塩化メチルのラット及びマウスを用いた
吸入によるがん原性試験報告書

APPENDIX

(J1～Q2)

試験番号：ラット/0210；マウス/0211

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIX J 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : DEAD AND MORIBUND ANIMALS

(TOW-YERA STUDY)

STUDY NO. : 0210
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				50 ppm				224 ppm				1000 ppm			
		No. of Animals on Study	8				9				14				9			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Integumentary system/appandage]																		
skin/app			< 8>				< 9>				<14>				< 9>			
	epidermal cyst		1 (13)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Respiratory system]																		
nasal cavit			< 8>				< 9>				<14>				< 9>			
	thrombus		2 (25)	0 (0)	0 (0)	0 (0)	2 (22)	0 (0)	0 (0)	0 (0)	5 (36)	0 (0)	0 (0)	0 (0)	5 (56)	0 (0)	0 (0)	0 (0)
	eosinophilic change:olfactory epithelium		3 (38)	0 (0)	0 (0)	0 (0)	4 (44)	1 (11)	0 (0)	0 (0)	2 (14)	2 (14)	0 (0)	0 (0)	1 (11)	0 (0)	0 (0)	0 (0)
	inflammation:foreign body		1 (13)	1 (13)	0 (0)	0 (0)	4 (44)	0 (0)	1 (11)	0 (0)	3 (21)	2 (14)	0 (0)	0 (0)	1 (11)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:olfactory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (11)	0 (0)	0 (0)	0 (0)
lung			< 8>				< 9>				<14>				< 9>			
	congestion		2 (25)	1 (13)	0 (0)	0 (0)	3 (33)	0 (0)	0 (0)	0 (0)	3 (21)	0 (0)	0 (0)	0 (0)	1 (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				50 ppm				224 ppm				1000 ppm			
		No. of Animals on Study	8				9				14				9			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
[Respiratory system]																		
lung			< 8>				< 9>				<14>				< 9>			
	pneumonia:NOS		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)	(0)	(0)
[Hematopoietic system]																		
bone marrow			< 8>				< 9>				<14>				< 9>			
	granulation		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)	(0)	(0)	(0)	(0)
	increased hematopoiesis		1	1	0	0	1	1	0	0	4	2	0	0	2	2	0	0
			(13)	(13)	(0)	(0)	(11)	(11)	(0)	(0)	(29)	(14)	(0)	(0)	(22)	(22)	(0)	(0)
spleen			< 8>				< 9>				<14>				< 9>			
	deposit of hemosiderin		0	1	1	0	2	2	0	0	1	2	0	0	2	3	1	0
			(0)	(13)	(13)	(0)	(22)	(22)	(0)	(0)	(7)	(14)	(0)	(0)	(22)	(33)	(11)	(0)
	fibrosis		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)	(0)	(0)	(0)	(0)
	extramedullary hematopoiesis		0	0	2	0	2	0	0	0	0	0	3	1	0	0	1	0
			(0)	(0)	(25)	(0)	(22)	(0)	(0)	(0)	(0)	(0)	(21)	(7)	(0)	(0)	(11)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
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 8				50 ppm 9				224 ppm 14				1000 ppm 9			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Circulatory system]																		
heart			< 8>				< 9>				<14>				< 9>			
	thrombus		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)
	mineralization		0	0	0	0	0	0	0	0	3	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(21)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	myocardial fibrosis		5	0	0	0	1	0	0	0	4	0	0	0	0	0	0	0 *
			(63)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(29)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]																		
stomach			< 8>				< 9>				<14>				< 9>			
	ulcer:forestomach		0	0	1	0	1	0	0	2	0	0	0	0	1	1	0	0
			(0)	(0)	(13)	(0)	(11)	(0)	(0)	(22)	(0)	(0)	(0)	(0)	(11)	(11)	(0)	(0)
	ulcer:glandular stomach		1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(13)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:glandular stomach		1	0	0	0	0	0	0	0	0	3	0	0	0	0	0	0
			(13)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(21)	(0)	(0)	(0)	(0)	(0)	(0)
liver			< 8>				< 9>				<14>				< 9>			
	herniation		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)	(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				50 ppm				224 ppm				1000 ppm			
		No. of Animals on Study	8				9				14				9			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
liver			< 8>				< 9>				<14>				< 9>			
	necrosis:central		2	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0
			(25)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(14)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	fatty change:central		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	clear cell focus		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)	(0)	(0)	(0)	(0)
	basophilic cell focus		1	0	0	0	1	0	0	0	4	0	0	0	0	0	0	0
			(13)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(29)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	spongiosis hepatis		0	0	0	0	1	0	0	0	3	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(21)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	bile duct hyperplasia		7	0	0	0	8	0	0	0	10	1	0	0	7	0	0	0
			(88)	(0)	(0)	(0)	(89)	(0)	(0)	(0)	(71)	(7)	(0)	(0)	(78)	(0)	(0)	(0)
pancreas			< 8>				< 9>				<14>				< 9>			
	atrophy		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Urinary system]																		
kidney			< 8>				< 9>				<14>				< 9>			
	chronic nephropathy		1	2	4	0	0	3	2	4	2	4	3	3	0	1	4	1
			(13)	(25)	(50)	(0)	(0)	(33)	(22)	(44)	(14)	(29)	(21)	(21)	(0)	(11)	(44)	(11)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
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 8				50 ppm 9				224 ppm 14				1000 ppm 9			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Endocrine system]																		
pituitary			< 8>				< 9>				<14>				< 9>			
	hyperplasia		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)	0 (0)
	Rathke pouch		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)	1 (11)	0 (0)	0 (0)	0 (0)
thyroid			< 8>				< 9>				<14>				< 9>			
	follicular 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 (11)	0 (0)	0 (0)	0 (0)
adrenal			< 8>				< 9>				<14>				< 9>			
	hemorrhage		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (11)	0 (0)	0 (0)	0 (0)
	hyperplasia:medulla		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 (22)	0 (0)	0 (0)	0 (0)
[Reproductive system]																		
testis			< 8>				< 9>				<14>				< 9>			
	atrophy		7 (88)	0 (0)	0 (0)	0 (0)	7 (78)	0 (0)	0 (0)	0 (0)	10 (71)	0 (0)	0 (0)	0 (0)	9 (100)	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 8				50 ppm 9				224 ppm 14				1000 ppm 9			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Reproductive system]																		
prostate			< 8>				< 9>				<14>				< 9>			
	inflammation		1	2	0	0	3	1	0	0	6	0	2	0	2	1	0	0
			(13)	(25)	(0)	(0)	(33)	(11)	(0)	(0)	(43)	(0)	(14)	(0)	(22)	(11)	(0)	(0)
	hyperplasia		2	0	0	0	2	0	0	0	0	0	0	0	2	0	0	0
			(25)	(0)	(0)	(0)	(22)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(22)	(0)	(0)	(0)
mammary gl			< 8>				< 9>				<14>				< 9>			
	galactocele		1	0	0	0	2	0	0	0	3	0	0	0	1	0	0	0
			(13)	(0)	(0)	(0)	(22)	(0)	(0)	(0)	(21)	(0)	(0)	(0)	(11)	(0)	(0)	(0)
[Special sense organs/appandage]																		
eye			< 8>				< 9>				<14>				< 9>			
	retinal atrophy		2	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(25)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	keratitis		0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(7)	(7)	(0)	(0)	(0)	(0)	(0)	(0)
[Musculoskeletal system]																		
muscle			< 8>				< 9>				<14>				< 9>			
	mineralization		0	0	0	0	2	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(22)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(11)	(0)	(0)	(0)

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

APPENDIX J 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : DEAD AND MORIBUND ANIMALS

(TOW-YERA STUDY)

Organ	Findings	Group Name	Control				50 ppm				224 ppm				1000 ppm			
		No. of Animals on Study	12				13				5				9			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
nasal cavit			<12>				<13>				< 5>				< 9>			
	thrombus		4	0	0	0	2	0	0	0	1	0	0	0	4	0	0	0
			(33)	(0)	(0)	(0)	(15)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(44)	(0)	(0)	(0)
	mineralization		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(11)	(0)	(0)	(0)
	eosinophilic change:olfactory epithelium		2	0	1	0	4	1	0	0	1	0	0	0	3	0	0	0
			(17)	(0)	(8)	(0)	(31)	(8)	(0)	(0)	(20)	(0)	(0)	(0)	(33)	(0)	(0)	(0)
	inflammation:foreign body		2	0	0	0	2	0	0	0	2	0	0	0	1	0	0	0
			(17)	(0)	(0)	(0)	(15)	(0)	(0)	(0)	(40)	(0)	(0)	(0)	(11)	(0)	(0)	(0)
	inflammation:squamous epithelium		0	0	0	0	2	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(15)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(11)	(0)	(0)	(0)
lung			<12>				<13>				< 5>				< 9>			
	congestion		4	0	0	0	6	0	0	0	0	0	0	0	2	0	0	0
			(33)	(0)	(0)	(0)	(46)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(22)	(0)	(0)	(0)
	inflammation		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)	(0)	(0)	(0)	(0)
	accumulation of foamy cells		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)	(11)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				50 ppm				224 ppm				1000 ppm			
		No. of Animals on Study	12				13				5				9			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
lung			<12>				<13>				< 5>				< 9>			
	bronchiolar-alveolar cell hyperplasia		1 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	thickening:alveolar wall		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 (11)	0 (0)	0 (0)	0 (0)
[Hematopoietic system]																		
bone marrow			<12>				<13>				< 5>				< 9>			
	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 (11)	1 (11)	0 (0)	0 (0)
	increased hematopoiesis		2 (17)	0 (0)	0 (0)	0 (0)	3 (23)	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	1 (20)	0 (0)	2 (22)	0 (0)	0 (0)	0 (0)
	osteosclerosis		0 (0)	0 (0)	0 (0)	0 (0)	2 (15)	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
spleen			<12>				<13>				< 5>				< 9>			
	deposit of hemosiderin		2 (17)	4 (33)	0 (0)	0 (0)	3 (23)	5 (38)	0 (0)	0 (0)	1 (20)	1 (20)	0 (0)	0 (0)	0 (0)	3 (33)	1 (11)	0 (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
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Organ	Findings	Group Name	Control				50 ppm				224 ppm				1000 ppm			
		No. of Animals on Study	12				13				5				9			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
spleen			<12>				<13>				< 5>				< 9>			
	fibrosis		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)	(0)	(0)	(0)	(0)
	extramedullary hematopoiesis		1	0	0	1	1	0	2	0	0	0	4	0 **	0	1	1	0
			(8)	(0)	(0)	(8)	(8)	(0)	(15)	(0)	(0)	(0)	(80)	(0)	(0)	(11)	(11)	(0)
[Circulatory system]																		
heart			<12>				<13>				< 5>				< 9>			
	thrombus		0	0	0	0	1	0	0	0	0	0	0	0	2	1	0	0
			(0)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(22)	(11)	(0)	(0)
	myocardial fibrosis		0	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(23)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]																		
stomach			<12>				<13>				< 5>				< 9>			
	ulcer:forestomach		4	2	0	0	2	1	0	0	0	1	0	0	0	1	0	0
			(33)	(17)	(0)	(0)	(15)	(8)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(11)	(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				50 ppm				224 ppm				1000 ppm			
		No. of Animals on Study	12				13				5				9			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
stomach			<12>				<13>				< 5>				< 9>			
	hyperplasia:forestomach		0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	erosion:glandular stomach		0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(0)	(0)	(0)	(11)	(0)	(0)	(0)
	ulcer:glandular stomach		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)	(0)	(0)	(0)	(0)
	mineralization:glandular stomach		0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(40)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
liver			<12>				<13>				< 5>				< 9>			
	herniation		2	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(17)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:central		1	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
			(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(22)	(0)	(0)	(0)
	fatty change		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	granulation		1	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0
			(8)	(0)	(0)	(0)	(15)	(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				50 ppm				224 ppm				1000 ppm			
		No. of Animals on Study	12				13				5				9			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
liver			<12>				<13>				< 5>				< 9>			
	clear cell focus		0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(8)	(0)	(0)	(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	spongiosis hepatis		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)	(11)	(0)	(0)	(0)
	bile duct hyperplasia		2	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0
			(17)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(11)	(0)	(0)
	biliary cyst		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
pancreas			<12>				<13>				< 5>				< 9>			
	atrophy		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)	(0)	(0)	(0)	(0)
[Urinary system]																		
kidney			<12>				<13>				< 5>				< 9>			
	chronic nephropathy		5	2	3	0	5	0	3	1	2	0	1	1	5	0	0	1
			(42)	(17)	(25)	(0)	(38)	(0)	(23)	(8)	(40)	(0)	(20)	(20)	(56)	(0)	(0)	(11)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
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				50 ppm				224 ppm				1000 ppm			
		No. of Animals on Study	12				13				5				9			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																		
kidney			<12>				<13>				< 5>				< 9>			
	hydronephrosis		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:cortico-medullary junction		0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)
[Endocrine system]																		
pituitary			<12>				<13>				< 5>				< 9>			
	cyst		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	Rathke pouch		0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(11)	(0)	(0)	(0)
thyroid			<12>				<13>				< 5>				< 9>			
	C-cell hyperplasia		2	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			<12>				<13>				< 5>				< 9>			
	focal fatty change:cortex		1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(11)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				50 ppm				224 ppm				1000 ppm			
		No. of Animals on Study	12				13				5				9			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Reproductive system]																		
mammary gl			<12>				<13>				< 5>				< 9>			
	galactocele		7	0	0	0	9	0	0	0	4	0	0	0	4	0	0	0
			(58)	(0)	(0)	(0)	(69)	(0)	(0)	(0)	(80)	(0)	(0)	(0)	(44)	(0)	(0)	(0)
[Special sense organs/appandage]																		
eye			<12>				<13>				< 5>				< 9>			
	retinal atrophy		2	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(17)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
Harder gl			<12>				<13>				< 5>				< 9>			
	granulation		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)	(0)	(0)	(0)	(0)

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

APPENDIX J 3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : SACRIFICED ANIMALS

(TOW-YERA STUDY)

Organ	Findings	Group Name	Control				50 ppm				224 ppm				1000 ppm			
		No. of Animals on Study	42				41				36				41			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
nasal cavit			<42>				<41>				<36>				<41>			
	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)	(2)	(0)	(0)	(0)
	eosinophilic change:olfactory epithelium		22	4	1	0	25	5	0	0	15	0	0	0	26	1	0	0
			(52)	(10)	(2)	(0)	(61)	(12)	(0)	(0)	(42)	(0)	(0)	(0)	(63)	(2)	(0)	(0)
	eosinophilic change:respiratory epithelium		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)
	inflammation:foreign body		12	0	0	0	15	2	1	0	10	0	0	0	2	1	0	0 *
			(29)	(0)	(0)	(0)	(37)	(5)	(2)	(0)	(28)	(0)	(0)	(0)	(5)	(2)	(0)	(0)
lung			<42>				<41>				<36>				<41>			
	congestion		2	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(5)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	accumulation of foamy cells		2	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(5)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	bronchiolar-alveolar cell hyperplasia		1	1	0	0	1	0	0	0	2	0	0	0	7	0	0	0
			(2)	(2)	(0)	(0)	(2)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(17)	(0)	(0)	(0)
	inflammation:foreign body		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)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
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 42				50 ppm 41				224 ppm 36				1000 ppm 41			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
lung			<42>				<41>				<36>				<41>			
	thickening:alveolar wall		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)
[Hematopoietic system]																		
bone marrow			<42>				<41>				<36>				<41>			
	granulation		2 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (6)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	increased hematopoiesis		0 (0)	1 (2)	0 (0)	0 (0)	3 (7)	1 (2)	0 (0)	0 (0)	2 (6)	0 (0)	0 (0)	0 (0)	3 (7)	0 (0)	0 (0)	0 (0)
	osteosclerosis		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)
lymph node			<42>				<41>				<36>				<41>			
	lymphadenitis		0 (0)	0 (0)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
spleen			<42>				<41>				<36>				<41>			
	deposit of hemosiderin		37 (88)	2 (5)	0 (0)	0 (0)	34 (83)	0 (0)	0 (0)	0 (0)	32 (89)	0 (0)	0 (0)	0 (0)	35 (85)	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 42 1 (%)	Control 42 2 (%)	Control 42 3 (%)	Control 42 4 (%)	50 ppm 41 1 (%)	50 ppm 41 2 (%)	50 ppm 41 3 (%)	50 ppm 41 4 (%)	224 ppm 36 1 (%)	224 ppm 36 2 (%)	224 ppm 36 3 (%)	224 ppm 36 4 (%)	1000 ppm 41 1 (%)	1000 ppm 41 2 (%)	1000 ppm 41 3 (%)	1000 ppm 41 4 (%)
[Hematopoietic system]																		
spleen			<42>				<41>				<36>				<41>			
	fibrosis		1 (2)	0 (0)	0 (0)	0 (0)	2 (5)	2 (5)	0 (0)	0 (0)	2 (6)	0 (0)	1 (3)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)
	extramedullary hematopoiesis		2 (5)	0 (0)	1 (2)	0 (0)	2 (5)	2 (5)	1 (2)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	lymphoid 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)
	capsule hyperplasia		2 (5)	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)
[Circulatory system]																		
heart			<42>				<41>				<36>				<41>			
	myocardial fibrosis		9 (21)	0 (0)	0 (0)	0 (0)	17 (41)	0 (0)	0 (0)	0 (0)	13 (36)	0 (0)	0 (0)	0 (0)	7 (17)	0 (0)	0 (0)	0 (0)
[Digestive system]																		
stomach			<42>				<41>				<36>				<41>			
	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)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
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 42				50 ppm 41				224 ppm 36				1000 ppm 41			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
stomach			<42>				<41>				<36>				<41>			
	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 (2)	0 (0)	0 (0)	0 (0)
	ulcer:forestomach		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)	1 (2)	0 (0)	0 (0)
	erosion:glandular stomach		2 (5)	0 (0)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	mineralization:glandular stomach		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)
liver			<42>				<41>				<36>				<41>			
	herniation		1 (2)	0 (0)	0 (0)	0 (0)	3 (7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	necrosis:central		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)
	necrosis:focal		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 (7)	0 (0)	0 (0)	0 (0)	6 (15)	0 (0)	0 (0)	0 (0)	3 (8)	1 (3)	0 (0)	0 (0)	5 (12)	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 42				50 ppm 41				224 ppm 36				1000 ppm 41			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver			<42>				<41>				<36>				<41>			
	clear cell focus		6 (14)	0 (0)	0 (0)	0 (0)	6 (15)	0 (0)	0 (0)	0 (0)	7 (19)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 * (0)
	acidophilic cell focus		5 (12)	0 (0)	0 (0)	0 (0)	3 (7)	0 (0)	0 (0)	0 (0)	5 (14)	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	basophilic cell focus		9 (21)	0 (0)	0 (0)	0 (0)	12 (29)	0 (0)	0 (0)	0 (0)	10 (28)	1 (3)	0 (0)	0 (0)	6 (15)	0 (0)	0 (0)	0 (0)
	vacuolated cell focus		2 (5)	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)
	spongiosis hepatis		5 (12)	1 (2)	0 (0)	0 (0)	8 (20)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	bile duct hyperplasia		41 (98)	0 (0)	1 (2)	0 (0)	40 (98)	0 (0)	0 (0)	0 (0)	36 (100)	0 (0)	0 (0)	0 (0)	37 (90)	1 (2)	0 (0)	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)	2 (5)	0 (0)	0 (0)	0 (0)
pancreas			<42>				<41>				<36>				<41>			
	atrophy		5 (12)	0 (0)	0 (0)	0 (0)	4 (10)	0 (0)	0 (0)	0 (0)	5 (14)	0 (0)	0 (0)	0 (0)	5 (12)	1 (2)	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 42				50 ppm 41				224 ppm 36				1000 ppm 41			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
pancreas			<42>				<41>				<36>				<41>			
	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)	1 (2)	0 (0)	0 (0)	0 (0)
	hyperplasia:acinar cell		3 (7)	0 (0)	0 (0)	0 (0)	3 (7)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	4 (10)	0 (0)	0 (0)	0 (0)
[Urinary system]																		
kidney			<42>				<41>				<36>				<41>			
	deposit of hemosiderin		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)	1 (2)	0 (0)
	chronic nephropathy		1 (2)	3 (7)	34 (81)	4 (10)	0 (0)	2 (5)	26 (63)	13 (32)	0 (0)	0 (0)	30 (83)	6 (17)	1 (2)	12 (29)	22 (54)	5 (12)
[Endocrine system]																		
pituitary			<42>				<41>				<36>				<41>			
	hyperplasia		10 (24)	0 (0)	0 (0)	0 (0)	8 (20)	0 (0)	0 (0)	0 (0)	5 (14)	0 (0)	0 (0)	0 (0)	4 (10)	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 42				50 ppm 41				224 ppm 36				1000 ppm 41			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Endocrine system]																		
pituitary			<42>				<41>				<36>				<41>			
	Rathke pouch		2 (5)	0 (0)	0 (0)	0 (0)	6 (15)	0 (0)	0 (0)	0 (0)	6 (17)	0 (0)	0 (0)	0 (0)	5 (12)	0 (0)	0 (0)	0 (0)
thyroid			<42>				<41>				<36>				<41>			
	ultimibranchial body remanet		1 (2)	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)
	follicular hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)
	C-cell hyperplasia		2 (5)	0 (0)	0 (0)	0 (0)	3 (7)	0 (0)	0 (0)	0 (0)	2 (6)	0 (0)	0 (0)	0 (0)	4 (10)	0 (0)	0 (0)	0 (0)
adrenal			<42>				<41>				<36>				<41>			
	hyperplasia:medulla		1 (2)	0 (0)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	focal fatty change:cortex		3 (7)	0 (0)	0 (0)	0 (0)	3 (7)	0 (0)	0 (0)	0 (0)	4 (11)	0 (0)	0 (0)	0 (0)	3 (7)	0 (0)	0 (0)	0 (0)
[Reproductive system]																		
testis			<42>				<41>				<36>				<41>			
	atrophy		41 (98)	0 (0)	0 (0)	0 (0)	41 (100)	0 (0)	0 (0)	0 (0)	36 (100)	0 (0)	0 (0)	0 (0)	41 (100)	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				50 ppm				224 ppm				1000 ppm			
		No. of Animals on Study	42				41				36				41			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Reproductive system]																		
prostate			<42>				<41>				<36>				<41>			
	inflammation		16 (38)	3 (7)	0 (0)	0 (0)	11 (27)	2 (5)	0 (0)	0 (0)	13 (36)	5 (14)	0 (0)	0 (0)	7 (17)	0 (0)	1 (2)	0 * (0)
	hyperplasia		7 (17)	0 (0)	0 (0)	0 (0)	9 (22)	0 (0)	0 (0)	0 (0)	4 (11)	0 (0)	0 (0)	0 (0)	7 (17)	0 (0)	0 (0)	0 (0)
mammary gl			<42>				<41>				<36>				<41>			
	galactocele		1 (2)	0 (0)	0 (0)	0 (0)	3 (7)	0 (0)	0 (0)	0 (0)	5 (14)	0 (0)	0 (0)	0 (0)	3 (7)	0 (0)	0 (0)	0 (0)
[Nervous system]																		
spinal cord			<42>				<41>				<36>				<41>			
	radiculoneuropathy		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)
[Special sense organs/appandage]																		
eye			<42>				<41>				<36>				<41>			
	retinal atrophy		8 (19)	0 (0)	0 (0)	0 (0)	15 (37)	0 (0)	0 (0)	0 (0)	12 (33)	0 (0)	0 (0)	0 (0)	7 (17)	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 42				50 ppm 41				224 ppm 36				1000 ppm 41			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Special sense organs/appandage]																		
eye			<42>				<41>				<36>				<41>			
	keratitis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
Harder gl			<42>				<41>				<36>				<41>			
	degeneration		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)
Zymbal gl			<42>				<41>				<36>				<41>			
	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 (2)	0 (0)	0 (0)	0 (0)

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

APPENDIX J 4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : SACRIFICED ANIMALS

(TOW-YERA STUDY)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 37				50 ppm 37				224 ppm 45				1000 ppm 41			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
nasal cavit			<37>				<37>				<45>				<41>			
	thrombus		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)
	eosinophilic change:olfactory epithelium		21 (57)	7 (19)	2 (5)	0 (0)	19 (51)	5 (14)	3 (8)	0 (0)	16 (36)	6 (13)	3 (7)	0 (0)	18 (44)	9 (22)	1 (2)	0 (0)
	inflammation:foreign body		1 (3)	0 (0)	0 (0)	0 (0)	6 (16)	0 (0)	0 (0)	0 (0)	3 (7)	1 (2)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	inflammation:squamous epithelium		2 (5)	0 (0)	0 (0)	0 (0)	4 (11)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
lung			<37>				<37>				<45>				<41>			
	congestion		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 (2)	0 (0)	0 (0)	0 (0)
	accumulation of foamy cells		1 (3)	0 (0)	0 (0)	0 (0)	5 (14)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (7)	0 (0)	0 (0)	0 (0)
	bronchiolar-alveolar cell hyperplasia		2 (5)	0 (0)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)	3 (7)	0 (0)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)
[Hematopoietic system]																		
bone marrow			<37>				<37>				<45>				<41>			
	granulation		2 (5)	2 (5)	0 (0)	0 (0)	3 (8)	0 (0)	1 (3)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)	8 (20)	0 (0)	1 (2)	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				50 ppm				224 ppm				1000 ppm			
		No. of Animals on Study	37				37				45				41			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
[Hematopoietic system]																		
bone marrow			<37>				<37>				<45>				<41>			
	increased hematopoiesis		3	0	0	0	2	0	0	0	3	1	0	0	0	1	0	0
			(8)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(7)	(2)	(0)	(0)	(0)	(2)	(0)	(0)
	osteosclerosis		6	0	0	0	4	0	0	0	5	0	0	0	1	0	0	0
			(16)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
lymph node			<37>				<37>				<45>				<41>			
	lymphadenitis		1	0	0	0	3	0	0	0	2	0	0	0	0	0	0	0
			(3)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen			<37>				<37>				<45>				<41>			
	deposit of hemosiderin		21	10	0	0	28	4	0	0	33	4	0	0	20	15	0	0
			(57)	(27)	(0)	(0)	(76)	(11)	(0)	(0)	(73)	(9)	(0)	(0)	(49)	(37)	(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)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	extramedullary hematopoiesis		18	2	0	0	15	1	1	0	14	0	1	0	16	0	1	0
			(49)	(5)	(0)	(0)	(41)	(3)	(3)	(0)	(31)	(0)	(2)	(0)	(39)	(0)	(2)	(0)
	lymphoid hyperplasia		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
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				50 ppm				224 ppm				1000 ppm			
		No. of Animals on Study	37				37				45				41			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
[Hematopoietic system]																		
spleen			<37>				<37>				<45>				<41>			
	capsule 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)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Circulatory system]																		
heart			<37>				<37>				<45>				<41>			
	myocardial fibrosis		2	0	0	0	2	0	0	0	5	1	0	0	2	0	0	0
			(5)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(11)	(2)	(0)	(0)	(5)	(0)	(0)	(0)
[Digestive system]																		
tongue			<37>				<37>				<45>				<41>			
	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)
stomach			<37>				<37>				<45>				<41>			
	epidermal cyst		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	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(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				50 ppm				224 ppm				1000 ppm			
		No. of Animals on Study	37				37				45				41			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
stomach			<37>				<37>				<45>				<41>			
	erosion: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)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
small intes			<37>				<37>				<45>				<41>			
	erosion		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
liver			<37>				<37>				<45>				<41>			
	herniation		1	0	0	0	2	0	0	0	3	0	0	0	1	0	0	0
			(3)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	peliosis-like lesion		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)
	granulation		15	1	1	0	14	1	0	0	11	3	0	0	14	0	0	0
			(41)	(3)	(3)	(0)	(38)	(3)	(0)	(0)	(24)	(7)	(0)	(0)	(34)	(0)	(0)	(0)
	clear cell focus		2	0	0	0	1	0	0	0	1	0	0	0	1	0	0	0
			(5)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	acidophilic cell focus		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)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
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				50 ppm				224 ppm				1000 ppm			
		No. of Animals on Study	37				37				45				41			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
liver			<37>				<37>				<45>				<41>			
	basophilic cell focus		4	0	0	0	3	0	0	0	1	0	0	0	3	0	0	0
			(11)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(7)	(0)	(0)	(0)
	vacuolated cell focus		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)	(0)	(0)	(0)	(0)
	bile duct hyperplasia		4	0	0	0	6	0	0	0	12	0	0	0	3	0	0	0
			(11)	(0)	(0)	(0)	(16)	(0)	(0)	(0)	(27)	(0)	(0)	(0)	(7)	(0)	(0)	(0)
	biliary cyst		0	0	0	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)
pancreas			<37>				<37>				<45>				<41>			
	atrophy		2	0	0	0	2	0	0	0	4	0	0	0	1	1	0	0
			(5)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(9)	(0)	(0)	(0)	(2)	(2)	(0)	(0)
[Urinary system]																		
kidney			<37>				<37>				<45>				<41>			
	infarct		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)	(2)	(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				50 ppm				224 ppm				1000 ppm			
		No. of Animals on Study	37				37				45				41			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																		
kidney			<37>				<37>				<45>				<41>			
	deposit of hemosiderin		0	0	0	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)
	chronic nephropathy		5	15	12	3	7	12	13	3	8	13	18	2	15	17	6	0 *
			(14)	(41)	(32)	(8)	(19)	(32)	(35)	(8)	(18)	(29)	(40)	(4)	(37)	(41)	(15)	(0)
	mineralization:cortico-medullary junction		0	0	0	0	3	0	0	0	4	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(9)	(0)	(0)	(0)	(7)	(0)	(0)	(0)
[Endocrine system]																		
pituitary			<37>				<37>				<45>				<41>			
	cyst		2	0	0	0	4	0	0	0	0	0	0	0	1	0	0	0
			(5)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	hyperplasia		11	0	0	0	6	0	0	0	10	0	0	0	11	0	0	0
			(30)	(0)	(0)	(0)	(16)	(0)	(0)	(0)	(22)	(0)	(0)	(0)	(27)	(0)	(0)	(0)
	Rathke pouch		3	0	0	0	2	0	0	0	2	0	0	0	1	0	0	0
			(8)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
thyroid			<37>				<37>				<45>				<41>			
	C-cell hyperplasia		2	0	0	0	3	0	0	0	1	0	0	0	2	0	0	0
			(5)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(5)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				50 ppm				224 ppm				1000 ppm			
		No. of Animals on Study	37				37				45				41			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]																		
adrenal			<37>				<37>				<45>				<41>			
	hyperplasia:medulla		0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	focal fatty change:cortex		5	0	0	0	4	0	0	0	2	0	0	0	6	0	0	0
			(14)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(15)	(0)	(0)	(0)
[Reproductive system]																		
ovary			<37>				<37>				<45>				<41>			
	cyst		0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
uterus			<37>				<37>				<45>				<41>			
	cyst		1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
mammary gl			<37>				<37>				<45>				<41>			
	galactocele		20	0	0	0	18	0	0	0	26	0	0	0	19	0	0	0
			(54)	(0)	(0)	(0)	(49)	(0)	(0)	(0)	(58)	(0)	(0)	(0)	(46)	(0)	(0)	(0)
[Special sense organs/appandage]																		
eye			<37>				<37>				<45>				<41>			
	retinal atrophy		10	0	0	0	13	0	0	0	15	0	0	0	20	0	0	0
			(27)	(0)	(0)	(0)	(35)	(0)	(0)	(0)	(33)	(0)	(0)	(0)	(49)	(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				50 ppm				224 ppm				1000 ppm			
		No. of Animals on Study	37				37				45				41			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Special sense organs/appandage]																		
eye			<37>				<37>				<45>				<41>			
	keratitis		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
Harder gl			<37>				<37>				<45>				<41>			
	granulation		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
Zymbal gl			<37>				<37>				<45>				<41>			
	cyst		0	0	0	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)

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

APPENDIX J 5

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOSUE : MALE : DEAD AND MORIBUND ANIMALS

MOSUE (TOW-YERA STUDY)

Organ	Findings	Group Name	Control				50 ppm				200 ppm				800 ppm			
		No. of Animals on Study	12				8				9				48			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Integumentary system/appandage]																		
skin/app			<12>				< 8>				< 9>				<48>			
	epidermal cyst		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Respiratory system]																		
nasal cavit			<12>				< 8>				< 9>				<48>			
	eosinophilic change:olfactory epithelium		0	0	0	0	1	1	0	0	1	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(13)	(13)	(0)	(0)	(11)	(0)	(0)	(0)	(0)	(2)	(0)	(0)
	eosinophilic change:respiratory epithelium		1	0	0	0	2	0	0	0	0	0	0	0	2	1	0	0
			(8)	(0)	(0)	(0)	(25)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(2)	(0)	(0)
	inflammation:foreign body		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lung			<12>				< 8>				< 9>				<48>			
	congestion		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)	(4)	(0)	(0)	(0)
	bronchiolar-alveolar cell hyperplasia		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(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	Grade	Control 12				50 ppm 8				200 ppm 9				800 ppm 48			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Hematopoietic system]																		
bone marrow			<12>				< 8>				< 9>				<48>			
	atrophy		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)
	granulopoiesis:increased		1 (8)	0 (0)	0 (0)	0 (0)	3 (38)	0 (0)	0 (0)	0 (0)	2 (22)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
spleen			<12>				< 8>				< 9>				<48>			
	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)	2 (4)	0 (0)	0 (0)	0 (0)
	extramedullary hematopoiesis		4 (33)	1 (8)	0 (0)	0 (0)	0 (0)	1 (13)	2 (25)	0 (0)	1 (11)	1 (11)	2 (22)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0) **
[Circulatory system]																		
heart			<12>				< 8>				< 9>				<48>			
	thrombus		0 (0)	0 (0)	0 (0)	0 (0)	1 (13)	0 (0)	0 (0)	0 (0)	1 (11)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	mineralization		1 (8)	0 (0)	0 (0)	0 (0)	2 (25)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	10 (21)	0 (0)	0 (0)	0 (0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 12				50 ppm 8				200 ppm 9				800 ppm 48			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Circulatory system]																		
heart			<12>				< 8>				< 9>				<48>			
	myocardial fibrosis		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)
	arteritis		1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]																		
tongue			<12>				< 8>				< 9>				<48>			
	arteritis		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
stomach			<12>				< 8>				< 9>				<48>			
	hyperplasia:forestomach		1	0	0	0	0	0	0	0	3	0	0	0	5	0	0	0
			(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(33)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	hyperplasia:glandular stomach		2	0	0	0	1	0	0	0	1	0	0	0	5	0	0	0
			(17)	(0)	(0)	(0)	(13)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
liver			<12>				< 7>				< 9>				<48>			
	granulation		0	0	0	0	0	0	0	0	0	1	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(11)	(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	Control				50 ppm				200 ppm				800 ppm			
		No. of Animals on Study	12				8				9				48			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
[Digestive system]																		
liver			<12>				< 7>				< 9>				<48>			
	basophilic cell focus		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
[Urinary system]																		
kidney			<12>				< 8>				< 9>				<48>			
	eosinophilic droplet:proximal tubule		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)
[Endocrine system]																		
pituitary			<11>				< 8>				< 8>				<47>			
	Rathke pouch		0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(25)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Reproductive system]																		
testis			<12>				< 8>				< 9>				<48>			
	atrophy		2	0	0	0	2	0	0	0	0	0	0	0	8	0	0	0
			(17)	(0)	(0)	(0)	(25)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(17)	(0)	(0)	(0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 12				50 ppm 8				200 ppm 9				800 ppm 48			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Reproductive system]																		
epididymis		<a>	<12>				< 8>				< 9>				<48>			
	spermatogenic granuloma	b	1	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0 *
		(c)	(8)	(8)	(0)	(0)	(13)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Nervous system]																		
brain		<a>	<12>				< 8>				< 9>				<48>			
	mineralization	b	7	0	0	0	3	0	0	0	2	0	0	0	17	0	0	0
		(c)	(58)	(0)	(0)	(0)	(38)	(0)	(0)	(0)	(22)	(0)	(0)	(0)	(35)	(0)	(0)	(0)

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

APPENDIX J 6

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOSUE : FEMALE : DEAD AND MORIBUND ANIMALS

(TOW-YERA STUDY)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 15				50 ppm 15				200 ppm 15				800 ppm 49			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
nasal cavit			<15>				<15>				<15>				<49>			
	eosinophilic change:olfactory epithelium		3 (20)	3 (20)	0 (0)	0 (0)	3 (20)	2 (13)	0 (0)	0 (0)	2 (13)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	1 (2)	0 (0) **
	eosinophilic change:respiratory epithelium		6 (40)	2 (13)	0 (0)	0 (0)	5 (33)	3 (20)	1 (7)	0 (0)	6 (40)	2 (13)	0 (0)	0 (0)	8 (16)	1 (2)	0 (0)	0 (0) *
lung			<15>				<15>				<15>				<49>			
	congestion		1 (7)	0 (0)	0 (0)	0 (0)	2 (13)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	6 (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 (2)	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)	2 (4)	0 (0)	0 (0)	0 (0)
[Hematopoietic system]																		
bone marrow			<15>				<15>				<15>				<49>			
	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 (2)	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				50 ppm				200 ppm				800 ppm			
		No. of Animals on Study	15				15				15				49			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
bone marrow			<15>				<15>				<15>				<49>			
	increased hematopoiesis		0	0	0	0	3	0	0	0	5	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(33)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	granulopoiesis:increased		2	1	0	0	1	0	0	0	1	0	0	0	0	1	0	0 *
			(13)	(7)	(0)	(0)	(7)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(0)	(2)	(0)	(0)
spleen			<15>				<15>				<15>				<49>			
	atrophy		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)	(6)	(0)	(0)	(0)
	extramedullary hematopoiesis		0	0	7	0	0	3	3	0	2	3	2	0	1	2	1	0 **
			(0)	(0)	(47)	(0)	(0)	(20)	(20)	(0)	(13)	(20)	(13)	(0)	(2)	(4)	(2)	(0)
[Circulatory system]																		
heart			<15>				<15>				<15>				<49>			
	thrombus		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)
	mineralization		0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(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	Control				50 ppm				200 ppm				800 ppm			
		No. of Animals on Study	15				15				15				49			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
[Circulatory system]																		
heart			<15>				<15>				<15>				<49>			
	myocardial fibrosis		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)
[Digestive system]																		
stomach			<15>				<15>				<15>				<49>			
	hyperplasia:forestomach		6	0	0	0	7	0	0	0	5	0	0	0	12	0	0	0
			(40)	(0)	(0)	(0)	(47)	(0)	(0)	(0)	(33)	(0)	(0)	(0)	(24)	(0)	(0)	(0)
	hyperplasia:glandular stomach		5	0	0	0	2	0	0	0	1	0	0	0	7	0	0	0
			(33)	(0)	(0)	(0)	(13)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(14)	(0)	(0)	(0)
liver			<15>				<15>				<15>				<49>			
	peliosis-like lesion		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
[Urinary system]																		
kidney			<15>				<15>				<15>				<49>			
	infarct		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
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				50 ppm 15				200 ppm 15				800 ppm 49			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Urinary system]																		
kidney			<15>				<15>				<15>				<49>			
	hydronephrosis		0 (0)	0 (0)	1 (7)	0 (0)	3 (20)	0 (0)	1 (7)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)
	eosinophilic droplet:proximal tubule		3 (20)	0 (0)	0 (0)	0 (0)	2 (13)	0 (0)	0 (0)	0 (0)	5 (33)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 * (0)
[Endocrine system]																		
pituitary			<15>				<15>				<15>				<48>			
	hyperplasia		1 (7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (13)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	Rathke pouch		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 (4)	0 (0)	0 (0)	0 (0)
[Reproductive system]																		
ovary			<15>				<15>				<15>				<49>			
	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)	1 (2)	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				50 ppm 15				200 ppm 15				800 ppm 49			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Reproductive system]																		
ovary			<15>				<15>				<15>				<49>			
	cyst		1 (7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)
uterus			<15>				<15>				<15>				<49>			
	dilatation		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 (2)	0 (0)	0 (0)	0 (0)
mammary gl			<15>				<15>				<15>				<49>			
	galactocele		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Nervous system]																		
brain			<15>				<15>				<15>				<49>			
	mineralization		7 (47)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0) **	2 (13)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0) **
[Special sense organs/appandage]																		
Harder gl			<15>				<15>				<15>				<49>			
	degeneration		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)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
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				50 ppm				200 ppm				800 ppm			
		No. of Animals on Study	15				15				15				49			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Musculoskeletal system]																		
muscle			<15>				<15>				<15>				<49>			
	mineralization		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
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

APPENDIX J 7

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOSUE : MALE : SACRIFICED ANIMALS

(TOW-YERA STUDY)

STUDY NO. : 0211
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 38 1 (%)	Control 38 2 (%)	Control 38 3 (%)	Control 38 4 (%)	50 ppm 42 1 (%)	50 ppm 42 2 (%)	50 ppm 42 3 (%)	50 ppm 42 4 (%)	200 ppm 41 1 (%)	200 ppm 41 2 (%)	200 ppm 41 3 (%)	200 ppm 41 4 (%)	800 ppm 0 1 (%)	800 ppm 0 2 (%)	800 ppm 0 3 (%)	800 ppm 0 4 (%)
[Integumentary system/appandage]																		
skin/app			<38>				<42>				<41>				< 0>			
	inflammation		0	0	0	0	0	0	0	0	1	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
	epidermal cyst		1	0	0	0	0	0	0	0	0	0	0	0	-	-	-	-
			(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
[Respiratory system]																		
nasal cavit			<38>				<42>				<41>				< 0>			
	eosinophilic change:olfactory epithelium		2	0	0	0	8	1	0	0	3	0	0	0	-	-	-	-
			(5)	(0)	(0)	(0)	(19)	(2)	(0)	(0)	(7)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
	eosinophilic change:respiratory epithelium		7	1	0	0	4	3	0	0	5	0	0	0	-	-	-	-
			(18)	(3)	(0)	(0)	(10)	(7)	(0)	(0)	(12)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
lung			<38>				<42>				<41>				< 0>			
	hemorrhage		0	0	0	0	0	0	0	0	1	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
	inflammation		0	0	0	0	1	0	0	0	0	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 38				50 ppm 42				200 ppm 41				800 ppm 0			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
lung			<38>				<42>				<41>				< 0>			
	bronchiolar-alveolar cell hyperplasia		1	0	0	0	1	0	0	0	0	0	0	0	-	-	-	-
			(3)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
[Hematopoietic system]																		
bone marrow			<38>				<42>				<41>				< 0>			
	granulation		2	0	0	0	2	0	0	0	3	0	0	0	-	-	-	-
			(5)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(7)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
	granulopoiesis:increased		5	0	0	0	2	0	0	0	1	0	0	0	-	-	-	-
			(13)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
spleen			<38>				<42>				<41>				< 0>			
	extramedullary hematopoiesis		2	0	0	0	1	1	0	0	2	1	0	0	-	-	-	-
			(5)	(0)	(0)	(0)	(2)	(2)	(0)	(0)	(5)	(2)	(0)	(0)	(-)	(-)	(-)	(-)
	megakaryocyte:increased		0	0	0	0	1	0	0	0	0	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
	follicular hyperplasia		3	0	0	0	1	0	0	0	4	0	0	0	-	-	-	-
			(8)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(-)	(-)	(-)	(-)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 38 1 (%)	Control 38 2 (%)	Control 38 3 (%)	Control 38 4 (%)	50 ppm 42 1 (%)	50 ppm 42 2 (%)	50 ppm 42 3 (%)	50 ppm 42 4 (%)	200 ppm 41 1 (%)	200 ppm 41 2 (%)	200 ppm 41 3 (%)	200 ppm 41 4 (%)	800 ppm 0 1 (%)	800 ppm 0 2 (%)	800 ppm 0 3 (%)	800 ppm 0 4 (%)
[Circulatory system]																		
heart			<38>				<42>				<41>				< 0>			
	mineralization		0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	- (-)	- (-)	- (-)	- (-)
	myocardial fibrosis		0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	- (-)	- (-)	- (-)	- (-)
[Digestive system]																		
tooth			<38>				<42>				<41>				< 0>			
	dysplasia		4 (11)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	- (-)	- (-)	- (-)	- (-)
stomach			<38>				<42>				<41>				< 0>			
	hyperplasia:glandular stomach		14 (37)	0 (0)	0 (0)	0 (0)	14 (33)	0 (0)	0 (0)	0 (0)	15 (37)	0 (0)	0 (0)	0 (0)	- (-)	- (-)	- (-)	- (-)
liver			<38>				<42>				<41>				< 0>			
	granulation		6 (16)	2 (5)	0 (0)	0 (0)	3 (7)	0 (0)	0 (0)	0 (0)	5 (12)	1 (2)	0 (0)	0 (0)	- (-)	- (-)	- (-)	- (-)
	clear cell focus		0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	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				50 ppm				200 ppm				800 ppm			
		No. of Animals on Study	38				42				41				0			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver			<38>				<42>				<41>				< 0>			
	basophilic cell focus		0	0	0	0	2	0	0	0	2	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(5)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
	biliary cyst		1	0	0	0	1	0	0	0	0	0	0	0	-	-	-	-
			(3)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
[Urinary system]																		
kidney			<38>				<42>				<41>				< 0>			
	infarct		0	0	0	0	1	0	0	0	0	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
	cyst		0	0	0	0	0	0	0	0	0	1	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(-)	(-)	(-)	(-)
	basophilic change		0	0	0	0	0	0	0	0	1	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
	hyaline cast		1	0	0	0	1	0	0	0	0	0	0	0	-	-	-	-
			(3)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
	hydronephrosis		0	0	0	0	1	1	0	0	0	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(2)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 38 1 (%)	Control 38 2 (%)	Control 38 3 (%)	Control 38 4 (%)	50 ppm 42 1 (%)	50 ppm 42 2 (%)	50 ppm 42 3 (%)	50 ppm 42 4 (%)	200 ppm 41 1 (%)	200 ppm 41 2 (%)	200 ppm 41 3 (%)	200 ppm 41 4 (%)	800 ppm 0 1 (%)	800 ppm 0 2 (%)	800 ppm 0 3 (%)	800 ppm 0 4 (%)
[Endocrine system]																		
pituitary			<38>				<42>				<40>				< 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)	- (-)	- (-)	- (-)	- (-)
	Rathke pouch		2 (5)	0 (0)	0 (0)	0 (0)	8 (19)	0 (0)	0 (0)	0 (0)	3 (8)	0 (0)	0 (0)	0 (0)	- (-)	- (-)	- (-)	- (-)
[Reproductive system]																		
testis			<38>				<42>				<41>				< 0>			
	atrophy		11 (29)	0 (0)	0 (0)	0 (0)	15 (36)	0 (0)	0 (0)	0 (0)	17 (41)	0 (0)	0 (0)	0 (0)	- (-)	- (-)	- (-)	- (-)
epididymis			<38>				<42>				<41>				< 0>			
	spermatogenic granuloma		1 (3)	1 (3)	0 (0)	0 (0)	2 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	- (-)	- (-)	- (-)	- (-)
prep/cli gl			<38>				<42>				<41>				< 0>			
	inflammation		2 (5)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	- (-)	- (-)	- (-)	- (-)
[Nervous system]																		
brain			<38>				<42>				<41>				< 0>			
	mineralization		26 (68)	0 (0)	0 (0)	0 (0)	24 (57)	0 (0)	0 (0)	0 (0)	19 (46)	0 (0)	0 (0)	0 (0)	- (-)	- (-)	- (-)	- (-)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 38 1 (%)	Control 38 2 (%)	Control 38 3 (%)	Control 38 4 (%)	50 ppm 42 1 (%)	50 ppm 42 2 (%)	50 ppm 42 3 (%)	50 ppm 42 4 (%)	200 ppm 41 1 (%)	200 ppm 41 2 (%)	200 ppm 41 3 (%)	200 ppm 41 4 (%)	800 ppm 0 1 (%)	800 ppm 0 2 (%)	800 ppm 0 3 (%)	800 ppm 0 4 (%)
[Nervous system]																		
spinal cord		<a>	<38>				<42>				<41>				< 0>			
	degeneration		0	0	0	0	0	0	0	0	1	0	0	0	-	-	-	-
		(c)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
[Special sense organs/appandage]																		
Harder gl		<a>	<38>				<42>				<41>				< 0>			
	hyperplasia		0	0	0	0	0	0	0	0	1	0	0	0	-	-	-	-
		(c)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(-)	(-)	(-)	(-)

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

APPENDIX J 8

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOSUE : FEMALE : SACRIFICED ANIMALS

(TOW-YERA STUDY)

Organ	Findings	Group Name	Control				50 ppm				200 ppm				800 ppm			
		No. of Animals on Study	35				35				34				0			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
nasal cavit			<35>				<35>				<34>				< 0>			
	eosinophilic change:olfactory epithelium		10	10	0	0	11	3	1	0	8	0	0	0 **	-	-	-	-
			(29)	(29)	(0)	(0)	(31)	(9)	(3)	(0)	(24)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
	eosinophilic change:respiratory epithelium		18	7	0	0	16	8	0	0	19	5	1	0	-	-	-	-
			(51)	(20)	(0)	(0)	(46)	(23)	(0)	(0)	(56)	(15)	(3)	(0)	(-)	(-)	(-)	(-)
lung			<35>				<35>				<34>				< 0>			
	congestion		0	0	0	0	1	0	0	0	0	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
	hemorrhage		2	0	0	0	0	0	0	0	0	0	0	0	-	-	-	-
			(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
	bronchiolar-alveolar cell hyperplasia		0	0	0	0	1	0	0	0	0	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
[Hematopoietic system]																		
bone marrow			<35>				<35>				<34>				< 0>			
	granulation		6	0	0	0	3	0	0	0	4	0	0	0	-	-	-	-
			(17)	(0)	(0)	(0)	(9)	(0)	(0)	(0)	(12)	(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				50 ppm				200 ppm				800 ppm			
		No. of Animals on Study	35				35				34				0			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
bone marrow			<35>				<35>				<34>				< 0>			
	granulopoiesis:increased		1	0	0	0	0	1	0	0	1	0	0	0	-	-	-	-
			(3)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(3)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
spleen			<35>				<35>				<34>				< 0>			
	extramedullary hematopoiesis		3	1	1	0	1	1	0	0	0	0	1	0	-	-	-	-
			(9)	(3)	(3)	(0)	(3)	(3)	(0)	(0)	(0)	(0)	(3)	(0)	(-)	(-)	(-)	(-)
	follicular hyperplasia		5	0	0	0	5	0	0	0	4	0	0	0	-	-	-	-
			(14)	(0)	(0)	(0)	(14)	(0)	(0)	(0)	(12)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
[Circulatory system]																		
heart			<35>				<35>				<34>				< 0>			
	myocardial fibrosis		0	0	0	0	1	0	0	0	0	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
	arteritis		0	0	0	0	0	0	0	0	1	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
[Digestive system]																		
stomach			<35>				<35>				<34>				< 0>			
	hyperplasia:forestomach		0	0	0	0	0	0	0	0	1	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 35				50 ppm 35				200 ppm 34				800 ppm 0			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
stomach			<35>				<35>				<34>				< 0>			
	hyperplasia:glandular stomach		16	0	0	0	19	0	0	0	12	0	0	0	-	-	-	-
			(46)	(0)	(0)	(0)	(54)	(0)	(0)	(0)	(35)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
liver			<35>				<35>				<34>				< 0>			
	granulation		8	0	0	0	6	1	0	0	6	2	0	0	-	-	-	-
			(23)	(0)	(0)	(0)	(17)	(3)	(0)	(0)	(18)	(6)	(0)	(0)	(-)	(-)	(-)	(-)
	clear cell focus		0	0	0	0	1	0	0	0	0	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
	biliary cyst		1	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			<35>				<35>				<34>				< 0>			
	hyaline cast		0	0	0	0	1	0	0	0	0	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
urin bladd			<35>				<35>				<34>				< 0>			
	inflammation		1	0	0	0	0	0	0	0	0	0	0	0	-	-	-	-
			(3)	(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				50 ppm 35				200 ppm 34				800 ppm 0			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Endocrine system]																		
pituitary			<35>				<35>				<34>				< 0>			
	hyperplasia		6	0	0	0	3	0	0	0	2	0	0	0	-	-	-	-
			(17)	(0)	(0)	(0)	(9)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
	Rathke pouch		0	0	0	0	1	0	0	0	2	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
adrenal			<35>				<35>				<34>				< 0>			
	fatty change		0	0	0	0	2	0	0	0	0	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
[Reproductive system]																		
ovary			<35>				<35>				<34>				< 0>			
	thrombus		0	0	0	0	0	0	0	0	1	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
	cyst		5	0	0	0	4	0	0	0	8	0	0	0	-	-	-	-
			(14)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(24)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
uterus			<35>				<35>				<34>				< 0>			
	thrombus		0	0	0	0	1	0	0	0	0	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)

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

Organ	Findings	Group Name	Control				50 ppm				200 ppm				800 ppm			
		No. of Animals on Study	35				35				34				0			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
[Reproductive system]																		
uterus			<35>				<35>				<34>				< 0>			
	cyst		1	0	0	0	0	0	0	0	0	0	0	0	-	-	-	-
			(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
[Nervous system]																		
brain			<35>				<35>				<34>				< 0>			
	mineralization		8	0	0	0	5	0	0	0	17	0	0	0 *	-	-	-	-
			(23)	(0)	(0)	(0)	(14)	(0)	(0)	(0)	(50)	(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 K 1

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

RAT : MALE

STUDY NO. : 0210
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	50 ppm	224 ppm	1000 ppm
0 - 52	NO. OF EXAMINED ANIMALS		0	0	1	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		0	2	1	1
	NO. OF ANIMALS WITH TUMORS		0	2	1	1
	NO. OF ANIMALS WITH SINGLE TUMORS		0	0	1	1
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	2	0	0
	NO. OF BENIGN TUMORS		0	2	1	0
	NO. OF MALIGNANT TUMORS		0	2	0	1
	NO. OF TOTAL TUMORS		0	4	1	1
79 - 104	NO. OF EXAMINED ANIMALS		8	7	12	8
	NO. OF ANIMALS WITH TUMORS		8	7	12	8
	NO. OF ANIMALS WITH SINGLE TUMORS		2	1	1	1
	NO. OF ANIMALS WITH MULTIPLE TUMORS		6	6	11	7
	NO. OF BENIGN TUMORS		16	11	17	13
	NO. OF MALIGNANT TUMORS		6	6	11	8
	NO. OF TOTAL TUMORS		22	17	28	21
105 - 105	NO. OF EXAMINED ANIMALS		42	41	36	41
	NO. OF ANIMALS WITH TUMORS		42	41	36	41
	NO. OF ANIMALS WITH SINGLE TUMORS		17	15	10	12
	NO. OF ANIMALS WITH MULTIPLE TUMORS		25	26	26	29
	NO. OF BENIGN TUMORS		77	78	76	74
	NO. OF MALIGNANT TUMORS		7	8	9	9
	NO. OF TOTAL TUMORS		84	86	85	83

STUDY NO. : 0210
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	50 ppm	224 ppm	1000 ppm
0 - 105	NO. OF EXAMINED ANIMALS		50	50	50	50
	NO. OF ANIMALS WITH TUMORS		50	50	49	50
	NO. OF ANIMALS WITH SINGLE TUMORS		19	16	12	14
	NO. OF ANIMALS WITH MULTIPLE TUMORS		31	34	37	36
	NO. OF BENIGN TUMORS		93	91	94	87
	NO. OF MALIGNANT TUMORS		13	16	20	18
	NO. OF TOTAL TUMORS		106	107	114	105

APPENDIX K 2

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

RAT : FEMALE

STUDY NO. : 0210
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	50 ppm	224 ppm	1000 ppm
0 - 52	NO. OF EXAMINED ANIMALS		0	0	0	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		5	2	1	2
	NO. OF ANIMALS WITH TUMORS		5	2	1	2
	NO. OF ANIMALS WITH SINGLE TUMORS		4	2	1	1
	NO. OF ANIMALS WITH MULTIPLE TUMORS		1	0	0	1
	NO. OF BENIGN TUMORS		2	1	0	2
	NO. OF MALIGNANT TUMORS		4	1	1	1
	NO. OF TOTAL TUMORS		6	2	1	3
79 - 104	NO. OF EXAMINED ANIMALS		7	11	4	6
	NO. OF ANIMALS WITH TUMORS		7	11	3	6
	NO. OF ANIMALS WITH SINGLE TUMORS		4	4	2	5
	NO. OF ANIMALS WITH MULTIPLE TUMORS		3	7	1	1
	NO. OF BENIGN TUMORS		6	12	2	4
	NO. OF MALIGNANT TUMORS		5	8	2	3
	NO. OF TOTAL TUMORS		11	20	4	7
105 - 105	NO. OF EXAMINED ANIMALS		37	37	45	41
	NO. OF ANIMALS WITH TUMORS		27	26	31	31
	NO. OF ANIMALS WITH SINGLE TUMORS		12	12	12	18
	NO. OF ANIMALS WITH MULTIPLE TUMORS		15	14	19	13
	NO. OF BENIGN TUMORS		40	38	41	43
	NO. OF MALIGNANT TUMORS		6	7	13	7
	NO. OF TOTAL TUMORS		46	45	54	50

STUDY NO. : 0210
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	50 ppm	224 ppm	1000 ppm
0 - 105	NO. OF EXAMINED ANIMALS		49	50	50	50
	NO. OF ANIMALS WITH TUMORS		39	39	35	40
	NO. OF ANIMALS WITH SINGLE TUMORS		20	18	15	25
	NO. OF ANIMALS WITH MULTIPLE TUMORS		19	21	20	15
	NO. OF BENIGN TUMORS		48	51	43	49
	NO. OF MALIGNANT TUMORS		15	16	16	12
	NO. OF TOTAL TUMORS		63	67	59	61

APPENDIX K 3

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

MOUSE : MALE

STUDY NO. : 0211
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	50 ppm	200 ppm	800 ppm
0 - 52	NO. OF EXAMINED ANIMALS		2	0	1	5
	NO. OF ANIMALS WITH TUMORS		2	0	0	0
	NO. OF ANIMALS WITH SINGLE TUMORS		2	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		2	0	0	0
	NO. OF TOTAL TUMORS		2	0	0	0
53 - 78	NO. OF EXAMINED ANIMALS		6	0	1	9
	NO. OF ANIMALS WITH TUMORS		5	0	1	2
	NO. OF ANIMALS WITH SINGLE TUMORS		2	0	0	2
	NO. OF ANIMALS WITH MULTIPLE TUMORS		3	0	1	0
	NO. OF BENIGN TUMORS		3	0	1	1
	NO. OF MALIGNANT TUMORS		5	0	1	1
	NO. OF TOTAL TUMORS		8	0	2	2
79 - 104	NO. OF EXAMINED ANIMALS		4	8	7	34
	NO. OF ANIMALS WITH TUMORS		3	6	7	11
	NO. OF ANIMALS WITH SINGLE TUMORS		1	3	5	7
	NO. OF ANIMALS WITH MULTIPLE TUMORS		2	3	2	4
	NO. OF BENIGN TUMORS		1	5	2	9
	NO. OF MALIGNANT TUMORS		5	7	9	7
	NO. OF TOTAL TUMORS		6	12	11	16
105 - 105	NO. OF EXAMINED ANIMALS		38	42	41	0
	NO. OF ANIMALS WITH TUMORS		26	36	25	0
	NO. OF ANIMALS WITH SINGLE TUMORS		12	23	19	0
	NO. OF ANIMALS WITH MULTIPLE TUMORS		14	13	6	0
	NO. OF BENIGN TUMORS		22	23	14	0
	NO. OF MALIGNANT TUMORS		22	32	17	0
	NO. OF TOTAL TUMORS		44	55	31	0

STUDY NO. : 0211
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	50 ppm	200 ppm	800 ppm
0 - 105	NO. OF EXAMINED ANIMALS		50	50	50	48
	NO. OF ANIMALS WITH TUMORS		36	42	33	13
	NO. OF ANIMALS WITH SINGLE TUMORS		17	26	24	9
	NO. OF ANIMALS WITH MULTIPLE TUMORS		19	16	9	4
	NO. OF BENIGN TUMORS		26	28	17	10
	NO. OF MALIGNANT TUMORS		34	39	27	8
	NO. OF TOTAL TUMORS		60	67	44	18

APPENDIX K 4

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

MOUSE: FEMALE

STUDY NO. : 0211
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	50 ppm	200 ppm	800 ppm
0 - 52	NO. OF EXAMINED ANIMALS		0	0	0	9
	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	5	4	8
	NO. OF ANIMALS WITH TUMORS		1	4	4	4
	NO. OF ANIMALS WITH SINGLE TUMORS		0	3	4	3
	NO. OF ANIMALS WITH MULTIPLE TUMORS		1	1	0	1
	NO. OF BENIGN TUMORS		1	1	0	2
	NO. OF MALIGNANT TUMORS		1	4	4	3
	NO. OF TOTAL TUMORS		2	5	4	5
79 - 104	NO. OF EXAMINED ANIMALS		14	10	11	32
	NO. OF ANIMALS WITH TUMORS		13	10	10	11
	NO. OF ANIMALS WITH SINGLE TUMORS		12	6	6	10
	NO. OF ANIMALS WITH MULTIPLE TUMORS		1	4	4	1
	NO. OF BENIGN TUMORS		1	5	5	6
	NO. OF MALIGNANT TUMORS		13	10	10	6
	NO. OF TOTAL TUMORS		14	15	15	12
105 - 105	NO. OF EXAMINED ANIMALS		35	35	34	0
	NO. OF ANIMALS WITH TUMORS		28	26	25	0
	NO. OF ANIMALS WITH SINGLE TUMORS		15	13	10	0
	NO. OF ANIMALS WITH MULTIPLE TUMORS		13	13	15	0
	NO. OF BENIGN TUMORS		21	23	30	0
	NO. OF MALIGNANT TUMORS		26	19	15	0
	NO. OF TOTAL TUMORS		47	42	45	0

STUDY NO. : 0211
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	50 ppm	200 ppm	800 ppm
0 - 105	NO. OF EXAMINED ANIMALS		50	50	49	49
	NO. OF ANIMALS WITH TUMORS		42	40	39	15
	NO. OF ANIMALS WITH SINGLE TUMORS		27	22	20	13
	NO. OF ANIMALS WITH MULTIPLE TUMORS		15	18	19	2
	NO. OF BENIGN TUMORS		23	29	35	8
	NO. OF MALIGNANT TUMORS		40	33	29	9
	NO. OF TOTAL TUMORS		63	62	64	17

APPENDIX L 1

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS : SUMMARY

RAT : MALE :

(TOW-YERA STUDY)

Organ	Findings	Group Name / No. of animals on Study	Control 50	50 ppm 50	224 ppm 50	1000 ppm 50
[Integumentary system/appandage]						
skin/app			<50>	<50>	<50>	<50>
	squamous cell papilloma		0 (0%)	0 (0%)	1 (2%)	1 (2%)
	trichoepithelioma		0 (0%)	1 (2%)	1 (2%)	0 (0%)
	keratoacanthoma		4 (8%)	1 (2%)	4 (8%)	0 (0%)
	sebaceous adenoma		2 (4%)	0 (0%)	0 (0%)	0 (0%)
	squamous cell carcinoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
subcutis			<50>	<50>	<50>	<50>
	fibroma		5 (10%)	5 (10%)	7 (14%)	2 (4%)
	lipoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
	schwannoma:malignant		1 (2%)	1 (2%)	0 (0%)	0 (0%)
	histiocytic sarcoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
[Respiratory system]						
lung			<50>	<50>	<50>	<50>
	bronchiolar-alveolar adenoma		0 (0%)	1 (2%)	3 (6%)	4 (8%)
	bronchiolar-alveolar carcinoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
[Hematopoietic system]						
bone marrow			<50>	<50>	<50>	<50>
	fibrosarcoma		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	50 ppm 50	224 ppm 50	1000 ppm 50
[Hematopoietic system]						
bone marrow			<50>	<50>	<50>	<50>
	malignant histiocytosis		0 (0%)	1 (2%)	0 (0%)	0 (0%)
thymus			<50>	<50>	<50>	<50>
	adenoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
spleen			<50>	<50>	<50>	<50>
	hemangioma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
	mononuclear cell leukemia		3 (6%)	7 (14%)	9 (18%)	6 (12%)
[Circulatory system]						
heart			<50>	<50>	<50>	<50>
	schwannoma:malignant		0 (0%)	1 (2%)	1 (2%)	1 (2%)
[Digestive system]						
tongue			<50>	<50>	<50>	<50>
	squamous cell papilloma		2 (4%)	0 (0%)	0 (0%)	0 (0%)
stomach			<50>	<50>	<50>	<50>
	squamous cell papilloma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
small intes			<50>	<50>	<50>	<50>
	adenocarcinoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
liver			<50>	<50>	<50>	<50>
	hepatocellular adenoma		1 (2%)	1 (2%)	0 (0%)	1 (2%)
	hepatocellular carcinoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
	cholangiocellular carcinoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)

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

Organ	Findings	Group Name / No. of animals on Study	Control 50	50 ppm 50	224 ppm 50	1000 ppm 50
[Urinary system]						
kidney			<50>	<50>	<50>	<50>
	transitional cell carcinoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
urin bladd			<50>	<50>	<50>	<50>
	transitional cell papilloma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
[Endocrine system]						
pituitary			<50>	<50>	<50>	<50>
	adenoma		10 (20%)	13 (26%)	12 (24%)	15 (30%)
	adenocarcinoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
thyroid			<50>	<50>	<50>	<50>
	C-cell adenoma		5 (10%)	7 (14%)	7 (14%)	4 (8%)
	follicular adenoma		1 (2%)	1 (2%)	1 (2%)	3 (6%)
	C-cell carcinoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
	follicular adenocarcinoma		2 (4%)	0 (0%)	2 (4%)	3 (6%)
panc islet			<50>	<50>	<50>	<50>
	adenoma		2 (4%)	4 (8%)	4 (8%)	1 (2%)
adrenal			<50>	<50>	<50>	<50>
	pheochromocytoma		7 (14%)	5 (10%)	4 (8%)	4 (8%)
	ganglioneuroma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
	cortical adenoma		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	50 ppm 50	224 ppm 50	1000 ppm 50
[Endocrine system]						
adrenal			<50>	<50>	<50>	<50>
	pheochromocytoma:malignant		1 (2%)	0 (0%)	2 (4%)	0 (0%)
[Reproductive system]						
testis			<50>	<50>	<50>	<50>
	interstitial cell tumor		48 (96%)	47 (94%)	45 (90%)	47 (94%)
mammary gl			<50>	<50>	<50>	<50>
	fibroadenoma		1 (2%)	1 (2%)	3 (6%)	1 (2%)
prep/cli gl			<50>	<50>	<50>	<50>
	adenoma		1 (2%)	2 (4%)	2 (4%)	1 (2%)
[Nervous system]						
brain			<50>	<50>	<50>	<50>
	malignant reticulosis		0 (0%)	0 (0%)	0 (0%)	2 (4%)
[Special sense organs/appandage]						
Harder gl			<50>	<50>	<50>	<50>
	adenoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
[Musculoskeletal system]						
bone			<50>	<50>	<50>	<50>
	osteosarcoma		1 (2%)	0 (0%)	0 (0%)	1 (2%)
vertebra			<50>	<50>	<50>	<50>
	chordoma:malignant		0 (0%)	0 (0%)	0 (0%)	1 (2%)
[Body cavities]						
pleura			<50>	<50>	<50>	<50>
	sarcoma:NOS		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	50 ppm 50	224 ppm 50	1000 ppm 50
[Body cavities]						
peritoneum			<50>	<50>	<50>	<50>
	mesothelioma		1 (2%)	4 (8%)	2 (4%)	2 (4%)
retroperit			<50>	<50>	<50>	<50>
	lipoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)

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

APPENDIX L 2

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE :

(TOW-YERA STUDY)

Organ	Findings	Group Name / No. of animals on Study	Control 49	50 ppm 50	224 ppm 50	1000 ppm 50
[Integumentary system/appandage]						
skin/app			<49>	<50>	<50>	<50>
	keratoacanthoma		0 (0%)	1 (2%)	2 (4%)	0 (0%)
	adenocarcinoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
subcutis			<49>	<50>	<50>	<50>
	fibroma		2 (4%)	1 (2%)	1 (2%)	0 (0%)
	lipoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
	xanthoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
	fibrosarcoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
[Respiratory system]						
lung			<49>	<50>	<50>	<50>
	bronchiolar-alveolar adenoma		5 (10%)	0 (0%)	0 (0%)	2 (4%)
	bronchiolar-alveolar carcinoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
[Hematopoietic system]						
bone marrow			<49>	<50>	<50>	<50>
	malignant histiocytosis		0 (0%)	0 (0%)	1 (2%)	0 (0%)
spleen			<49>	<50>	<50>	<50>
	mononuclear cell leukemia		8 (16%)	10 (20%)	7 (14%)	6 (12%)
[Digestive system]						
oral cavity			<49>	<50>	<50>	<50>
	squamous cell papilloma		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 49	50 ppm 50	224 ppm 50	1000 ppm 50
[Digestive system]						
tongue			<49>	<50>	<50>	<50>
	squamous cell carcinoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
salivary gl			<49>	<50>	<50>	<50>
	adenoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
small intes			<49>	<50>	<50>	<50>
	fibrosarcoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
[Urinary system]						
urin bladd			<49>	<50>	<50>	<50>
	transitional cell papilloma		0 (0%)	1 (2%)	0 (0%)	1 (2%)
	transitional cell carcinoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
[Endocrine system]						
pituitary			<49>	<50>	<50>	<50>
	adenoma		20 (41%)	20 (40%)	19 (38%)	16 (32%)
	adenocarcinoma		1 (2%)	1 (2%)	1 (2%)	0 (0%)
thyroid			<49>	<50>	<50>	<50>
	C-cell adenoma		4 (8%)	6 (12%)	4 (8%)	3 (6%)
	follicular adenoma		2 (4%)	0 (0%)	0 (0%)	1 (2%)
	C-cell carcinoma		0 (0%)	0 (0%)	1 (2%)	1 (2%)
	follicular adenocarcinoma		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 49	50 ppm 50	224 ppm 50	1000 ppm 50
[Endocrine system]						
panc islet			<49>	<50>	<50>	<50>
	adenoma		0 (0%)	2 (4%)	0 (0%)	0 (0%)
adrenal			<49>	<50>	<50>	<50>
	pheochromocytoma		1 (2%)	0 (0%)	2 (4%)	1 (2%)
	ganglioneuroma		0 (0%)	2 (4%)	0 (0%)	0 (0%)
	cortical adenoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
	pheochromocytoma:malignant		1 (2%)	1 (2%)	0 (0%)	0 (0%)
[Reproductive system]						
ovary			<49>	<50>	<50>	<50>
	sertoli cell tumor		0 (0%)	0 (0%)	0 (0%)	1 (2%)
	granulosa-theca cell tumor:malignant		1 (2%)	0 (0%)	0 (0%)	0 (0%)
uterus			<49>	<50>	<50>	<50>
	squamous cell papilloma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
	adenoma		1 (2%)	0 (0%)	0 (0%)	1 (2%)
	leiomyoma		0 (0%)	0 (0%)	0 (0%)	2 (4%)
	endometrial stromal polyp		3 (6%)	9 (18%)	5 (10%)	11 (22%)
	endometrial stromal sarcoma		0 (0%)	0 (0%)	1 (2%)	1 (2%)

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

Organ	Findings	Group Name / No. of animals on Study	Control 49	50 ppm 50	224 ppm 50	1000 ppm 50
[Reproductive system]						
mammary gl			<49>	<50>	<50>	<50>
	adenoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
	fibroadenoma		7 (14%)	6 (12%)	6 (12%)	4 (8%)
	adenocarcinoma		0 (0%)	2 (4%)	1 (2%)	1 (2%)
prep/cli gl			<49>	<50>	<50>	<50>
	adenoma		1 (2%)	1 (2%)	1 (2%)	3 (6%)
[Nervous system]						
brain			<49>	<50>	<50>	<50>
	malignant reticulosis		2 (4%)	0 (0%)	0 (0%)	0 (0%)
	glioma		1 (2%)	0 (0%)	0 (0%)	1 (2%)
periph nerv			<49>	<50>	<50>	<50>
	carcinoid tumor		1 (2%)	0 (0%)	0 (0%)	0 (0%)
[Special sense organs/appandage]						
Harder gl			<49>	<50>	<50>	<50>
	adenoma		1 (2%)	0 (0%)	1 (2%)	0 (0%)
[Musculoskeletal system]						
muscle			<49>	<50>	<50>	<50>
	sarcoma:NOS		1 (2%)	0 (0%)	0 (0%)	0 (0%)
[Body cavities]						
mediastinum			<49>	<50>	<50>	<50>
	squamous cell carcinoma		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 L 3

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS : SUMMARY

MOUSE: MALE

(TOW-YERA STUDY)

STUDY NO. : 0211
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name / No. of animals on Study	Control 50	50 ppm 50	200 ppm 50	800 ppm 48
[Integumentary system/appandage]						
skin/app			<50>	<50>	<50>	<48>
	keratoacanthoma		0 (0%)	0 (0%)	2 (4%)	0 (0%)
	squamous cell carcinoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
subcutis			<50>	<50>	<50>	<48>
	histiocytic sarcoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
	hemangiosarcoma		1 (2%)	0 (0%)	1 (2%)	0 (0%)
[Respiratory system]						
lung			<50>	<50>	<50>	<48>
	bronchiolar-alveolar adenoma		8 (16%)	10 (20%)	5 (10%)	2 (4%)
	bronchiolar-alveolar carcinoma		6 (12%)	6 (12%)	3 (6%)	0 (0%)
[Hematopoietic system]						
bone marrow			<50>	<50>	<50>	<48>
	histiocytic sarcoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
lymph node			<50>	<50>	<50>	<48>
	malignant lymphoma		4 (8%)	5 (10%)	4 (8%)	1 (2%)
spleen			<50>	<50>	<50>	<48>
	hemangioma		0 (0%)	2 (4%)	0 (0%)	0 (0%)
	malignant lymphoma		4 (8%)	8 (16%)	4 (8%)	2 (4%)
	mastcytoma:malignant		0 (0%)	0 (0%)	2 (4%)	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	50 ppm 50	200 ppm 50	800 ppm 48
[Hematopoietic system]						
spleen			<50>	<50>	<50>	<48>
	hemangiosarcoma		1 (2%)	1 (2%)	2 (4%)	0 (0%)
[Digestive system]						
salivary gl			<50>	<50>	<50>	<48>
	histiocytic sarcoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
liver			<50>	<49>	<50>	<48>
	hemangioma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
	hepatocellular adenoma		13 (26%)	12 (24%)	9 (18%)	2 (4%)
	histiocytic sarcoma		0 (0%)	3 (6%)	2 (4%)	0 (0%)
	hemangiosarcoma		3 (6%)	5 (10%)	2 (4%)	0 (0%)
	hepatocellular carcinoma		5 (10%)	8 (16%)	4 (8%)	2 (4%)
[Urinary system]						
kidney			<50>	<50>	<50>	<48>
	renal cell adenoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
	liposarcoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
	renal cell carcinoma		0 (0%)	0 (0%)	1 (2%)	1 (2%)
urin bladd			<50>	<50>	<50>	<48>
	histiocytic sarcoma		2 (4%)	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	Control	50 ppm	200 ppm	800 ppm
		No. of animals on Study	50	50	50	48
[Endocrine system]						
pituitary			<49>	<50>	<48>	<47>
	adenoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
[Reproductive system]						
testis			<50>	<50>	<50>	<48>
	interstitial cell tumor		1 (2%)	1 (2%)	0 (0%)	0 (0%)
epididymis			<50>	<50>	<50>	<48>
	histiocytic sarcoma		1 (2%)	1 (2%)	0 (0%)	0 (0%)
[Nervous system]						
brain			<50>	<50>	<50>	<48>
	histiocytic sarcoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
periph nerv			<50>	<50>	<50>	<48>
	schwannoma:malignant		1 (2%)	0 (0%)	0 (0%)	0 (0%)
	histiocytic sarcoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
[Special sense organs/appandage]						
Harder gl			<50>	<50>	<50>	<48>
	adenoma		3 (6%)	2 (4%)	1 (2%)	5 (10%)
[Musculoskeletal system]						
muscle			<50>	<50>	<50>	<48>
	leiomyosarcoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
[Body cavities]						
pleura			<50>	<50>	<50>	<48>
	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

STUDY NO. : 0211
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control	50 ppm	200 ppm	800 ppm
		No. of animals on Study	50	50	50	48
[Body cavities]						
mediastinum			<50>	<50>	<50>	<48>
	histiocytic sarcoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)

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

APPENDIX L 4

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS : SUMMARY

MOUSE: FEMALE

(TOW-YERA STUDY)

Organ	Findings	Group Name	Control	50 ppm	200 ppm	800 ppm
		No. of animals on Study	50	50	49	49
[Integumentary system/appandage]						
subcutis			<50>	<50>	<49>	<49>
	malignant fibrous histiocytoma		0 (0%)	1 (2%)	0 (0%)	1 (2%)
	histiocytic sarcoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
[Respiratory system]						
lung			<50>	<50>	<49>	<49>
	bronchiolar-alveolar adenoma		4 (8%)	3 (6%)	9 (18%)	3 (6%)
	bronchiolar-alveolar carcinoma		0 (0%)	1 (2%)	1 (2%)	0 (0%)
[Hematopoietic system]						
bone marrow			<50>	<50>	<49>	<49>
	hemangioma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
lymph node			<50>	<50>	<49>	<49>
	malignant lymphoma		9 (18%)	9 (18%)	3 (6%)	0 (0%)
spleen			<50>	<50>	<49>	<49>
	malignant lymphoma		14 (28%)	9 (18%)	9 (18%)	2 (4%)
	mastcytoma:malignant		0 (0%)	0 (0%)	0 (0%)	1 (2%)
	hemangiosarcoma		0 (0%)	1 (2%)	1 (2%)	0 (0%)
[Digestive system]						
stomach			<50>	<50>	<49>	<49>
	squamous cell papilloma		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	50 ppm 50	200 ppm 49	800 ppm 49
[Digestive system]						
stomach			<50>	<50>	<49>	<49>
	squamous cell carcinoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
liver			<50>	<50>	<49>	<49>
	hemangioma		1 (2%)	2 (4%)	0 (0%)	0 (0%)
	hepatocellular adenoma		2 (4%)	5 (10%)	7 (14%)	3 (6%)
	hemangiosarcoma		2 (4%)	1 (2%)	2 (4%)	0 (0%)
	hepatocellular carcinoma		4 (8%)	3 (6%)	0 (0%)	0 (0%)
[Endocrine system]						
pituitary			<50>	<50>	<49>	<48>
	adenoma		9 (18%)	10 (20%)	12 (24%)	1 (2%)
adrenal			<50>	<50>	<49>	<49>
	pheochromocytoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
[Reproductive system]						
ovary			<50>	<50>	<49>	<49>
	cystadenoma		2 (4%)	3 (6%)	4 (8%)	1 (2%)
	histiocytic sarcoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
uterus			<50>	<50>	<49>	<49>
	adenoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
	endometrial stromal polyp		3 (6%)	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	50 ppm 50	200 ppm 49	800 ppm 49
[Reproductive system]						
uterus			<50>	<50>	<49>	<49>
	histiocytic sarcoma		6 (12%)	7 (14%)	11 (22%)	5 (10%)
	hemangiosarcoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
	endometrial stromal sarcoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
mammary gl			<50>	<50>	<49>	<49>
	adenocarcinoma		1 (2%)	1 (2%)	0 (0%)	0 (0%)
[Special sense organs/appandage]						
Harder gl			<50>	<50>	<49>	<49>
	adenoma		2 (4%)	3 (6%)	1 (2%)	0 (0%)
[Body cavities]						
peritoneum			<50>	<50>	<49>	<49>
	leiomyosarcoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)

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

APPENDIX M 1

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

RAT : MALE

(TOW-YERA STUDY)

Group Name	Control	50 ppm	224 ppm	1000 ppm
	SITE : skin/appendage TUMOR : keratoacanthoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	1/50(2.0)	4/50(8.0)	0/50(0.0)
Adjusted rates(b)	9.52	2.44	11.11	0.0
Terminal rates(c)	4/42(9.5)	1/41(2.4)	4/36(11.1)	0/41(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.9593			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.1033			
Fisher Exact test(e)		P = 0.1998	P = 0.3579	P = 0.0688
	SITE : subcutis TUMOR : fibroma			
Tumor rate				
Overall rates(a)	5/50(10.0)	5/50(10.0)	7/50(14.0)	2/50(4.0)
Adjusted rates(b)	10.20	10.87	11.36	4.88
Terminal rates(c)	3/42(7.1)	4/41(9.8)	4/36(11.1)	2/41(4.9)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5373			
Prevalence method(d)	P = 0.9079			
Combined analysis(d)	P = 0.9142			
Cochran-Armitage test(e)	P = 0.1805			
Fisher Exact test(e)		P = 0.3710	P = 0.4062	P = 0.2425
	SITE : lung TUMOR : bronchiolar-alveolar adenoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	1/50(2.0)	3/50(6.0)	4/50(8.0)
Adjusted rates(b)	0.0	2.44	8.33	9.52
Terminal rates(c)	0/42(0.0)	1/41(2.4)	3/36(8.3)	3/41(7.3)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.0376*			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.0511			
Fisher Exact test(e)		P = 0.4950	P = 0.1325	P = 0.0688

Group Name	Control	50 ppm	224 ppm	1000 ppm
	SITE : lung TUMOR : bronchiolar-alveolar adenoma,bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	1/50(2.0)	3/50(6.0)	4/50(8.0)
Adjusted rates(b)	2.38	2.44	8.33	9.52
Terminal rates(c)	1/42(2.4)	1/41(2.4)	3/36(8.3)	3/41(7.3)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.0730			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.1155			
Fisher Exact test(e)		P = 0.2475	P = 0.3235	P = 0.1998
	SITE : spleen TUMOR : mononuclear cell leukemia			
Tumor rate				
Overall rates(a)	3/50(6.0)	7/50(14.0)	9/50(18.0)	6/50(12.0)
Adjusted rates(b)	2.38	9.76	8.33	8.70
Terminal rates(c)	1/42(2.4)	4/41(9.8)	3/36(8.3)	3/41(7.3)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.6508			
Prevalence method(d)	P = 0.2330			
Combined analysis(d)	P = 0.4185			
Cochran-Armitage test(e)	P = 0.8301			
Fisher Exact test(e)		P = 0.1917	P = 0.0899	P = 0.2728
	SITE : pituitary gland TUMOR : adenoma			
Tumor rate				
Overall rates(a)	10/50(20.0)	13/50(26.0)	12/50(24.0)	15/50(30.0)
Adjusted rates(b)	20.83	25.58	30.56	31.82
Terminal rates(c)	8/42(19.0)	9/41(22.0)	11/36(30.6)	13/41(31.7)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3062			
Prevalence method(d)	P = 0.1895			
Combined analysis(d)	P = 0.1665			
Cochran-Armitage test(e)	P = 0.3272			
Fisher Exact test(e)		P = 0.3703	P = 0.4406	P = 0.2516

Group Name	Control	50 ppm	224 ppm	1000 ppm
	SITE : pituitary gland TUMOR : adenoma,adenocarcinoma			
Tumor rate				
Overall rates(a)	10/50(20.0)	14/50(28.0)	12/50(24.0)	15/50(30.0)
Adjusted rates(b)	20.83	26.09	30.56	31.82
Terminal rates(c)	8/42(19.0)	9/41(22.0)	11/36(30.6)	13/41(31.7)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.4356			
Prevalence method(d)	P = 0.1962			
Combined analysis(d)	P = 0.2028			
Cochran-Armitage test(e)	P = 0.3870			
Fisher Exact test(e)		P = 0.3071	P = 0.4406	P = 0.2516
	SITE : thyroid TUMOR : C-cell adenoma			
Tumor rate				
Overall rates(a)	5/50(10.0)	7/50(14.0)	7/50(14.0)	4/50(8.0)
Adjusted rates(b)	11.90	17.07	19.44	9.76
Terminal rates(c)	5/42(11.9)	7/41(17.1)	7/36(19.4)	4/41(9.8)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.7796			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.4379			
Fisher Exact test(e)		P = 0.4062	P = 0.4062	P = 0.4883
	SITE : thyroid TUMOR : follicular adenoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	1/50(2.0)	1/50(2.0)	3/50(6.0)
Adjusted rates(b)	2.13	2.44	2.70	7.32
Terminal rates(c)	0/42(0.0)	1/41(2.4)	0/36(0.0)	3/41(7.3)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.0886			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.1601			
Fisher Exact test(e)		P = 0.2475	P = 0.2475	P = 0.3235

Group Name	Control	50 ppm	224 ppm	1000 ppm
	SITE : thyroid TUMOR : follicular adenocarcinoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	0/50(0.0)	2/50(4.0)	3/50(6.0)
Adjusted rates(b)	4.76	0.0	5.56	6.98
Terminal rates(c)	2/42(4.8)	0/41(0.0)	2/36(5.6)	2/41(4.9)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.1282			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.2437			
Fisher Exact test(e)		P = 0.2574	P = 0.3088	P = 0.4909
	SITE : thyroid TUMOR : C-cell adenoma,C-cell carcinoma			
Tumor rate				
Overall rates(a)	5/50(10.0)	7/50(14.0)	7/50(14.0)	5/50(10.0)
Adjusted rates(b)	11.90	17.07	19.44	12.20
Terminal rates(c)	5/42(11.9)	7/41(17.1)	7/36(19.4)	5/41(12.2)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.6478			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.6944			
Fisher Exact test(e)		P = 0.4062	P = 0.4062	P = 0.3710
	SITE : thyroid TUMOR : follicular adenoma,follicular adenocarcinoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	1/50(2.0)	3/50(6.0)	6/50(12.0)
Adjusted rates(b)	6.38	2.44	8.11	13.95
Terminal rates(c)	2/42(4.8)	1/41(2.4)	2/36(5.6)	5/41(12.2)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.0359*			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.0656			
Fisher Exact test(e)		P = 0.3235	P = 0.3392	P = 0.2728

Group Name	Control	50 ppm	224 ppm	1000 ppm
	SITE : pancreas islet TUMOR : adenoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	4/50(8.0)	4/50(8.0)	1/50(2.0)
Adjusted rates(b)	4.76	8.51	11.11	2.44
Terminal rates(c)	2/42(4.8)	3/41(7.3)	4/36(11.1)	1/41(2.4)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.8615			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.2777			
Fisher Exact test(e)		P = 0.3574	P = 0.3574	P = 0.4926
	SITE : adrenal gland TUMOR : pheochromocytoma			
Tumor rate				
Overall rates(a)	7/50(14.0)	5/50(10.0)	4/50(8.0)	4/50(8.0)
Adjusted rates(b)	14.89	10.87	9.52	8.89
Terminal rates(c)	5/42(11.9)	4/41(9.8)	3/36(8.3)	3/41(7.3)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.7515			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.4731			
Fisher Exact test(e)		P = 0.4062	P = 0.2958	P = 0.2958
	SITE : testis TUMOR : interstitial cell tumor			
Tumor rate				
Overall rates(a)	48/50(96.0)	47/50(94.0)	45/50(90.0)	47/50(94.0)
Adjusted rates(b)	97.96	100.00	95.74	97.67
Terminal rates(c)	41/42(97.6)	41/41(100.0)	34/36(94.4)	40/41(97.6)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.5333			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.9264			
Fisher Exact test(e)		P = 0.4722	P = 0.4682	P = 0.4722

Group Name	Control	50 ppm	224 ppm	1000 ppm
	SITE : mammary gland TUMOR : fibroadenoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	1/50(2.0)	3/50(6.0)	1/50(2.0)
Adjusted rates(b)	2.38	2.44	8.33	2.44
Terminal rates(c)	1/42(2.4)	1/41(2.4)	3/36(8.3)	1/41(2.4)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.5464			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.8455			
Fisher Exact test(e)		P = 0.2475	P = 0.3235	P = 0.2475
	SITE : peritoneum TUMOR : mesothelioma			
Tumor rate				
Overall rates(a)	1/50(2.0)	4/50(8.0)	2/50(4.0)	2/50(4.0)
Adjusted rates(b)	0.0	4.88	0.0	0.0
Terminal rates(c)	0/42(0.0)	2/41(4.9)	0/36(0.0)	0/41(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3626			
Prevalence method(d)	P = 0.8006			
Combined analysis(d)	P = 0.5459			
Cochran-Armitage test(e)	P = 0.8530			
Fisher Exact test(e)		P = 0.1998	P = 0.4926	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 M 2

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

RAT : FEMALE

(TOW-YERA STUDY)

Group Name	Control	50 ppm	224 ppm	1000 ppm
	SITE : lung TUMOR : bronchiolar-alveolar adenoma			
Tumor rate				
Overall rates(a)	5/49(10.2)	0/50(0.0)	0/50(0.0)	2/50(4.0)
Adjusted rates(b)	13.51	0.0	0.0	4.88
Terminal rates(c)	5/37(13.5)	0/37(0.0)	0/45(0.0)	2/41(4.9)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.5913			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.8180			
Fisher Exact test(e)		P = 0.0344*	P = 0.0344*	P = 0.2345
	SITE : lung TUMOR : bronchiolar-alveolar adenoma,bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	5/49(10.2)	1/50(2.0)	0/50(0.0)	2/50(4.0)
Adjusted rates(b)	13.51	2.70	0.0	4.88
Terminal rates(c)	5/37(13.5)	1/37(2.7)	0/45(0.0)	2/41(4.9)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.6833			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.6470			
Fisher Exact test(e)		P = 0.1163	P = 0.0344*	P = 0.2345
	SITE : spleen TUMOR : mononuclear cell leukemia			
Tumor rate				
Overall rates(a)	8/49(16.3)	10/50(20.0)	7/50(14.0)	6/50(12.0)
Adjusted rates(b)	8.11	14.63	15.56	7.32
Terminal rates(c)	3/37(8.1)	5/37(13.5)	7/45(15.6)	3/41(7.3)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.6620			
Prevalence method(d)	P = 0.7756			
Combined analysis(d)	P = 0.8126			
Cochran-Armitage test(e)	P = 0.3677			
Fisher Exact test(e)		P = 0.4459	P = 0.5000	P = 0.4019

Group Name	Control	50 ppm	224 ppm	1000 ppm
	SITE : pituitary gland TUMOR : adenoma			
Tumor rate				
Overall rates(a)	20/49(40.8)	20/50(40.0)	19/50(38.0)	16/50(32.0)
Adjusted rates(b)	45.95	38.10	40.00	31.71
Terminal rates(c)	17/37(45.9)	14/37(37.8)	18/45(40.0)	13/41(31.7)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.4219			
Prevalence method(d)	P = 0.9105			
Combined analysis(d)	P = 0.8723			
Cochran-Armitage test(e)	P = 0.3173			
Fisher Exact test(e)		P = 0.4047	P = 0.5000	P = 0.3346
	SITE : pituitary gland TUMOR : adenoma,adenocarcinoma			
Tumor rate				
Overall rates(a)	21/49(42.9)	21/50(42.0)	20/50(40.0)	16/50(32.0)
Adjusted rates(b)	45.95	38.10	42.22	31.71
Terminal rates(c)	17/37(45.9)	14/37(37.8)	19/45(42.2)	13/41(31.7)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5964			
Prevalence method(d)	P = 0.9217			
Combined analysis(d)	P = 0.9179			
Cochran-Armitage test(e)	P = 0.2149			
Fisher Exact test(e)		P = 0.4056	P = 0.5000	P = 0.2877
	SITE : thyroid TUMOR : C-cell adenoma			
Tumor rate				
Overall rates(a)	4/49(8.2)	6/50(12.0)	4/50(8.0)	3/50(6.0)
Adjusted rates(b)	10.81	14.29	8.89	7.32
Terminal rates(c)	4/37(10.8)	4/37(10.8)	4/45(8.9)	3/41(7.3)
Statistical analysis				
Peto test				
Standard method(d)	P = -------			
Prevalence method(d)	P = 0.7677			
Combined analysis(d)	P = -------			
Cochran-Armitage test(e)	P = 0.4325			
Fisher Exact test(e)		P = 0.4066	P = 0.3474	P = 0.5000

Group Name	Control	50 ppm	224 ppm	1000 ppm
	SITE : thyroid TUMOR : C-cell adenoma,C-cell carcinoma			
Tumor rate				
Overall rates(a)	4/49(8.2)	6/50(12.0)	5/50(10.0)	4/50(8.0)
Adjusted rates(b)	10.81	14.29	11.11	9.76
Terminal rates(c)	4/37(10.8)	4/37(10.8)	5/45(11.1)	4/41(9.8)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.6265			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.6916			
Fisher Exact test(e)		P = 0.4066	P = 0.4763	P = 0.3474
	SITE : uterus TUMOR : endometrial stromal polyp			
Tumor rate				
Overall rates(a)	3/49(6.1)	9/50(18.0)	5/50(10.0)	11/50(22.0)
Adjusted rates(b)	7.32	19.05	11.11	24.39
Terminal rates(c)	2/37(5.4)	5/37(13.5)	5/45(11.1)	10/41(24.4)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5031			
Prevalence method(d)	P = 0.0274*			
Combined analysis(d)	P = 0.0399*			
Cochran-Armitage test(e)	P = 0.0677			
Fisher Exact test(e)		P = 0.0955	P = 0.3899	P = 0.0434*
	SITE : uterus TUMOR : endometrial stromal polyp,endometrial stromal sarcoma			
Tumor rate				
Overall rates(a)	3/49(6.1)	9/50(18.0)	6/50(12.0)	12/50(24.0)
Adjusted rates(b)	7.32	19.05	11.11	24.39
Terminal rates(c)	2/37(5.4)	5/37(13.5)	5/45(11.1)	10/41(24.4)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3063			
Prevalence method(d)	P = 0.0245*			
Combined analysis(d)	P = 0.0228*			
Cochran-Armitage test(e)	P = 0.0391*			
Fisher Exact test(e)		P = 0.0955	P = 0.2829	P = 0.0290*

Group Name	Control	50 ppm	224 ppm	1000 ppm
	SITE : mammary gland TUMOR : fibroadenoma			
Tumor rate				
Overall rates(a)	7/49(14.3)	6/50(12.0)	6/50(12.0)	4/50(8.0)
Adjusted rates(b)	17.95	16.22	13.04	9.76
Terminal rates(c)	6/37(16.2)	6/37(16.2)	5/45(11.1)	4/41(9.8)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.8399			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.3439			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.2850
	SITE : preputial/clitoral gland TUMOR : adenoma			
Tumor rate				
Overall rates(a)	1/49(2.0)	1/50(2.0)	1/50(2.0)	3/50(6.0)
Adjusted rates(b)	2.70	2.70	2.22	4.88
Terminal rates(c)	1/37(2.7)	1/37(2.7)	1/45(2.2)	2/41(4.9)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1688			
Prevalence method(d)	P = 0.2395			
Combined analysis(d)	P = 0.1047			
Cochran-Armitage test(e)	P = 0.1634			
Fisher Exact test(e)		P = 0.2426	P = 0.2426	P = 0.3312

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

APPENDIX M 3

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

MOSUE : MALE

(TOW-YERA STUDY)

Group Name	Control	50 ppm	200 ppm
	SITE : lung TUMOR : bronchiolar-alveolar adenoma		
Tumor rate			
Overall rates(a)	8/50(16.0)	10/50(20.0)	5/50(10.0)
Adjusted rates(b)	18.60	21.74	11.90
Terminal rates(c)	7/38(18.4)	8/42(19.0)	4/41(9.8)
Statistical analysis			
Peto test			
Standard method(d)	P = ------		
Prevalence method(d)	P = 0.8970		
Combined analysis(d)	P = ------		
Cochran-Armitage test(e)	P = 0.2665		
Fisher Exact test(e)		P = 0.4300	P = 0.3141
	SITE : lung TUMOR : bronchiolar-alveolar carcinoma		
Tumor rate			
Overall rates(a)	6/50(12.0)	6/50(12.0)	3/50(6.0)
Adjusted rates(b)	12.50	14.29	7.32
Terminal rates(c)	4/38(10.5)	6/42(14.3)	3/41(7.3)
Statistical analysis			
Peto test			
Standard method(d)	P = 1.0000 ?		
Prevalence method(d)	P = 0.8503		
Combined analysis(d)	P = 0.9007		
Cochran-Armitage test(e)	P = 0.2623		
Fisher Exact test(e)		P = 0.3807	P = 0.2728
	SITE : lung TUMOR : bronchiolar-alveolar adenoma,bronchiolar-alveolar carcinoma		
Tumor rate			
Overall rates(a)	14/50(28.0)	16/50(32.0)	8/50(16.0)
Adjusted rates(b)	30.95	34.78	19.05
Terminal rates(c)	11/38(28.9)	14/42(33.3)	7/41(17.1)
Statistical analysis			
Peto test			
Standard method(d)	P = 1.0000 ?		
Prevalence method(d)	P = 0.9680		
Combined analysis(d)	P = 0.9781		
Cochran-Armitage test(e)	P = 0.0903		
Fisher Exact test(e)		P = 0.4557	P = 0.1781

Group Name	Control	50 ppm	200 ppm
	SITE : lymph node TUMOR : malignant lymphoma		
Tumor rate			
Overall rates(a)	4/50(8.0)	5/50(10.0)	4/50(8.0)
Adjusted rates(b)	7.89	9.52	7.32
Terminal rates(c)	3/38(7.9)	4/42(9.5)	3/41(7.3)
Statistical analysis			
Peto test			
Standard method(d)	P = 0.4902		
Prevalence method(d)	P = 0.5677		
Combined analysis(d)	P = 0.5670		
Cochran-Armitage test(e)	P = 0.9094		
Fisher Exact test(e)		P = 0.4883	P = 0.3579
	SITE : spleen TUMOR : malignant lymphoma		
Tumor rate			
Overall rates(a)	4/50(8.0)	8/50(16.0)	4/50(8.0)
Adjusted rates(b)	10.53	14.29	4.88
Terminal rates(c)	4/38(10.5)	6/42(14.3)	2/41(4.9)
Statistical analysis			
Peto test			
Standard method(d)	P = 0.1893		
Prevalence method(d)	P = 0.8741		
Combined analysis(d)	P = 0.6866		
Cochran-Armitage test(e)	P = 0.6781		
Fisher Exact test(e)		P = 0.2169	P = 0.3579
	SITE : liver TUMOR : hepatocellular adenoma		
Tumor rate			
Overall rates(a)	13/50(26.0)	12/49(24.5)	9/50(18.0)
Adjusted rates(b)	30.77	26.19	18.37
Terminal rates(c)	11/38(28.9)	11/42(26.2)	7/41(17.1)
Statistical analysis			
Peto test			
Standard method(d)	P = 1.0000 ?		
Prevalence method(d)	P = 0.8383		
Combined analysis(d)	P = 0.8780		
Cochran-Armitage test(e)	P = 0.3125		
Fisher Exact test(e)		P = 0.4638	P = 0.2965

Group Name	Control	50 ppm	200 ppm
	SITE : liver TUMOR : histiocytic sarcoma		
Tumor rate			
Overall rates(a)	0/50(0.0)	3/49(6.1)	2/50(4.0)
Adjusted rates(b)	0.0	2.38	0.0
Terminal rates(c)	0/38(0.0)	1/42(2.4)	0/41(0.0)
Statistical analysis			
Peto test			
Standard method(d)	P = 0.1861		
Prevalence method(d)	P = 0.4648		
Combined analysis(d)	P = 0.2604		
Cochran-Armitage test(e)	P = 0.4804		
Fisher Exact test(e)		P = 0.1287	P = 0.2574
	SITE : liver TUMOR : hemangiosarcoma		
Tumor rate			
Overall rates(a)	3/50(6.0)	5/49(10.2)	2/50(4.0)
Adjusted rates(b)	5.26	11.90	4.76
Terminal rates(c)	2/38(5.3)	5/42(11.9)	1/41(2.4)
Statistical analysis			
Peto test			
Standard method(d)	P = 1.0000 ?		
Prevalence method(d)	P = 0.6824		
Combined analysis(d)	P = 0.7832		
Cochran-Armitage test(e)	P = 0.4759		
Fisher Exact test(e)		P = 0.3685	P = 0.4909
	SITE : liver TUMOR : hepatocellular carcinoma		
Tumor rate			
Overall rates(a)	5/50(10.0)	8/49(16.3)	4/50(8.0)
Adjusted rates(b)	10.53	15.56	9.52
Terminal rates(c)	4/38(10.5)	6/42(14.3)	3/41(7.3)
Statistical analysis			
Peto test			
Standard method(d)	P = 0.8202		
Prevalence method(d)	P = 0.6609		
Combined analysis(d)	P = 0.7760		
Cochran-Armitage test(e)	P = 0.5050		
Fisher Exact test(e)		P = 0.3021	P = 0.4883

Group Name	Control	50 ppm	200 ppm
	SITE : liver		
	TUMOR : hemangioma,hemangiosarcoma		
Tumor rate			
Overall rates(a)	3/50(6.0)	6/49(12.2)	2/50(4.0)
Adjusted rates(b)	5.26	13.95	4.76
Terminal rates(c)	2/38(5.3)	5/42(11.9)	1/41(2.4)
Statistical analysis			
Peto test			
Standard method(d)	P = 1.0000 ?		
Prevalence method(d)	P = 0.7320		
Combined analysis(d)	P = 0.8188		
Cochran-Armitage test(e)	P = 0.4205		
Fisher Exact test(e)		P = 0.2632	P = 0.4909
	SITE : liver		
	TUMOR : hepatocellular adenoma,hepatocellular carcinoma		
Tumor rate			
Overall rates(a)	16/50(32.0)	17/49(34.7)	13/50(26.0)
Adjusted rates(b)	35.90	35.71	26.53
Terminal rates(c)	13/38(34.2)	15/42(35.7)	10/41(24.4)
Statistical analysis			
Peto test			
Standard method(d)	P = 0.9285		
Prevalence method(d)	P = 0.7472		
Combined analysis(d)	P = 0.8555		
Cochran-Armitage test(e)	P = 0.4128		
Fisher Exact test(e)		P = 0.5000	P = 0.3904

Group Name	Control	50 ppm	200 ppm
	SITE : Harderian gland TUMOR : adenoma		
Tumor rate			
Overall rates(a)	3/50(6.0)	2/50(4.0)	1/50(2.0)
Adjusted rates(b)	6.98	4.76	2.44
Terminal rates(c)	2/38(5.3)	2/42(4.8)	1/41(2.4)
Statistical analysis			
Peto test			
Standard method(d)	P = ------		
Prevalence method(d)	P = 0.8500		
Combined analysis(d)	P = ------		
Cochran-Armitage test(e)	P = 0.3268		
Fisher Exact test(e)		P = 0.4909	P = 0.3235

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

STUDY No. : 0211
ANIMAL : MOUSE BDF1
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

Group Name	Control	50 ppm	200 ppm
	SITE : ALL SITE TUMOR : malignant lymphoma		
Tumor rate			
Overall rates(a)	8/50(16.0)	13/50(26.0)	8/50(16.0)
Adjusted rates(b)	18.42	23.81	12.20
Terminal rates(c)	7/38(18.4)	10/42(23.8)	5/41(12.2)
Statistical analysis			
Peto test			
Standard method(d)	P = 0.2531		
Prevalence method(d)	P = 0.8481		
Combined analysis(d)	P = 0.6960		
Cochran-Armitage test(e)	P = 0.6851		
Fisher Exact test(e)		P = 0.2265	P = 0.3943

(HPT360A)

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

APPENDIX M 4

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

MOSUE :FEMALE

(TOW-YERA STUDY)

Group Name	Control	50 ppm	200 ppm
	SITE : lung TUMOR : bronchiolar-alveolar adenoma		
Tumor rate			
Overall rates(a)	4/50(8.0)	3/50(6.0)	9/49(18.4)
Adjusted rates(b)	11.43	6.12	25.71
Terminal rates(c)	4/35(11.4)	1/35(2.9)	8/34(23.5)
Statistical analysis			
Peto test			
Standard method(d)	P = -------		
Prevalence method(d)	P = 0.0242*		
Combined analysis(d)	P = -------		
Cochran-Armitage test(e)	P = 0.0494*		
Fisher Exact test(e)		P = 0.4895	P = 0.1483
	SITE : lung TUMOR : bronchiolar-alveolar adenoma,bronchiolar-alveolar carcinoma		
Tumor rate			
Overall rates(a)	4/50(8.0)	4/50(8.0)	10/49(20.4)
Adjusted rates(b)	11.43	8.16	28.57
Terminal rates(c)	4/35(11.4)	2/35(5.7)	9/34(26.5)
Statistical analysis			
Peto test			
Standard method(d)	P = -------		
Prevalence method(d)	P = 0.0161*		
Combined analysis(d)	P = -------		
Cochran-Armitage test(e)	P = 0.0341*		
Fisher Exact test(e)		P = 0.3579	P = 0.1045
	SITE : lymph node TUMOR : malignant lymphoma		
Tumor rate			
Overall rates(a)	9/50(18.0)	9/50(18.0)	3/49(6.1)
Adjusted rates(b)	8.57	11.43	2.94
Terminal rates(c)	3/35(8.6)	4/35(11.4)	1/34(2.9)
Statistical analysis			
Peto test			
Standard method(d)	P = 0.9104		
Prevalence method(d)	P = 0.8657		
Combined analysis(d)	P = 0.9624		
Cochran-Armitage test(e)	P = 0.0575		
Fisher Exact test(e)		P = 0.3993	P = 0.0955

Group Name	Control	50 ppm	200 ppm
	SITE : spleen TUMOR : malignant lymphoma		
Tumor rate			
Overall rates(a)	14/50(28.0)	9/50(18.0)	9/49(18.4)
Adjusted rates(b)	34.29	17.14	14.71
Terminal rates(c)	12/35(34.3)	6/35(17.1)	5/34(14.7)
Statistical analysis			
Peto test			
Standard method(d)	P = 0.1963		
Prevalence method(d)	P = 0.9519		
Combined analysis(d)	P = 0.7975		
Cochran-Armitage test(e)	P = 0.3565		
Fisher Exact test(e)		P = 0.2397	P = 0.2538
	SITE : liver TUMOR : hepatocellular adenoma		
Tumor rate			
Overall rates(a)	2/50(4.0)	5/50(10.0)	7/49(14.3)
Adjusted rates(b)	5.71	13.16	20.00
Terminal rates(c)	2/35(5.7)	4/35(11.4)	6/34(17.6)
Statistical analysis			
Peto test			
Standard method(d)	P = ------		
Prevalence method(d)	P = 0.0449*		
Combined analysis(d)	P = -------		
Cochran-Armitage test(e)	P = 0.1014		
Fisher Exact test(e)		P = 0.2425	P = 0.0994
	SITE : liver TUMOR : hepatocellular carcinoma		
Tumor rate			
Overall rates(a)	4/50(8.0)	3/50(6.0)	0/49(0.0)
Adjusted rates(b)	11.43	8.57	0.0
Terminal rates(c)	4/35(11.4)	3/35(8.6)	0/34(0.0)
Statistical analysis			
Peto test			
Standard method(d)	P = -------		
Prevalence method(d)	P = 0.9830		
Combined analysis(d)	P = -------		
Cochran-Armitage test(e)	P = 0.0506		
Fisher Exact test(e)		P = 0.4895	P = 0.0715

Group Name	Control	50 ppm	200 ppm
	SITE : liver		
	TUMOR : hemangioma,hemangiosarcoma		
Tumor rate			
Overall rates(a)	3/50(6.0)	3/50(6.0)	2/49(4.1)
Adjusted rates(b)	8.57	5.71	2.94
Terminal rates(c)	3/35(8.6)	2/35(5.7)	1/34(2.9)
Statistical analysis			
Peto test			
Standard method(d)	P = 0.2452		
Prevalence method(d)	P = 0.8229		
Combined analysis(d)	P = 0.6561		
Cochran-Armitage test(e)	P = 0.6358		
Fisher Exact test(e)		P = 0.3392	P = 0.4816
	SITE : liver		
	TUMOR : hepatocellular adenoma,hepatocellular carcinoma		
Tumor rate			
Overall rates(a)	6/50(12.0)	8/50(16.0)	7/49(14.3)
Adjusted rates(b)	17.14	21.05	20.00
Terminal rates(c)	6/35(17.1)	7/35(20.0)	6/34(17.6)
Statistical analysis			
Peto test			
Standard method(d)	P = ------		
Prevalence method(d)	P = 0.3822		
Combined analysis(d)	P = ------		
Cochran-Armitage test(e)	P = 0.8535		
Fisher Exact test(e)		P = 0.4157	P = 0.5000
	SITE : pituitary gland		
	TUMOR : adenoma		
Tumor rate			
Overall rates(a)	9/50(18.0)	10/50(20.0)	12/49(24.5)
Adjusted rates(b)	22.86	25.71	29.41
Terminal rates(c)	8/35(22.9)	9/35(25.7)	10/34(29.4)
Statistical analysis			
Peto test			
Standard method(d)	P = ------		
Prevalence method(d)	P = 0.1685		
Combined analysis(d)	P = ------		
Cochran-Armitage test(e)	P = 0.4167		
Fisher Exact test(e)		P = 0.4839	P = 0.3465

Group Name	Control	50 ppm	200 ppm
	SITE : ovary TUMOR : cystadenoma		
Tumor rate			
Overall rates(a)	2/50(4.0)	3/50(6.0)	4/49(8.2)
Adjusted rates(b)	5.71	4.88	11.76
Terminal rates(c)	2/35(5.7)	1/35(2.9)	4/34(11.8)
Statistical analysis			
Peto test			
Standard method(d)	P = 0.4428		
Prevalence method(d)	P = 0.1495		
Combined analysis(d)	P = 0.1936		
Cochran-Armitage test(e)	P = 0.4007		
Fisher Exact test(e)		P = 0.4909	P = 0.3483
	SITE : uterus TUMOR : endometrial stromal polyp		
Tumor rate			
Overall rates(a)	3/50(6.0)	1/50(2.0)	0/49(0.0)
Adjusted rates(b)	6.00	2.86	0.0
Terminal rates(c)	2/35(5.7)	1/35(2.9)	0/34(0.0)
Statistical analysis			
Peto test			
Standard method(d)	P = ------		
Prevalence method(d)	P = 0.9657		
Combined analysis(d)	P = ------		
Cochran-Armitage test(e)	P = 0.0937		
Fisher Exact test(e)		P = 0.3235	P = 0.1364
	SITE : uterus TUMOR : histiocytic sarcoma		
Tumor rate			
Overall rates(a)	6/50(12.0)	7/50(14.0)	11/49(22.4)
Adjusted rates(b)	8.57	11.43	16.22
Terminal rates(c)	3/35(8.6)	4/35(11.4)	5/34(14.7)
Statistical analysis			
Peto test			
Standard method(d)	P = 0.1847		
Prevalence method(d)	P = 0.1202		
Combined analysis(d)	P = 0.0718		
Cochran-Armitage test(e)	P = 0.1346		
Fisher Exact test(e)		P = 0.4863	P = 0.1853

Group Name	Control	50 ppm	200 ppm
	SITE : uterus		
	TUMOR : endometrial stromal polyp,endometrial stromal sarcoma		
Tumor rate			
Overall rates(a)	3/50(6.0)	1/50(2.0)	1/49(2.0)
Adjusted rates(b)	6.00	2.86	0.0
Terminal rates(c)	2/35(5.7)	1/35(2.9)	0/34(0.0)
Statistical analysis			
Peto test			
Standard method(d)	P = 0.2096		
Prevalence method(d)	P = 0.9648		
Combined analysis(d)	P = 0.7886		
Cochran-Armitage test(e)	P = 0.3822		
Fisher Exact test(e)		P = 0.3235	P = 0.3312
	SITE : Harderian gland		
	TUMOR : adenoma		
Tumor rate			
Overall rates(a)	2/50(4.0)	3/50(6.0)	1/49(2.0)
Adjusted rates(b)	5.71	8.57	2.94
Terminal rates(c)	2/35(5.7)	3/35(8.6)	1/34(2.9)
Statistical analysis			
Peto test			
Standard method(d)	P = ------		
Prevalence method(d)	P = 0.7468		
Combined analysis(d)	P = ------		
Cochran-Armitage test(e)	P = 0.4748		
Fisher Exact test(e)		P = 0.4909	P = 0.4851

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

Group Name	Control	50 ppm	200 ppm
	SITE : ALL SITE TUMOR : malignant lymphoma		
Tumor rate			
Overall rates(a)	22/50(44.0)	17/50(34.0)	12/49(24.5)
Adjusted rates(b)	40.00	25.71	17.65
Terminal rates(c)	14/35(40.0)	9/35(25.7)	6/34(17.6)
Statistical analysis			
Peto test			
Standard method(d)	P = 0.6726		
Prevalence method(d)	P = 0.9723		
Combined analysis(d)	P = 0.9528		
Cochran-Armitage test(e)	P = 0.0504		
Fisher Exact test(e)		P = 0.3123	P = 0.1081

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

APPENDIX N 1

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

RAT: MALE : DEAD AND MORIBUND ANIMALS

(TOW-YERA STUDY)

STUDY NO. : 0210
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	50 ppm	224 ppm	1000 ppm
			8	9	14	9
[Respiratory system]						
nasal cavit			< 8>	< 9>	<14>	< 9>
	leukemic cell infiltration		0	0	2	0
lung			< 8>	< 9>	<14>	< 9>
	leukemic cell infiltration		2	3	6	3
	metastasis:vertebra tumor		0	0	0	1
[Hematopoietic system]						
bone marrow			< 8>	< 9>	<14>	< 9>
	leukemic cell infiltration		1	1	3	1
lymph node			< 8>	< 9>	<14>	< 9>
	leukemic cell infiltration		0	1	5	1
[Digestive system]						
liver			< 8>	< 9>	<14>	< 9>
	leukemic cell infiltration		2	3	5	3
[Urinary system]						
kidney			< 8>	< 9>	<14>	< 9>
	leukemic cell infiltration		0	2	2	1
[Nervous system]						
brain			< 8>	< 9>	<14>	< 9>
	leukemic cell infiltration		1	0	3	2
spinal cord			< 8>	< 8>	<14>	< 9>
	leukemic cell infiltration		0	0	1	0

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

APPENDIX N 2

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

RAT: FEMALE : DEAD AND MORIBUND ANIMALS

(TOW-YERA STUDY)

STUDY NO. : 0210
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	50 ppm	224 ppm	1000 ppm
			12	13	5	9
[Respiratory system]						
lung			<12>	<13>	< 5>	< 9>
	leukemic cell infiltration		4	3	0	3
	metastasis:mammary gland tumor		0	1	0	0
[Hematopoietic system]						
bone marrow			<12>	<13>	< 5>	< 9>
	leukemic cell infiltration		3	2	0	2
lymph node			<12>	<13>	< 5>	< 9>
	leukemic cell infiltration		2	1	0	0
[Digestive system]						
liver			<12>	<13>	< 5>	< 9>
	leukemic cell infiltration		5	5	0	3
pancreas			<12>	<13>	< 5>	< 9>
	leukemic cell infiltration		2	0	0	0
[Urinary system]						
kidney			<12>	<13>	< 5>	< 9>
	leukemic cell infiltration		1	1	0	1
[Reproductive system]						
uterus			<12>	<13>	< 5>	< 9>
	leukemic cell infiltration		0	0	0	1
[Body cavities]						
peritoneum			<12>	<13>	< 5>	< 9>
	metastasis:urinary bladder tumor		0	0	1	0

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

APPENDIX N 3

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

RAT: MALE : SACRIFICED ANIMALS

(TOW-YERA STUDY)

STUDY NO. : 0210
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name / No. of Animals on Study	Control	50 ppm	224 ppm	1000 ppm
			42	41	36	41
[Respiratory system]						
lung			<42>	<41>	<36>	<41>
	leukemic cell infiltration		1	1	1	3
[Hematopoietic system]						
bone marrow			<42>	<41>	<36>	<41>
	leukemic cell infiltration		0	0	1	1
lymph node			<42>	<41>	<36>	<41>
	leukemic cell infiltration		0	1	1	1
[Digestive system]						
liver			<42>	<41>	<36>	<41>
	leukemic cell infiltration		1	1	1	3
[Urinary system]						
kidney			<42>	<41>	<36>	<41>
	leukemic cell infiltration		0	0	0	1
[Nervous system]						
brain			<42>	<41>	<36>	<41>
	leukemic cell infiltration		0	1	0	0

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

APPENDIX N 4

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

RAT: FEMALE : SACRIFICED ANIMALS

(TOW-YERA STUDY)

Organ	Findings	Group Name / No. of Animals on Study	Control 37	50 ppm 37	224 ppm 45	1000 ppm 41
[Respiratory system]						
lung			<37>	<37>	<45>	<41>
	leukemic cell infiltration		0	1	6	1
	metastasis:adrenal tumor		1	0	0	0
	metastasis:subcutis tumor		1	0	0	0
	metastasis:skin/appendage tumor		0	0	1	0
[Hematopoietic system]						
bone marrow			<37>	<37>	<45>	<41>
	leukemic cell infiltration		0	0	2	1
lymph node			<37>	<37>	<45>	<41>
	leukemic cell infiltration		0	0	2	0
[Digestive system]						
liver			<37>	<37>	<45>	<41>
	leukemic cell infiltration		1	3	6	2
	metastasis:muscle tumor		1	0	0	0

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

APPENDIX N 5

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

MOUSE: MALE : DEAD AND MORIBUND ANIMALS

(TOW-YERA STUDY)

STUDY NO. : 0211
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name / No. of Animals on Study	Control	50 ppm	200 ppm	800 ppm
			12	8	9	48
[Respiratory system]						
lung			<12>	< 8>	< 9>	<48>
	leukemic cell infiltration		0	1	2	0
	metastasis:liver tumor		0	1	0	1
	metastasis:mediastinum tumor		1	0	0	0
[Hematopoietic system]						
bone marrow			<12>	< 8>	< 9>	<48>
	leukemic cell infiltration		0	1	0	0
lymph node			<12>	< 8>	< 9>	<48>
	leukemic cell infiltration		0	1	2	0
	metastasis:liver tumor		0	0	1	0
spleen			<12>	< 8>	< 9>	<48>
	leukemic cell infiltration		0	1	1	0
[Circulatory system]						
heart			<12>	< 8>	< 9>	<48>
	metastasis:mediastinum tumor		1	0	0	0
[Digestive system]						
liver			<12>	< 7>	< 9>	<48>
	leukemic cell infiltration		0	3	2	1
[Urinary system]						
kidney			<12>	< 8>	< 9>	<48>
	leukemic cell infiltration		0	2	1	0

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

STUDY NO. : 0211
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name / No. of Animals on Study	Control	50 ppm	200 ppm	800 ppm
			12	8	9	48
[Urinary system]						
urin bladd			<12>	< 8>	< 9>	<48>
	metastasis:liver tumor		0	1	0	0

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

APPENDIX N 6

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

MOUSE: FEMALE : DEAD AND MORIBUND ANIMALS

(TOW-YERA STUDY)

Organ	Findings	Control	50 ppm	200 ppm	800 ppm
Group Name		Control	50 ppm	200 ppm	800 ppm
No. of Animals on Study		15	15	15	49
[Integumentary system/appandage]					
subcutis		<15>	<15>	<15>	<49>
	leukemic cell infiltration	1	0	0	0
[Respiratory system]					
nasal cavit		<15>	<15>	<15>	<49>
	metastasis:uterus tumor	1	0	0	0
lung		<15>	<15>	<15>	<49>
	leukemic cell infiltration	7	7	6	2
	metastasis:uterus tumor	2	0	3	1
[Hematopoietic system]					
bone marrow		<15>	<15>	<15>	<49>
	leukemic cell infiltration	1	0	1	2
	metastasis:liver tumor	1	0	0	0
	metastasis:uterus tumor	0	0	1	1
lymph node		<15>	<15>	<15>	<49>
	leukemic cell infiltration	0	1	3	1
	metastasis:uterus tumor	0	0	1	0
	metastasis:stomach tumor	1	0	0	0
spleen		<15>	<15>	<15>	<49>
	leukemic cell infiltration	3	0	2	0
[Digestive system]					
salivary gl		<15>	<15>	<15>	<49>
	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	Control	50 ppm	200 ppm	800 ppm
	Group Name	Control	50 ppm	200 ppm	800 ppm
	No. of Animals on Study	15	15	15	49
[Digestive system]					
liver		<15>	<15>	<15>	<49>
	leukemic cell infiltration	4	2	5	2
	metastasis:uterus tumor	3	3	5	1
	metastasis:stomach tumor	1	0	0	0
[Urinary system]					
kidney		<15>	<15>	<15>	<49>
	leukemic cell infiltration	1	0	3	0
	metastasis:uterus tumor	2	0	1	0
urin bladd		<15>	<15>	<15>	<49>
	leukemic cell infiltration	2	0	0	0
[Reproductive system]					
ovary		<15>	<15>	<15>	<49>
	leukemic cell infiltration	2	2	4	1
	metastasis:uterus tumor	1	2	4	0
	metastasis:stomach tumor	1	0	0	0
uterus		<15>	<15>	<15>	<49>
	leukemic cell infiltration	2	1	4	0
[Nervous system]					
brain		<15>	<15>	<15>	<49>
	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. : 0211
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name / No. of Animals on Study	Control 15	50 ppm 15	200 ppm 15	800 ppm 49
[Special sense organs/appandage]						
Harder gl			<15>	<15>	<15>	<49>
	leukemic cell infiltration		0	1	0	0
[Body cavities]						
peritoneum			<15>	<15>	<15>	<49>
	metastasis:uterus tumor		0	1	0	0

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

APPENDIX N 7

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

MOUSE: MALE : SACRIFICED ANIMALS

(TOW-YERA STUDY)

STUDY NO. : 0211
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name / No. of Animals on Study	Control 38	50 ppm 42	200 ppm 41	800 ppm 0
[Respiratory system]						
nasal cavit			<38>	<42>	<41>	< 0>
	leukemic cell infiltration		0	0	1	-
lung			<38>	<42>	<41>	< 0>
	leukemic cell infiltration		0	2	0	-
	metastasis:liver tumor		0	1	0	-
[Hematopoietic system]						
bone marrow			<38>	<42>	<41>	< 0>
	leukemic cell infiltration		0	0	1	-
lymph node			<38>	<42>	<41>	< 0>
	leukemic cell infiltration		1	3	0	-
spleen			<38>	<42>	<41>	< 0>
	leukemic cell infiltration		3	0	2	-
[Digestive system]						
salivary gl			<38>	<42>	<41>	< 0>
	leukemic cell infiltration		0	1	0	-
	metastasis:liver tumor		0	1	0	-
liver			<38>	<42>	<41>	< 0>
	leukemic cell infiltration		1	0	2	-
[Urinary system]						
kidney			<38>	<42>	<41>	< 0>
	leukemic cell infiltration		1	0	2	-

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

STUDY NO. : 0211
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name / No. of Animals on Study	Control	50 ppm	200 ppm	800 ppm
			38	42	41	0
[Urinary system]						
urin bladd			<38>	<42>	<41>	< 0>
	leukemic cell infiltration		0	1	0	-

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

APPENDIX N 8

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR : SUMMARY

MOUSE: FEMALE : SACRIFICED ANIMALS

(TOW-YERA STUDY)

Organ	Findings	Group Name / No. of Animals on Study	Control 35	50 ppm 35	200 ppm 34	800 ppm 0
[Respiratory system]						
lung			<35>	<35>	<34>	< 0>
	leukemic cell infiltration		3	0	2	-
[Hematopoietic system]						
bone marrow			<35>	<35>	<34>	< 0>
	leukemic cell infiltration		0	1	0	-
lymph node			<35>	<35>	<34>	< 0>
	leukemic cell infiltration		5	2	1	-
spleen			<35>	<35>	<34>	< 0>
	leukemic cell infiltration		1	2	1	-
[Digestive system]						
liver			<35>	<35>	<34>	< 0>
	leukemic cell infiltration		6	3	2	-
	metastasis:uterus tumor		1	1	0	-
[Urinary system]						
kidney			<35>	<35>	<34>	< 0>
	leukemic cell infiltration		2	1	1	-
[Reproductive system]						
ovary			<35>	<35>	<34>	< 0>
	metastasis:liver tumor		0	1	0	-
uterus			<35>	<35>	<34>	< 0>
	leukemic cell infiltration		2	0	0	-

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

STUDY NO. : 0211
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	50 ppm	200 ppm	800 ppm
			35	35	34	0
[Nervous system]						
brain			<35>	<35>	<34>	< 0>
	leukemic cell infiltration		1	0	0	-

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

APPENDIX O 1

CHARACTERIZATION OF METHYL CHLORIDE

(TOW-YERA STUDY)

CHARACTERIZATION OF METHYL CHLORIDE(TWO-YEAR STUDIES)

Lot no. P91031

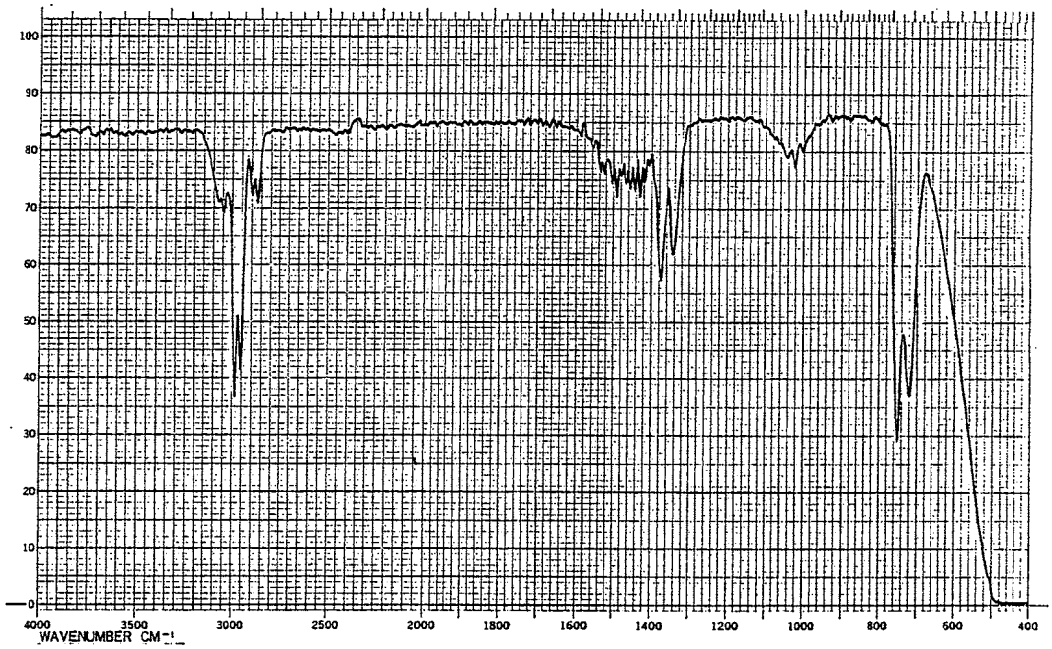
1. Spectral data

Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : Gass cell

Slit : Medium



Infrared Spectrum of Test Substance

Results:

Determined Value
Wave Number(cm^{-1})
700～ 740
740～ 770
1320～1360
1360～1400
2930～3000

2. Gas Chromatography

Instrument	: Hewlett Packard 5890A Gas Chromatograph
Column	: Methyl Silicone(0.2mmϕ × 50m)
Column Temperature	: 80°C
Flow Rate	: 1 ml/min
Detector	: FID(Flame Ionization Detector)
Injection Volume	: 1 ml

Results: Gas chromatography indicated only one major peak.

Peak	Retention Time(min)	Area Count
1	2.100	44114

APPENDIX O 2

IDENTITY OF METHYL CHLORIDE

(TOW-YERA STUDY)

IDENTITY OF METHYL CHLORIDE(TWO-YEAR STUDIES)

A. Lot no. P91031

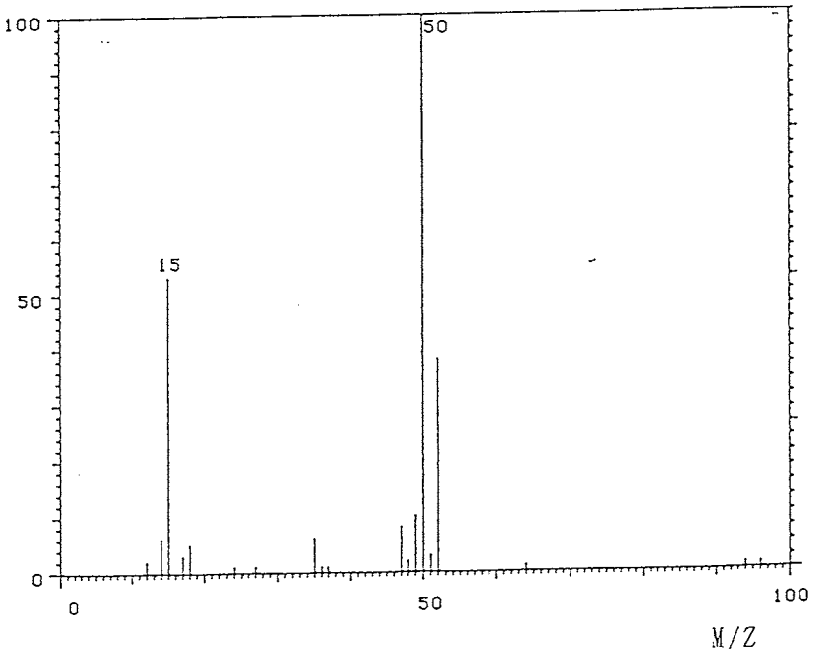
1. Spectral data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI(Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Results: The mass spectrum was consistent with literature spectrum.

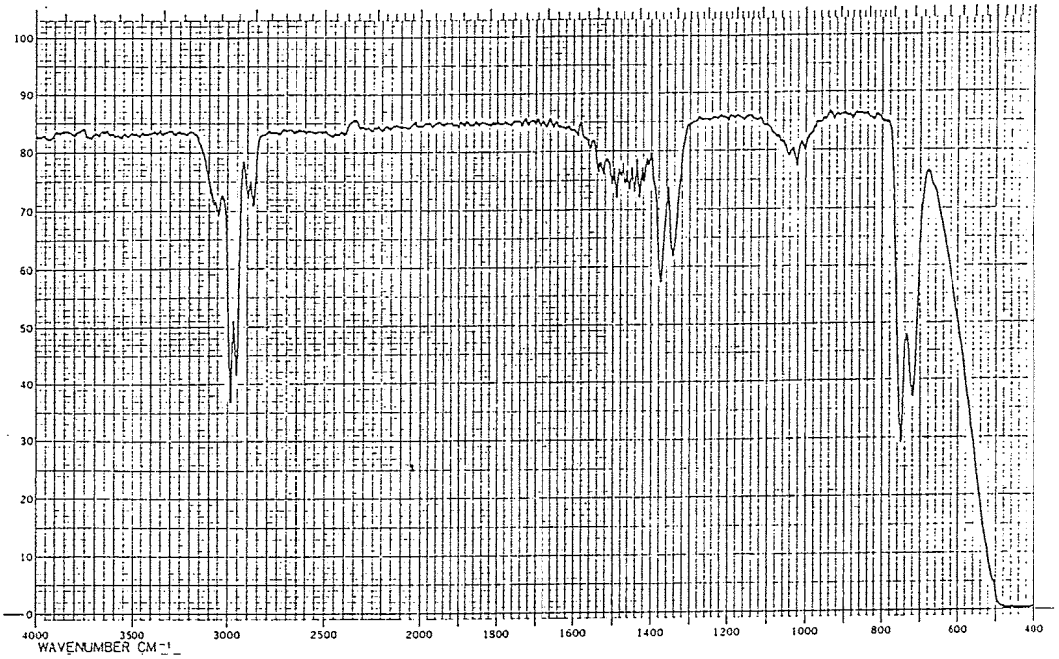
Determined Value Fragment Peak(M/Z)	Literature Value* Fragment Peak(M/Z)
15 50(Base Peak)	15 50 (*EPA/NIH Mass Spectral Data Base (1978) Vol. 1, p. 5.)

Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : Gass cell

Slit : Medium



Infrared Spectrum of Test Substance

Results: The infrared spectrum was consistent with literature spectrum.

Determined Value Wave Number(cm^{-1})	Literature Value* Wave Number(cm^{-1})
700～ 740	700～ 740
740～ 770	740～ 770
1320～1360	1320～1360
1360～1400	1360～1400
2930～3000	2930～3000

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

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

B. Lot no. 83610

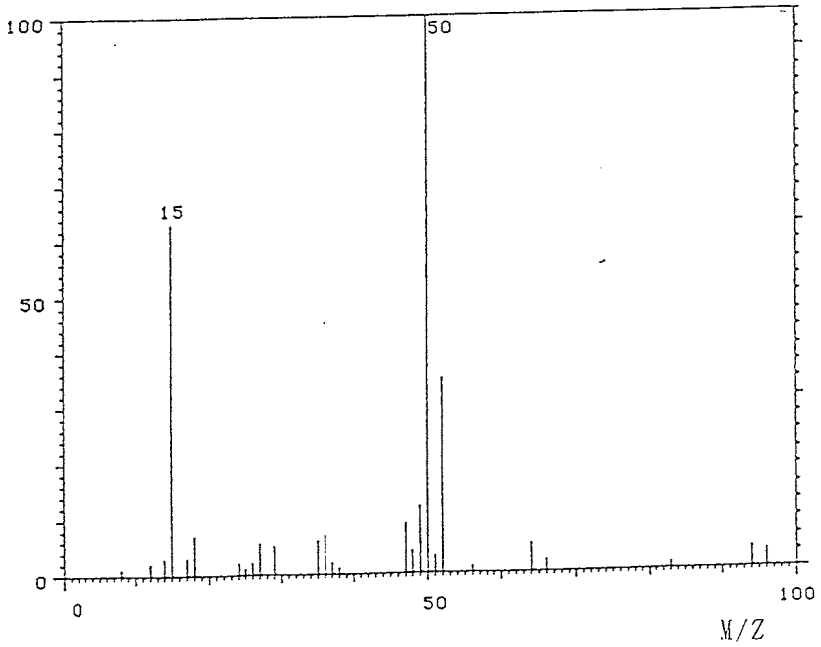
1. Spectral data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI(Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Results: The mass spectrum was consistent with literature spectrum.

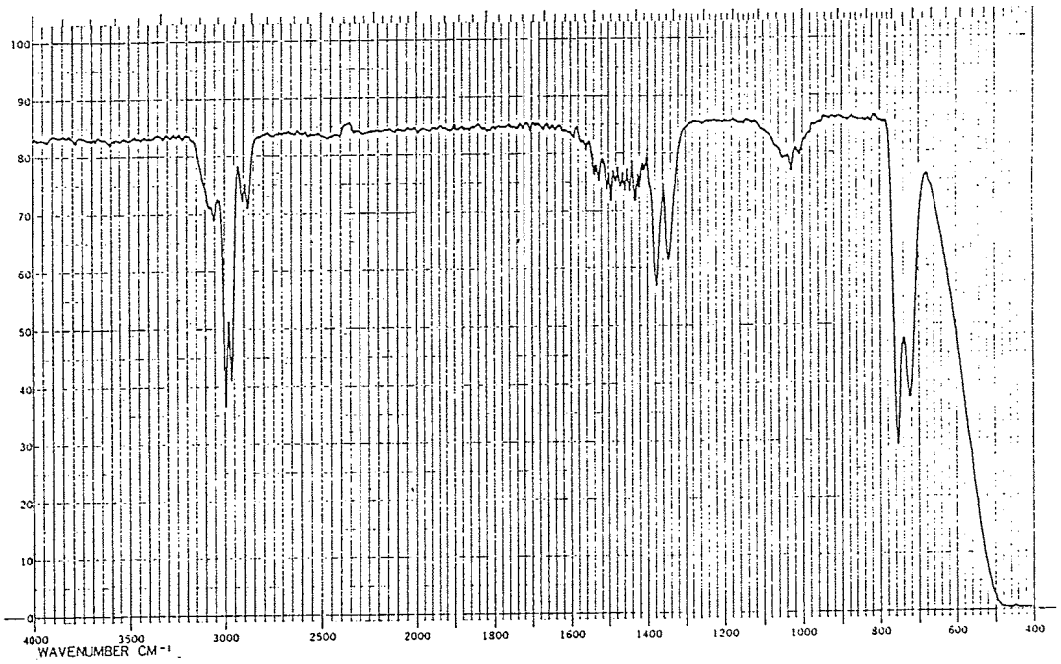
Determined Value Fragment Peak(M/Z)	Literature Value* Fragment Peak(M/Z)
15	15
50(Base Peak)	50
	(*EPA/NIH Mass Spectral Data Base (1978) Vol. 1, p. 5.)

Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : Gass cell

Slit : Medium



Infrared Spectrum of Test Substance

Results: The infrared spectrum was consistent with literature spectrum.

Determined Value Wave Number(cm^{-1})	Literature Value* Wave Number(cm^{-1})
700～ 740	700～ 740
740～ 770	740～ 770
1320～1360	1320～1360
1360～1400	1360～1400
2930～3000	2930～3000

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

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

C. Lot no. 90388-01

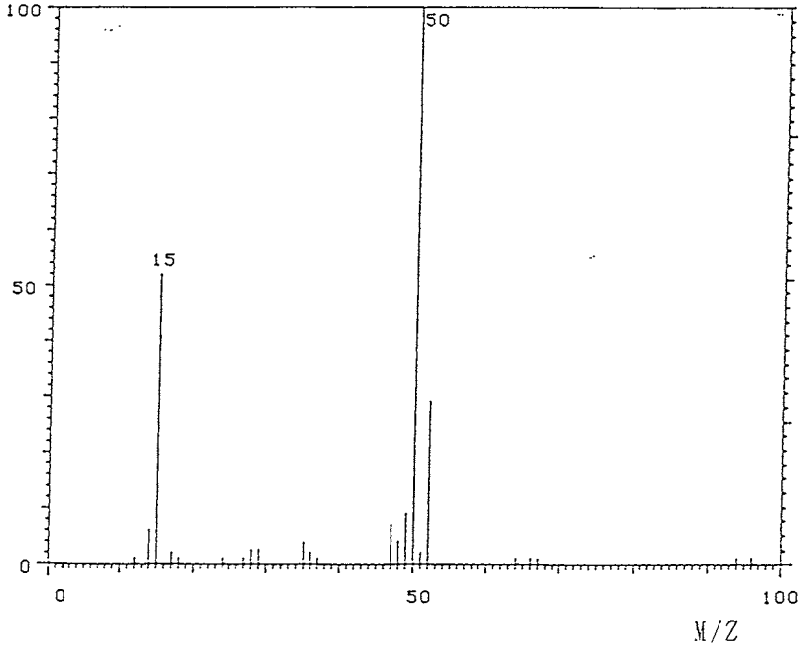
1. Spectral data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI(Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Results: The mass spectrum was consistent with literature spectrum.

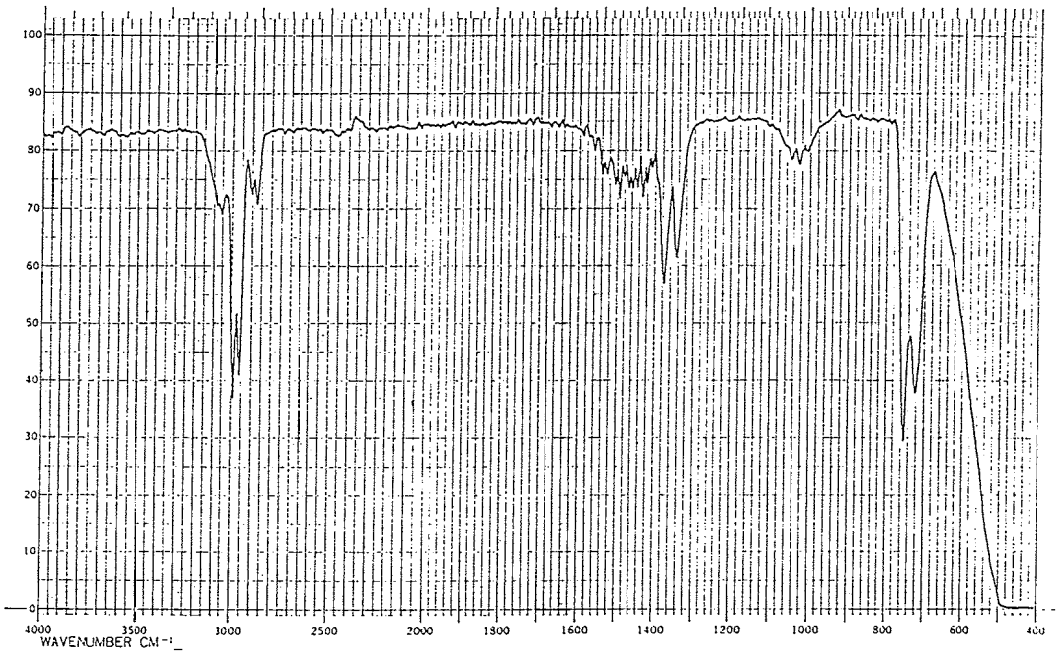
Determined Value Fragment Peak(M/Z)	Literature Value* Fragment Peak(M/Z)
15	15
50(Base Peak)	50
	(*EPA/NIH Mass Spectral Data Base (1978) Vol. 1, p. 5.)

Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : Gass cell

Slit : Medium



Infrared Spectrum of Test Substance

Results: The infrared spectrum was consistent with literature spectrum.

Determined Value Wave Number(cm^{-1})	Literature Value* Wave Number(cm^{-1})
700～ 740	700～ 740
740～ 770	740～ 770
1320～1360	1320～1360
1360～1400	1360～1400
2930～3000	2930～3000

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

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

D. Lot no. 93344

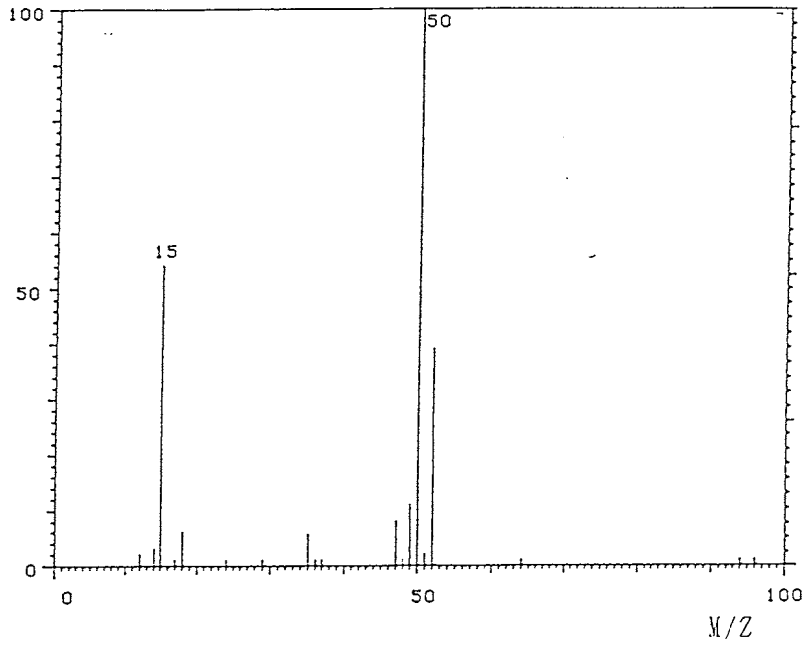
1. Spectral data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI(Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Results: The mass spectrum was consistent with literature spectrum.

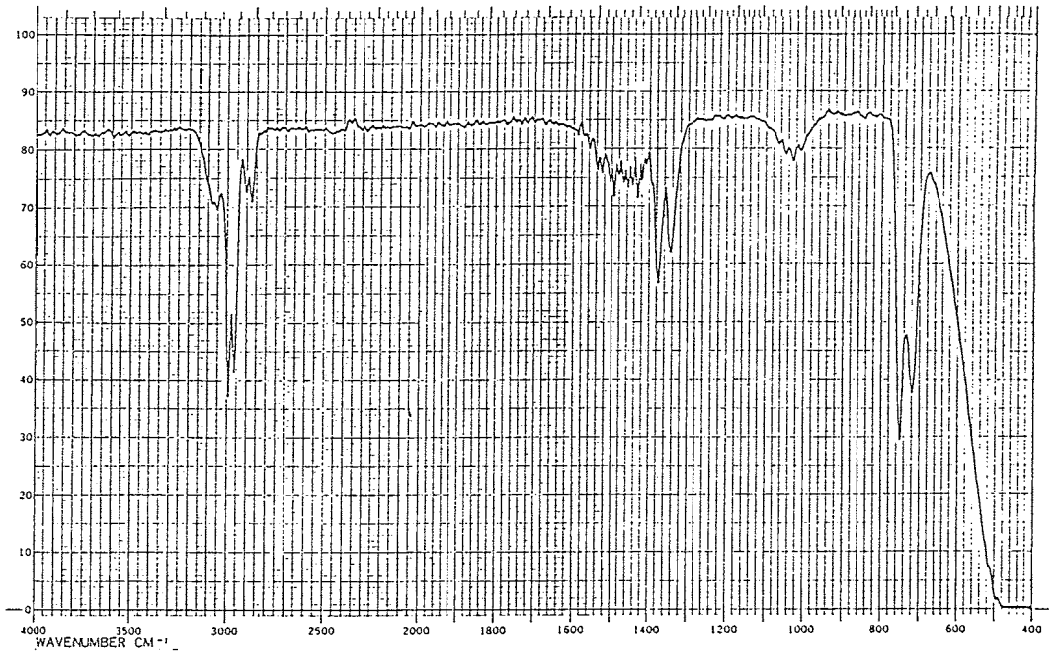
Determined Value Fragment Peak(M/Z)	Literature Value* Fragment Peak(M/Z)
15 50(Base Peak)	15 50 (*EPA/NIH Mass Spectral Data Base (1978) Vol. 1, p. 5.)

Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : Gass cell

Slit : Medium



Infrared Spectrum of Test Substance

Results: The infrared spectrum was consistent with literature spectrum.

Determined Value Wave Number(cm^{-1})	Literature Value* Wave Number(cm^{-1})
700～ 740	700～ 740
740～ 770	740～ 770
1320～1360	1320～1360
1360～1400	1360～1400
2930～3000	2930～3000

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

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

APPENDIX O 3

STABILITY OF METHYL CHLORIDE

(TOW-YERA STUDY)

STABILITY OF METHYL CHLORIDE(TWO-YEAR STUDIES)

A. Lot no. P91031

1. Sample storage: This lot was used from 1992.10.22 to 1992.11.2. Test substance was stored at room temperature.

2. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : Methyl Silicone(0.2mmϕ × 50m)

Column Temperature : 80°C

Flow Rate : 1 ml/min

Detector : FID(Flame Ionization Detector)

Injection Volume : 1 ml

Results: Gas chromatography indicated one major peak analyzed at 1992.10.21 and one major peak analyzed at 1992.11.4. No new treace impurity peak in the test substance analyzed at 1992.11.4 was detected.

Date	Retention Time(min)	Area Count
1992.10.21 (date analyzed)	2.100	44114
1992.11.04 (date analyzed)	2.097	45377

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

B. Lot no. 83610

1. Sample storage: This lot was used from 1992.11.2 to 1992.11.25. Test substance was stored at room temperature.

2. Gas Chromatography

Instrument	: Hewlett Packard 5890A Gas Chromatograph
Column	: Methyl Silicone(0.2mmϕ × 50m)
Column Temperature	: 80°C
Flow Rate	: 1 ml/min
Detector	: FID(Flame Ionization Detector)
Injection Volume	: 1 ml

Results: Gas chromatography indicated one major peak analyzed at 1992.10.29 and one major peak analyzed at 1992.11.26. No new treace impurity peak in the test substance analyzed at 1992.11.26 was detected.

Date	Retention Time(min)	Area Count
1992.10.29 (date analyzed)	2.098	45771
1992.11.26 (date analyzed)	2.102	46656

3. Conclusions: The results indicated that the test substance did not change when stored in the dark at room temperature during this period for about 4 weeks).

C. Lot no. 90388-01

1. Sample storage: This lot was used from 1992.11.25 to 1993.12.8. Test substance was stored at room temperature.

2. Gas Chromatography

Instrument	: Hewlett Packard 5890A Gas Chromatograph
Column	: Methyl Silicone(0.2mmϕ × 50m)
Column Temperature	: 80°C
Flow Rate	: 1 ml/min
Detector	: FID(Flame Ionization Detector)
Injection Volume	: 1 ml

Results: Gas chromatography indicated one major peak analyzed at 1992.11.24 and one major peak analyzed at 1993.12.9. No new treace impurity peak in the test substance analyzed at 1993.12.9 was detected.

Date	Retention Time(min)	Area Count
1992.11.24 (date analyzed)	2.102	45143
1993.12.09 (date analyzed)	2.103	45178

3. Conclusions: The results indicated that the test substance did not change when stored in the dark at room temperature during this period for about 1 years).

D. Lot no. 93344

1. Sample storage: This lot was used from 1993.12.8 to 1994.11.10. Test substance was stored at room temperature.

2. Gas Chromatography

Instrument	: Hewlett Packard 5890A Gas Chromatograph
Column	: Methyl Silicone(0.2mmϕ × 50m)
Column Temperature	: 80°C
Flow Rate	: 1 ml/min
Detector	: FID(Flame Ionization Detector)
Injection Volume	: 1 ml

Results: Gas chromatography indicated one major peak analyzed at 1993.12.7 and one major peak analyzed at 1994.11.14. No new treace impurity peak in the test substance analyzed at 1994.11.14 was detected.

Date	Retention Time(min)	Area Count
1993.12.07 (date analyzed)	2.105	46015
1994.11.14 (date analyzed)	2.103	44625

3. Conclusions: The results indicated that the test substance did not change when stored in the dark at room temperature during this period for about 1 years).

APPENDIX P 1

CONDETRATION OF METHYL CHLORIDE IN INHALATION CHAMBER

(TOW-YERA STUDY)

CONCENTRATION OF Methyl chloride
IN INHALTION CHAMBER
(RAT : TWO-YEAR STUDY)

Group Name	Concentration (ppm) Mean ± S.D.
Control	0.0 ± 0.0
50ppm	50.1 ± 0.6
224ppm	222.8 ± 2.3
1000ppm	999.0 ± 11.3

CONCENTRATION OF Methyl chloride
IN INHALTION CHAMBER
(MOUSE : TWO-YEAR STUDY)

Group Name	Concentration (ppm) Mean ± S.D.
Control	0.0 ± 0.0
50ppm	49.9 ± 0.5
200ppm	200.3 ± 2.6
800ppm	800.3 ± 16.0

APPENDIX P 2

ENVIRONMET OF INHALATION CHAMBER

(TOW-YERA STUDY)

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

Group Name	Temperature(℃) Mean ± S.D.	Humidity(%) Mean ± S.D.	Ventilation Rate(L/min) Mean ± S.D.	Room Air Change(time/h) Mean
Control	22.8 ± 0.3	54.0 ± 2.3	1538.9 ± 25.9 (764.4 ± 9.4)	12.1 (6.0)
50ppm	22.8 ± 0.2	54.6 ± 2.1	1539.2 ± 28.7 (764.3 ± 7.6)	12.2 (6.0)
224ppm	22.9 ± 0.2	53.1 ± 2.2	1540.3 ± 29.8 (767.5 ± 8.1)	12.2 (6.1)
1000ppm	22.9 ± 0.2	54.2 ± 2.6	1531.1 ± 26.5 (768.2 ± 7.6)	12.1 (6.1)

( ) : during exposure

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

Group Name	Temperature(℃) Mean ± S.D.	Humidity(%) Mean ± S.D.	Ventilation Rate(L/min) Mean ± S.D.	Room Air Change(time/h) Mean
Control	22.5 ± 0.1	54.1 ± 1.8	736.4 ± 13.1 (376.5 ± 6.3)	11.9 (6.1)
50ppm	22.7 ± 0.1	53.9 ± 2.1	731.7 ± 12.7 (376.8 ± 5.7)	11.9 (6.1)
200ppm	22.7 ± 0.2	53.5 ± 2.3	734.4 ± 13.7 (377.4 ± 6.0)	11.9 (6.1)
800ppm	22.6 ± 0.1	52.0 ± 2.4	739.3 ± 16.6 (377.4 ± 6.7)	12.0 (6.1)

( ) : during exposure

APPENDIX Q 1

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS

METHODS FOR HEMATOLOGY,BIOCHEMISTRY AND URINALYSIS

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

1) Automatic blood cell analyzer (Technicon H·1 : Technicon Instruments Corporation,USA)

2) Automatic blood cell differential analyzer (Hitachi 8200 : Hitachi,Ltd.,Japan)

3) Automatic analyzer (Hitachi 7070 : Hitachi,Ltd.,Japan)

4) Ames reagent strips for urinalysis (Multistix,Uro–Labstix : Bayer–Sankyo Co.,Ltd.,Japan)

APPENDIX Q 2

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

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