

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

## APPENDIX

(L1～R2)

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## APPENDIX L 1

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

RAT : MALE : DEAD AND MORIBUND ANIMALS

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

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

PAGE : 1

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	12				11				16				20			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
nasal cavit	ulcer		<12>				<11>				<16>				<20>			
			0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 8)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
	thrombus		0	0	1	0	1	0	0	0	0	4	1	0	0	4	4	0
			( 0)	( 0)	( 8)	( 0)	( 9)	( 0)	( 0)	( 0)	( 0)	( 25)	( 6)	( 0)	( 0)	( 20)	( 20)	( 0)
	mineralization		5	0	0	0	9	0	0	0	4	0	0	0	11	0	0	0
			( 42)	( 0)	( 0)	( 0)	( 82)	( 0)	( 0)	( 0)	( 25)	( 0)	( 0)	( 0)	( 55)	( 0)	( 0)	( 0)
	eosinophilic change:olfactory epithelium		7	1	0	0	8	0	0	0	7	0	0	0	4	0	0	0 *
		( 58)	( 8)	( 0)	( 0)	( 73)	( 0)	( 0)	( 0)	( 44)	( 0)	( 0)	( 0)	( 20)	( 0)	( 0)	( 0)	
eosinophilic change:respiratory epithelium		2	0	0	0	2	0	0	0	5	0	0	0	2	0	0	0	
		( 17)	( 0)	( 0)	( 0)	( 18)	( 0)	( 0)	( 0)	( 31)	( 0)	( 0)	( 0)	( 10)	( 0)	( 0)	( 0)	
inflammation:foreign body		4	2	0	0	1	0	0	0	3	0	0	0	3	0	1	0	
		( 33)	( 17)	( 0)	( 0)	( 9)	( 0)	( 0)	( 0)	( 19)	( 0)	( 0)	( 0)	( 15)	( 0)	( 5)	( 0)	
inflammation:respiratory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	
		( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 5)	( 0)	( 0)	( 0)	
respiratory metaplasia:olfactory epithelium		2	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	
		( 17)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 13)	( 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 : Number of animals with lesion  
( c ) c : b / a \* 100  
Significant difference ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$  Test of Chi Square

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

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

PAGE : 2

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

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b : Number of animals with lesion

( c ) c : b / a \* 100

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

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

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

PAGE : 3

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

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b : Number of animals with lesion

( c ) c : b / a \* 100

Significant difference : \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square



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

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

PAGE : 4

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

( c ) c : b / a \* 100

Significant difference ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$  Test of Chi Square

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

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

PAGE : 5

Organ_____	Findings_____	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	12				11				16				20			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Circulatory system]																		
heart	mineralization		<12>				<11>				<16>				<20>			
		1	1	0	0	0	0	0	0	0	1	0	0	0	3	6	2	0
		( 8)	( 8)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 6)	( 0)	( 0)	( 0)	( 15)	( 30)	( 10)	( 0)	
	myocardial fibrosis		5	6	0	0	4	7	0	0	1	12	1	0	2	16	1	0
			( 42)	( 50)	( 0)	( 0)	( 36)	( 64)	( 0)	( 0)	( 6)	( 75)	( 6)	( 0)	( 10)	( 80)	( 5)	( 0)
[Digestive system]																		
esophagus	necrosis		<12>				<11>				<16>				<20>			
		0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	
		( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 9)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	
stomach	edema		<12>				<11>				<16>				<20>			
		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)	( 0)	( 6)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
	mineralization		0	1	1	0	0	0	0	0	0	0	0	0	3	2	0	0
			( 0)	( 8)	( 8)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 15)	( 10)	( 0)	( 0)
	erosion:forestomach		0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0
			( 0)	( 8)	( 0)	( 0)	( 0)	( 0)	( 9)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
Grade	1 : Slight	2 : Moderate	3 : Marked	4 : Severe														
< a >	a : Number of animals examined at the site																	
b	b : Number of animals with lesion																	
( c )	c : b / a * 100																	
Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square																		

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

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

PAGE : 6

Organ	Findings	Control No. of Animals on Study Grade				7500 ppm 11				15000 ppm 16				30000 ppm 20			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																	
stomach		<12>				<11>				<16>				<20>			
	ulcer:forestomach	0	0	3	0	0	1	0	0	1	0	0	1	1	0	0	0
		( 0)	( 0)	( 25)	( 0)	( 0)	( 9)	( 0)	( 0)	( 6)	( 0)	( 0)	( 6)	( 5)	( 0)	( 0)	( 0)
	hyperplasia:forestomach	0	0	0	0	1	0	1	0	1	0	0	0	0	0	0	0
		( 0)	( 0)	( 0)	( 0)	( 9)	( 0)	( 9)	( 0)	( 6)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
	erosion:glandular stomach	3	1	0	0	1	1	0	0	2	0	0	0	1	0	0	0
		( 25)	( 8)	( 0)	( 0)	( 9)	( 9)	( 0)	( 0)	( 13)	( 0)	( 0)	( 0)	( 5)	( 0)	( 0)	( 0)
	ulcer:glandular stomach	0	0	0	0	0	0	0	0	3	0	0	0	0	0	0	0
		( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 19)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
liver		<12>				<11>				<16>				<20>			
	herniation	0	0	0	0	0	0	0	0	2	0	0	0	1	0	0	0
		( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 13)	( 0)	( 0)	( 0)	( 5)	( 0)	( 0)	( 0)
	congestion	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		( 0)	( 8)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
	hemorrhage	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
		( 8)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 5)	( 0)	( 0)	( 0)
	peliosis-like lesion	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
		( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 5)	( 0)	( 0)	( 0)

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

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

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

PAGE : 7

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

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

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

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

PAGE : 8

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

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

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

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

PAGE : 9

Organ_____	Findings_____	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	12				11				16				20			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
pancreas			<12>				<11>				<16>				<20>			
	hyperplasia:acinar cell		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			( 8)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
[Urinary system]																		
kidney			<12>				<11>				<16>				<20>			
	congestion		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			( 0)	( 0)	( 0)	( 0)	( 9)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
	hyaline droplet		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 6)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
	deposit of hemosiderin		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			( 8)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
	chronic nephropathy		7	0	1	2	5	3	2	0	5	3	3	1	3	9	6	0 **
			( 58)	( 0)	( 8)	( 17)	( 45)	( 27)	( 18)	( 0)	( 31)	( 19)	( 19)	( 6)	( 15)	( 45)	( 30)	( 0)
	papillary necrosis		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			( 8)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
	mineralization:cortico-medullary junction		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 5)	( 0)	( 0)	( 0)
Grade	1 : Slight	2 : Moderate	3 : Marked	4 : Severe														
< a >	a : Number of animals examined at the site																	
b	b : Number of animals with lesion																	
( c )	c : b / a * 100																	
Significant difference : * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square																		

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

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

PAGE : 10

Organ_____	Findings_____	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	12				11				16				20			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																		
kidney			<12>				<11>				<16>				<20>			
	mineralization:papilla		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			( 8)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
	mineralization:cortex		1	1	0	0	0	0	0	0	2	0	0	0	8	3	0	0
			( 8)	( 8)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 13)	( 0)	( 0)	( 0)	( 40)	( 15)	( 0)	( 0)
	urothelial hyperplasia:pelvis		0	0	0	0	0	0	0	0	1	0	0	1	2	0	0	
			( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 6)	( 0)	( 0)	( 5)	( 10)	( 0)	( 0)	
urin bladd			<12>				<11>				<16>				<20>			
	simple hyperplasia:transitional epithelium		0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			( 0)	( 8)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 6)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
	nodular hyperplasia:transitional epithelium		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			( 0)	( 0)	( 0)	( 0)	( 9)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	
[Endocrine system]																		
pituitary			<12>				<11>				<16>				<20>			
	hyperplasia		0	0	0	0	0	1	0	0	0	1	0	0	1	0	0	0
			( 0)	( 0)	( 0)	( 0)	( 0)	( 9)	( 0)	( 0)	( 0)	( 6)	( 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 : Number of animals with lesion  
 ( c ) c : b / a \* 100  
 Significant difference ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$  Test of Chi Square

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

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

PAGE : 11

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	12				11				16				20			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]																		
pituitary	Rathke pouch		<12>				<11>				<16>				<20>			
		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
thyroid	ultimibranhial body remanet		<12>				<11>				<16>				<20>			
		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 )	( 10 )	( 0 )	( 0 )	( 0 )
	C-cell hyperplasia		0	0	0	0	2	0	0	0	2	0	0	0	1	1	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 18 )	( 0 )	( 0 )	( 0 )	( 13 )	( 0 )	( 0 )	( 0 )	( 5 )	( 5 )	( 0 )	( 0 )
adrenal	hyperplasia:cortical cell		<12>				<11>				<16>				<20>			
		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	hyperplasia:medulla		0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 9 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )	
	focal fatty change:cortex		1	0	0	0	1	0	0	0	3	0	0	0	1	1	0	0
			( 8 )	( 0 )	( 0 )	( 0 )	( 9 )	( 0 )	( 0 )	( 0 )	( 19 )	( 0 )	( 0 )	( 0 )	( 5 )	( 5 )	( 0 )	( 0 )
[Reproductive system]																		
testis	atrophy		<12>				<11>				<16>				<20>			
		1	1	5	0	0	1	6	0	1	2	8	0	1	1	11	0	
		( 8 )	( 8 )	( 42 )	( 0 )	( 0 )	( 9 )	( 55 )	( 0 )	( 6 )	( 13 )	( 50 )	( 0 )	( 5 )	( 5 )	( 55 )	( 0 )	
Grade	1 : Slight	2 : Moderate	3 : Marked	4 : Severe														
< a >	a : Number of animals examined at the site																	
b	b : Number of animals with lesion																	
( c )	c : b / a * 100																	
Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square																		



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

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

PAGE : 12

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

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

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

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

PAGE : 13

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

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

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

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

PAGE : 14

Organ_____	Findings_____	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	12				11				16				20			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

[Special sense organs/appandage]

eye	cataract	<12>				<11>				<16>				<20>			
		0	1	0	0	0	0	0	0	0	1	0	0	0	1	0	0
		( 0 )	( 8 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )
	retinal atrophy	3	6	2	0	4	5	2	0	0	12	4	0	5	7	8	0
		( 25 )	( 50 )	( 17 )	( 0 )	( 36 )	( 45 )	( 18 )	( 0 )	( 0 )	( 75 )	( 25 )	( 0 )	( 25 )	( 35 )	( 40 )	( 0 )
	keratitis	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 )	( 10 )	( 0 )	( 0 )
	iritis	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )
Harder gl	inflammatory infiltration	<12>				<11>				<16>				<20>			
		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 9 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	lymphocytic infiltration	2	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0
		( 17 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )

[Musculoskeletal system]

muscle	atrophy	<12>				<11>				<16>				<20>			
		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		( 8 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )

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

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

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

PAGE : 15

Organ	Findings	Group Name No. of Animals on Study				Control 12				7500 ppm 11				15000 ppm 16				30000 ppm 20			
		Grade				1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)				(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

[Musculoskeletal system]

		<12>				<11>				<16>				<20>			
muscle	mineralization	0	1	0	0	2	0	0	0	0	0	0	0	0	0	0	0
		( 0 )	( 8 )	( 0 )	( 0 )	( 18 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )

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

(HPT150)

BAIS3

## APPENDIX L 2

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

RAT : FEMALE : DEAD AND MORIBUND ANIMALS

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

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

PAGE : 16

		Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	3				11				15				36			
Organ	Findings	Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Integumentary system/appandage]																		
skin/app			< 3>				<11>				<15>				<36>			
	epidermal cyst		0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )
[Respiratory system]																		
nasal cavit			< 3>				<11>				<15>				<36>			
	thrombus		0	0	0	0	0	0	0	0	1	0	1	0	2	4	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 7 )	( 0 )	( 7 )	( 0 )	( 6 )	( 11 )	( 0 )	( 0 )
	mineralization		1	0	0	0	5	0	0	0	1	0	0	0	7	0	0	0
			( 33 )	( 0 )	( 0 )	( 0 )	( 45 )	( 0 )	( 0 )	( 0 )	( 7 )	( 0 )	( 0 )	( 0 )	( 19 )	( 0 )	( 0 )	( 0 )
	eosinophilic change:olfactory epithelium		1	0	1	0	4	0	0	0	7	3	0	0	4	4	0	0 **
			( 33 )	( 0 )	( 33 )	( 0 )	( 36 )	( 0 )	( 0 )	( 0 )	( 47 )	( 20 )	( 0 )	( 0 )	( 11 )	( 11 )	( 0 )	( 0 )
	eosinophilic change:respiratory epithelium		1	0	0	0	2	0	0	0	2	0	0	0	3	0	0	0
			( 33 )	( 0 )	( 0 )	( 0 )	( 18 )	( 0 )	( 0 )	( 0 )	( 13 )	( 0 )	( 0 )	( 0 )	( 8 )	( 0 )	( 0 )	( 0 )
	inflammation:respiratory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )
	respiratory metaplasia:olfactory epithelium		0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 9 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )
Grade	1 : Slight      2 : Moderate      3 : Marked      4 : Severe																	
< a >	a : Number of animals examined at the site																	
b	b : Number of animals with lesion																	
( c )	c : b / a * 100																	
Significant difference ;    * : P ≤ 0.05    ** : P ≤ 0.01    Test of Chi Square																		

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

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

PAGE : 17

Organ_____	Findings_____	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	3				11				15				36			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

---

[Respiratory system]

nasal cavit

respiratory metaplasia:gland

< 3>

10000

70000

130000

310000

erythropoiesis:increased

0000

1000

0000

0000

lung

hemorrhage

< 3>

0000

0000

0000

1000

edema

0000

0100

0000

0000

thrombus

0000

0000

0100

0000

osseous metaplasia

0000

0000

1000

0000

accumulation of foamy cells

0000

1000

0000

1000

bronchiolar-alveolar cell hyperplasia

0000

2000

0000

0000

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

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

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

PAGE : 18

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

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



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

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

PAGE : 19

Organ	Findings	Group Name No. of Animals on Study Grade	Control 3				7500 ppm 11				15000 ppm 15				30000 ppm 36			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Hematopoietic system]																		
spleen			< 3>				<11>				<15>				<36>			
	deposit of hemosiderin		0 ( 0)	1 ( 33)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 9)	0 ( 0)	0 ( 0)	0 ( 0)	3 ( 20)	0 ( 0)	0 ( 0)	1 ( 3)	26 ( 72)	0 ( 0)	0 ( 0)
	extramedullary hematopoiesis		0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 9)	2 ( 18)	0 ( 0)	0 ( 0)	4 ( 27)	3 ( 20)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
	capsule hyperplasia		0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 7)	0 ( 0)	0 ( 0)	1 ( 3)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
[Circulatory system]																		
heart			< 3>				<11>				<15>				<36>			
	mineralization		1 ( 33)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	2 ( 13)	0 ( 0)	2 ( 6)	12 ( 33)	4 ( 11)	0 ( 0)
	myocardial fibrosis		0 ( 0)	1 ( 33)	0 ( 0)	0 ( 0)	3 ( 27)	2 ( 18)	0 ( 0)	0 ( 0)	8 ( 53)	4 ( 27)	0 ( 0)	0 ( 0)	27 ( 75)	5 ( 14)	1 ( 3)	0 * ( 0)
[Digestive system]																		
tooth			< 3>				<11>				<15>				<36>			
	inflammation		0 ( 0)	1 ( 33)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
Grade	1 : Slight	2 : Moderate	3 : Marked	4 : Severe														
< a >	a : Number of animals examined at the site																	
b	b : Number of animals with lesion																	
( c )	c : b / a * 100																	
Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square																		

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

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

PAGE : 20

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

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

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

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

PAGE : 21

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

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

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

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

PAGE : 22

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

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

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

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

PAGE : 23

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

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

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

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

PAGE : 24

Organ_____	Findings_____	Group Name No. of Animals on Study Grade	Control 3				7500 ppm 11				15000 ppm 15				30000 ppm 36			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Urinary system]																		
kidney	mineralization:cortico-medullary junction		< 3>				<11>				<15>				<36>			
		1 ( 33)	0 ( 0)	0 ( 0)	0 ( 0)	7 ( 64)	0 ( 0)	0 ( 0)	0 ( 0)	7 ( 47)	1 ( 7)	0 ( 0)	0 ( 0)	12 ( 33)	1 ( 3)	1 ( 3)	0 ( 0)	
		0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	2 ( 18)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 3)	0 ( 0)	0 ( 0)	0 ( 0)	
		1 ( 33)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 9)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 7)	0 ( 0)	10 ( 28)	9 ( 25)	6 ( 17)	1 ( 3)	
		0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 7)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 3)	0 ( 0)	0 ( 0)	
urin bladd	simple hyperplasia:transitional epithelium		< 3>				<11>				<15>				<36>			
		0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 7)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 3)	0 ( 0)	0 ( 0)	0 ( 0)	
		0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 3)	0 ( 0)	0 ( 0)	0 ( 0)	
pituitary	angiectasis		< 3>				<11>				<15>				<36>			
		0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	2 ( 13)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	3 ( 8)	0 ( 0)	0 ( 0)	
		0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	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 : Number of animals with lesion  
( c ) c : b / a \* 100  
Significant difference : \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

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

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

PAGE : 25

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

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

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

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

PAGE : 26

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

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



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

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

PAGE : 27

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

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

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

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

PAGE : 28

Organ	Findings	Group Name No. of Animals on Study Grade	Control 3				7500 ppm 11				15000 ppm 15				30000 ppm 36			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

[Special sense organs/appandage]

eye	cataract		< 3>				<11>				<15>				<36>			
			0	0	0	0	0	1	0	0	0	0	1	0	1	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 9 )	( 0 )	( 0 )	( 0 )	( 0 )	( 7 )	( 0 )	( 3 )	( 0 )	( 3 )	( 0 )
	retinal atrophy		0	2	1	0	0	6	3	1	4	4	6	1	8	7	16	1
			( 0 )	( 67 )	( 33 )	( 0 )	( 0 )	( 55 )	( 27 )	( 9 )	( 27 )	( 27 )	( 40 )	( 7 )	( 22 )	( 19 )	( 44 )	( 3 )
	keratitis		0	0	1	0	0	0	0	0	0	1	0	0	1	1	1	0
			( 0 )	( 0 )	( 33 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 7 )	( 0 )	( 0 )	( 3 )	( 3 )	( 3 )	( 0 )
	iritis		0	0	0	0	0	0	0	0	0	0	0	0	2	1	1	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 6 )	( 3 )	( 3 )	( 0 )
Harder gl	degeneration		< 3>				<11>				<15>				<36>			
			0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 7 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )
	inflammatory infiltration		0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 33 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	Lymphocytic infiltration		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )

[Musculoskeletal system]

bone	osteosclerosis		< 3>				<11>				<15>				<36>			
			1	0	0	0	0	2	0	0	3	1	0	0	4	2	2	0
			( 33 )	( 0 )	( 0 )	( 0 )	( 0 )	( 18 )	( 0 )	( 0 )	( 20 )	( 7 )	( 0 )	( 0 )	( 11 )	( 6 )	( 6 )	( 0 )

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

## APPENDIX L 3

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

RAT : MALE : SACRIFICED ANIMALS

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

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

PAGE : 1

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

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

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

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

PAGE : 2

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

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

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

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

PAGE : 3

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

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

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

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

PAGE : 4

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

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

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

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

PAGE : 5

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

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



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

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

PAGE : 6

		Control 38				7500 ppm 39				15000 ppm 34				30000 ppm 30			
		Grade				Grade				Grade				Grade			
Organ	Findings	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																	
tooth		<38>				<39>				<34>				<30>			
	dysplasia	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 3 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
stomach		<38>				<39>				<34>				<30>			
	atrophy	0 ( 0 )	0 ( 0 )	1 ( 3 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
	ulcer:forestomach	1 ( 3 )	0 ( 0 )	1 ( 3 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 3 )	0 ( 0 )	0 ( 0 )
	erosion:glandular stomach	2 ( 5 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 3 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 3 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	3 ( 10 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
liver		<38>				<39>				<34>				<30>			
	herniation	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 3 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 3 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 3 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
	peliasis-like lesion	1 ( 3 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 3 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
	necrosis:zonal	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 3 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )

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

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

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

PAGE : 7

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

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

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

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

PAGE : 8

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

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

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

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

PAGE : 9

Organ	Findings	Group Name	Control				7500 ppm				15000 ppm				30000 ppm			
		No. of Animals on Study	38				39				34				30			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																		
kidney			<38>				<39>				<34>				<30>			
	inflammatory infiltration		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	chronic nephropathy		1	16	17	4	0	14	22	3	2	12	20	0	4	17	9	0
			( 3 )	( 42 )	( 45 )	( 11 )	( 0 )	( 36 )	( 56 )	( 8 )	( 6 )	( 35 )	( 59 )	( 0 )	( 13 )	( 57 )	( 30 )	( 0 )
	mineralization:papilla		1	0	0	0	0	0	1	0	0	0	0	2	0	0	0	
			( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 7 )	( 0 )	( 0 )	( 0 )	
	mineralization:cortex		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 )	( 7 )	( 0 )	( 0 )	( 0 )	
	urothelial hyperplasia:pelvis		1	2	0	0	0	1	0	0	0	2	0	1	3	0	0	
			( 3 )	( 5 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 6 )	( 0 )	( 3 )	( 10 )	( 0 )	( 0 )	
urin bladd			<38>				<39>				<34>				<30>			
	simple hyperplasia:transitional epithelium		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
[Endocrine system]																		
pituitary			<38>				<39>				<34>				<30>			
	angiectasis		0	0	0	0	1	0	1	0	0	0	0	0	1	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 3 )	( 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 : Number of animals with lesion  
( c ) c : b / a \* 100  
Significant difference ; \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

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

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

PAGE : 10

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

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

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

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

PAGE : 11

Organ	Findings	Group Name No. of Animals on Study Grade	Control 38				7500 ppm 39				15000 ppm 34				30000 ppm 30			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)

[Endocrine system]

adrenal	cyst	<38>	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 3)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
	hyperplasia:cortical cell		1 ( 3)	0 ( 0)	0 ( 0)	0 ( 0)	3 ( 8)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 3)	1 ( 3)	0 ( 0)	0 ( 0)	2 ( 7)	0 ( 0)	0 ( 0)	0 ( 0)
	hyperplasia:medulla		3 ( 8)	1 ( 3)	0 ( 0)	0 ( 0)	3 ( 8)	4 (10)	0 ( 0)	0 ( 0)	1 ( 3)	2 ( 6)	0 ( 0)	0 ( 0)	3 (10)	0 ( 0)	0 ( 0)	0 ( 0)
	focal fatty change:cortex		7 (18)	0 ( 0)	0 ( 0)	0 ( 0)	5 (13)	0 ( 0)	0 ( 0)	0 ( 0)	8 (24)	0 ( 0)	0 ( 0)	0 ( 0)	3 (10)	0 ( 0)	0 ( 0)	0 ( 0)

[Reproductive system]

testis	atrophy	<38>	2 ( 5)	3 ( 8)	30 (79)	0 ( 0)	3 ( 8)	3 ( 8)	31 (79)	0 ( 0)	2 ( 6)	3 ( 9)	28 (82)	0 ( 0)	3 (10)	1 ( 3)	22 (73)	0 ( 0)
	mineralization		3 ( 8)	1 ( 3)	0 ( 0)	0 ( 0)	2 ( 5)	0 ( 0)	0 ( 0)	0 ( 0)	3 ( 9)	0 ( 0)	0 ( 0)	0 ( 0)	3 (10)	0 ( 0)	0 ( 0)	0 ( 0)
	arteritis		1 ( 3)	0 ( 0)	0 ( 0)	0 ( 0)	2 ( 5)	2 ( 5)	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 : Number of animals with lesion

( c ) c : b / a \* 100

Significant difference ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$  Test of Chi Square

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

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

PAGE : 12

Organ	Findings	Control 38				7500 ppm 39				15000 ppm 34				30000 ppm 30			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Reproductive system]																	
testis		<38>				<39>				<34>				<30>			
	interstitial cell hyperplasia	3	0	0	0	2	0	0	0	4	1	0	0	3	0	0	0
		( 8 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )	( 12 )	( 3 )	( 0 )	( 0 )	( 10 )	( 0 )	( 0 )	( 0 )
epididymis		<38>				<39>				<34>				<30>			
	inflammation	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
prostate		<38>				<39>				<34>				<30>			
	inflammation	9	3	0	0	8	2	0	0	8	3	0	0	6	2	0	0
		( 24 )	( 8 )	( 0 )	( 0 )	( 21 )	( 5 )	( 0 )	( 0 )	( 24 )	( 9 )	( 0 )	( 0 )	( 20 )	( 7 )	( 0 )	( 0 )
	hyperplasia	4	0	0	0	9	0	0	0	4	0	0	0	1	0	0	0
		( 11 )	( 0 )	( 0 )	( 0 )	( 23 )	( 0 )	( 0 )	( 0 )	( 12 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )
mammary gl		<38>				<39>				<34>				<30>			
	duct ectasia	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	hyperplasia	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
		( 3 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	galactocoele	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b b : Number of animals with lesion

( c ) c : b / a \* 100

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

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

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

PAGE : 13

Organ	Findings	Group Name No. of Animals on Study Grade				Control 38				7500 ppm 39				15000 ppm 34				30000 ppm 30			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Reproductive system]																					
prep/cli gl		<38>				<39>				<34>				<30>							
	duct ectasia	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		( 3)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
[Nervous system]																					
brain		<38>				<39>				<34>				<30>							
	necrosis:focal	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
		( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 3)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
[Special sense organs/appandage]																					
eye		<38>				<39>				<34>				<30>							
	cataract	1	2	0	0	0	3	1	0	0	5	0	0	0	0	0	0	0	0	0	0
		( 3)	( 5)	( 0)	( 0)	( 0)	( 8)	( 3)	( 0)	( 0)	( 15)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
	retinal atrophy	7	14	15	1	2	14	23	0	0	13	20	1	2	12	16	0				
		( 18)	( 37)	( 39)	( 3)	( 5)	( 36)	( 59)	( 0)	( 0)	( 38)	( 59)	( 3)	( 7)	( 40)	( 53)	( 0)				
	keratitis	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		( 5)	( 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 : Number of animals with lesion  
( c ) c : b / a \* 100  
Significant difference : \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$  Test of Chi Square



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

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

PAGE : 14

Organ	Findings	Control 38				7500 ppm 39				15000 ppm 34				30000 ppm 30			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

[Special sense organs/appandage]

eye	iritis	<38>				<39>				<34>				<30>			
		1	2	0	0	0	1	0	0	0	0	0	0	0	0	0	0
		( 3 )	( 5 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
Harder gl	degeneration	<38>				<39>				<34>				<30>			
		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	inflammatory infiltration	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	Lymphocytic infiltration	2	1	0	0	1	1	0	0	1	0	0	0	1	0	0	0
		( 5 )	( 3 )	( 0 )	( 0 )	( 3 )	( 3 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )

[Musculoskeletal system]

muscle	atrophy	<38>				<39>				<34>				<30>			
		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b : Number of animals with lesion

( c ) c : b / a \* 100

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

## APPENDIX L 4

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

RAT : FEMALE : SACRIFICED ANIMALS

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

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

PAGE : 15

Organ	Findings	Group Name No. of Animals on Study Grade	Control 47				7500 ppm 39				15000 ppm 35				30000 ppm 14			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

[Integumentary system/appandage]

skin/app	ulcer	<47>	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	inflammation		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	scab		0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	epidermal cyst		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 7 )	( 0 )	( 0 )

[Respiratory system]

nasal cavit	mineralization	<47>	6	0	0	0	15	0	0	0 *	2	0	0	0	0	0	0	0
			( 13 )	( 0 )	( 0 )	( 0 )	( 38 )	( 0 )	( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	eosinophilic change:olfactory epithelium		18	16	3	0	20	10	1	0	12	15	3	0	2	6	4	0
			( 38 )	( 34 )	( 6 )	( 0 )	( 51 )	( 26 )	( 3 )	( 0 )	( 34 )	( 43 )	( 9 )	( 0 )	( 14 )	( 43 )	( 29 )	( 0 )
	eosinophilic change:respiratory epithelium		15	0	0	0	16	0	0	0	14	0	0	0	4	0	0	0
			( 32 )	( 0 )	( 0 )	( 0 )	( 41 )	( 0 )	( 0 )	( 0 )	( 40 )	( 0 )	( 0 )	( 0 )	( 29 )	( 0 )	( 0 )	( 0 )

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b : Number of animals with lesion

( c ) c : b / a \* 100

Significant difference ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$  Test of Chi Square

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

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

PAGE : 16

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

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

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

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

PAGE : 17

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

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

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

PAGE : 18

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

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

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

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

PAGE : 19

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

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

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

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

PAGE : 20

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

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b : Number of animals with lesion

( c ) c : b / a \* 100

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



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

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

PAGE : 21

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

[Endocrine system]

pituitary		<46>				<39>				<35>				<14>							
	angiectasis	1	2	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0
		( 2 )	( 4 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 7 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b : Number of animals with lesion

( c ) c : b / a \* 100

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

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

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

PAGE : 22

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

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b : Number of animals with lesion

( c ) c : b / a \* 100

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

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

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

PAGE : 23

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

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

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

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

PAGE : 24

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

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

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

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

PAGE : 25

Organ	Findings	Control No. of Animals on Study Grade				7500 ppm 39				15000 ppm 35				30000 ppm 14			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

[Special sense organs/appandage]

Harder gl		<47>				<39>				<35>				<14>			
	Lymphocytic infiltration	4	0	0	0	0	0	0	0	4	0	0	0	0	0	0	0
		( 9)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 11)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
	granulation	2	0	0	0	6	0	0	0	1	1	0	0	0	0	0	0
		( 4)	( 0)	( 0)	( 0)	( 15)	( 0)	( 0)	( 0)	( 3)	( 3)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
	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)

[Musculoskeletal system]

bone		<47>				<39>				<35>				<14>			
	osteosclerosis	3	3	2	0	7	3	0	0	4	3	3	0	2	2	1	0
		( 6)	( 6)	( 4)	( 0)	( 18)	( 8)	( 0)	( 0)	( 11)	( 9)	( 9)	( 0)	( 14)	( 14)	( 7)	( 0)

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

(HPT150)

BAIS3

## APPENDIX L 5

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

MOSUE : MALE : DEAD AND MORIBUND ANIMALS

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

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

PAGE : 1

Organ_____	Findings_____	Group Name	Control				10000 ppm				20000 ppm				40000 ppm			
		No. of Animals on Study	16				15				20				25			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

[Integumentary system/appandage]																		
skin/app			<16>				<15>				<20>				<25>			
	inflammation		0	0	0	0	0	2	0	0	0	0	0	0	0	1	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 13 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )
subcutis			<16>				<15>				<20>				<25>			
	xanthogranuloma		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )

[Respiratory system]																		
nasal cavit			<16>				<15>				<20>				<25>			
	inflammation		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 )	( 0 )	( 0 )	( 0 )
	eosinophilic change:olfactory epithelium		2	0	0	0	4	0	0	0	5	0	0	0	4	0	0	0
			( 13 )	( 0 )	( 0 )	( 0 )	( 27 )	( 0 )	( 0 )	( 0 )	( 25 )	( 0 )	( 0 )	( 0 )	( 16 )	( 0 )	( 0 )	( 0 )
	eosinophilic change:respiratory epithelium		5	1	0	0	3	2	0	0	2	1	0	0	4	2	0	0
			( 31 )	( 6 )	( 0 )	( 0 )	( 20 )	( 13 )	( 0 )	( 0 )	( 10 )	( 5 )	( 0 )	( 0 )	( 16 )	( 8 )	( 0 )	( 0 )
	respiratory metaplasia:olfactory epithelium		2	0	0	0	1	0	0	0	8	0	0	0	12	2	0	0 *
			( 13 )	( 0 )	( 0 )	( 0 )	( 7 )	( 0 )	( 0 )	( 0 )	( 40 )	( 0 )	( 0 )	( 0 )	( 48 )	( 8 )	( 0 )	( 0 )

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b : Number of animals with lesion

( c ) c : b / a \* 100

Significant difference ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$  Test of Chi Square

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

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

PAGE : 2

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

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b : Number of animals with lesion

( c ) c : b / a \* 100

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



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

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

PAGE : 3

Organ	Findings	Group Name No. of Animals on Study Grade	Control 16				10000 ppm 15				20000 ppm 20				40000 ppm 25			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

[Hematopoietic system]

bone marrow	hyperplasia:vascular	<16>				<15>				<20>				<25>			
		0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	2 ( 10 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
spleen	thrombus	<16>				<15>				<20>				<25>			
		0 ( 0 )	1 ( 6 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
	deposit of melanin	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 4 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
		extramedullary hematopoiesis	2 ( 13 )	2 ( 13 )	2 ( 13 )	0 ( 0 )	1 ( 7 )	4 ( 27 )	3 ( 20 )	0 ( 0 )	0 ( 0 )	3 ( 15 )	4 ( 20 )	0 ( 0 )	1 ( 4 )	1 ( 4 )	2 ( 8 )
	hyperplasia:vascular		0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 5 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )

[Circulatory system]

heart				<16>			<15>			<20>			<25>	
necrosis	0	1	0	0	0	0	0	0	0	1	0	0	0	0
	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )	( 0 )

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

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

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

PAGE : 4

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

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b b : Number of animals with lesion

( c ) c : b / a \* 100

Significant difference : \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

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

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

PAGE : 5

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

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b : Number of animals with lesion

( c ) c : b / a \* 100

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

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

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

PAGE : 6

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

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

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

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

PAGE : 7

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

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b b : Number of animals with lesion

( c ) c : b / a \* 100

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

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

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

PAGE : 8

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

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

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

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

PAGE : 9

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

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b : Number of animals with lesion

( c ) c : b / a \* 100

Significant difference : \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

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

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

PAGE : 10

		Group Name	Control				10000 ppm				20000 ppm				40000 ppm			
		No. of Animals on Study	16				15				20				25			
Organ	Findings	Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Reproductive system]																		
prostate			<16>				<15>				<20>				<25>			
	inflammation		0	0	0	0	2	0	1	0	0	0	1	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 13 )	( 0 )	( 7 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
prep/cli gl			<16>				<15>				<20>				<25>			
	duct ectasia		0	0	0	0	0	2	0	0	0	3	1	0	0	2	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 13 )	( 0 )	( 0 )	( 0 )	( 15 )	( 5 )	( 0 )	( 0 )	( 8 )	( 0 )	( 0 )
[Nervous system]																		
brain			<16>				<15>				<20>				<25>			
	hemorrhage		1	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			( 6 )	( 6 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	mineralization		7	0	0	0	8	0	0	0	11	0	0	0	11	0	0	0
			( 44 )	( 0 )	( 0 )	( 0 )	( 53 )	( 0 )	( 0 )	( 0 )	( 55 )	( 0 )	( 0 )	( 0 )	( 44 )	( 0 )	( 0 )	( 0 )
spinal cord			<16>				<15>				<20>				<24>			
	hemorrhage		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
[Special sense organs/appandage]																		
Harder gl			<16>				<15>				<20>				<25>			
	hyperplasia		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			( 0 )	( 6 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )

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



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

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

PAGE : 11

Organ	Findings	Group Name No. of Animals on Study Grade	Control 16				10000 ppm 15				20000 ppm 20				40000 ppm 25			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

[Musculoskeletal system]

muscle	mineralization	<16>				<15>				<20>				<25>			
		2	0	0	0	2	0	0	0	0	0	0	0	1	0	0	0
		( 13)	( 0)	( 0)	( 0)	( 13)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 4)	( 0)	( 0)	( 0)

[Body cavities]

peritoneum	inflammation	<16>				<15>				<20>				<25>			
		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)	( 0)	( 0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b : Number of animals with lesion

( c ) c : b / a \* 100

Significant difference : \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$  Test of Chi Square

(HPT150)

BAIS3

## APPENDIX L 6

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

MOSUE : FEMALE : DEAD AND MORIBUND ANIMALS

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

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

PAGE : 12

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

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b b : Number of animals with lesion

( c ) c : b / a \* 100

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

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

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

PAGE : 13

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

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

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

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

PAGE : 14

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

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b : Number of animals with lesion

( c ) c : b / a \* 100

Significant difference : \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

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

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

PAGE : 15

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

( c ) c : b / a \* 100

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

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

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

PAGE : 16

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

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b : Number of animals with lesion

( c ) c : b / a \* 100

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

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

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

PAGE : 17

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

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b : Number of animals with lesion

( c ) c : b / a \* 100

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



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

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

PAGE : 18

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

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

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

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

PAGE : 19

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

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b : Number of animals with lesion

( c ) c : b / a \* 100

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

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

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

PAGE : 20

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

[Reproductive system]

ovary	angiectasis	<20>				<26>				<31>				<21>							
		0	0	0	0	0	0	0	0	0	1	1	0	0	1	0	0	0	1	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 3 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )
	hemorrhage	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 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 : Number of animals with lesion  
( c ) c : b / a \* 100  
Significant difference ; \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

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

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

PAGE : 21

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

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

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

PAGE : 22

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

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b : Number of animals with lesion

( c ) c : b / a \* 100

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

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

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

PAGE : 23

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

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

(HPT150)

BAIS3

## APPENDIX L 7

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

MOSUE : MALE : SACRIFICED ANIMALS

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

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

PAGE : 1

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

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



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

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

PAGE : 2

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

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

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

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

PAGE : 3

Organ	Findings	Group Name No. of Animals on Study Grade	Control 34				10000 ppm 35				20000 ppm 30				40000 ppm 25			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

[Hematopoietic system]

spleen			<34>				<35>				<30>				<25>			
	deposit of melanin		1	0	0	0	4	0	0	0	2	0	0	0	1	0	0	0
			( 3 )	( 0 )	( 0 )	( 0 )	( 11 )	( 0 )	( 0 )	( 0 )	( 7 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )
	extramedullary hematopoiesis		3	1	0	0	1	0	0	0	2	1	0	0	1	2	0	0
			( 9 )	( 3 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 7 )	( 3 )	( 0 )	( 0 )	( 4 )	( 8 )	( 0 )	( 0 )
	hyperplasia:vascular		1	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0
			( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 4 )	( 4 )	( 0 )	( 0 )
	follicular hyperplasia		2	2	1	0	2	1	1	0	4	3	0	0	1	1	0	0
			( 6 )	( 6 )	( 3 )	( 0 )	( 6 )	( 3 )	( 3 )	( 0 )	( 13 )	( 10 )	( 0 )	( 0 )	( 4 )	( 4 )	( 0 )	( 0 )

[Circulatory system]

heart			<34>				<35>				<30>				<25>			
	necrosis		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	mineralization		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )

[Digestive system]

tooth			<34>				<35>				<30>				<25>			
	dysplasia		22	3	2	1	21	6	0	0	9	6	2	0 *	15	2	1	0
			( 65 )	( 9 )	( 6 )	( 3 )	( 60 )	( 17 )	( 0 )	( 0 )	( 30 )	( 20 )	( 7 )	( 0 )	( 60 )	( 8 )	( 4 )	( 0 )

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b : Number of animals with lesion

( c ) c : b / a \* 100

Significant difference : \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

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

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

PAGE : 4

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

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b b : Number of animals with lesion

( c ) c : b / a \* 100

Significant difference ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$  Test of Chi Square

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

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

PAGE : 5

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

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b b : Number of animals with lesion

( c ) c : b / a \* 100

Significant difference ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$  Test of Chi Square

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

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

PAGE : 6

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

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

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

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

PAGE : 7

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

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b : Number of animals with lesion

( c ) c : b / a \* 100

Significant difference ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$  Test of Chi Square

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

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

PAGE : 8

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

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

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

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

PAGE : 9

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

( c ) c : b / a \* 100

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



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

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

PAGE : 10

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

( c ) c : b / a \* 100

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

## APPENDIX L 8

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

MOSUE : FEMALE : SACRIFICED ANIMALS

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

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

PAGE : 11

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

( c ) c : b / a \* 100

Significant difference ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$  Test of Chi Square

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

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

PAGE : 12

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

( c ) c : b / a \* 100

Significant difference : \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

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

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

PAGE : 13

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

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

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

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
SACRIFICED ANIMALS (1050)

PAGE : 14

Organ	Findings	Group Name No. of Animals on Study Grade	Control 29				10000 ppm 24				20000 ppm 19				40000 ppm 28			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Circulatory system]																		
heart			<29>				<24>				<19>				<28>			
	inflammation		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
[Digestive system]																		
tooth			<29>				<24>				<19>				<28>			
	dysplasia		5	0	0	0	2	0	0	0	0	0	0	0	4	0	0	0
			( 17 )	( 0 )	( 0 )	( 0 )	( 8 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 14 )	( 0 )	( 0 )	( 0 )
tongue			<29>				<24>				<19>				<28>			
	arteritis		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
salivary gl			<29>				<24>				<19>				<28>			
	inflammation		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	lymphocytic infiltration		9	0	0	0	8	0	0	0	4	0	0	0	6	1	0	0
			( 31 )	( 0 )	( 0 )	( 0 )	( 33 )	( 0 )	( 0 )	( 0 )	( 21 )	( 0 )	( 0 )	( 0 )	( 21 )	( 4 )	( 0 )	( 0 )
stomach			<29>				<24>				<19>				<28>			
	mineralization		2	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 : Number of animals with lesion  
( c ) c : b / a \* 100  
Significant difference ; \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

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

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

PAGE : 15

Organ	Findings	Group Name No. of Animals on Study Grade				Control 29				10000 ppm 24				20000 ppm 19				40000 ppm 28			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																					
stomach		<29>				<24>				<19>				<28>							
	inflammation	1 ( 3)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
	erosion:forestomach	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 4)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
	erosion:glandular stomach	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 4)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 5)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 5)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
	hyperplasia:glandular stomach	11 ( 38)	4 ( 14)	0 ( 0)	0 ( 0)	6 ( 25)	2 ( 8)	0 ( 0)	0 ( 0)	6 ( 32)	3 ( 16)	0 ( 0)	0 ( 0)	6 ( 32)	3 ( 16)	0 ( 0)	0 ( 0)	8 ( 29)	1 ( 4)	0 ( 0)	0 ( 0)
liver		<29>				<24>				<19>				<28>							
	angiectasis	0 ( 0)	2 ( 7)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 5)	0 ( 0)	0 ( 0)	0 ( 0)	2 ( 7)	0 ( 0)	0 ( 0)	0 ( 0)	2 ( 7)	0 ( 0)	0 ( 0)
	necrosis:focal	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 4)	0 ( 0)	0 ( 0)
	deposit of hemosiderin	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 4)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
	inflammatory infiltration	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	2 ( 8)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 4)	1 ( 4)	2 ( 7)	0 ( 0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b : Number of animals with lesion

( c ) c : b / a \* 100

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

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

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

PAGE : 16

Organ	Findings	Group Name No. of Animals on Study Grade	Control 29				10000 ppm 24				20000 ppm 19				40000 ppm 28			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

[Digestive system]

liver		<29>				<24>				<19>				<28>			
	lymphocytic infiltration	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 7 )	( 0 )	( 0 )	( 0 )
	granulation	22	0	0	0	17	2	0	0	11	0	0	0	17	2	0	0
		( 76 )	( 0 )	( 0 )	( 0 )	( 71 )	( 8 )	( 0 )	( 0 )	( 58 )	( 0 )	( 0 )	( 0 )	( 61 )	( 7 )	( 0 )	( 0 )
	clear cell focus	1	0	0	0	2	0	0	0	2	0	0	0	2	0	1	0
		( 3 )	( 0 )	( 0 )	( 0 )	( 8 )	( 0 )	( 0 )	( 0 )	( 11 )	( 0 )	( 0 )	( 0 )	( 7 )	( 0 )	( 4 )	( 0 )
acidophilic cell focus	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	
	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 5 )	( 5 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	
basophilic cell focus	1	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0	
	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	
biliary cyst	1	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	
	( 3 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	

[Urinary system]

kidney		<29>				<24>				<19>				<28>			
	hyaline droplet	0	1	0	0	0	0	0	0	3	0	0	0	0	1	0	0
		( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 16 )	( 0 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b b : Number of animals with lesion

( c ) c : b / a \* 100

Significant difference ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$  Test of Chi Square



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

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

PAGE : 17

		Group Name	Control				10000 ppm				20000 ppm				40000 ppm			
		No. of Animals on Study	29				24				19				28			
Organ	Findings	Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																		
kidney			<29>				<24>				<19>				<28>			
	deposit of hemosiderin		0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 4 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
	hyaline cast		0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 5 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
	lymphocytic infiltration		3 ( 10 )	1 ( 3 )	0 ( 0 )	0 ( 0 )	5 ( 21 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	3 ( 16 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	6 ( 21 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
	granulation		1 ( 3 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
	inflammatory polyp		0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 4 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
	hydronephrosis		0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 4 )	0 ( 0 )
urin bladd			<29>				<24>				<19>				<28>			
	inflammation		1 ( 3 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 4 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 5 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 4 )	1 ( 4 )	0 ( 0 )
[Endocrine system]																		
pituitary			<29>				<24>				<18>				<28>			
	angiectasis		1 ( 3 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 4 )	0 ( 0 )	0 ( 0 )	0 ( 0 )

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b : Number of animals with lesion

( c ) c : b / a \* 100

Significant difference ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$  Test of Chi Square

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

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

PAGE : 18

Organ	Findings	Group Name No. of Animals on Study Grade				Control 29				10000 ppm 24				20000 ppm 19				40000 ppm 28			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

[Endocrine system]

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

[Reproductive system]

ovary	angiectasis	<29>				<24>				<19>				<28>			
		0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
		( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 4)	( 0)

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

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

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

PAGE : 19

		Group Name	Control				10000 ppm				20000 ppm				40000 ppm				
		No. of Animals on Study	29				24				19				28				
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	
Organ	Findings		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	
[Reproductive system]																			
ovary			<29>				<24>				<19>				<28>				
	cyst		3 ( 10)	6 ( 21)	0 ( 0)	0 ( 0)	4 ( 17)	5 ( 21)	0 ( 0)	0 ( 0)	1 ( 5)	3 ( 16)	0 ( 0)	0 ( 0)	3 ( 11)	2 ( 7)	0 ( 0)	0 ( 0)	
uterus			<29>				<24>				<19>				<28>				
	thrombus		0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 4)	0 ( 0)	
	decidual change		0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 4)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	
	cystic endometrial hyperplasia		8 ( 28)	6 ( 21)	0 ( 0)	0 ( 0)	5 ( 21)	12 ( 50)	0 ( 0)	0 ( 0)	4 ( 21)	8 ( 42)	0 ( 0)	0 ( 0)	8 ( 29)	7 ( 25)	0 ( 0)	0 ( 0)	
	mammary gl			<29>				<24>				<19>				<28>			
		lymphocytic infiltration		0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 5)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 4)	0 ( 0)	0 ( 0)	0 ( 0)
hyperplasia			3 ( 10)	1 ( 3)	0 ( 0)	0 ( 0)	5 ( 21)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 5)	0 ( 0)	0 ( 0)	0 ( 0)	2 ( 7)	0 ( 0)	0 ( 0)	0 ( 0)	
	atypical hyperplasia		0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 4)	0 ( 0)	0 ( 0)	0 ( 0)		

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b : Number of animals with lesion

( c ) c : b / a \* 100

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

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

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

PAGE : 20

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

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

(HPT150)

BAIS3

APPENDIX M 1

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

RAT : MALE

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

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

PAGE : 1

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

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

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

PAGE : 2

Time-related Weeks	Items	Group Name	Control	7500 ppm	15000 ppm	30000 ppm
0 - 105	NO. OF EXAMINED ANIMALS		50	50	50	50
	NO. OF ANIMALS WITH TUMORS		50	50	48	50
	NO. OF ANIMALS WITH SINGLE TUMORS		18	12	15	11
	NO. OF ANIMALS WITH MULTIPLE TUMORS		32	38	33	39
	NO. OF BENIGN TUMORS		92	93	83	101
	NO. OF MALIGNANT TUMORS		16	20	17	18
	NO. OF TOTAL TUMORS		108	113	100	119
(HPT070)						BAIS3

APPENDIX M 2

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

RAT : FEMALE



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

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

PAGE : 3

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

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

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

PAGE : 4

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

(HPT070)

BAIS3

APPENDIX M 3

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

MOUSE : MALE

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

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

PAGE : 1

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

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

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

PAGE : 2

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

(HPT070)

BAIS3

APPENDIX M 4

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

MOUSE: FEMALE

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

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

PAGE : 3

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

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

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

PAGE : 4

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

(HPT070)

BAIS3



## APPENDIX N 1

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

RAT : MALE :

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

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

PAGE : 1

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

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

(HPT085)

BAIS3

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

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

PAGE : 2

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

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

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

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

PAGE : 3

Organ	Findings	Group Name No. of animals on Study	Control 50	7500 ppm 50	15000 ppm 50	30000 ppm 50
[Digestive system]						
liver	histiocytic sarcoma		<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 1 ( 2%)	<50> 1 ( 2%)
	hepatocellular carcinoma		0 ( 0%)	2 ( 4%)	0 ( 0%)	1 ( 2%)
pancreas	islet cell adenoma		<50> 4 ( 8%)	<50> 3 ( 6%)	<50> 4 ( 8%)	<50> 3 ( 6%)
	islet cell adenocarcinoma		1 ( 2%)	0 ( 0%)	0 ( 0%)	0 ( 0%)
[Urinary system]						
kidney	nephroblastoma		<50> 1 ( 2%)	<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 0 ( 0%)
	transitional cell papilloma		<50> 0 ( 0%)	<50> 1 ( 2%)	<50> 1 ( 2%)	<50> 0 ( 0%)
[Endocrine system]						
pituitary	adenoma		<50> 14 ( 28%)	<50> 14 ( 28%)	<50> 11 ( 22%)	<50> 18 ( 36%)
	adenocarcinoma		3 ( 6%)	1 ( 2%)	3 ( 6%)	1 ( 2%)
thyroid	C-cell adenoma		<50> 12 ( 24%)	<50> 5 ( 10%)	<50> 5 ( 10%)	<50> 4 ( 8%)
	follicular adenocarcinoma		1 ( 2%)	1 ( 2%)	2 ( 4%)	1 ( 2%)
adrenal	pheochromocytoma		<50> 4 ( 8%)	<50> 7 ( 14%)	<50> 5 ( 10%)	<50> 7 ( 14%)
< a >      a : Number of animals examined at the site b ( c )      b : Number of animals with neoplasm      c : b / a * 100						

(HPT085)

BAIS3

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

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

PAGE : 4

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

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

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

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

PAGE : 5

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

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

(HPT085)

BAIS3

## APPENDIX N 2

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

RAT : FEMALE :

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

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

PAGE : 6

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

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



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

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

PAGE : 7

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

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

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

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

PAGE : 8

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

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

(HPT085)

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

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

PAGE : 9

Organ	Findings	Group Name No. of animals on Study	Control 50	7500 ppm 50	15000 ppm 50	30000 ppm 50
[Reproductive system]						
mammary gl			<50>	<50>	<50>	<50>
	adenocarcinoma		0 ( 0%)	1 ( 2%)	1 ( 2%)	0 ( 0%)
prep/cli gl			<50>	<50>	<50>	<50>
	squamous cell papilloma		0 ( 0%)	1 ( 2%)	0 ( 0%)	0 ( 0%)
	adenoma		1 ( 2%)	3 ( 6%)	1 ( 2%)	3 ( 6%)
[Nervous system]						
brain			<50>	<50>	<50>	<50>
	malignant reticulosis		0 ( 0%)	1 ( 2%)	1 ( 2%)	0 ( 0%)
[Special sense organs/appandage]						
Zymbal gl			<50>	<50>	<50>	<50>
	adenoma		1 ( 2%)	0 ( 0%)	0 ( 0%)	0 ( 0%)
	squamous cell carcinoma		0 ( 0%)	0 ( 0%)	1 ( 2%)	0 ( 0%)
[Body cavities]						
peritoneum			<50>	<50>	<50>	<50>
	mesothelioma		0 ( 0%)	0 ( 0%)	0 ( 0%)	1 ( 2%)
< a >      a : Number of animals examined at the site b ( c )      b : Number of animals with neoplasm      c : b / a * 100						

(HPT085)

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APPENDIX N 3

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

MOUSE: MALE

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

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

PAGE : 1

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

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

(HPT085)

BAIS3

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

Organ	Findings	Group Name No. of animals on Study	Control 50	10000 ppm 50	20000 ppm 50	40000 ppm 50	
[Hematopoietic system]							
Lymph node			<50>	<50>	<50>	<50>	
	malignant lymphoma	7	( 14%)	3	( 6%)	6	( 12%)
	mastcytoma:malignant	0	( 0%)	1	( 2%)	0	( 0%)
spleen			<50>	<50>	<50>	<50>	
	hemangioma	1	( 2%)	0	( 0%)	3	( 6%)
	malignant lymphoma	1	( 2%)	0	( 0%)	3	( 6%)
	mastcytoma:malignant	0	( 0%)	0	( 0%)	0	( 0%)
	hemangiosarcoma	1	( 2%)	3	( 6%)	3	( 6%)
[Digestive system]							
tongue			<50>	<50>	<50>	<50>	
	squamous cell papilloma	0	( 0%)	0	( 0%)	1	( 2%)
small intes			<50>	<50>	<50>	<50>	
	adenoma	0	( 0%)	0	( 0%)	1	( 2%)
	adenocarcinoma	0	( 0%)	0	( 0%)	1	( 2%)
liver			<50>	<50>	<50>	<50>	
	hemangioma	5	( 10%)	8	( 16%)	1	( 2%)
	hepatocellular adenoma	6	( 12%)	13	( 26%)	13	( 26%)
	histiocytic sarcoma	2	( 4%)	3	( 6%)	1	( 2%)
<div> <div> <div>&lt; a &gt;</div> <div>a : Number of animals examined at the site</div> </div> <div> <div>b ( c )</div> <div>b : Number of animals with neoplasm</div> </div> <div> <div>c : b / a * 100</div> </div> </div>							

(HPT085)

BAIS3

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

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

PAGE : 3

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

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

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

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)  
ALL ANIMALS (0-1050)

PAGE : 4

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

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

(HPT085)

BAIS3



APPENDIX N 4

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

MOUSE: FEMALE

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

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

PAGE : 5

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

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

(HPT085)

BAIS3

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

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

PAGE : 6

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

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

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

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

PAGE : 7

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

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

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

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

PAGE : 8

Organ	Findings	Group Name No. of animals on Study	Control 50	10000 ppm 50	20000 ppm 50	40000 ppm 50
[Reproductive system]						
mammary gl	adenocarcinoma		<50> 1 ( 2%)	<50> 1 ( 2%)	<50> 2 ( 4%)	<50> 3 ( 6%)
[Nervous system]						
periph nerv	histiocytic sarcoma		<50> 0 ( 0%)	<50> 1 ( 2%)	<50> 0 ( 0%)	<50> 0 ( 0%)
[Special sense organs/appandage]						
Harder gl	adenoma		<50> 2 ( 4%)	<50> 1 ( 2%)	<50> 0 ( 0%)	<50> 4 ( 8%)
[Body cavities]						
peritoneum	hemangioma		<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 1 ( 2%)
< a >      a : Number of animals examined at the site b ( c )      b : Number of animals with neoplasm      c : b / a * 100						
(HPT085)						BAISS

APPENDIX O 1

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

RAT : MALE

STUDY No. : 0224  
ANIMAL : RAT F344  
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 1

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

STUDY No. : 0224  
ANIMAL : RAT F344  
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 2

Group Name	Control	7500 ppm	15000 ppm	30000 ppm
SITE : subcutis TUMOR : fibroma,fibrosarcoma				
Tumor rate				
Overall rates(a)	5/50( 10.0)	4/50( 8.0)	4/50( 8.0)	6/50( 12.0)
Adjusted rates(b)	10.53	7.69	8.89	13.64
Terminal rates(c)	4/38( 10.5)	3/39( 7.7)	3/34( 8.8)	3/30( 10.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8773			
Prevalence method(d)	P = 0.1850			
Combined analysis(d)	P = 0.3375			
Cochran-Armitage test(e)	P = 0.6539			
Fisher Exact test(e)		P = 0.4883	P = 0.4883	P = 0.4872
SITE : lung TUMOR : bronchiolar-alveolar adenoma				
Tumor rate				
Overall rates(a)	3/50( 6.0)	3/50( 6.0)	3/50( 6.0)	5/50( 10.0)
Adjusted rates(b)	7.89	6.52	8.82	16.67
Terminal rates(c)	3/38( 7.9)	2/39( 5.1)	3/34( 8.8)	5/30( 16.7)
Statistical analysis				
Peto test				
Standard method(d)	P = -----			
Prevalence method(d)	P = 0.1328			
Combined analysis(d)	P = -----			
Cochran-Armitage test(e)	P = 0.3991			
Fisher Exact test(e)		P = 0.3392	P = 0.3392	P = 0.3790
SITE : lung TUMOR : bronchiolar-alveolar adenoma,bronchiolar-alveolar carcinoma				
Tumor rate				
Overall rates(a)	3/50( 6.0)	3/50( 6.0)	3/50( 6.0)	6/50( 12.0)
Adjusted rates(b)	7.89	6.52	8.82	20.00
Terminal rates(c)	3/38( 7.9)	2/39( 5.1)	3/34( 8.8)	6/30( 20.0)
Statistical analysis				
Peto test				
Standard method(d)	P = -----			
Prevalence method(d)	P = 0.0655			
Combined analysis(d)	P = -----			
Cochran-Armitage test(e)	P = 0.2205			
Fisher Exact test(e)		P = 0.3392	P = 0.3392	P = 0.2728



STUDY No. : 0224  
ANIMAL : RAT F344  
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 3

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

STUDY No. : 0224  
ANIMAL : RAT F344  
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 4

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

STUDY No. : 0224  
ANIMAL : RAT F344  
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 5

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

STUDY No. : 0224  
ANIMAL : RAT F344  
SEX : MALE

# NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 6

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

STUDY No. : 0224  
ANIMAL : RAT F344  
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 7

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

(HPT360A)

BAIS3

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

APPENDIX O 2

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

RAT : FEMALE

STUDY No. : 0224  
ANIMAL : RAT F344  
SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 8

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

STUDY No. : 0224  
ANIMAL : RAT F344  
SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 9

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



STUDY No. : 0224  
ANIMAL : RAT F344  
SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 10

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

STUDY No. : 0224  
ANIMAL : RAT F344  
SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 11

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

STUDY No. : 0224  
ANIMAL : RAT F344  
SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 12

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

(HPT360A)

BAIS3

STUDY No. : 0224  
ANIMAL : RAT F344  
SEX : FEMALE

# NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 13

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

(HPT360A)

BAIS3

- (a): Number of tumor-bearing animals/number of animals examined at the site.  
(b): Kaplan-Meire estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.  
(c): Observed tumor incidence at terminal kill.  
(d): Beneath the control incidence are the P-values associated with the trend test.  
Standard method : Death analysis  
Prevalence method : Incidental tumor test  
Combined analysis : Death analysis + Incidental tumor test  
(e): The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.  
? : The conditional probabilities 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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

APPENDIX O 3

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

MOSUE : MALE

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

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 1

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

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

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 2

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

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

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 3

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



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

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 4

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

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

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 5

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

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

# NEOPLASTIC LESIONS—INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 6

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

(HPT360A)

BAIS3

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

APPENDIX O 4

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

MOSUE :FEMALE

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

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 7

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

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

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 8

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

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

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 9

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

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

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 10

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



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

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 11

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

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

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 12

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

(HPT360A)

BAIS3

- (a): Number of tumor-bearing animals/number of animals examined at the site.  
 (b): Kaplan-Meire estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.  
 (c): Observed tumor incidence at terminal kill.  
 (d): Beneath the control incidence are the P-values associated with the trend test.  
     Standard method : Death analysis  
     Prevalence method : Incidental tumor test  
     Combined analysis : Death analysis + Incidental tumor test  
 (e): The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.  
 ? : The conditional probabilities 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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

## APPENDIX P 1

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

RAT: MALE : DEAD AND MORIBUND ANIMALS

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

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

PAGE : 1

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

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

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

PAGE : 2

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

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

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

PAGE : 3

		Group Name	Control	7500 ppm	15000 ppm	30000 ppm
		No. of Animals on Study	12	11	16	20
Organ_____	Findings_____					
<hr/>						
[Special sense organs/appandage]						
Harder gl			<12>	<11>	<16>	<20>
	leukemic cell infiltration		2	0	0	0
<hr/>						
< a >	a : Number of animals examined at the site					
b	b : Number of animals with lesion					
<hr/>						
(JPT150)						
<hr/>						

BAIS3

## APPENDIX P 2

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

RAT: FEMALE : DEAD AND MORIBUND ANIMALS

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

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

PAGE : 4

Group Name No. of Animals on Study		Control 3	7500 ppm 11	15000 ppm 15	30000 ppm 36
Organ	Findings				
[Respiratory system]					
lung	leukemic cell infiltration	< 3> 0	<11> 3	<15> 1	<36> 3
	metastasis:liver tumor	0	0	1	0
	metastasis:uterus tumor	0	0	1	0
[Hematopoietic system]					
bone marrow	leukemic cell infiltration	< 3> 0	<11> 1	<15> 0	<36> 1
	metastasis:liver tumor	0	0	1	0
Lymph node	leukemic cell infiltration	< 3> 0	<11> 4	<15> 1	<36> 0
	metastasis:liver tumor	0	0	1	0
	metastasis:uterus tumor	0	0	1	0
[Digestive system]					
liver	leukemic cell infiltration	< 3> 0	<11> 4	<15> 1	<36> 3
[Urinary system]					
kidney	leukemic cell infiltration	< 3> 0	<11> 1	<15> 0	<36> 0
[Nervous system]					
brain	leukemic cell infiltration	< 3> 0	<11> 2	<15> 0	<36> 0
< a >		a : Number of animals examined at the site			
b		b : Number of animals with lesion			



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

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

PAGE : 5

		Group Name	Control	7500 ppm	15000 ppm	30000 ppm
		No. of Animals on Study	3	11	15	36
Organ_____	Findings_____					
<hr/>						
[Nervous system]						
spinal cord			< 3>	<11>	<15>	<36>
	leukemic cell infiltration		0	1	0	0
 [Special sense organs/appandage]						
eye			< 3>	<11>	<15>	<36>
	leukemic cell infiltration		0	1	0	0
< a >	a : Number of animals examined at the site					
b	b : Number of animals with lesion					
<hr/>						
(JPT150)						

BAIS3

## APPENDIX P 3

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

RAT: MALE : SACRIFICED ANIMALS

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

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

PAGE : 1

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

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

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

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

PAGE : 2

		Group Name	Control	7500 ppm	15000 ppm	30000 ppm
		No. of Animals on Study	38	39	34	30
Organ	Findings					

[Endocrine system]

adrenal		<38>	<39>	<34>	<30>
	leukemic cell infiltration	0	1	0	0

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

(JPT150)

BAIS3

## APPENDIX P 4

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

RAT: FEMALE : SACRIFICED ANIMALS

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

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

PAGE : 3

		Group Name	Control	7500 ppm	15000 ppm	30000 ppm
		No. of Animals on Study	47	39	35	14
Organ	Findings					
[Respiratory system]						
Lung			<47>	<39>	<35>	<14>
	leukemic cell infiltration		0	3	1	1
	metastasis:uterus tumor		0	0	1	0
[Hematopoietic system]						
Lymph node			<47>	<39>	<35>	<14>
	leukemic cell infiltration		0	1	0	0
[Digestive system]						
Liver			<47>	<39>	<35>	<14>
	leukemic cell infiltration		0	3	2	1
[Nervous system]						
brain			<47>	<39>	<35>	<14>
	leukemic cell infiltration		0	0	1	0
< a >	a : Number of animals examined at the site					
b	b : Number of animals with lesion					

APPENDIX P 5

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

MOUSE: MALE : DEAD AND MORIBUND ANIMALS

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

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

PAGE : 1

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

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



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

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

PAGE : 2

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

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

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

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

PAGE : 3

Group Name No. of Animals on Study		Control 16	10000 ppm 15	20000 ppm 20	40000 ppm 25
Organ	Findings				
[Reproductive system]					
semin ves		<16>	<15>	<20>	<25>
	leukemic cell infiltration	1	0	0	1
	metastasis:liver tumor	0	0	1	0
prostate		<16>	<15>	<20>	<25>
	leukemic cell infiltration	0	0	0	1
[Nervous system]					
brain		<16>	<15>	<20>	<25>
	leukemic cell infiltration	0	1	0	0
[Special sense organs/appandage]					
Harder gl		<16>	<15>	<20>	<25>
	leukemic cell infiltration	0	1	0	0
< a >      a : Number of animals examined at the site b : Number of animals with lesion					
(JPT150)					

BAIS3

## APPENDIX P 6

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

MOUSE: FEMALE : DEAD AND MORIBUND ANIMALS

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

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

PAGE : 4

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

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

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

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

PAGE : 5

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

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

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

PAGE : 6

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

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

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

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

## APPENDIX P 7

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

MOUSE: MALE : SACRIFICED ANIMALS



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

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

PAGE : 1

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

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

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

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

PAGE : 2

		Group Name	Control	10000 ppm	20000 ppm	40000 ppm
		No. of Animals on Study	34	35	30	25
Organ	Findings					
[Urinary system]						
kidney	leukemic cell infiltration		<34> 1	<35> 0	<30> 2	<25> 0
< a >	a : Number of animals examined at the site					
b	b : Number of animals with lesion					
(JPT150)						

BAIS3

## APPENDIX P 8

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

MOUSE: FEMALE : SACRIFICED ANIMALS

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

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

PAGE : 3

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

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

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

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

PAGE : 4

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

(JPT150)

BAIS3

APPENDIX Q 1

IDENTITY OF UROTROPIN

(TOW-YEAR STUDY)

IDENTITY OF 1,3,5,7-TETRAAZATRICYCLO[3.3.1.1<sup>3,7</sup>]DECANE(TWO-YEAR STUDIES)

A.Lot no. TWH2454

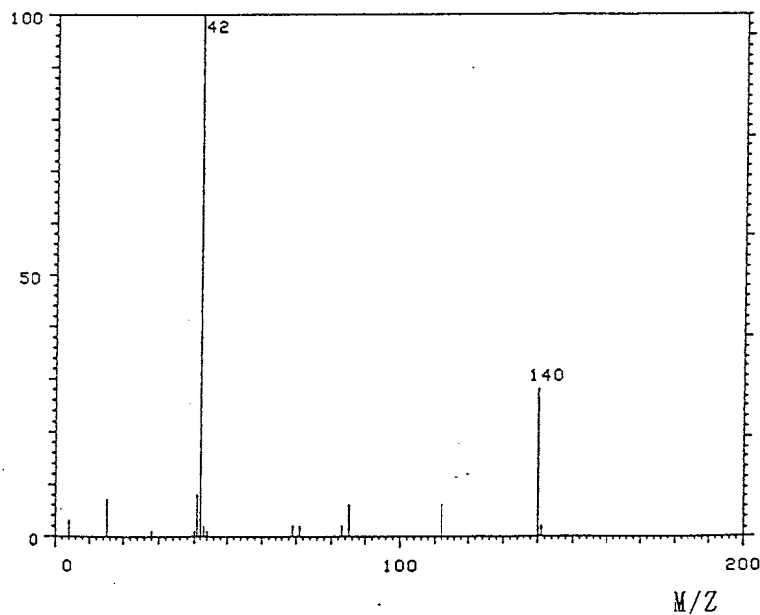
## 1. Spectral data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI(Electron Ionization)

Ionization Voltage : 70eV



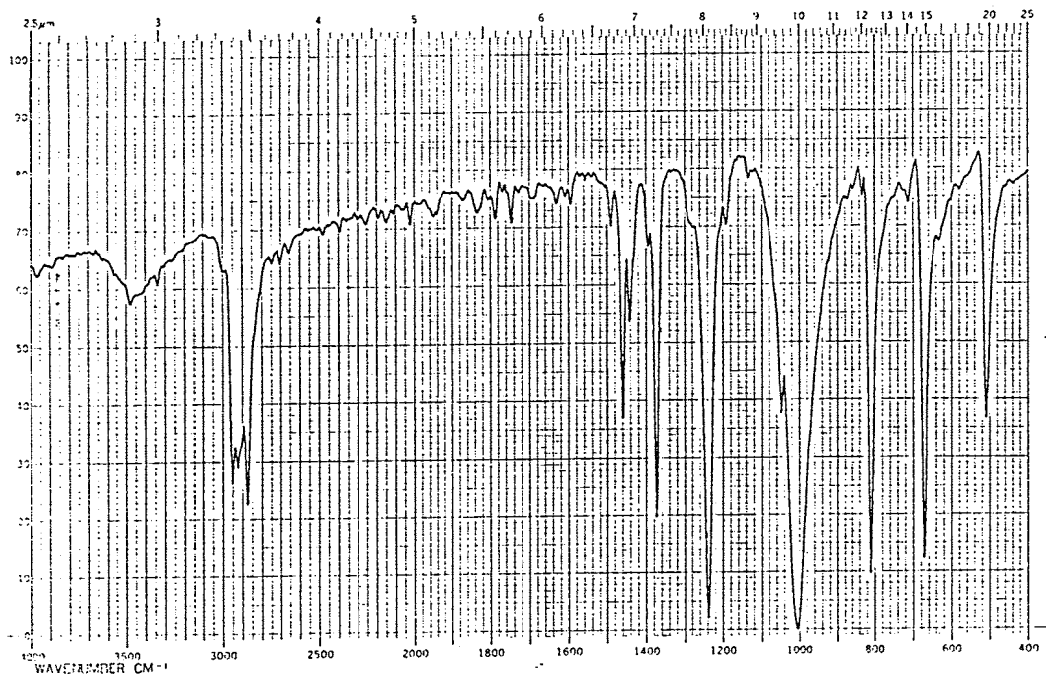
Mass Spectrum of Test Substance

Results: The mass spectrum was consistent with literature spectrum.

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

Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer  
 Cell : KBr  
 Slit : Medium



Infrared Spectrum of Test Substance

Results: The infrared spectrum was consistent with literature spectrum.

<u>Determined Value</u>	<u>Literature Value*</u>
Wave Number(cm <sup>-1</sup> )	Wave Number(cm <sup>-1</sup> )
480~ 530	480~ 530
640~ 700	640~ 700
780~ 830	780~ 830
910~1100	910~1100
1200~1270	1200~1270
1350~1420	1350~1420
1420~1490	1420~1490
2800~3000	2800~3000

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

2. Conclusions: The result of the mass spectrum and the infrared spectrum agreed with the literature values.  
 Consequently, the test substance was identified as  
 1, 3, 5, 7-Tetraazatricyclo[3.3.1.1<sup>3,7</sup>]decane.



B.Lot no. APR5276

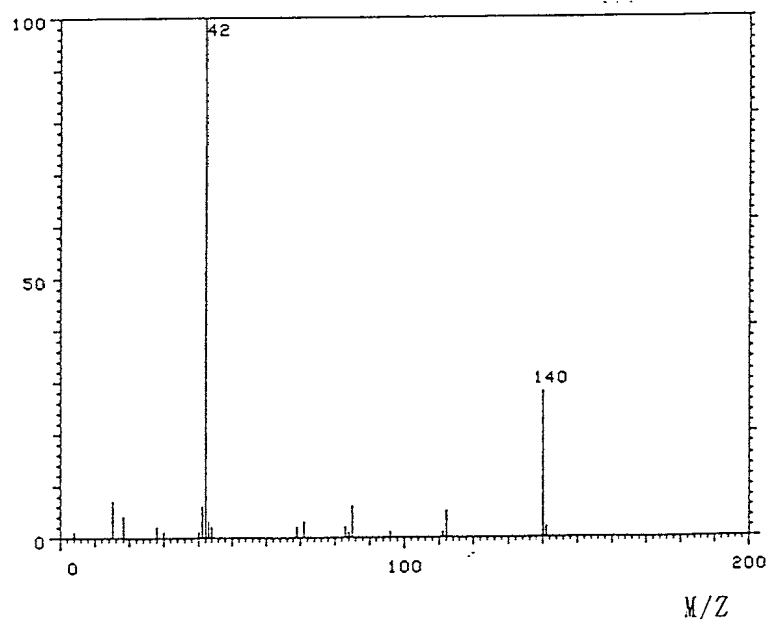
## 1. Spectral data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI(Electron Ionization)

Ionization Voltage : 70eV



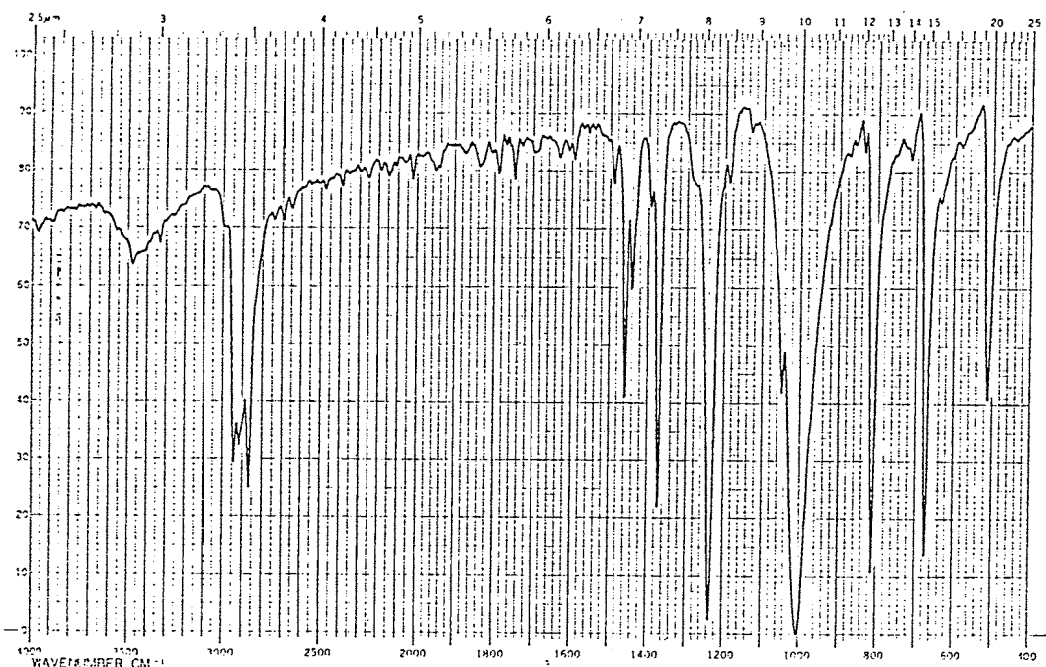
Mass Spectrum of Test Substance

Results: The mass spectrum was consistent with literature spectrum.

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

Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer  
 Cell : KBr  
 Slit : Medium



Infrared Spectrum of Test Substance

Results: The infrared spectrum was consistent with literature spectrum.

<u>Determined Value</u>	<u>Literature Value*</u>
Wave Number(cm <sup>-1</sup> )	Wave Number(cm <sup>-1</sup> )
480~ 530	480~ 530
640~ 700	640~ 700
780~ 830	780~ 830
910~1100	910~1100
1200~1270	1200~1270
1350~1420	1350~1420
1420~1490	1420~1490
2800~3000	2800~3000

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

2. Conclusions: The result of the mass spectrum and the infrared spectrum agreed with the literature values.  
 Consequently, the test substance was identified as  
 1,3,5,7-Tetraazatricyclo[3.3.1.1<sup>3,7</sup>]decane.

C.Lot no. APF5582

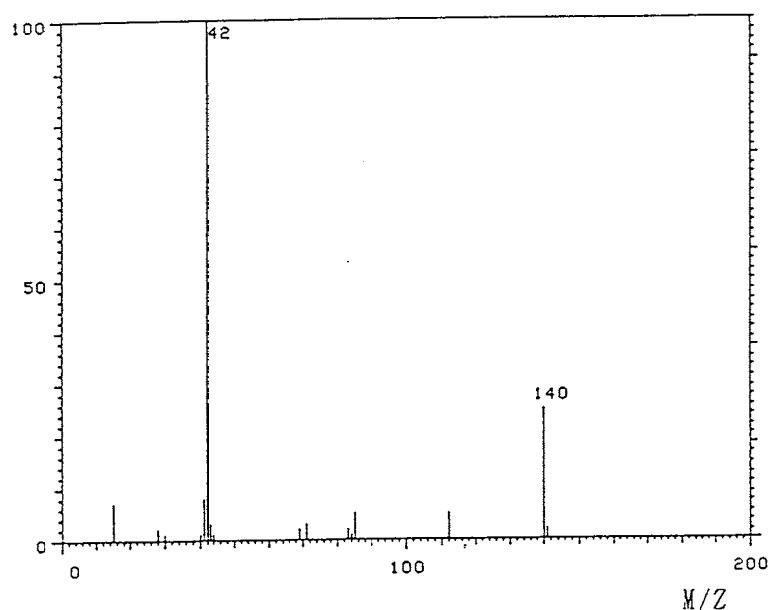
## 1. Spectral data

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.

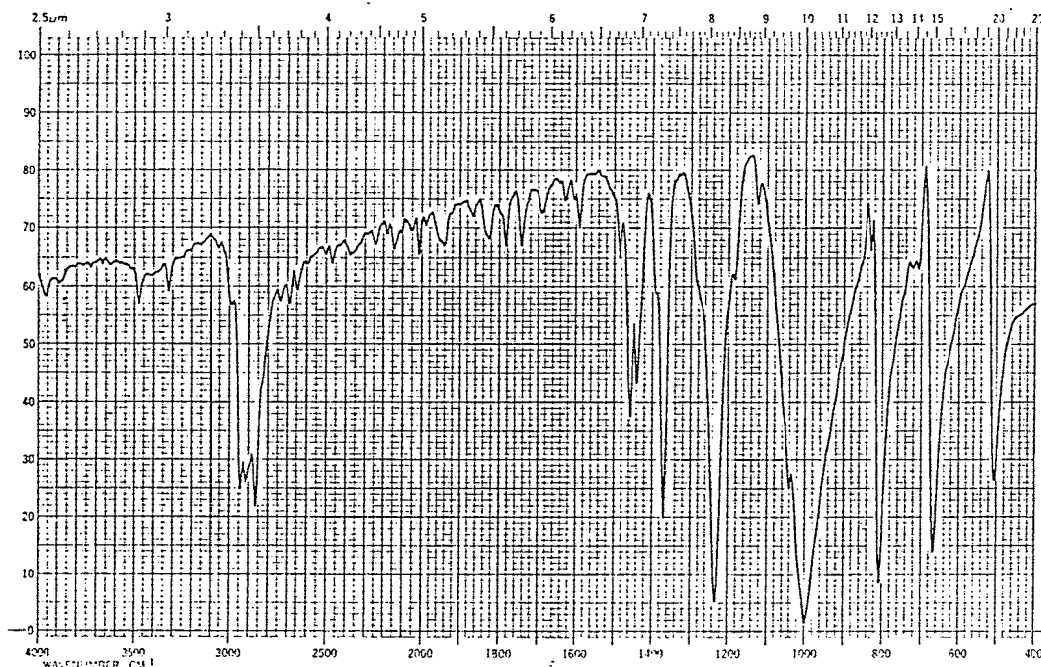
Determined Value  
Fragment Peak(M/Z)42(Base Peak)  
140Literature Value\*  
Fragment Peak(M/Z)42(Base Peak)  
140  
(\*EPA/NIH Mass Spectral  
Data Base (1978) Vol. 1,  
p. 348.)

Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium



Infrared Spectrum of Test Substance

Results: The infrared spectrum was consistent with literature spectrum.

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

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

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

D.Lot no. KCR6018

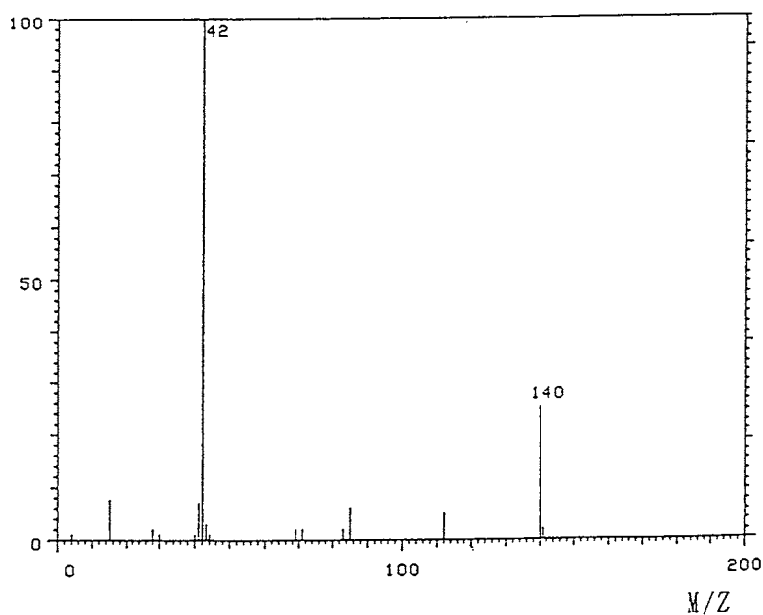
## 1. Spectral data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI(Electron Ionization)

Ionization Voltage : 70eV



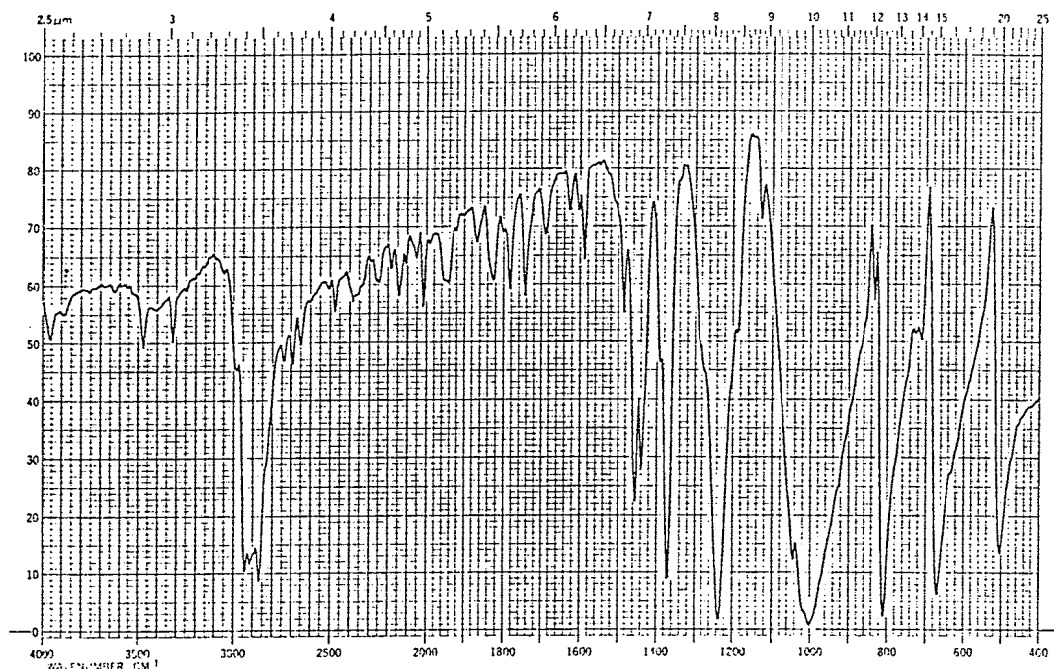
Mass Spectrum of Test Substance

Results: The mass spectrum was consistent with literature spectrum.

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

Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer  
 Cell : KBr  
 Slit : Medium



Infrared Spectrum of Test Substance

Results: The infrared spectrum was consistent with literature spectrum.

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

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

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

APPENDIX Q 2

STABILITY OF UROTROPIN

(TOW-YEAR STUDY)

STABILITY OF 1,3,5,7-TETRAAZATRICYCLO[3.3.1.1<sup>3,7</sup>]DECANE(TWO-YEAR STUDIES)

A.Lot no. TWH2454

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

2. Gas Chromatography

Instrument: Hewlett Packard 5890A Gas Chromatograph

Column: 4% Carbowax 20M / 0.8% KOH(2mm  $\phi$   $\times$  2m)

Column Temperature: 215°C

Flow Rate: 35ml/min

Detector: FID(Flame Ionization Detector)

Injection Volume: 1  $\mu$ l

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

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

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



B. Lot no. APR5276

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

2. Gas Chromatography

Instrument: Hewlett Packard 5890A Gas Chromatograph

Column: 4% Carbowax 20M / 0.8% KOH(2mm  $\phi$   $\times$  2m)

Column Temperature: 215°C

Flow Rate: 35ml/min

Detector: FID(Flame Ionization Detector)

Injection Volume: 1  $\mu$ l

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

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

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

C. Lot no. APF5582

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

2. Gas Chromatography

Instrument: Hewlett Packard 5890A Gas Chromatograph

Column: 4% Carbowax 20M / 0.8% KOH(2mm  $\phi$   $\times$  2m)

Column Temperature: 215°C

Flow Rate: 35ml/min

Detector: FID(Flame Ionization Detector)

Injection Volume: 1  $\mu$ l

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

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

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

D.Lot no. KCR6018

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

2. Gas Chromatography

Instrument: Hewlett Packard 5890A Gas Chromatograph

Column: 4% Carbowax 20M / 0.8% KOH(2mm $\phi$   $\times$  2m)

Column Temperature: 215°C

Flow Rate: 35ml/min

Detector: FID(Flame Ionization Detector)

Injection Volume: 1  $\mu$ l

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

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

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

APPENDIX Q 3

CONCENTRATION OF UROTROPIN IN DRINKING WATER

(TOW-YEAR STUDY: RAT)

CONCENTRATION OF 1,3,5,7-TETRAAZATRICYCLO[3.3.1.1<sup>3,7</sup>]DECANE IN DRINKING WATER(TWO-YEAR STUDY)

(Rat)

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

\* : % of target concentration

Analytical method: The samples were analyzed by the GC.

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

APPENDIX Q 4

CONCENTRATION OF UROTROPIN IN DRINKING WATER

(TOW-YEAR STUDY: MOUSE)

CONCENTRATION OF 1,3,5,7-TETRAAZATRICYCLO[3.3.1.1<sup>3,7</sup>]DECANE IN DRINKING WATER(TWO-YEAR STUDY)

(Mouse)

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

\* : % of target concentration

Analytical method: The samples were analyzed by the GC.

Instrument	: Hewlett Packard 5890A	Flow Rate	: 35ml/min
Column	: 4% Carbowax 20M / 0.8% KOH	Detector	: FID(Hydrogen Flame Ionization)
	/ 60/80 Carbopack B (2mm $\phi$ $\times$ 2m)	Injection Volume	: 1 $\mu$ l
Column Temperature:	215°C		

APPENDIX Q 5

STABILITY OF UROTROPIN IN DRINKING WATER

(TOW-YEAR STUDY)



# STABILITY OF 1,3,5,7-TETRAAZATRICYCLO[3.3.1.1<sup>3,7</sup>]DECANE IN DRINKING WATER(TWO-YEAR STUDIES)

(Rat)

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

(Mouse)

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

a : Date of preparation

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

Analytical method: The samples were analyzed by the GC.

Instrument	: Hewlett Packard 5890A	Flow Rate	: 35ml/min
Column	: 4% Carbowax 20M / 0.8% KOH	Detector	: FID(Hydrogen Flame Ionization)
	/ 60/80 Carbowax B (2mm $\phi$ $\times$ 2m)	Injection Volume	: 1 $\mu$ l
Column Temperature:	215°C		

## APPENDIX R 1

### METHODS FOR HEMATOLOGY,BIOCHEMISTRY AND URINALYSIS

## METHODS FOR HEMATOLOGY,BIOCHEMISTRY AND URINALYSIS

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

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

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

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

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

## APPENDIX R 2

### UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

# UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

Item	Unit	Decimal place
<b>Hematology</b>		
Red blood cell (RBC)	$\times 10^6 / \mu\text{L}$	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	$\times 10^3 / \mu\text{L}$	0
White blood cell (WBC)	$\times 10^3 / \mu\text{L}$	2
Differential WBC	%	0
<b>Biochemistry</b>		
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
$\gamma$ - Glutamyl transpeptidase ( $\gamma$ - 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