.04.16 (date analyzed)	3.305	231946

4. Conclusions: The results indicated that the test substance did not change when stored in the dark at 5°C during this period(for about 6 weeks).

APPENDIX Q 3

CONDETRATION OF VINYL ACETATE IN DRINKING WATER

(2-YEAR STUDY)

CONCENTRATION OF VINYL ACETATE IN DRINKING WATER(TWO-YEAR STUDIES)

(Rat)

	Target Concentration(ppm)		
Date analyzed	400	2000	10000
1991.03.26	412.5(103.1)*	1910.5(95.5)	9611.5(96.1)
1991.07.05	430.2(107.5)	2038.4(101.9)	10254.8(102.5)
1991.10.11	370.1(92.5)	1791.6(89.6)	7137.3(71.4)
1992.01.24	483.0(120.8)	1990.9(99.5)	10519.4(105.2)
1992.04.03	398.0(99.5)	2053.3(102.7)	10025.6(100.3)
1992.06.19	372.4(93.1)	1998.3(99.9)	10843.8(108.4)
1992.09.18	349.3(87.3)	1779.4(89.0)	9144.7(91.4)
1992.12.18	409.3(102.3)	1953.1(97.7)	11204.3(112.0)
1993.03.19	323.9(81.0)	1826.4(91.3)	9225.6(92.3)

(*) % of target concentration

Analytical method: The sample were analyzed by the GC.

Instrument : Hewlett Packard 5890A
Column : METHYL SILICONE(0.2mmϕ × 38m)
Column Temperature: 40℃
Carrier : He
Flow Rate : 1ml/min
Detector : FID(Flame Ionization)
Injection Volume : 10μl

CONCENTRATION OF VINYL ACETATE IN DRINKING WATER(TWO-YEAR STUDIES)

(Mouse)

	Target Concentration(ppm)		
Date analyzed	400	2000	10000
1991.04.16	371.3(92.8)*	1898.8(94.9)	9881.1(98.8)
1991.07.05	409.8(102.4)	1990.9(99.5)	9791.5(97.9)
1991.10.11	374.9(93.7)	1911.3(95.6)	7409.6(74.1)
1992.01.24	453.1(113.3)	1899.1(95.0)	9629.1(96.3)
1992.04.03	352.2(88.0)	1905.8(95.3)	9410.1(94.1)
1992.06.19	430.0(107.5)	2367.2(118.4)	11996.2(120.0)
1992.09.18	349.8(87.5)	1767.2(88.4)	9166.8(91.7)
1992.12.18	399.1(99.8)	1921.9(96.1)	9950.1(99.5)
1993.03.19	323.8(81.0)	1791.0(89.6)	9327.8(93.3)

(*) % of target concentration

Analytical method: The sample were analyzed by the GC.

Instrument : Hewlett Packard 5890A
Column : METHYL SILICONE(0.2mmϕ × 38m)
Column Temperature: 40℃
Carrier : He
Flow Rate : 1ml/min
Detector : FID(Flame Ionization)
Injection Volume : 10μl

APPENDIX Q 4

STABILITY OF β-CHLOROPROPIONIC ACID IN DRINKING WATER

(2-YEAR STUDY)

STABILITY OF VINYL ACETATE IN DRINKING WATER(TWO-YEAR STUDIES)

(Rat)

	Target Concentration(ppm)		
Date analyzed	400	2000	10000
1991.03.29(a)	369.6	1959.1	10083.4
1991.04.02(b)	318.5	1444.8	7391.3

(Mouse)

	Target Concentration(ppm)		
Date analyzed	400	2000	10000
1991.04.26(a)	433.1	1975.4	10274.3
1991.04.30(b)	374.6	1929.1	8608.8

(a) Date of preparation
(b) The stability of vinyl acetate in drinking water was established for 4 days when stored at 25℃.

Analytical method: The sample were analyzed by the GC.

Instrument	: Hewlett Packard 5890A	Flow Rate	: 1ml/min
Column	: METHYL SILICONE(0.2mmϕ × 38m)	Detector	: FID(Flame Ionization)
Column Temperature	: 40℃	Injection Volume	: 10μl
Carrier	: He		

APPENDIX R 1

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS

METHODS FOR HEMATOLOGY,BIOCHEMISTRY AND URINALYSIS

Item	Method	Unit
Hematology		
Red blood cell (RBC)	Light scattering method [1]	$\times 10^6/\mu l$
Hemoglobin (Hgb)	Cyanmethemoglobin method [1]	g/dl
Hematocrit (Hct)	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 (TP)	Biuret method [3]	g/dl
Albumin (Alb)	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 R 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	$10^6/\mu l$
	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
	γ-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