

アントラセ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予備試験(混餌試験)報告書

試験番号：ラット/0242；マウス/0243

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(K1～S4)

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## APPENDIX K 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (2-YEAR STUDY: SUMMARY)

RAT : MALE : ALL ANIMALS

STUDY NO. : 0242  
ANIMAL : RAT F344/DuCrJ  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 1

Organ	Findings	Group Name No. of Animals on Study Grade	Control 50				8000 ppm 50				20000 ppm 50				50000 ppm 50			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Integumentary system/appandage]																		
skin/app			<50>				<50>				<50>				<50>			
	hemorrhage		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 )
	epidermal cyst		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	sebaceous hyperplasia		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )
subcutis			<50>				<50>				<50>				<50>			
	abscess		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
[Respiratory system]																		
nasal cavit			<50>				<50>				<50>				<50>			
	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 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	inflammation		1	0	0	0	0	0	0	0	1	0	0	0	3	0	0	0
			( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )

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

STUDY NO. : 0242  
 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 2

Organ	Findings	Group Name No. of Animals on Study Grade				Control 50				8000 ppm 50				20000 ppm 50				50000 ppm 50			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																					
nasal cavit		<50>				<50>				<50>				<50>				<50>			
	eosinophilic change:olfactory epithelium	22	23	0	0	1	0	0	0 **	0	0	0	0 **	0	0	0	0	0	0	0	0 **
		( 44)	( 46)	( 0)	( 0)	( 2)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
	eosinophilic change:respiratory epithelium	35	1	0	0	1	0	0	0 **	0	0	0	0 **	0	0	0	0	0	0	0	0 **
		( 70)	( 2)	( 0)	( 0)	( 2)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
lung	inflammation:foreign body	10	11	0	0	7	10	0	0	12	13	2	0	6	7	1	0				
		( 20)	( 22)	( 0)	( 0)	( 14)	( 20)	( 0)	( 0)	( 24)	( 26)	( 4)	( 0)	( 12)	( 14)	( 2)	( 0)				
	respiratory metaplasia:olfactory epithelium	7	0	0	0	3	1	0	0	4	0	0	0	5	0	0	0				
		( 14)	( 0)	( 0)	( 0)	( 6)	( 2)	( 0)	( 0)	( 8)	( 0)	( 0)	( 0)	( 10)	( 0)	( 0)	( 0)				
	respiratory metaplasia:gland	31	3	0	0	27	4	0	0	19	0	0	0 **	18	1	0	0 **				
		( 62)	( 6)	( 0)	( 0)	( 54)	( 8)	( 0)	( 0)	( 38)	( 0)	( 0)	( 0)	( 36)	( 2)	( 0)	( 0)				
larynx		<50>				<50>				<50>				<50>				<50>			
	inflammatory infiltration	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)				
lung		<50>				<50>				<50>				<50>				<50>			
	congestion	3	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0				
		( 6)	( 0)	( 0)	( 0)	( 2)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)				

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



STUDY NO. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 3

Organ	Findings	Control 50				8000 ppm 50				20000 ppm 50				50000 ppm 50			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																	
Lung	deposit of hemosiderin	<50>				<50>				<50>				<50>			
		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	inflammation	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 )	( 2 )	( 0 )	( 0 )
	inflammatory infiltration	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 )
	osseous metaplasia	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	bronchiolar-alveolar cell hyperplasia	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )
[Hematopoietic system]																	
bone marrow	congestion	<50>				<50>				<50>				<50>			
		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 )
	granulation	1	2	0	0	2	1	0	0	0	0	0	0	3	0	0	0
		( 2 )	( 4 )	( 0 )	( 0 )	( 4 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )

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

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

b : 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. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 4

Organ	Findings	Control 50				8000 ppm 50				20000 ppm 50				50000 ppm 50			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																	
bone marrow		<50>				<50>				<50>				<50>			
	increased hematopoiesis	2	0	0	0	4	1	0	0	4	1	0	0	4	0	0	0
		( 4 )	( 0 )	( 0 )	( 0 )	( 8 )	( 2 )	( 0 )	( 0 )	( 8 )	( 2 )	( 0 )	( 0 )	( 8 )	( 0 )	( 0 )	( 0 )
	decreased hematopoiesis	0	0	1	0	2	0	0	0	0	2	0	0	0	1	1	0
		( 0 )	( 0 )	( 2 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )
	granulopoiesis:increased	2	0	0	0	2	0	0	0	0	0	0	0	1	0	0	0
		( 4 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )
Lymph node		<50>				<50>				<50>				<50>			
	Lymphocytic infiltration	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
spleen		<50>				<50>				<50>				<50>			
	atrophy	2	0	0	0	1	0	1	0	1	2	0	0	0	1	1	0
		( 4 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 2 )	( 0 )	( 2 )	( 4 )	( 0 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )
	congestion	7	4	0	0	8	1	0	0	12	0	0	0	6	0	0	0
		( 14 )	( 8 )	( 0 )	( 0 )	( 16 )	( 2 )	( 0 )	( 0 )	( 24 )	( 0 )	( 0 )	( 0 )	( 12 )	( 0 )	( 0 )	( 0 )
	deposit of hemosiderin	1	1	1	0	4	1	0	0	8	1	0	0	9	5	0	0 **
		( 2 )	( 2 )	( 2 )	( 0 )	( 8 )	( 2 )	( 0 )	( 0 )	( 16 )	( 2 )	( 0 )	( 0 )	( 18 )	( 10 )	( 0 )	( 0 )

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

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

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. : 0242  
 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 5

Organ	Findings	Group Name No. of Animals on Study Grade	Control 50				8000 ppm 50				20000 ppm 50				50000 ppm 50			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
spleen			<50>				<50>				<50>				<50>			
	fibrosis		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	extramedullary hematopoiesis		2	2	0	0	3	2	0	0	2	2	0	0	5	3	1	0
			( 4 )	( 4 )	( 0 )	( 0 )	( 6 )	( 4 )	( 0 )	( 0 )	( 4 )	( 4 )	( 0 )	( 0 )	( 10 )	( 6 )	( 2 )	( 0 )
	engorgement of erythrocyte		0	0	0	0	13	2	0	0 **	14	0	0	0 **	10	0	0	0 **
			( 0 )	( 0 )	( 0 )	( 0 )	( 26 )	( 4 )	( 0 )	( 0 )	( 28 )	( 0 )	( 0 )	( 0 )	( 20 )	( 0 )	( 0 )	( 0 )
[Circulatory system]																		
heart			<50>				<50>				<50>				<50>			
	thrombus		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	myocardial fibrosis		3	0	0	0	2	0	0	0	3	0	0	0	4	4	0	0
			( 6 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )	( 8 )	( 8 )	( 0 )	( 0 )
	arteritis		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
artery/aort			<50>				<50>				<50>				<50>			
	mineralization		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 )	( 2 )	( 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. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 6

Organ	Findings	Group Name No. of Animals on Study Control Grade				8000 ppm 50				20000 ppm 50				50000 ppm 50			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Circulatory system]																	
artery/aort	arteritis	<50>				<50>				<50>				<50>			
		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
[Digestive system]																	
tongue	arteritis	<50>				<50>				<50>				<50>			
		3	1	0	0	3	0	0	0	3	0	0	0	2	1	0	0
		( 6 )	( 2 )	( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )	( 4 )	( 2 )	( 0 )	( 0 )
salivary gl	inflammation	<50>				<50>				<50>				<50>			
		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 )	( 2 )	( 0 )	( 0 )
stomach	mineralization	<50>				<50>				<50>				<50>			
		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 )	( 2 )	( 0 )	( 0 )
	ulcer:forestomach	1	1	0	0	1	1	0	0	1	2	0	0	0	0	0	0
		( 2 )	( 2 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )	( 0 )	( 2 )	( 4 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	hyperplasia:forestomach	1	0	0	0	1	0	0	0	0	1	0	0	0	1	0	0
		( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )

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

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

b b : Number of animals with lesion

( c ) c : b / a \* 100

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

STUDY NO. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 7

Organ	Findings	Control No. of Animals on Study Grade				8000 ppm No. of Animals on Study Grade				20000 ppm No. of Animals on Study Grade				50000 ppm No. of Animals on Study Grade			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																	
stomach		<50>				<50>				<50>				<50>			
	erosion:glandular stomach	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)	2 ( 4)	0 ( 0)	0 ( 0)	0 ( 0)
	ulcer:glandular stomach	4 ( 8)	3 ( 6)	0 ( 0)	0 ( 0)	5 ( 10)	0 ( 0)	0 ( 0)	0 ( 0)	2 ( 4)	1 ( 2)	0 ( 0)	0 ( 0)	2 ( 4)	0 ( 0)	0 ( 0)	0 ( 0)
	hyperplasia:glandular stomach	2 ( 4)	0 ( 0)	0 ( 0)	0 ( 0)	2 ( 4)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)	1 ( 2)	0 ( 0)	0 ( 0)	3 ( 6)	1 ( 2)	0 ( 0)	0 ( 0)
small intes		<50>				<50>				<50>				<50>			
	diverticula	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
liver		<50>				<50>				<50>				<50>			
	herniation	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	3 ( 6)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
	necrosis:central	1 ( 2)	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
	necrosis:focal	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)	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. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 8

Organ	Findings	Group Name No. of Animals on Study Grade				Control 50				8000 ppm 50				20000 ppm 50				50000 ppm 50			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																					
Liver	collapse	<50>				<50>				<50>				<50>				<50>			
		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 )	( 2 )	( 0 )	( 0 )
	fatty change	0	2	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
		( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	degeneration:central	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 )
	granulation	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )
	clear cell focus	6	2	1	0	2	12	17	11 **	2	13	14	14 **	5	20	8	5 **	( 10 )	( 40 )	( 16 )	( 10 )
		( 12 )	( 4 )	( 2 )	( 0 )	( 4 )	( 24 )	( 34 )	( 22 )	( 4 )	( 26 )	( 28 )	( 28 )	( 6 )	( 18 )	( 16 )	( 30 )	( 6 )	( 12 )	( 16 )	( 30 )
	acidophilic cell focus	4	0	0	0	5	14	14	7 **	3	9	13	15 **	3	6	8	15 **	( 8 )	( 0 )	( 0 )	( 0 )
		( 8 )	( 0 )	( 0 )	( 0 )	( 10 )	( 28 )	( 28 )	( 14 )	( 6 )	( 18 )	( 26 )	( 30 )	( 6 )	( 12 )	( 16 )	( 30 )	( 6 )	( 12 )	( 16 )	( 30 )
	basophilic cell focus	5	8	0	0	8	9	4	0	6	13	0	1	11	9	3	0	( 10 )	( 16 )	( 0 )	( 0 )
		( 10 )	( 16 )	( 0 )	( 0 )	( 16 )	( 18 )	( 8 )	( 0 )	( 12 )	( 26 )	( 0 )	( 2 )	( 22 )	( 18 )	( 6 )	( 0 )	( 22 )	( 18 )	( 6 )	( 0 )
	spongiosis hepatitis	0	1	0	0	11	3	0	0 **	8	3	1	0 **	9	5	1	0 **	( 0 )	( 2 )	( 0 )	( 0 )
		( 0 )	( 2 )	( 0 )	( 0 )	( 22 )	( 6 )	( 0 )	( 0 )	( 16 )	( 6 )	( 2 )	( 0 )	( 18 )	( 10 )	( 2 )	( 0 )	( 18 )	( 10 )	( 2 )	( 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. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 9

Organ	Findings	Control No. of Animals on Study Grade				8000 ppm 50				20000 ppm 50				50000 ppm 50			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																	
liver	bile duct hyperplasia	10 ( 20 )	36 ( 72 )	0 ( 0 )	0 ( 0 )	10 ( 20 )	37 ( 74 )	0 ( 0 )	0 ( 0 )	18 ( 36 )	22 ( 44 )	2 ( 4 )	0 * ( 0 )	18 ( 36 )	22 ( 44 )	1 ( 2 )	0 * ( 0 )
	cholangiofibrosis	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	2 ( 4 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
	biliary cyst	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
pancreas	atrophy	3 ( 6 )	3 ( 6 )	0 ( 0 )	0 ( 0 )	5 ( 10 )	7 ( 14 )	2 ( 4 )	0 ( 0 )	7 ( 14 )	5 ( 10 )	1 ( 2 )	0 ( 0 )	10 ( 20 )	6 ( 12 )	0 ( 0 )	0 * ( 0 )
	hyperplasia	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
	arteritis	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	2 ( 4 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
[Urinary system]																	
kidney	hyperplasia:tubular epithelial cell	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	4 ( 8 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	2 ( 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. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 10

Organ	Findings	Control 50				8000 ppm 50				20000 ppm 50				50000 ppm 50			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																	
kidney		<50>				<50>				<50>				<50>			
	infarct	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	cyst	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	deposit of hemosiderin	0	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )
	eosinophilic body	0	0	0	0	0	1	0	0	0	0	0	0	0	1	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )
	chronic nephropathy	6	12	17	10	1	15	11	15	3	13	14	15	7	13	16	7
		( 12 )	( 24 )	( 34 )	( 20 )	( 2 )	( 30 )	( 22 )	( 30 )	( 6 )	( 26 )	( 28 )	( 30 )	( 14 )	( 26 )	( 32 )	( 14 )
	tubular necrosis	0	0	2	0	0	0	1	0	0	0	2	0	0	1	1	0
		( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )
	papillary necrosis	0	1	0	0	4	0	0	0	5	1	0	0	1	1	0	0
		( 0 )	( 2 )	( 0 )	( 0 )	( 8 )	( 0 )	( 0 )	( 0 )	( 10 )	( 2 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )	( 0 )
	mineralization:cortico-medullary junction	0	2	0	0	0	1	0	0	0	0	0	0	0	1	0	0
		( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 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. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 11

Organ	Findings	Group Name No. of Animals on Study Grade	Control 50				8000 ppm 50				20000 ppm 50				50000 ppm 50			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																		
kidney	mineralization:papilla		<50>				<50>				<50>				<50>			
			2	0	0	0	4	2	0	0	8	0	0	0	6	1	0	0
			( 4 )	( 0 )	( 0 )	( 0 )	( 8 )	( 4 )	( 0 )	( 0 )	( 16 )	( 0 )	( 0 )	( 0 )	( 12 )	( 2 )	( 0 )	( 0 )
	mineralization:pelvis		0	0	0	0	1	1	0	0	1	1	0	0	2	2	0	1
			( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )	( 0 )	( 4 )	( 4 )	( 0 )	( 2 )
	mineralization:cortex		0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	simple hyperplasia:transitional epithelium		2	0	0	0	5	0	0	0	4	1	0	0	7	0	0	0
			( 4 )	( 0 )	( 0 )	( 0 )	( 10 )	( 0 )	( 0 )	( 0 )	( 8 )	( 2 )	( 0 )	( 0 )	( 14 )	( 0 )	( 0 )	( 0 )
	nodular hyperplasia:transitional epithelium		4	0	0	0	5	3	0	0	8	0	0	0	5	0	0	0
			( 8 )	( 0 )	( 0 )	( 0 )	( 10 )	( 6 )	( 0 )	( 0 )	( 16 )	( 0 )	( 0 )	( 0 )	( 10 )	( 0 )	( 0 )	( 0 )
	eosinophilic droplet:proximal tubule		1	0	0	0	19	4	0	0 **	27	5	0	0 **	23	13	0	0 **
			( 2 )	( 0 )	( 0 )	( 0 )	( 38 )	( 8 )	( 0 )	( 0 )	( 54 )	( 10 )	( 0 )	( 0 )	( 46 )	( 26 )	( 0 )	( 0 )
urin bladd	hemorrhage		<50>				<50>				<50>				<50>			
			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 )
	simple hyperplasia:transitional epithelium		0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )

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

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

b b : Number of animals with lesion

( c ) c : b / a \* 100

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

STUDY NO. : 0242  
 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 12

Organ	Findings	Control No. of Animals on Study Grade				8000 ppm 50				20000 ppm 50				50000 ppm 50			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																	
urin bladd		<50>				<50>				<50>				<50>			
	nodular hyperplasia:transitional epithelium	0	0	0	0	0	0	0	0	1	0	0	0	2	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )
[Endocrine system]																	
pituitary		<49>				<50>				<50>				<50>			
	angiectasis	2	1	0	0	1	0	0	0	0	0	0	0	1	2	0	0
		( 4 )	( 2 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 4 )	( 0 )	( 0 )
	cyst	1	0	0	0	1	0	0	0	1	0	0	0	1	0	0	0
		( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )
	hyperplasia	6	2	0	0	5	1	0	0	6	3	0	0	7	2	0	0
		( 12 )	( 4 )	( 0 )	( 0 )	( 10 )	( 2 )	( 0 )	( 0 )	( 12 )	( 6 )	( 0 )	( 0 )	( 14 )	( 4 )	( 0 )	( 0 )
	hyperplasia:gland	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	Rathke pouch	0	0	0	0	2	0	0	0	2	0	0	0	2	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )
thyroid		<50>				<50>				<50>				<50>			
	C-cell hyperplasia	1	2	0	0	4	0	0	0	3	0	0	0	2	3	0	0
		( 2 )	( 4 )	( 0 )	( 0 )	( 8 )	( 0 )	( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )	( 4 )	( 6 )	( 0 )	( 0 )

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

STUDY NO. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 13

Organ	Findings	Control No. of Animals on Study Grade				8000 ppm 50				20000 ppm 50				50000 ppm 50			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]																	
thyroid		<50>				<50>				<50>				<50>			
	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 )	( 2 )	( 0 )	( 0 )	( 0 )
panc islet		<50>				<50>				<50>				<50>			
	islet cell hyperplasia	1	1	0	0	2	0	0	0	1	1	0	0	0	0	0	0
		( 2 )	( 2 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
adrenal		<50>				<50>				<50>				<50>			
	peliosis-like lesion	0	0	0	0	1	0	0	0	2	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	hyperplasia:medulla	3	5	0	0	4	7	0	0	7	4	0	0	5	1	0	0
		( 6 )	( 10 )	( 0 )	( 0 )	( 8 )	( 14 )	( 0 )	( 0 )	( 14 )	( 8 )	( 0 )	( 0 )	( 10 )	( 2 )	( 0 )	( 0 )
	focal fatty change:cortex	1	0	0	0	1	0	0	0	2	0	0	0	0	0	0	0
		( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
[Reproductive system]																	
testis		<50>				<50>				<50>				<50>			
	atrophy	1	0	0	0	1	0	0	0	1	0	0	0	3	0	0	0
		( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )

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

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

b b : Number of animals with lesion

( c ) c : b / a \* 100

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

STUDY NO. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 14

Organ	Findings	Control No. of Animals on Study Grade				8000 ppm 50				20000 ppm 50				50000 ppm 50			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Reproductive system]																	
testis	mineralization	6 ( 12)	0 ( 0)	0 ( 0)	0 ( 0)	7 ( 14)	0 ( 0)	0 ( 0)	0 ( 0)	14 ( 28)	1 ( 2)	0 ( 0)	0 ( 0)	16 ( 32)	1 ( 2)	0 ( 0)	0 * ( 0)
	arteritis	5 ( 10)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	3 ( 6)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)
	interstitial cell hyperplasia	8 ( 16)	0 ( 0)	0 ( 0)	0 ( 0)	2 ( 4)	0 ( 0)	0 ( 0)	0 ( 0)	2 ( 4)	0 ( 0)	0 ( 0)	0 ( 0)	3 ( 6)	0 ( 0)	0 ( 0)	0 ( 0)
prostate	inflammation	4 ( 8)	0 ( 0)	0 ( 0)	0 ( 0)	7 ( 14)	0 ( 0)	0 ( 0)	0 ( 0)	4 ( 8)	0 ( 0)	1 ( 2)	0 ( 0)	7 ( 14)	0 ( 0)	0 ( 0)	0 ( 0)
	hyperplasia	8 ( 16)	0 ( 0)	0 ( 0)	0 ( 0)	6 ( 12)	0 ( 0)	0 ( 0)	0 ( 0)	11 ( 22)	0 ( 0)	0 ( 0)	0 ( 0)	11 ( 22)	0 ( 0)	0 ( 0)	0 ( 0)
mammary gl	hyperplasia	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
	galactocoele	0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)	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. : 0242  
 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 15

Organ	Findings	Control 50				8000 ppm 50				20000 ppm 50				50000 ppm 50			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Nervous system]																	
periph nerv	adhesion	<50>				<50>				<50>				<50>			
		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 )	( 2 )	( 0 )	( 0 )
[Special sense organs/appandage]																	
eye	hemorrhage	<50>				<50>				<50>				<50>			
		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	inflammatory infiltration	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )
	cataract	0	5	0	0	0	4	0	0	0	3	0	0	0	4	0	0
		( 0 )	( 10 )	( 0 )	( 0 )	( 0 )	( 8 )	( 0 )	( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )	( 8 )	( 0 )	( 0 )
	retinal atrophy	2	10	0	0	2	16	0	0	0	9	0	0	4	9	0	0
		( 4 )	( 20 )	( 0 )	( 0 )	( 4 )	( 32 )	( 0 )	( 0 )	( 0 )	( 18 )	( 0 )	( 0 )	( 8 )	( 18 )	( 0 )	( 0 )
	keratitis	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 )
Harder gl	degeneration	<50>				<50>				<50>				<50>			
		2	0	0	0	1	0	0	0	0	0	0	0	0	2	0	0
		( 4 )	( 0 )	( 0 )	( 0 )	( 2 )	( 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. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 16

Organ	Findings	Group Name No. of Animals on Study Grade	Control 50				8000 ppm 50				20000 ppm 50				50000 ppm 50			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Special sense organs/appandage]																		
Harder gl	inflammatory infiltration		<50>				<50>				<50>				<50>			
			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 )	( 2 )	( 0 )	( 0 )
	Lymphocytic infiltration		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 )
nasolacr d	inflammation		<50>				<50>				<50>				<50>			
			0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )
[Body cavities]																		
retroperit	hemorrhage		<50>				<50>				<50>				<50>			
			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 )	( 2 )	( 0 )	( 0 )
adipose	necrosis		<50>				<50>				<50>				<50>			
			0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )

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

## APPENDIX K 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (2-YEAR STUDY: SUMMARY)

RAT : FEMALE : ALL ANIMALS

STUDY NO. : 0242  
 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 1

		Group Name	Control				8000 ppm				20000 ppm				50000 ppm			
		No. of Animals on Study	50				50				50				50			
Organ	Findings	Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Integumentary system/appandage]																		
skin/app			<50>				<50>				<50>				<50>			
	inflammation		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 )	( 2 )	( 0 )	( 0 )
[Respiratory system]																		
nasal cavit			<50>				<50>				<50>				<50>			
	follicle		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 )
	atrophy		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )
	eosinophilic change:olfactory epithelium		4	29	16	0	0	0	0	0 **	0	0	0	0 **	0	0	0	0 **
			( 8 )	( 58 )	( 32 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	eosinophilic change:respiratory epithelium		36	0	0	0	0	0	0	0 **	0	0	0	0 **	0	0	0	0 **
			( 72 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	inflammation:foreign body		5	2	0	0	1	1	0	0	2	1	0	0	6	1	0	0
			( 10 )	( 4 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )	( 0 )	( 4 )	( 2 )	( 0 )	( 0 )	( 12 )	( 2 )	( 0 )	( 0 )
	disarrangement:olfactory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )

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



STUDY NO. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 2

Organ	Findings	Group Name No. of Animals on Study Grade	Control 50				8000 ppm 50				20000 ppm 50				50000 ppm 50			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
nasal cavit			<50>				<50>				<50>				<50>			
	respiratory metaplasia:olfactory epithelium		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 )	( 16 )	( 0 )	( 0 )	( 0 )
	respiratory metaplasia:gland		30	2	0	0	18	0	0	0 *	23	0	0	0	15	0	0	0 **
			( 60 )	( 4 )	( 0 )	( 0 )	( 36 )	( 0 )	( 0 )	( 0 )	( 46 )	( 0 )	( 0 )	( 0 )	( 30 )	( 0 )	( 0 )	( 0 )
	necrosis:olfactory epithelium		0	0	0	0	3	0	0	0	14	0	0	0 **	25	0	0	0 **
			( 0 )	( 0 )	( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )	( 28 )	( 0 )	( 0 )	( 0 )	( 50 )	( 0 )	( 0 )	( 0 )
lung			<50>				<50>				<50>				<50>			
	congestion		1	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0
			( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	hemorrhage		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	inflammation		0	0	0	0	2	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 )
	inflammatory infiltration		1	0	0	0	1	0	0	0	3	0	0	0	1	0	0	0
			( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )
	lymphocytic infiltration		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe  
< a > a : Number of animals examined at the site  
b : 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. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 3

Organ	Findings	Group Name	Control				8000 ppm				20000 ppm				50000 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
lung			<50>				<50>				<50>				<50>			
	accumulation of foamy cells		0	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )
	bronchiolar-alveolar cell hyperplasia		1	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0
			( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
[Hematopoietic system]																		
bone marrow			<50>				<50>				<50>				<50>			
	granulation		2	4	0	0	2	5	0	0	1	2	0	0	5	5	0	0
			( 4 )	( 8 )	( 0 )	( 0 )	( 4 )	( 10 )	( 0 )	( 0 )	( 2 )	( 4 )	( 0 )	( 0 )	( 10 )	( 10 )	( 0 )	( 0 )
	increased hematopoiesis		5	0	0	0	2	0	0	0	4	0	0	0	4	1	0	0
			( 10 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 8 )	( 0 )	( 0 )	( 0 )	( 8 )	( 2 )	( 0 )	( 0 )
	decreased hematopoiesis		0	1	0	0	0	0	0	0	0	0	0	0	2	0	0	
			( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	
	granulopoiesis:increased		0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	
			( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	
spleen			<50>				<50>				<50>				<50>			
	atrophy		1	0	0	0	0	1	0	0	0	2	0	0	0	1	0	0
			( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 2 )	( 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. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 4

Organ	Findings	Group Name No. of Animals on Study Grade	Control 50				8000 ppm 50				20000 ppm 50				50000 ppm 50			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
spleen			<50>				<50>				<50>				<50>			
	congestion		6 ( 12)	0 ( 0)	0 ( 0)	0 ( 0)	6 ( 12)	0 ( 0)	0 ( 0)	0 ( 0)	2 ( 4)	0 ( 0)	0 ( 0)	0 ( 0)	7 ( 14)	0 ( 0)	0 ( 0)	0 ( 0)
	deposit of hemosiderin		15 ( 30)	9 ( 18)	0 ( 0)	0 ( 0)	22 ( 44)	8 ( 16)	1 ( 2)	0 ( 0)	28 ( 56)	7 ( 14)	1 ( 2)	0 * ( 0)	21 ( 42)	9 ( 18)	0 ( 0)	0 ( 0)
	extramedullary hematopoiesis		3 ( 6)	3 ( 6)	0 ( 0)	0 ( 0)	2 ( 4)	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)	2 ( 4)	0 ( 0)	0 ( 0)	2 ( 4)	3 ( 6)	0 ( 0)	0 ( 0)
	engorgement of erythrocyte		0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	22 ( 44)	6 ( 12)	0 ( 0)	0 ** ( 0)	29 ( 58)	4 ( 8)	0 ( 0)	0 ** ( 0)	20 ( 40)	8 ( 16)	0 ( 0)	0 ** ( 0)
[Circulatory system]																		
heart			<50>				<50>				<50>				<50>			
	thrombus		0 ( 0)	0 ( 0)	1 ( 2)	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)
	necrosis:focal		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)
	mineralization		0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)

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

STUDY NO. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 5

Organ	Findings	Group Name No. of Animals on Study Grade	Control 50				8000 ppm 50				20000 ppm 50				50000 ppm 50			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Circulatory system]																		
heart	myocardial fibrosis		<50>				<50>				<50>				<50>			
			1	0	0	0	2	0	0	0	0	1	0	0	3	0	0	0
			( 2 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )
artery/aort	arteritis		<50>				<50>				<50>				<50>			
			0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
[Digestive system]																		
tooth	epidermal cyst		<50>				<50>				<50>				<50>			
			0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
tongue	arteritis		<50>				<50>				<50>				<50>			
			1	0	0	0	1	1	0	0	2	1	0	0	1	0	0	0
			( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )	( 0 )	( 4 )	( 2 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )
stomach	mineralization		<50>				<50>				<50>				<50>			
			0	0	0	0	1	0	0	0	1	1	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	arteritis		<50>				<50>				<50>				<50>			
			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 )	( 2 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )

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

STUDY NO. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 6

Organ	Findings	Group Name No. of Animals on Study Grade	Control 50				8000 ppm 50				20000 ppm 50				50000 ppm 50			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
stomach	ulcer:forestomach		<50>				<50>				<50>				<50>			
			0	0	0	0	0	1	0	0	0	0	1	0	1	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )
	hyperplasia:forestomach		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	erosion:glandular stomach		0	0	0	0	2	0	0	0	1	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	ulcer:glandular stomach		2	0	0	0	0	0	0	1	0	0	0	0	1	1	0	0
			( 4 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )	( 0 )
	hyperplasia:glandular stomach		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )
small intes	inflammation		<50>				<50>				<50>				<50>			
			0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
liver	herniation		<50>				<50>				<50>				<50>			
			3	0	0	0	2	0	0	0	1	0	0	0	1	0	0	0
			( 6 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )

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

STUDY NO. : 0242  
 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 7

Organ	Findings	Group Name No. of Animals on Study Grade	Control 50				8000 ppm 50				20000 ppm 50				50000 ppm 50			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
Liver																		
	peliosis-like lesion		<50>				<50>				<50>				<50>			
			0	0	0	0	2	0	0	0	1	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	necrosis:central		0	2	0	0	0	0	0	0	0	1	0	0	0	1	1	0
			( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )
	necrosis:focal		0	1	0	0	0	0	0	0	2	0	0	0	0	0	0	0
			( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	fatty change		1	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0
			( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	lymphocytic infiltration		0	1	0	0	0	1	0	0	1	1	0	0	0	0	0	0
			( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	granulation		17	9	0	0	20	8	1	0	24	10	2	0	20	12	2	0
			( 34 )	( 18 )	( 0 )	( 0 )	( 40 )	( 16 )	( 2 )	( 0 )	( 48 )	( 20 )	( 4 )	( 0 )	( 40 )	( 24 )	( 4 )	( 0 )
	extramedullary hematopoiesis		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	clear cell focus		1	0	0	0	3	6	0	0 *	8	7	0	0 **	5	6	2	0 **
			( 2 )	( 0 )	( 0 )	( 0 )	( 6 )	( 12 )	( 0 )	( 0 )	( 16 )	( 14 )	( 0 )	( 0 )	( 10 )	( 12 )	( 4 )	( 0 )

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

STUDY NO. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 8

Organ	Findings	Group Name No. of Animals on Study Grade	Control 50				8000 ppm 50				20000 ppm 50				50000 ppm 50			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
liver			<50>				<50>				<50>				<50>			
	acidophilic cell focus		0	0	0	0	6	11	3	0 **	6	10	3	1 **	10	5	1	1 **
			( 0 )	( 0 )	( 0 )	( 0 )	( 12 )	( 22 )	( 6 )	( 0 )	( 12 )	( 20 )	( 6 )	( 2 )	( 20 )	( 10 )	( 2 )	( 2 )
	basophilic cell focus		12	10	0	0	7	11	0	0	9	10	1	1	9	5	1	0
			( 24 )	( 20 )	( 0 )	( 0 )	( 14 )	( 22 )	( 0 )	( 0 )	( 18 )	( 20 )	( 2 )	( 2 )	( 18 )	( 10 )	( 2 )	( 0 )
	mixed cell focus		0	0	0	0	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 )	( 2 )	( 0 )	( 0 )
pancreas	spongiosis hepatitis		0	0	0	0	1	0	0	0	2	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	bile duct hyperplasia		4	0	0	0	3	1	0	0	1	1	0	0	1	1	0	0
			( 8 )	( 0 )	( 0 )	( 0 )	( 6 )	( 2 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )	( 0 )
	cholangiofibrosis		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )
	biliary cyst		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
pancreas			<50>				<50>				<50>				<50>			
	atrophy		4	0	0	0	3	3	0	0	3	7	0	0 *	5	3	0	0
			( 8 )	( 0 )	( 0 )	( 0 )	( 6 )	( 6 )	( 0 )	( 0 )	( 6 )	( 14 )	( 0 )	( 0 )	( 10 )	( 6 )	( 0 )	( 0 )

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

STUDY NO. : 0242  
 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 9

Organ	Findings	Group Name No. of Animals on Study Grade	Control 50				8000 ppm 50				20000 ppm 50				50000 ppm 50			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																		
kidney			<50>				<50>				<50>				<50>			
	infarct		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	cyst		0	1	0	0	1	0	0	0	0	0	0	0	1	0	0	0
			( 0 )	( 2 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )
	chronic nephropathy		23	11	3	3	10	15	15	4 **	10	21	8	5 *	17	18	7	0
			( 46 )	( 22 )	( 6 )	( 6 )	( 20 )	( 30 )	( 30 )	( 8 )	( 20 )	( 42 )	( 16 )	( 10 )	( 34 )	( 36 )	( 14 )	( 0 )
	hydronephrosis		0	0	1	0	0	0	0	0	0	1	0	0	0	1	0	0
			( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )
	tubular necrosis		0	3	4	0	0	1	3	0	0	1	1	0	0	1	2	0
			( 0 )	( 6 )	( 8 )	( 0 )	( 0 )	( 2 )	( 6 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )	( 0 )	( 2 )	( 4 )	( 0 )
	papillary necrosis		0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	mineralization:cortico-medullary junction		21	2	0	0	13	4	0	0	15	0	0	0	13	0	0	0
			( 42 )	( 4 )	( 0 )	( 0 )	( 26 )	( 8 )	( 0 )	( 0 )	( 30 )	( 0 )	( 0 )	( 0 )	( 26 )	( 0 )	( 0 )	( 0 )
	mineralization:papilla		2	0	0	0	11	1	0	0 *	7	0	0	0	5	0	0	0
			( 4 )	( 0 )	( 0 )	( 0 )	( 22 )	( 2 )	( 0 )	( 0 )	( 14 )	( 0 )	( 0 )	( 0 )	( 10 )	( 0 )	( 0 )	( 0 )

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



STUDY NO. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 10

Organ	Findings	Group Name No. of Animals on Study Grade	Control 50				8000 ppm 50				20000 ppm 50				50000 ppm 50			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																		
kidney			<50>				<50>				<50>				<50>			
	mineralization:pelvis		5	1	0	0	4	2	0	0	7	0	0	0	7	1	0	0
			( 10 )	( 2 )	( 0 )	( 0 )	( 8 )	( 4 )	( 0 )	( 0 )	( 14 )	( 0 )	( 0 )	( 0 )	( 14 )	( 2 )	( 0 )	( 0 )
	mineralization:cortex		0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	dilatation:tubular lumen		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	simple tubule hyperplasia		0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	atypical tubule hyperplasia		0	0	0	0	12	0	0	0 **	13	0	0	0 **	7	0	0	0 *
			( 0 )	( 0 )	( 0 )	( 0 )	( 24 )	( 0 )	( 0 )	( 0 )	( 26 )	( 0 )	( 0 )	( 0 )	( 14 )	( 0 )	( 0 )	( 0 )
	eosinophilic droplet:proximal tubule		2	0	0	0	14	32	0	0 **	4	38	0	0 **	8	37	0	0 **
			( 4 )	( 0 )	( 0 )	( 0 )	( 28 )	( 64 )	( 0 )	( 0 )	( 8 )	( 76 )	( 0 )	( 0 )	( 16 )	( 74 )	( 0 )	( 0 )
urin bladd			<50>				<50>				<50>				<50>			
	nodular hyperplasia:transitional epithelium		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
[Endocrine system]																		
pituitary			<50>				<50>				<50>				<50>			
	angiectasis		6	5	0	0	0	1	0	0 **	1	0	0	0 **	4	0	0	0
			( 12 )	( 10 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 8 )	( 0 )	( 0 )	( 0 )

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

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

b b : Number of animals with lesion

( c ) c : b / a \* 100

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

STUDY NO. : 0242  
 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 11

Organ	Findings	Group Name No. of Animals on Study Grade	Control 50				8000 ppm 50				20000 ppm 50				50000 ppm 50			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]																		
pituitary	cyst		<50>				<50>				<50>				<50>			
			3	0	0	0	8	0	0	0	1	1	0	0	9	0	0	0
			( 6 )	( 0 )	( 0 )	( 0 )	( 16 )	( 0 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )	( 0 )	( 18 )	( 0 )	( 0 )	( 0 )
	hyperplasia		6	0	0	0	6	1	0	0	4	1	0	0	7	1	0	0
			( 12 )	( 0 )	( 0 )	( 0 )	( 12 )	( 2 )	( 0 )	( 0 )	( 8 )	( 2 )	( 0 )	( 0 )	( 14 )	( 2 )	( 0 )	( 0 )
	Rathke pouch		0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
thyroid	cyst		<50>				<50>				<50>				<49>			
			0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	ultimibranhial body remanet		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	C-cell hyperplasia		4	0	0	0	3	1	0	0	2	0	0	0	1	0	0	0
			( 8 )	( 0 )	( 0 )	( 0 )	( 6 )	( 2 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )
	focal follicular cell hyperplasia		0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )
adrenal	peliosis-like lesion		<50>				<50>				<50>				<50>			
			6	0	0	0	5	0	0	0	2	1	0	0	5	0	0	0
			( 12 )	( 0 )	( 0 )	( 0 )	( 10 )	( 0 )	( 0 )	( 0 )	( 4 )	( 2 )	( 0 )	( 0 )	( 10 )	( 0 )	( 0 )	( 0 )

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

STUDY NO. : 0242  
 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 12

		Group Name	Control				8000 ppm				20000 ppm				50000 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
Organ	Findings		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
<hr/>																		
[Endocrine system]																		
adrenal			<50>				<50>				<50>				<50>			
	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 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
	hyperplasia:cortical cell		0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
	hyperplasia:medulla		6 ( 12 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	6 ( 12 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	3 ( 6 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	9 ( 18 )	2 ( 4 )	0 ( 0 )	0 ( 0 )
	focal fatty change:cortex		2 ( 4 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	3 ( 6 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	3 ( 6 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
[Reproductive system]																		
ovary			<50>				<50>				<50>				<50>			
	cyst		0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	2 ( 4 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
uterus			<50>				<50>				<50>				<50>			
	dilatation		1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )

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

STUDY NO. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 13

Organ	Findings	Group Name No. of Animals on Study Grade	Control 50				8000 ppm 50				20000 ppm 50				50000 ppm 50			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Reproductive system]																		
uterus	cystic endometrial hyperplasia		<50>				<50>				<50>				<50>			
			3	2	0	0	4	1	0	0	4	5	0	0	9	2	0	0
			( 6 )	( 4 )	( 0 )	( 0 )	( 8 )	( 2 )	( 0 )	( 0 )	( 8 )	( 10 )	( 0 )	( 0 )	( 18 )	( 4 )	( 0 )	( 0 )
mammary gl	duct ectasia		<50>				<50>				<50>				<50>			
			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 )
	hyperplasia		3	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 )
[Nervous system]																		
brain	hemorrhage		<50>				<50>				<50>				<50>			
			0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
[Special sense organs/appandage]																		
eye	cataract		<50>				<50>				<50>				<50>			
			0	3	0	0	0	2	0	0	0	3	0	0	0	2	0	0
			( 0 )	( 6 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )

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

STUDY NO. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 14

Organ	Findings	Group Name No. of Animals on Study Grade	Control 50				8000 ppm 50				20000 ppm 50				50000 ppm 50			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Special sense organs/appandage]																		
eye	retinal atrophy		<50>				<50>				<50>				<50>			
			9	4	0	0	5	4	1	0	1	9	0	0 *	2	5	0	0
			( 18 )	( 8 )	( 0 )	( 0 )	( 10 )	( 8 )	( 2 )	( 0 )	( 2 )	( 18 )	( 0 )	( 0 )	( 4 )	( 10 )	( 0 )	( 0 )
	keratitis		0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )
	vascularization:cornea		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
Harder gl	atrophy		<50>				<50>				<50>				<50>			
			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 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )
	degeneration		0	1	0	0	2	0	0	0	0	0	0	0	2	0	0	0
			( 0 )	( 2 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )
	inflammatory infiltration		0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )	( 0 )
	Lymphocytic infiltration		3	1	0	0	1	1	0	0	0	1	0	0	2	0	0	0
			( 6 )	( 2 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )
nasolacr d	inflammation		<50>				<50>				<50>				<50>			
			1	0	0	0	3	0	0	0	1	0	0	0	1	0	0	0
			( 2 )	( 0 )	( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )

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

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

b : Number of animals with lesion

( c ) c : b / a \* 100

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

STUDY NO. : 0242  
 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 15

Organ	Findings	Group Name No. of Animals on Study Grade	Control 50				8000 ppm 50				20000 ppm 50				50000 ppm 50			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Musculoskeletal system]																		
muscle			<50>				<50>				<50>				<50>			
	hematoma		0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	mineralization		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
bone			<50>				<50>				<50>				<50>			
	osteosclerosis		5	6	0	0	4	3	3	0	2	4	1	0	2	2	2	0
			( 10 )	( 12 )	( 0 )	( 0 )	( 8 )	( 6 )	( 6 )	( 0 )	( 4 )	( 8 )	( 2 )	( 0 )	( 4 )	( 4 )	( 4 )	( 0 )
[Body cavities]																		
pleura			<50>				<50>				<50>				<50>			
	inflammation		0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
peritoneum			<50>				<50>				<50>				<50>			
	inflammation		0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
retroperit			<50>				<50>				<50>				<50>			
	hematoma		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 )	( 2 )

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

< 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

## APPENDIX K 3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (2-YEAR STUDY: SUMMARY)

RAT : MALE : SACRIFICED ANIMALS

STUDY NO. : 0242  
 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 1

Organ	Findings	Group Name No. of Animals on Study Control 33 Grade				8000 ppm 43				20000 ppm 43				50000 ppm 38			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Integumentary system/appandage]																	
skin/app	epidermal cyst	<33>				<43>				<43>				<38>			
		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
subcutis	abscess	<33>				<43>				<43>				<38>			
		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
[Respiratory system]																	
nasal cavit	inflammation	<33>				<43>				<43>				<38>			
		0	0	0	0	0	0	0	0	1	0	0	0	2	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )
	eosinophilic change:olfactory epithelium	15	18	0	0	1	0	0	0 **	0	0	0	0 **	0	0	0	0 **
		( 45 )	( 55 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	eosinophilic change:respiratory epithelium	26	1	0	0	1	0	0	0 **	0	0	0	0 **	0	0	0	0 **
		( 79 )	( 3 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	inflammation:foreign body	8	7	0	0	7	10	0	0	12	10	2	0	2	7	1	0
		( 24 )	( 21 )	( 0 )	( 0 )	( 16 )	( 23 )	( 0 )	( 0 )	( 28 )	( 23 )	( 5 )	( 0 )	( 5 )	( 18 )	( 3 )	( 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. : 0242  
ANIMAL : RAT F344/DuCrj  
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 33				8000 ppm 43				20000 ppm 43				50000 ppm 38			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																					
nasal cavity		<33>				<43>				<43>				<38>							
	respiratory metaplasia:olfactory epithelium	4 ( 12)	0 ( 0)	0 ( 0)	0 ( 0)	2 ( 5)	0 ( 0)	0 ( 0)	0 ( 0)	4 ( 9)	0 ( 0)	0 ( 0)	0 ( 0)	4 ( 11)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
	respiratory metaplasia:gland	24 ( 73)	3 ( 9)	0 ( 0)	0 ( 0)	25 ( 58)	3 ( 7)	0 ( 0)	0 ( 0)	18 ( 42)	0 ( 0)	0 ( 0)	0 ( 0)	15 ( 39)	1 ( 3)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
lung		<33>				<43>				<43>				<38>							
	osseous metaplasia	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
	bronchiolar-alveolar cell hyperplasia	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 3)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
[Hematopoietic system]																					
bone marrow		<33>				<43>				<43>				<38>							
	granulation	1 ( 3)	2 ( 6)	0 ( 0)	0 ( 0)	2 ( 5)	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	3 ( 8)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
	increased hematopoiesis	1 ( 3)	0 ( 0)	0 ( 0)	0 ( 0)	2 ( 5)	1 ( 2)	0 ( 0)	0 ( 0)	3 ( 7)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)

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

STUDY NO. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 3

Organ	Findings	Group Name No. of Animals on Study Grade				Control 33				8000 ppm 43				20000 ppm 43				50000 ppm 38			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																					
bone marrow		<33>				<43>				<43>				<38>							
	decreased hematopoiesis	0	0	0	0	1	0	0	0	0	1	0	0	0	1	0	0	0	1	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	granulopoiesis:increased	1	0	0	0	2	0	0	0	0	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 )	( 0 )	( 0 )	( 0 )	( 0 )
Lymph node		<33>				<43>				<43>				<38>							
	Lymphocytic infiltration	0	0	0	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 )
spleen		<33>				<43>				<43>				<38>							
	atrophy	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 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	congestion	6	4	0	0	8	1	0	0	12	0	0	0	6	0	0	0	6	0	0	0
		( 18 )	( 12 )	( 0 )	( 0 )	( 19 )	( 2 )	( 0 )	( 0 )	( 28 )	( 0 )	( 0 )	( 0 )	( 16 )	( 0 )	( 0 )	( 0 )	( 16 )	( 0 )	( 0 )	( 0 )
	deposit of hemosiderin	0	0	0	0	2	1	0	0	7	0	0	0 *	7	3	0	0 **	7	3	0	0 **
		( 0 )	( 0 )	( 0 )	( 0 )	( 5 )	( 2 )	( 0 )	( 0 )	( 16 )	( 0 )	( 0 )	( 0 )	( 18 )	( 8 )	( 0 )	( 0 )	( 18 )	( 8 )	( 0 )	( 0 )
	fibrosis	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 )	( 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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$  Test of Chi Square

STUDY NO. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 4

Organ	Findings	Group Name No. of Animals on Study Grade	Control 33				8000 ppm 43				20000 ppm 43				50000 ppm 38			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
spleen			<33>				<43>				<43>				<38>			
	extramedullary hematopoiesis		2	0	0	0	2	2	0	0	1	1	0	0	2	2	0	0
			( 6 )	( 0 )	( 0 )	( 0 )	( 5 )	( 5 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )	( 0 )	( 5 )	( 5 )	( 0 )	( 0 )
	engorgement of erythrocyte		0	0	0	0	12	2	0	0 **	14	0	0	0 **	10	0	0	0 **
			( 0 )	( 0 )	( 0 )	( 0 )	( 28 )	( 5 )	( 0 )	( 0 )	( 33 )	( 0 )	( 0 )	( 0 )	( 26 )	( 0 )	( 0 )	( 0 )
[Circulatory system]																		
heart			<33>				<43>				<43>				<38>			
	myocardial fibrosis		3	0	0	0	2	0	0	0	1	0	0	0	2	3	0	0
			( 9 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 5 )	( 8 )	( 0 )	( 0 )
	arteritis		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
artery/aort			<33>				<43>				<43>				<38>			
	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 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
[Digestive system]																		
tongue			<33>				<43>				<43>				<38>			
	arteritis		3	1	0	0	3	0	0	0	3	0	0	0	2	1	0	0
			( 9 )	( 3 )	( 0 )	( 0 )	( 7 )	( 0 )	( 0 )	( 0 )	( 7 )	( 0 )	( 0 )	( 0 )	( 5 )	( 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. : 0242  
 ANIMAL : RAT F344/DuCrj  
 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 33				8000 ppm 43				20000 ppm 43				50000 ppm 38			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																					
salivary gl		<33>				<43>				<43>				<38>							
	inflammation	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 )
stomach		<33>				<43>				<43>				<38>							
	ulcer:forestomach	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	erosion:glandular stomach	1	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	2	0	0	0
		( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )
	ulcer:glandular stomach	2	0	0	0	5	0	0	0	2	0	0	0	2	0	0	0	2	0	0	0
		( 6 )	( 0 )	( 0 )	( 0 )	( 12 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )
	hyperplasia:glandular stomach	1	0	0	0	2	0	0	0	1	1	0	0	2	1	0	0	2	1	0	0
		( 3 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )	( 0 )	( 5 )	( 3 )	( 0 )	( 0 )	( 5 )	( 3 )	( 0 )	( 0 )
small intes		<33>				<43>				<43>				<38>							
	diverticula	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 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
liver		<33>				<43>				<43>				<38>							
	herniation	0	0	0	0	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 )

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. : 0242  
ANIMAL : RAT F344/DuCrj  
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 Control 33 Grade				8000 ppm 43				20000 ppm 43				50000 ppm 38			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																	
Liver		<33>				<43>				<43>				<38>			
	necrosis:focal	1 ( 3)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
	granulation	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 3)	0 ( 0)	0 ( 0)	0 ( 0)
	clear cell focus	6 ( 18)	2 ( 6)	1 ( 3)	0 ( 0)	2 ( 5)	10 ( 23)	17 ( 40)	11 ** ( 26)	1 ( 2)	12 ( 28)	14 ( 33)	14 ** ( 33)	2 ( 5)	19 ( 50)	8 ( 21)	5 ** ( 13)
	acidophilic cell focus	4 ( 12)	0 ( 0)	0 ( 0)	0 ( 0)	4 ( 9)	13 ( 30)	14 ( 33)	7 ** ( 16)	2 ( 5)	9 ( 21)	13 ( 30)	15 ** ( 35)	2 ( 5)	5 ( 13)	8 ( 21)	15 ** ( 39)
	basophilic cell focus	5 ( 15)	7 ( 21)	0 ( 0)	0 ( 0)	8 ( 19)	9 ( 21)	4 ( 9)	0 ( 0)	6 ( 14)	13 ( 30)	0 ( 0)	1 ( 2)	9 ( 24)	8 ( 21)	3 ( 8)	0 ( 0)
	spongiosis hepatitis	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	9 ( 21)	3 ( 7)	0 ( 0)	0 ** ( 0)	7 ( 16)	3 ( 7)	1 ( 2)	0 * ( 0)	9 ( 24)	5 ( 13)	0 ( 0)	0 ** ( 0)
	bile duct hyperplasia	4 ( 12)	28 ( 85)	0 ( 0)	0 ( 0)	9 ( 21)	33 ( 77)	0 ( 0)	0 ( 0)	16 ( 37)	22 ( 51)	2 ( 5)	0 * ( 0)	15 ( 39)	19 ( 50)	1 ( 3)	0 * ( 0)
	cholangiofibrosis	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)	2 ( 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. : 0242  
ANIMAL : RAT F344/DuCrj  
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 33				8000 ppm 43				20000 ppm 43				50000 ppm 38			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
Liver	biliary cyst		<33>				<43>				<43>				<38>			
		0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	
pancreas	atrophy		<33>				<43>				<43>				<38>			
		3 ( 9 )	3 ( 9 )	0 ( 0 )	0 ( 0 )	5 ( 12 )	6 ( 14 )	2 ( 5 )	0 ( 0 )	7 ( 16 )	5 ( 12 )	1 ( 2 )	0 ( 0 )	9 ( 24 )	6 ( 16 )	0 ( 0 )	0 ( 0 )	
	hyperplasia		0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	
		arteritis		0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	2 ( 5 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
[Urinary system]																		
kidney	hyperplasia:tubular epithelial cell		<33>				<43>				<43>				<38>			
		0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	4 ( 9 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	2 ( 5 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	
infarct		0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	

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

STUDY NO. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 8

Organ	Findings	Control 33				8000 ppm 43				20000 ppm 43				50000 ppm 38			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																	
kidney	cyst	<33>				<43>				<43>				<38>			
		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	deposit of hemosiderin	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	eosinophilic body	0	0	0	0	0	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 )
	chronic nephropathy	3	9	14	7	1	15	11	15	3	11	14	14	4	11	15	6
		( 9 )	( 27 )	( 42 )	( 21 )	( 2 )	( 35 )	( 26 )	( 35 )	( 7 )	( 26 )	( 33 )	( 33 )	( 11 )	( 29 )	( 39 )	( 16 )
	papillary necrosis	0	0	0	0	4	0	0	0	5	1	0	0	1	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 9 )	( 0 )	( 0 )	( 0 )	( 12 )	( 2 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )
	mineralization:cortico-medullary junction	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	mineralization:papilla	2	0	0	0	3	1	0	0	6	0	0	0	5	1	0	0
		( 6 )	( 0 )	( 0 )	( 0 )	( 7 )	( 2 )	( 0 )	( 0 )	( 14 )	( 0 )	( 0 )	( 0 )	( 13 )	( 3 )	( 0 )	( 0 )
	mineralization:pelvis	0	0	0	0	1	1	0	0	0	1	0	0	2	1	0	1
		( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 5 )	( 3 )	( 0 )	( 3 )

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe  
< a > a : Number of animals examined at the site  
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. : 0242  
 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 9

Organ	Findings	Control 33				8000 ppm 43				20000 ppm 43				50000 ppm 38			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																	
kidney		<33>				<43>				<43>				<38>			
	simple hyperplasia:transitional epithelium	2	0	0	0	5	0	0	0	4	1	0	0	7	0	0	0
		( 6 )	( 0 )	( 0 )	( 0 )	( 12 )	( 0 )	( 0 )	( 0 )	( 9 )	( 2 )	( 0 )	( 0 )	( 18 )	( 0 )	( 0 )	( 0 )
	nodular hyperplasia:transitional epithelium	3	0	0	0	5	3	0	0	8	0	0	0	4	0	0	0
		( 9 )	( 0 )	( 0 )	( 0 )	( 12 )	( 7 )	( 0 )	( 0 )	( 19 )	( 0 )	( 0 )	( 0 )	( 11 )	( 0 )	( 0 )	( 0 )
	eosinophilic droplet:proximal tubule	1	0	0	0	19	4	0	0 **	26	5	0	0 **	20	13	0	0 **
		( 3 )	( 0 )	( 0 )	( 0 )	( 44 )	( 9 )	( 0 )	( 0 )	( 60 )	( 12 )	( 0 )	( 0 )	( 53 )	( 34 )	( 0 )	( 0 )
urin bladd		<33>				<43>				<43>				<38>			
	simple hyperplasia:transitional epithelium	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	nodular hyperplasia:transitional epithelium	0	0	0	0	0	0	0	0	1	0	0	0	2	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )
[Endocrine system]																	
pituitary		<32>				<43>				<43>				<38>			
	angiectasis	2	1	0	0	1	0	0	0	0	0	0	0	1	1	0	0
		( 6 )	( 3 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 3 )	( 0 )	( 0 )

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



STUDY NO. : 0242  
 ANIMAL : RAT F344/DuCrj  
 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 33				8000 ppm 43				20000 ppm 43				50000 ppm 38			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Endocrine system]																		
pituitary	cyst		<32>				<43>				<43>				<38>			
		1 ( 3 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 3 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	
	hyperplasia	5 ( 16 )	2 ( 6 )	0 ( 0 )	0 ( 0 )	4 ( 9 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	6 ( 14 )	3 ( 7 )	0 ( 0 )	0 ( 0 )	7 ( 18 )	2 ( 5 )	0 ( 0 )	0 ( 0 )	
		hyperplasia:gland	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
thyroid	Rathke pouch	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	2 ( 5 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	2 ( 5 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	2 ( 5 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	
		C-cell hyperplasia	0 ( 0 )	1 ( 3 )	0 ( 0 )	0 ( 0 )	4 ( 9 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	3 ( 7 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 3 )	3 ( 8 )	0 ( 0 )	0 ( 0 )
	panc islet	islet cell hyperplasia	1 ( 3 )	1 ( 3 )	0 ( 0 )	0 ( 0 )	2 ( 5 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
			adrenal	peliosis-like lesion	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	2 ( 5 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )

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. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 11

		Group Name No. of Animals on Study Grade	Control 33				8000 ppm 43				20000 ppm 43				50000 ppm 38			
Organ	Findings		1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Endocrine system]																		
adrenal			<33>				<43>				<43>				<38>			
	hyperplasia:medulla		3 ( 9 )	4 ( 12 )	0 ( 0 )	0 ( 0 )	4 ( 9 )	7 ( 16 )	0 ( 0 )	0 ( 0 )	7 ( 16 )	4 ( 9 )	0 ( 0 )	0 ( 0 )	5 ( 13 )	1 ( 3 )	0 ( 0 )	0 ( 0 )
	focal fatty change:cortex		0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
[Reproductive system]																		
testis			<33>				<43>				<43>				<38>			
	atrophy		1 ( 3 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 3 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
	mineralization		5 ( 15 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	7 ( 16 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	13 ( 30 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	10 ( 26 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
	arteritis		3 ( 9 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	2 ( 5 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 3 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
	interstitial cell hyperplasia		3 ( 9 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
prostate			<33>				<43>				<43>				<38>			
	inflammation		3 ( 9 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	6 ( 14 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	2 ( 5 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	7 ( 18 )	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. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 12

		Group Name No. of Animals on Study Grade	Control 33				8000 ppm 43				20000 ppm 43				50000 ppm 38			
Organ	Findings		1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Reproductive system]																		
prostate	hyperplasia		<33>				<43>				<43>				<38>			
			8 ( 24)	0 ( 0)	0 ( 0)	0 ( 0)	6 ( 14)	0 ( 0)	0 ( 0)	0 ( 0)	10 ( 23)	0 ( 0)	0 ( 0)	0 ( 0)	11 ( 29)	0 ( 0)	0 ( 0)	0 ( 0)
mammary gl	hyperplasia		<33>				<43>				<43>				<38>			
			0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
	galactoele		0 ( 0)	1 ( 3)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
[Special sense organs/appandage]																		
eye	cataract		<33>				<43>				<43>				<38>			
			0 ( 0)	4 ( 12)	0 ( 0)	0 ( 0)	0 ( 0)	4 ( 9)	0 ( 0)	0 ( 0)	0 ( 0)	3 ( 7)	0 ( 0)	0 ( 0)	0 ( 0)	4 ( 11)	0 ( 0)	0 ( 0)
	retinal atrophy		2 ( 6)	7 ( 21)	0 ( 0)	0 ( 0)	1 ( 2)	16 ( 37)	0 ( 0)	0 ( 0)	0 ( 0)	9 ( 21)	0 ( 0)	0 ( 0)	4 ( 11)	9 ( 24)	0 ( 0)	0 ( 0)
Harder gl	degeneration		<33>				<43>				<43>				<38>			
			0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	2 ( 5)	0 ( 0)	0 ( 0)

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

STUDY NO. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 13

Organ	Findings	Control No. of Animals on Study Grade				8000 ppm 43				20000 ppm 43				50000 ppm 38			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Special sense organs/appandage]																	
Harder gl	Lymphocytic infiltration	<33>				<43>				<43>				<38>			
		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)
nasolacr d	inflammation	<33>				<43>				<43>				<38>			
		0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0
		( 0)	( 0)	( 0)	( 0)	( 0)	( 2)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 3)	( 0)	( 0)	( 0)
[Body cavities]																	
retroperit	hemorrhage	<33>				<43>				<43>				<38>			
		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)
adipose	necrosis	<33>				<43>				<43>				<38>			
		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
		( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 2)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe  
< a > a : Number of animals examined at the site  
b : 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 K 4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (2-YEAR STUDY: SUMMARY)

RAT : FEMALE : SACRIFICED ANIMALS

STUDY NO. : 0242  
 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 1

Organ	Findings	Group Name No. of Animals on Study Grade	Control 40				8000 ppm 40				20000 ppm 40				50000 ppm 37			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Integumentary system/appandage]																		
skin/app			<40>				<40>				<40>				<37>			
	inflammation		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )
[Respiratory system]																		
nasal cavit			<40>				<40>				<40>				<37>			
	follicle		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 )
	atrophy		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 )
	eosinophilic change:olfactory epithelium		3	22	15	0	0	0	0	0 **	0	0	0	0 **	0	0	0	0 **
			( 8 )	( 55 )	( 38 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	eosinophilic change:respiratory epithelium		30	0	0	0	0	0	0	0 **	0	0	0	0 **	0	0	0	0 **
			( 75 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	inflammation:foreign body		4	2	0	0	1	1	0	0	2	1	0	0	4	1	0	0
			( 10 )	( 5 )	( 0 )	( 0 )	( 3 )	( 3 )	( 0 )	( 0 )	( 5 )	( 3 )	( 0 )	( 0 )	( 11 )	( 3 )	( 0 )	( 0 )
	disarrangement:olfactory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 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. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 2

Organ	Findings	Control No. of Animals on Study Grade				8000 ppm 40				20000 ppm 40				50000 ppm 37			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																	
nasal cavit		<40>				<40>				<40>				<37>			
	respiratory metaplasia:olfactory epithelium	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	6 ( 16 )	0 ( 0 )	0 ( 0 )	0 * ( 0 )
	respiratory metaplasia:gland	24 ( 60 )	1 ( 3 )	0 ( 0 )	0 ( 0 )	17 ( 43 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	21 ( 53 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	14 ( 38 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
	necrosis:olfactory epithelium	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	3 ( 8 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	14 ( 35 )	0 ( 0 )	0 ( 0 )	0 ** ( 0 )	24 ( 65 )	0 ( 0 )	0 ( 0 )	0 ** ( 0 )
lung		<40>				<40>				<40>				<37>			
	hemorrhage	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 )
	inflammation	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 3 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
	inflammatory infiltration	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 3 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
	lymphocytic infiltration	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 )
	accumulation of foamy cells	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 )	1 ( 3 )	0 ( 0 )	0 ( 0 )

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

STUDY NO. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 3

Organ	Findings	Control 40				8000 ppm 40				20000 ppm 40				50000 ppm 37			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																	
Lung		<40>				<40>				<40>				<37>			
	bronchiolar-alveolar cell hyperplasia	1	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0
		( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
[Hematopoietic system]																	
bone marrow		<40>				<40>				<40>				<37>			
	granulation	2	3	0	0	2	5	0	0	1	2	0	0	5	5	0	0
		( 5 )	( 8 )	( 0 )	( 0 )	( 5 )	( 13 )	( 0 )	( 0 )	( 3 )	( 5 )	( 0 )	( 0 )	( 14 )	( 14 )	( 0 )	( 0 )
	increased hematopoiesis	1	0	0	0	0	0	0	0	2	0	0	0	1	0	0	0
		( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )
	granulopoiesis:increased	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 )
spleen		<40>				<40>				<40>				<37>			
	congestion	6	0	0	0	6	0	0	0	2	0	0	0	7	0	0	0
		( 15 )	( 0 )	( 0 )	( 0 )	( 15 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )	( 19 )	( 0 )	( 0 )	( 0 )
	deposit of hemosiderin	14	8	0	0	21	7	0	0	25	5	0	0 *	21	6	0	0
		( 35 )	( 20 )	( 0 )	( 0 )	( 53 )	( 18 )	( 0 )	( 0 )	( 63 )	( 13 )	( 0 )	( 0 )	( 57 )	( 16 )	( 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. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 4

Organ	Findings	Group Name No. of Animals on Study Grade	Control 40				8000 ppm 40				20000 ppm 40				50000 ppm 37						
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)			
[Hematopoietic system]																					
spleen			<40>				<40>				<40>				<37>						
	extramedullary hematopoiesis		2 ( 5)	1 ( 3)	0 ( 0)	0 ( 0)	1 ( 3)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 3)	0 ( 0)	0 ( 0)	0 ( 0)			
	engorgement of erythrocyte		0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	21 ( 53)	6 ( 15)	0 ( 0)	0 ( 0)	**	27 ( 68)	4 ( 10)	0 ( 0)	0 ( 0)	**	17 ( 46)	7 ( 19)	0 ( 0)	0 ( 0)	**
[Circulatory system]																					
heart			<40>				<40>				<40>				<37>						
	thrombus		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)	0 ( 0)	
	myocardial fibrosis		0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	2 ( 5)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 3)	0 ( 0)	0 ( 0)	0 ( 0)	3 ( 8)	0 ( 0)	0 ( 0)	0 ( 0)	
artery/aort			<40>				<40>				<40>				<37>						
	arteritis		0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 3)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	
[Digestive system]																					
tongue			<40>				<40>				<40>				<37>						
	arteritis		0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 3)	1 ( 3)	0 ( 0)	0 ( 0)	2 ( 5)	1 ( 3)	0 ( 0)	0 ( 0)	1 ( 3)	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. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 5

Organ	Findings	Group Name No. of Animals on Study Grade				Control 40				8000 ppm 40				20000 ppm 40				50000 ppm 37			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																					
stomach		<40>				<40>				<40>				<37>							
	arteritis	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	ulcer:forestomach	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 )
	hyperplasia:forestomach	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 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	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 )
	ulcer:glandular stomach	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 )	( 3 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )
liver		<40>				<40>				<40>				<37>							
	herniation	3	0	0	0	2	0	0	0	1	0	0	0	1	0	0	0	1	0	0	0
		( 8 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )
	peliosis-like lesion	0	0	0	0	2	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	lymphocytic infiltration	0	1	0	0	0	1	0	0	1	1	0	0	0	0	0	0	0	0	0	0
		( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 3 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe  
< a > a : Number of animals examined at the site  
b : 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. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 6

Organ	Findings	Group Name No. of Animals on Study Grade				Control 40				8000 ppm 40				20000 ppm 40				50000 ppm 37			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																					
Liver		<40>				<40>				<40>				<37>							
	granulation	15 ( 38)	9 ( 23)	0 ( 0)	0 ( 0)	20 ( 50)	8 ( 20)	1 ( 3)	0 ( 0)	21 ( 53)	9 ( 23)	2 ( 5)	0 ( 0)	18 ( 49)	10 ( 27)	2 ( 5)	0 ( 0)				
	clear cell focus	1 ( 3)	0 ( 0)	0 ( 0)	0 ( 0)	3 ( 8)	6 ( 15)	0 ( 0)	0 * ( 0)	8 ( 20)	7 ( 18)	0 ( 0)	0 ** ( 0)	5 ( 14)	6 ( 16)	2 ( 5)	0 ** ( 0)				
	acidophilic cell focus	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	6 ( 15)	11 ( 28)	3 ( 8)	0 ** ( 0)	6 ( 15)	10 ( 25)	3 ( 8)	1 ** ( 3)	7 ( 19)	4 ( 11)	1 ( 3)	1 ** ( 3)				
	basophilic cell focus	10 ( 25)	10 ( 25)	0 ( 0)	0 ( 0)	7 ( 18)	10 ( 25)	0 ( 0)	0 ( 0)	9 ( 23)	10 ( 25)	1 ( 3)	1 ( 3)	8 ( 22)	4 ( 11)	1 ( 3)	0 ( 0)				
	mixed cell focus	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 3)	1 ( 3)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 3)	0 ( 0)	0 ( 0)				
	spongiosis hepatitis	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 3)	0 ( 0)	0 ( 0)	0 ( 0)	2 ( 5)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)				
	bile duct hyperplasia	4 ( 10)	0 ( 0)	0 ( 0)	0 ( 0)	3 ( 8)	1 ( 3)	0 ( 0)	0 ( 0)	1 ( 3)	1 ( 3)	0 ( 0)	0 ( 0)	1 ( 3)	0 ( 0)	0 ( 0)	0 ( 0)				
	cholangiofibrosis	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 3)	0 ( 0)	0 ( 0)	0 ( 0)				

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

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

b : 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. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 7

Organ	Findings	Group Name No. of Animals on Study Control 40 Grade				8000 ppm 40				20000 ppm 40				50000 ppm 37			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																	
liver	biliary cyst	<40>				<40>				<40>				<37>			
		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 )
pancreas	atrophy	<40>				<40>				<40>				<37>			
		3	0	0	0	3	2	0	0	2	7	0	0 *	5	3	0	0
		( 8 )	( 0 )	( 0 )	( 0 )	( 8 )	( 5 )	( 0 )	( 0 )	( 5 )	( 18 )	( 0 )	( 0 )	( 14 )	( 8 )	( 0 )	( 0 )
[Urinary system]																	
kidney	infarct	<40>				<40>				<40>				<37>			
		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 )
	cyst	<40>				<40>				<40>				<37>			
		0	1	0	0	1	0	0	0	0	0	0	0	1	0	0	0
		( 0 )	( 3 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )
	chronic nephropathy	<40>				<40>				<40>				<37>			
		22	10	2	3	7	15	15	2 **	8	20	7	4 **	14	16	6	0
		( 55 )	( 25 )	( 5 )	( 8 )	( 18 )	( 38 )	( 38 )	( 5 )	( 20 )	( 50 )	( 18 )	( 10 )	( 38 )	( 43 )	( 16 )	( 0 )
	papillary necrosis	<40>				<40>				<40>				<37>			
		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 )

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

< 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. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 8

Organ	Findings	Group Name No. of Animals on Study Grade				Control 40				8000 ppm 40				20000 ppm 40				50000 ppm 37			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																					
kidney		<40>				<40>				<40>				<37>							
	mineralization:cortico-medullary junction	18 ( 45)	1 ( 3)	0 ( 0)	0 ( 0)	13 ( 33)	2 ( 5)	0 ( 0)	0 ( 0)	13 ( 33)	0 ( 0)	0 ( 0)	0 ( 0)	9 ( 24)	0 ( 0)	0 ( 0)	0 ( 0)				
	mineralization:papilla	1 ( 3)	0 ( 0)	0 ( 0)	0 ( 0)	10 ( 25)	0 ( 0)	0 ( 0)	0 ( 0)	6 ( 15)	0 ( 0)	0 ( 0)	0 ( 0)	3 ( 8)	0 ( 0)	0 ( 0)	0 ( 0)				
	mineralization:pelvis	5 ( 13)	0 ( 0)	0 ( 0)	0 ( 0)	3 ( 8)	1 ( 3)	0 ( 0)	0 ( 0)	4 ( 10)	0 ( 0)	0 ( 0)	0 ( 0)	6 ( 16)	0 ( 0)	0 ( 0)	0 ( 0)				
	mineralization:cortex	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)				
	dilatation:tubular lumen	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)				
	simple tubule hyperplasia	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	2 ( 5)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)				
	atypical tubule hyperplasia	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	10 ( 25)	0 ( 0)	0 ( 0)	0 ( 0)	13 ( 33)	0 ( 0)	0 ( 0)	0 ( 0)	7 ( 19)	0 ( 0)	0 ( 0)	0 ( 0)				
	eosinophilic droplet:proximal tubule	2 ( 5)	0 ( 0)	0 ( 0)	0 ( 0)	11 ( 28)	29 ( 73)	0 ( 0)	0 ( 0)	1 ( 3)	37 ( 93)	0 ( 0)	0 ( 0)	4 ( 11)	33 ( 89)	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. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 9

Organ	Findings	Control No. of Animals on Study Grade				8000 ppm 40				20000 ppm 40				50000 ppm 37			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																	
urin bladd		<40>				<40>				<40>				<37>			
	nodular hyperplasia:transitional epithelium	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
[Endocrine system]																	
pituitary		<40>				<40>				<40>				<37>			
	angiectasis	6	3	0	0	0	1	0	0 *	1	0	0	0 *	3	0	0	0
		( 15 )	( 8 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 8 )	( 0 )	( 0 )	( 0 )
	cyst	3	0	0	0	7	0	0	0	1	1	0	0	9	0	0	0
		( 8 )	( 0 )	( 0 )	( 0 )	( 18 )	( 0 )	( 0 )	( 0 )	( 3 )	( 3 )	( 0 )	( 0 )	( 24 )	( 0 )	( 0 )	( 0 )
	hyperplasia	5	0	0	0	6	1	0	0	4	1	0	0	7	1	0	0
		( 13 )	( 0 )	( 0 )	( 0 )	( 15 )	( 3 )	( 0 )	( 0 )	( 10 )	( 3 )	( 0 )	( 0 )	( 19 )	( 3 )	( 0 )	( 0 )
	Rathke pouch	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
thyroid		<40>				<40>				<40>				<37>			
	ultimibranhial body remanet	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )

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

< 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. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 10

Organ	Findings	Group Name No. of Animals on Study Grade	Control 40				8000 ppm 40				20000 ppm 40				50000 ppm 37			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]																		
thyroid	C-cell hyperplasia		<40>				<40>				<40>				<37>			
			4	0	0	0	3	1	0	0	2	0	0	0	1	0	0	0
			( 10)	( 0)	( 0)	( 0)	( 8)	( 3)	( 0)	( 0)	( 5)	( 0)	( 0)	( 0)	( 3)	( 0)	( 0)	( 0)
	focal follicular cell hyperplasia		<40>				<40>				<40>				<37>			
			0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 3)	( 0)	( 0)	( 0)	( 3)	( 0)	( 0)	( 0)
adrenal	peliosis-like lesion		<40>				<40>				<40>				<37>			
			6	0	0	0	5	0	0	0	2	0	0	0	5	0	0	0
			( 15)	( 0)	( 0)	( 0)	( 13)	( 0)	( 0)	( 0)	( 5)	( 0)	( 0)	( 0)	( 14)	( 0)	( 0)	( 0)
	cyst		<40>				<40>				<40>				<37>			
			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)
	hyperplasia:cortical cell		<40>				<40>				<40>				<37>			
			0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			( 0)	( 3)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 3)	( 0)	( 0)	( 0)
	hyperplasia:medulla		<40>				<40>				<40>				<37>			
			6	0	0	0	5	0	0	0	3	1	0	0	8	2	0	0
			( 15)	( 0)	( 0)	( 0)	( 13)	( 0)	( 0)	( 0)	( 8)	( 3)	( 0)	( 0)	( 22)	( 5)	( 0)	( 0)
	focal fatty change:cortex		<40>				<40>				<40>				<37>			
			2	1	0	0	1	0	0	0	3	0	0	0	0	0	0	0
			( 5)	( 3)	( 0)	( 0)	( 3)	( 0)	( 0)	( 0)	( 8)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
[Reproductive system]																		
ovary	cyst		<40>				<40>				<40>				<37>			
			0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0
			( 0)	( 0)	( 0)	( 0)	( 3)	( 0)	( 0)	( 0)	( 0)	( 3)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)

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. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 11

Organ	Findings	Control No. of Animals on Study Grade				8000 ppm 40				20000 ppm 40				50000 ppm 37			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Reproductive system]																	
uterus	dilatation	<40>				<40>				<40>				<37>			
		0	0	0	0	0	1	0	0	1	0	0	0	1	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )
	cystic endometrial hyperplasia	<40>				<40>				<40>				<37>			
		3	2	0	0	3	1	0	0	4	4	0	0	7	2	0	0
		( 8 )	( 5 )	( 0 )	( 0 )	( 8 )	( 3 )	( 0 )	( 0 )	( 10 )	( 10 )	( 0 )	( 0 )	( 19 )	( 5 )	( 0 )	( 0 )
mammary gl	duct ectasia	<40>				<40>				<40>				<37>			
		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 )
	hyperplasia	<40>				<40>				<40>				<37>			
		3	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 )
[Special sense organs/appandage]																	
eye	cataract	<40>				<40>				<40>				<37>			
		0	1	0	0	0	1	0	0	0	2	0	0	0	1	0	0
		( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )
	retinal atrophy	<40>				<40>				<40>				<37>			
		8	3	0	0	5	4	1	0	1	8	0	0 *	2	5	0	0
		( 20 )	( 8 )	( 0 )	( 0 )	( 13 )	( 10 )	( 3 )	( 0 )	( 3 )	( 20 )	( 0 )	( 0 )	( 5 )	( 14 )	( 0 )	( 0 )

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe  
< a > a : Number of animals examined at the site  
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. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 12

Organ	Findings	Control No. of Animals on Study Grade				8000 ppm 40				20000 ppm 40				50000 ppm 37			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Special sense organs/appandage]																	
eye	keratitis	<40>				<40>				<40>				<37>			
		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 )
	vascularization:cornea	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
Harder gl	atrophy	<40>				<40>				<40>				<37>			
		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 )
	degeneration	0	1	0	0	2	0	0	0	0	0	0	0	0	0	0	0
		( 0 )	( 3 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	inflammatory infiltration	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 3 )	( 0 )	( 0 )
	lymphocytic infiltration	3	1	0	0	1	1	0	0	0	1	0	0	2	0	0	0
		( 8 )	( 3 )	( 0 )	( 0 )	( 3 )	( 3 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )
nasolacr d	inflammation	<40>				<40>				<40>				<37>			
		1	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
		( 3 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe  
< a > a : Number of animals examined at the site  
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. : 0242  
 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 13

Organ	Findings	Control No. of Animals on Study Grade				8000 ppm No. of Animals on Study Grade				20000 ppm No. of Animals on Study Grade				50000 ppm No. of Animals on Study Grade			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

[Musculoskeletal system]

bone	osteosclerosis	<40>				<40>				<40>				<37>			
		4	4	0	0	2	3	2	0	1	3	1	0	2	2	2	0
		( 10)	( 10)	( 0)	( 0)	( 5)	( 8)	( 5)	( 0)	( 3)	( 8)	( 3)	( 0)	( 5)	( 5)	( 5)	( 0)

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

## APPENDIX K 5

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (2-YEAR STUDY: SUMMARY)

MOSUE : MALE :ALL ANIMALS

STUDY NO. : 0243  
ANIMAL : MOUSE Crj:BDF1  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 1

Organ	Findings	Control 49				3200 ppm 50				8000 ppm 50				20000 ppm 50			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Integumentary system/appandage]																	
subcutis		<49>				<50>				<50>				<50>			
	inflammation	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
[Respiratory system]																	
nasal cavit		<49>				<50>				<50>				<50>			
	inflammation	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 )
	inflammatory infiltration	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	eosinophilic change:olfactory epithelium	3	1	0	0	7	0	0	0	5	0	0	0	5	0	0	0
		( 6 )	( 2 )	( 0 )	( 0 )	( 14 )	( 0 )	( 0 )	( 0 )	( 10 )	( 0 )	( 0 )	( 0 )	( 10 )	( 0 )	( 0 )	( 0 )
	eosinophilic change:respiratory epithelium	3	2	1	0	4	0	0	0	2	2	1	0	6	1	0	0
		( 6 )	( 4 )	( 2 )	( 0 )	( 8 )	( 0 )	( 0 )	( 0 )	( 4 )	( 4 )	( 2 )	( 0 )	( 12 )	( 2 )	( 0 )	( 0 )
	respiratory metaplasia:olfactory epithelium	6	1	0	0	7	0	0	0	1	3	0	0	11	2	0	0
		( 12 )	( 2 )	( 0 )	( 0 )	( 14 )	( 0 )	( 0 )	( 0 )	( 2 )	( 6 )	( 0 )	( 0 )	( 22 )	( 4 )	( 0 )	( 0 )
	respiratory metaplasia:gland	7	2	0	0	12	2	0	0	5	3	1	0	11	2	1	0
		( 14 )	( 4 )	( 0 )	( 0 )	( 24 )	( 4 )	( 0 )	( 0 )	( 10 )	( 6 )	( 2 )	( 0 )	( 22 )	( 4 )	( 2 )	( 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. : 0243  
ANIMAL : MOUSE Crj:BDF1  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 2

Organ	Findings	Group Name No. of Animals on Study Grade				Control 49				3200 ppm 50				8000 ppm 50				20000 ppm 50			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																					
lung		<49>				<50>				<50>				<50>				<50>			
	congestion	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	hemorrhage	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 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	inflammatory infiltration	0	1	0	0	2	0	0	0	3	0	0	0	0	1	0	0	0	0	1	0
		( 0 )	( 2 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )
	bronchiolar-alveolar cell hyperplasia	1	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		( 2 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
[Hematopoietic system]																					
spleen		<49>				<50>				<50>				<50>				<50>			
	atrophy	0	0	3	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0
		( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )
	deposit of melanin	0	3	0	0	2	2	0	0	0	0	0	0	1	0	0	0	0	0	0	0
		( 0 )	( 6 )	( 0 )	( 0 )	( 4 )	( 4 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	extramedullary hematopoiesis	1	2	0	0	0	5	2	0	1	4	2	0	1	3	1	0	0	0	0	0
		( 2 )	( 4 )	( 0 )	( 0 )	( 0 )	( 10 )	( 4 )	( 0 )	( 2 )	( 8 )	( 4 )	( 0 )	( 2 )	( 6 )	( 2 )	( 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. : 0243  
 ANIMAL : MOUSE Crj:BDF1  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 3

		Group Name No. of Animals on Study	Control 49				3200 ppm 50				8000 ppm 50				20000 ppm 50			
Organ_____	Findings_____	Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Hematopoietic system]																		
spleen			<49>				<50>				<50>				<50>			
	follicular hyperplasia		3 ( 6 )	1 ( 2 )	2 ( 4 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	2 ( 4 )	0 ( 0 )	3 ( 6 )	3 ( 6 )	1 ( 2 )	0 ( 0 )	3 ( 6 )	2 ( 4 )	1 ( 2 )	0 ( 0 )
[Circulatory system]																		
heart			<49>				<50>				<50>				<50>			
	arteritis		0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
[Digestive system]																		
oral cavity			<49>				<50>				<50>				<50>			
	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 ( 2 )	0 ( 0 )	0 ( 0 )
	inflammation		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 )
tooth			<49>				<50>				<50>				<50>			
	cyst		0 ( 0 )	2 ( 4 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )

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

STUDY NO. : 0243  
 ANIMAL : MOUSE Crj:BDF1  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 4

Organ	Findings	Group Name No. of Animals on Study Grade	Control 49				3200 ppm 50				8000 ppm 50				20000 ppm 50			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
tooth	inflammation		<49>				<50>				<50>				<50>			
			0	0	0	0	0	0	0	0	1	0	0	0	5	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 10 )	( 0 )	( 0 )	( 0 )
	foreign body granuloma		1	0	0	0	0	0	0	0	1	0	0	0	3	2	0	0
			( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 6 )	( 4 )	( 0 )	( 0 )
			( 27 )	( 8 )	( 0 )	( 0 )	( 14 )	( 4 )	( 0 )	( 0 )	( 8 )	( 0 )	( 4 )	( 0 )	( 16 )	( 10 )	( 0 )	( 0 )
	dysplasia		13	4	0	0	7	2	0	0	4	0	2	0 **	8	5	0	0
			( 27 )	( 8 )	( 0 )	( 0 )	( 14 )	( 4 )	( 0 )	( 0 )	( 8 )	( 0 )	( 4 )	( 0 )	( 16 )	( 10 )	( 0 )	( 0 )
tongue	arteritis		<49>				<50>				<50>				<50>			
			0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
stomach	ulcer:forestomach		<49>				<50>				<50>				<50>			
			1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	hyperplasia:forestomach		0	0	0	0	1	1	0	0	0	0	0	0	1	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )
	erosion:glandular stomach		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )

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

STUDY NO. : 0243  
 ANIMAL : MOUSE Crj:BDF1  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 5

Organ	Findings	Group Name No. of Animals on Study Grade	Control 49				3200 ppm 50				8000 ppm 50				20000 ppm 50			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
stomach	ulcer:glandular stomach		<49>				<50>				<50>				<50>			
			0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	hyperplasia:glandular stomach		1	1	0	0	0	2	0	0	2	1	0	0	1	1	0	0
			( 2 )	( 2 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 4 )	( 2 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )	( 0 )
liver	angiectasis		<49>				<50>				<50>				<50>			
			0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	necrosis		0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	leucocytic 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 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	granulation		10	1	0	0	8	2	0	0	7	0	0	0	7	0	0	0
			( 20 )	( 2 )	( 0 )	( 0 )	( 16 )	( 4 )	( 0 )	( 0 )	( 14 )	( 0 )	( 0 )	( 0 )	( 14 )	( 0 )	( 0 )	( 0 )
	clear cell focus		0	1	0	0	0	0	0	1	0	0	1	0	0	0	0	0
			( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	basophilic cell focus		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 )	( 2 )	( 0 )	( 0 )

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



STUDY NO. : 0243  
 ANIMAL : MOUSE Crj:BDF1  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 6

Organ	Findings	Group Name No. of Animals on Study Grade				Control 49				3200 ppm 50				8000 ppm 50				20000 ppm 50			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																					
kidney		<49>				<50>				<50>				<50>				<50>			
	hyperplasia:tubular epithelial cell	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0	1	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )
	infarct	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 )
	hyaline droplet	2	0	0	0	3	0	0	0	6	0	0	0	3	0	0	0	3	0	0	0
		( 4 )	( 0 )	( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )	( 12 )	( 0 )	( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )
	basophilic change	16	0	0	0	21	0	0	0	21	0	0	0	20	0	0	0	20	0	0	0
		( 33 )	( 0 )	( 0 )	( 0 )	( 42 )	( 0 )	( 0 )	( 0 )	( 42 )	( 0 )	( 0 )	( 0 )	( 40 )	( 0 )	( 0 )	( 0 )	( 40 )	( 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 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	Lymphocytic infiltration	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 )
	inflammatory polyp	0	0	0	0	0	1	1	0	0	0	1	0	0	0	1	0	0	0	1	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )
	vacuolization of proximal tubule	21	1	0	0	14	0	0	0	0	0	0	0 **	0	0	0	0 **	0	0	0	0 **
		( 43 )	( 2 )	( 0 )	( 0 )	( 28 )	( 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. : 0243  
ANIMAL : MOUSE Crj:BDF1  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 7

		Group Name	Control				3200 ppm				8000 ppm				20000 ppm			
		No. of Animals on Study	49				50				50				50			
Organ_____	Findings_____	Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																		
kidney			<49>				<50>				<50>				<50>			
	hydronephrosis		0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)	2 ( 4)	0 ( 0)	3 ( 6)	2 ( 4)	1 ( 2)	0 ( 0)	1 ( 2)	0 ( 0)	2 ( 4)	0 ( 0)
	mineralization:papilla		1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)	3 ( 6)	0 ( 0)	0 ( 0)	0 ( 0)	3 ( 6)	0 ( 0)	0 ( 0)	0 ( 0)
	mineralization:pelvis		3 ( 6)	0 ( 0)	0 ( 0)	0 ( 0)	2 ( 4)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)	4 ( 8)	0 ( 0)	0 ( 0)	0 ( 0)
	mineralization:cortex		33 ( 67)	1 ( 2)	0 ( 0)	0 ( 0)	34 ( 68)	1 ( 2)	0 ( 0)	0 ( 0)	33 ( 66)	3 ( 6)	0 ( 0)	0 ( 0)	33 ( 66)	0 ( 0)	0 ( 0)	0 ( 0)
urin bladd			<49>				<50>				<50>				<50>			
	hyaline droplet degeneration:superficial cell of transitional epithelium		0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	28 ( 56)	0 ( 0)	0 ( 0)	0 ( 0) **	38 ( 76)	4 ( 8)	0 ( 0)	0 ( 0) **	20 ( 40)	27 ( 54)	0 ( 0)	0 ( 0) **
[Endocrine system]																		
pituitary			<49>				<50>				<49>				<50>			
	angiectasis		0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)

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

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

b b : Number of animals with lesion

( c ) c : b / a \* 100

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

STUDY NO. : 0243  
ANIMAL : MOUSE Crj:BDF1  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 8

Organ	Findings	Group Name No. of Animals on Study				Control 49				3200 ppm 50				8000 ppm 50				20000 ppm 50			
		Grade				1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]																					
pituitary	cyst	<49>				4	2	0	0	3	0	0	0	4	0	0	0	9	0	0	0
		( 8 )	( 4 )	( 0 )	( 0 )	( 8 )	( 4 )	( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )	( 8 )	( 0 )	( 0 )	( 0 )	( 18 )	( 0 )	( 0 )	( 0 )
	hyperplasia	<49>				0	0	0	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 )
thyroid	Rathke pouch	<49>				1	0	0	0	1	0	0	0	2	0	0	0	3	0	0	0
		( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )
	focal follicular cell hyperplasia	<49>				0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
adrenal	extramedullary hematopoiesis	<49>				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 )	( 2 )	( 0 )	( 0 )	( 0 )
	spindle-cell hyperplasia	<49>				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 )	( 0 )	( 0 )	( 0 )	( 0 )
	hyperplasia:cortical cell	<49>				5	3	0	0	5	3	0	0	6	1	0	0	7	4	0	0
		( 10 )	( 6 )	( 0 )	( 0 )	( 10 )	( 6 )	( 0 )	( 0 )	( 10 )	( 6 )	( 0 )	( 0 )	( 12 )	( 2 )	( 0 )	( 0 )	( 14 )	( 8 )	( 0 )	( 0 )
		<50>																			

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. : 0243  
ANIMAL : MOUSE Crj:BDF1  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 9

Organ	Findings	Group Name No. of Animals on Study Grade				Control 49				3200 ppm 50				8000 ppm 50				20000 ppm 50			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]																					
adrenal	hyperplasia:medulla	<49>				<50>				<50>				<50>				<50>			
		0	0	0	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 )
[Reproductive system]																					
testis	atrophy	<49>				<50>				<50>				<50>				<50>			
		0	0	0	0	0	0	0	0	1	2	0	0	1	0	0	0	1	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 4 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )
	mineralization	12	0	0	0	6	0	0	0	7	1	0	0	11	0	0	0	11	0	0	0
		( 24 )	( 0 )	( 0 )	( 0 )	( 12 )	( 0 )	( 0 )	( 0 )	( 14 )	( 2 )	( 0 )	( 0 )	( 22 )	( 0 )	( 0 )	( 0 )	( 22 )	( 0 )	( 0 )	( 0 )
epididymis	lymphocytic infiltration	<49>				<50>				<50>				<50>				<50>			
		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 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	spermatogenic granuloma	0	3	0	0	1	0	0	0	0	2	0	0	1	1	0	0	1	1	0	0
		( 0 )	( 6 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )	( 0 )
prep/cli gl	duct ectasia	<49>				<50>				<50>				<50>				<50>			
		0	5	0	0	0	2	0	0	0	1	0	0	0	2	0	0	0	2	0	0
		( 0 )	( 10 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 4 )	( 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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$  Test of Chi Square

STUDY NO. : 0243  
 ANIMAL : MOUSE Crj:BDF1  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 10

Organ	Findings	Group Name No. of Animals on Study Grade				Control 49				3200 ppm 50				8000 ppm 50				20000 ppm 50			
		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		<49>				<50>				<50>				<50>				<50>			
	inflammation	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 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
[Nervous system]																					
brain		<49>				<50>				<50>				<50>				<50>			
	mineralization	17	16	0	0	18	24	0	0	9	22	0	0	14	29	0	0 *				
		( 35 )	( 33 )	( 0 )	( 0 )	( 36 )	( 48 )	( 0 )	( 0 )	( 18 )	( 44 )	( 0 )	( 0 )	( 28 )	( 58 )	( 0 )	( 0 )				
[Special sense organs/appandage]																					
Harder gl		<49>				<50>				<50>				<50>				<50>			
	degeneration	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 )
	hyperplasia	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
[Musculoskeletal system]																					
muscle		<49>				<50>				<50>				<50>				<50>			
	mineralization	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		( 0 )	( 2 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )

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

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

b : 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. : 0243  
 ANIMAL : MOUSE Crj:BDF1  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 11

Organ	Findings	Group Name No. of Animals on Study				Control 49				3200 ppm 50				8000 ppm 50				20000 ppm 50			
		Grade				1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

[Musculoskeletal system]

muscle	inflammatory infiltration	<49>				<50>				<50>				<50>			
		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )

[Body cavities]

adipose	hemorrhage	<49>				<50>				<50>				<50>			
		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )

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

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

b b : Number of animals with lesion

( c ) c : b / a \* 100

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

(HPT150)

BAIS3

## APPENDIX K 6

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (2-YEAR STUDY: SUMMARY)

MOSUE : FEMALE : ALL ANIMALS

STUDY NO. : 0243  
ANIMAL : MOUSE Crj:BDF1  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 12

Organ	Findings	Group Name No. of Animals on Study Grade	Control 50				8000 ppm 50				20000 ppm 50				50000 ppm 50			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
nasal cavit	atrophy		<50>				<50>				<50>				<50>			
			0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	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 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	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 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	eosinophilic change:olfactory epithelium		2	0	0	0	1	1	0	0	1	0	0	0	3	1	0	0
			( 4 )	( 0 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 6 )	( 2 )	( 0 )	( 0 )
	eosinophilic change:respiratory epithelium		13	4	0	0	14	7	0	0	14	10	2	0	14	10	2	0
			( 26 )	( 8 )	( 0 )	( 0 )	( 28 )	( 14 )	( 0 )	( 0 )	( 28 )	( 20 )	( 4 )	( 0 )	( 28 )	( 20 )	( 4 )	( 0 )
	disarrangement:olfactory epithelium		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	respiratory metaplasia:olfactory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )
	respiratory metaplasia:gland		4	3	0	0	6	5	0	0	2	2	0	0	5	4	0	0
			( 8 )	( 6 )	( 0 )	( 0 )	( 12 )	( 10 )	( 0 )	( 0 )	( 4 )	( 4 )	( 0 )	( 0 )	( 10 )	( 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 ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square



STUDY NO. : 0243  
 ANIMAL : MOUSE Crj:BDF1  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 13

Organ	Findings	Group Name	Control				8000 ppm				20000 ppm				50000 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
Lung			<50>				<50>				<50>				<50>			
	congestion		0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
	hemorrhage		0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
	inflammatory infiltration		1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )
	lymphocytic infiltration		0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )
	bronchiolar-alveolar cell hyperplasia		0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
[Hematopoietic system]																		
bone marrow			<50>				<50>				<50>				<50>			
	granulation		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 )
spleen			<50>				<50>				<50>				<49>			
	atrophy		0 ( 0 )	3 ( 6 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	2 ( 4 )
Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe																		
< a >		a : Number of animals examined at the site																
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. : 0243  
 ANIMAL : MOUSE Crj:BDF1  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 14

Organ	Findings	Group Name No. of Animals on Study Grade				Control 50				8000 ppm 50				20000 ppm 50				50000 ppm 50			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																					
spleen		<50>				<50>				<50>				<49>							
	deposit of melanin	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		( 2 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	extramedullary hematopoiesis	0	3	2	0	3	4	4	0	0	5	5	0	2	5	1	0				
		( 0 )	( 6 )	( 4 )	( 0 )	( 6 )	( 8 )	( 8 )	( 0 )	( 0 )	( 10 )	( 10 )	( 0 )	( 4 )	( 10 )	( 2 )	( 0 )				
	follicular hyperplasia	6	1	1	0	0	3	0	0 *	2	1	2	0	1	1	1	0				
		( 12 )	( 2 )	( 2 )	( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 4 )	( 2 )	( 4 )	( 0 )	( 2 )	( 2 )	( 2 )	( 0 )				
[Circulatory system]																					
heart		<50>				<50>				<50>				<50>							
	thrombus	0	1	0	0	0	0	0	0	1	0	0	0	1	0	0	0				
		( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )				
	mineralization	1	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0				
		( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )				
	granulation	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0				
		( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )				
	arteritis	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 )	( 2 )	( 0 )	( 0 )				
Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe																					
< a > a : Number of animals examined at the site																					
b b : Number of animals with lesion																					
( c ) c : b / a * 100																					
Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square																					

STUDY NO. : 0243  
ANIMAL : MOUSE Crj:BDF1  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 15

Organ	Findings	Group Name No. of Animals on Study Grade				Control 50				8000 ppm 50				20000 ppm 50				50000 ppm 50			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																					
tooth	cyst	<50>				<50>				<50>				<50>				<50>			
		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 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	inflammation	3	0	0	0	0	0	0	0	1	0	0	0	2	0	0	0	2	0	0	0
		( 6 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )
	foreign body granuloma	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 )	( 2 )	( 0 )	( 0 )	( 0 )
	dysplasia	1	0	0	0	1	1	0	0	2	1	1	0	1	3	2	0	1	3	2	0
		( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )	( 0 )	( 4 )	( 2 )	( 2 )	( 0 )	( 2 )	( 6 )	( 4 )	( 0 )	( 2 )	( 6 )	( 4 )	( 0 )
tongue	arteritis	<49>				<50>				<50>				<50>				<50>			
		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 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )
stomach	hyperplasia:forestomach	<49>				<50>				<50>				<50>				<50>			
		0	1	0	0	0	0	0	0	0	0	0	0	2	1	0	0	2	1	0	0
		( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 4 )	( 2 )	( 0 )	( 0 )	( 4 )	( 2 )	( 0 )	( 0 )
	inflammation:forestomach	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 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 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. : 0243  
 ANIMAL : MOUSE Crj:BDF1  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 16

Organ	Findings	Group Name No. of Animals on Study Grade	Control 50				8000 ppm 50				20000 ppm 50				50000 ppm 50			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
stomach	erosion:glandular stomach		<49>				<50>				<50>				<50>			
			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)
	hyperplasia:glandular stomach		2	1	0	0	4	0	0	0	4	0	0	0	1	0	0	0
			( 4)	( 2)	( 0)	( 0)	( 8)	( 0)	( 0)	( 0)	( 8)	( 0)	( 0)	( 0)	( 2)	( 0)	( 0)	( 0)
small intes	ulcer		<50>				<50>				<50>				<50>			
			0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
			( 0)	( 0)	( 2)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
liver	angiectasis		<50>				<50>				<50>				<50>			
			0	0	2	0	0	0	1	0	0	3	0	0	2	1	0	0
			( 0)	( 0)	( 4)	( 0)	( 0)	( 0)	( 2)	( 0)	( 0)	( 6)	( 0)	( 0)	( 4)	( 2)	( 0)	( 0)
	necrosis		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 2)	( 0)	( 0)	( 0)
	granulation		7	18	3	0	6	12	0	0	14	5	1	0 **	6	10	1	0
			( 14)	( 36)	( 6)	( 0)	( 12)	( 24)	( 0)	( 0)	( 28)	( 10)	( 2)	( 0)	( 12)	( 20)	( 2)	( 0)
	extramedullary hematopoiesis		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			( 2)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)

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

STUDY NO. : 0243  
ANIMAL : MOUSE Crj:BDF1  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 17

Organ	Findings	Group Name No. of Animals on Study Grade	Control 50				8000 ppm 50				20000 ppm 50				50000 ppm 50			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
liver	clear cell focus		<50>				<50>				<50>				<50>			
			1	1	0	3	1	1	0	0	0	3	0	1	1	10	3	1 *
			( 2 )	( 2 )	( 0 )	( 6 )	( 2 )	( 2 )	( 0 )	( 0 )	( 0 )	( 6 )	( 0 )	( 2 )	( 2 )	( 20 )	( 6 )	( 2 )
	acidophilic cell focus		0	0	1	1	1	1	0	3	0	0	1	0	0	1	1	3
			( 0 )	( 0 )	( 2 )	( 2 )	( 2 )	( 2 )	( 0 )	( 6 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 2 )	( 2 )	( 6 )
	basophilic cell focus		0	0	0	0	1	1	0	0	2	4	0	0 *	0	8	4	2 **
			( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )	( 0 )	( 4 )	( 8 )	( 0 )	( 0 )	( 0 )	( 16 )	( 8 )	( 4 )
pancreas	atrophy		<50>				<50>				<50>				<50>			
			0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )
[Urinary system]																		
kidney	atrophy		<50>				<50>				<50>				<50>			
			0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	hyaline droplet		5	0	0	0	9	1	0	0	8	0	0	0	6	0	0	0
			( 10 )	( 0 )	( 0 )	( 0 )	( 18 )	( 2 )	( 0 )	( 0 )	( 16 )	( 0 )	( 0 )	( 0 )	( 12 )	( 0 )	( 0 )	( 0 )

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

STUDY NO. : 0243  
 ANIMAL : MOUSE Crj:BDF1  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 18

Organ	Findings	Group Name No. of Animals on Study Grade				Control 50				8000 ppm 50				20000 ppm 50				50000 ppm 50			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																					
kidney		<50>				<50>				<50>				<50>				<50>			
	deposit of amyloid	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 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 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	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )
	lymphocytic infiltration	1	0	0	0	2	0	0	0	2	0	0	0	2	0	0	0	0	1	0	0
		( 2 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )
	hydronephrosis	0	2	0	0	1	1	0	0	0	0	1	0	0	0	1	0	0	0	1	1
		( 0 )	( 4 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 2 )
	tubular necrosis	0	0	0	0	0	1	0	0	0	1	0	0	0	1	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	mineralization:papilla	2	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0
		( 4 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )
	mineralization:pelvis	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )
urin bladd		<50>				<50>				<50>				<50>				<49>			
	lymphocytic infiltration	0	0	0	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 )

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe  
 < a > a : Number of animals examined at the site  
 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. : 0243  
ANIMAL : MOUSE Crj:BDF1  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 19

Organ	Findings	Group Name No. of Animals on Study Grade	Control 50				8000 ppm 50				20000 ppm 50				50000 ppm 50			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																		
urin bladd			<50>				<50>				<50>				<49>			
	hyaline droplet degeneration:superficial cell of transit		0	0	0	0	5	0	0	0	12	0	0	0 **	24	0	0	0 **
	ional epithelium		( 0 )	( 0 )	( 0 )	( 0 )	( 10 )	( 0 )	( 0 )	( 0 )	( 24 )	( 0 )	( 0 )	( 0 )	( 49 )	( 0 )	( 0 )	( 0 )
[Endocrine system]																		
pituitary			<50>				<50>				<50>				<50>			
	cyst		7	0	0	0	8	0	0	0	8	0	0	0	6	0	0	0
			( 14 )	( 0 )	( 0 )	( 0 )	( 16 )	( 0 )	( 0 )	( 0 )	( 16 )	( 0 )	( 0 )	( 0 )	( 12 )	( 0 )	( 0 )	( 0 )
	hyperplasia		1	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	Rathke pouch		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
adrenal			<50>				<50>				<50>				<50>			
	hyperplasia:cortical cell		0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	focal fatty change:cortex		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )

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

STUDY NO. : 0243  
ANIMAL : MOUSE Crj:BDF1  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 20

Organ	Findings	Group Name No. of Animals on Study				Control 50				8000 ppm 50				20000 ppm 50				50000 ppm 50			
		Grade				1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Reproductive system]																					
ovary		<50>				<50>				<50>				<50>				<50>			
	angiectasis	0	1	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0
		( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	cyst	4	0	0	0	5	0	0	0	7	0	0	0	4	0	0	0	4	0	0	0
		( 8 )	( 0 )	( 0 )	( 0 )	( 10 )	( 0 )	( 0 )	( 0 )	( 14 )	( 0 )	( 0 )	( 0 )	( 8 )	( 0 )	( 0 )	( 0 )	( 8 )	( 0 )	( 0 )	( 0 )
	mineralization	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 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
uterus		<50>				<50>				<50>				<50>				<50>			
	dilatation	0	1	0	0	0	0	0	0	0	1	0	0	0	2	0	0	0	4	0	0
		( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )	( 0 )	( 4 )	( 0 )	( 0 )
	cystic endometrial hyperplasia	13	14	0	0	13	11	0	0	18	13	0	0	12	15	0	0	12	15	0	0
		( 26 )	( 28 )	( 0 )	( 0 )	( 26 )	( 22 )	( 0 )	( 0 )	( 36 )	( 26 )	( 0 )	( 0 )	( 24 )	( 30 )	( 0 )	( 0 )	( 24 )	( 30 )	( 0 )	( 0 )
	xanthogranuloma	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 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
[Nervous system]																					
brain		<50>				<50>				<50>				<50>				<50>			
	mineralization	4	13	0	0	8	13	0	0	10	10	0	0	6	14	0	0	6	14	0	0
		( 8 )	( 26 )	( 0 )	( 0 )	( 16 )	( 26 )	( 0 )	( 0 )	( 20 )	( 20 )	( 0 )	( 0 )	( 12 )	( 28 )	( 0 )	( 0 )	( 12 )	( 28 )	( 0 )	( 0 )

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe  
< a > a : Number of animals examined at the site  
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. : 0243  
ANIMAL : MOUSE Crj:BDF1  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 21

Organ	Findings	Group Name No. of Animals on Study Grade	Control 50				8000 ppm 50				20000 ppm 50				50000 ppm 50			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

[Special sense organs/appandage]

Harder gl	degeneration	<50>				<50>				<50>				<50>			
		1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
		( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )
	hyperplasia	<50>				<50>				<50>				<50>			
		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )

[Musculoskeletal system]

bone	fracture	<50>				<50>				<50>				<50>			
		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe  
< 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 K 7

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (2-YEAR STUDY: SUMMARY)

MOSUE : MALE : SACRIFICED ANIMALS

STUDY NO. : 0243  
ANIMAL : MOUSE Crj:BDF1  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 1

Organ	Findings	Group Name No. of Animals on Study Grade	Control 41				3200 ppm 41				8000 ppm 37				20000 ppm 42			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
nasal cavit	inflammation		<41>				<41>				<37>				<42>			
			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 )
	eosinophilic change:olfactory epithelium		3	1	0	0	6	0	0	0	4	0	0	0	3	0	0	0
			( 7 )	( 2 )	( 0 )	( 0 )	( 15 )	( 0 )	( 0 )	( 0 )	( 11 )	( 0 )	( 0 )	( 0 )	( 7 )	( 0 )	( 0 )	( 0 )
	eosinophilic change:respiratory epithelium		3	2	1	0	4	0	0	0	1	1	1	0	6	1	0	0
			( 7 )	( 5 )	( 2 )	( 0 )	( 10 )	( 0 )	( 0 )	( 0 )	( 3 )	( 3 )	( 3 )	( 0 )	( 14 )	( 2 )	( 0 )	( 0 )
	respiratory metaplasia:olfactory epithelium		5	1	0	0	7	0	0	0	1	3	0	0	10	2	0	0
			( 12 )	( 2 )	( 0 )	( 0 )	( 17 )	( 0 )	( 0 )	( 0 )	( 3 )	( 8 )	( 0 )	( 0 )	( 24 )	( 5 )	( 0 )	( 0 )
	respiratory metaplasia:gland		7	2	0	0	11	2	0	0	5	3	1	0	10	2	1	0
			( 17 )	( 5 )	( 0 )	( 0 )	( 27 )	( 5 )	( 0 )	( 0 )	( 14 )	( 8 )	( 3 )	( 0 )	( 24 )	( 5 )	( 2 )	( 0 )
lung	bronchiolar-alveolar cell hyperplasia		<41>				<41>				<37>				<42>			
			1	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0
			( 2 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
[Hematopoietic system]																		
spleen	deposit of melanin		<41>				<41>				<37>				<42>			
			0	2	0	0	2	2	0	0	0	0	0	0	1	0	0	0
			( 0 )	( 5 )	( 0 )	( 0 )	( 5 )	( 5 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )

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

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

b b : Number of animals with lesion

( c ) c : b / a \* 100

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

STUDY NO. : 0243  
ANIMAL : MOUSE Crj:BDF1  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 2

Organ	Findings	Group Name	Control				3200 ppm				8000 ppm				20000 ppm			
		No. of Animals on Study	41				41				37				42			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
spleen	extramedullary hematopoiesis		<41>				<41>				<37>				<42>			
		1	0	0	0	0	2	0	0	1	0	0	0	0	1	0	0	
			( 2)	( 0)	( 0)	( 0)	( 0)	( 5)	( 0)	( 0)	( 3)	( 0)	( 0)	( 0)	( 0)	( 2)	( 0)	( 0)
	follicular hyperplasia		3	1	2	0	1	0	2	0	3	3	1	0	3	2	1	0
		( 7)	( 2)	( 5)	( 0)	( 2)	( 0)	( 5)	( 0)	( 8)	( 8)	( 3)	( 0)	( 7)	( 5)	( 2)	( 0)	
[Digestive system]																		
tooth	cyst		<41>				<41>				<37>				<42>			
		0	2	0	0	1	1	0	0	0	0	0	0	0	0	0	0	
		( 0)	( 5)	( 0)	( 0)	( 2)	( 2)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	
	inflammation		0	0	0	0	0	0	0	0	1	0	0	0	5	0	0	0
		( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 3)	( 0)	( 0)	( 0)	( 12)	( 0)	( 0)	( 0)	
	foreign body granuloma		1	0	0	0	0	0	0	0	0	0	0	0	3	1	0	0
		( 2)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 7)	( 2)	( 0)	( 0)	
	dysplasia		13	2	0	0	7	2	0	0	4	0	2	0 *	8	4	0	0
		( 32)	( 5)	( 0)	( 0)	( 17)	( 5)	( 0)	( 0)	( 11)	( 0)	( 5)	( 0)	( 19)	( 10)	( 0)	( 0)	
tongue	arteritis		<41>				<41>				<37>				<42>			
		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	
			( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 3)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe																		
< a > a : Number of animals examined at the site																		
b b : Number of animals with lesion																		
( c ) c : b / a * 100																		
Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square																		

STUDY NO. : 0243  
ANIMAL : MOUSE Crj:BDF1  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 3

Organ	Findings	Group Name No. of Animals on Study Grade				Control 41				3200 ppm 41				8000 ppm 37				20000 ppm 42			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																					
stomach		<41>				<41>				<37>				<42>							
	ulcer:forestomach	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
	hyperplasia:forestomach	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)
	hyperplasia:glandular stomach	1 ( 2)	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)	2 ( 5)	0 ( 0)	0 ( 0)	2 ( 5)	1 ( 3)	0 ( 0)	0 ( 0)	2 ( 5)	1 ( 3)	0 ( 0)	0 ( 0)	1 ( 2)	1 ( 2)	0 ( 0)	0 ( 0)
liver		<41>				<41>				<37>				<42>							
	angiectasis	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)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
	leucocytic infiltration	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 3)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
	granulation	10 ( 24)	1 ( 2)	0 ( 0)	0 ( 0)	8 ( 20)	2 ( 5)	0 ( 0)	0 ( 0)	7 ( 19)	0 ( 0)	0 ( 0)	0 ( 0)	7 ( 17)	0 ( 0)	0 ( 0)	0 ( 0)	7 ( 17)	0 ( 0)	0 ( 0)	0 ( 0)
	clear cell focus	0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)	1 ( 3)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 3)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
	basophilic cell focus	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 2)	0 ( 0)	0 ( 0)

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

STUDY NO. : 0243  
ANIMAL : MOUSE Crj:BDF1  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 4

Organ	Findings	Group Name No. of Animals on Study Grade				Control 41				3200 ppm 41				8000 ppm 37				20000 ppm 42			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																					
kidney		<41>				<41>				<37>				<42>							
	hyperplasia:tubular epithelial cell	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 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
	infarct	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 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
	hyaline droplet	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
	basophilic change	16 ( 39 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	21 ( 51 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	21 ( 57 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	19 ( 45 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
	inflammation	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	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 )
	lymphocytic infiltration	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 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
	vacuolization of proximal tubule	21 ( 51 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	13 ( 32 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
	hydronephrosis	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	3 ( 8 )	2 ( 5 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	1 ( 2 )	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. : 0243  
ANIMAL : MOUSE Crj:BDF1  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 5

		Group Name No. of Animals on Study Grade				Control 41				3200 ppm 41				8000 ppm 37				20000 ppm 42			
Organ	Findings	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)				
[Urinary system]																					
kidney		<41>				<41>				<37>				<42>							
	mineralization:papilla	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	2 ( 5 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	3 ( 7 )	0 ( 0 )	0 ( 0 )	0 ( 0 )				
	mineralization:pelvis	3 ( 7 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	4 ( 10 )	0 ( 0 )	0 ( 0 )	0 ( 0 )				
	mineralization:cortex	30 ( 73 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	29 ( 71 )	1 ( 2 )	0 ( 0 )	0 ( 0 )	30 ( 81 )	3 ( 8 )	0 ( 0 )	0 ( 0 )	31 ( 74 )	0 ( 0 )	0 ( 0 )	0 ( 0 )				
urin bladd		<41>				<41>				<37>				<42>							
	hyaline droplet degeneration:superficial cell of transitional epithelium	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	26 ( 63 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	** ( 0 )	30 ( 81 )	4 ( 11 )	0 ( 0 )	0 ( 0 )	** ( 0 )	16 ( 38 )	26 ( 62 )	0 ( 0 )			
[Endocrine system]																					
pituitary		<41>				<41>				<36>				<42>							
	angiectasis	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 )				
	cyst	3 ( 7 )	2 ( 5 )	0 ( 0 )	0 ( 0 )	3 ( 7 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	4 ( 11 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	7 ( 17 )	0 ( 0 )	0 ( 0 )	0 ( 0 )				
Grade	1 : Slight      2 : Moderate      3 : Marked      4 : Severe																				
< a >	a : Number of animals examined at the site																				
b	b : Number of animals with lesion																				
( c )	c : b / a * 100																				
Significant difference :      * : P ≤ 0.05      ** : P ≤ 0.01      Test of Chi Square																					

STUDY NO. : 0243  
ANIMAL : MOUSE Crj: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				Control 41				3200 ppm 41				8000 ppm 37				20000 ppm 42			
		Grade				1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]																					
pituitary		<41>				<41>				<36>				<42>							
	hyperplasia	0	0	0	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 )
	Rathke pouch	1	0	0	0	1	0	0	0	2	0	0	0	2	0	0	0	2	0	0	0
		( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )
thyroid		<41>				<41>				<37>				<42>							
	focal follicular cell hyperplasia	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 )
adrenal		<41>				<41>				<37>				<42>							
	extramedullary hematopoiesis	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	2	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )
	spindle-cell hyperplasia	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 )
	hyperplasia:cortical cell	5	3	0	0	5	3	0	0	6	1	0	0	7	4	0	0	17	10	0	0
		( 12 )	( 7 )	( 0 )	( 0 )	( 12 )	( 7 )	( 0 )	( 0 )	( 16 )	( 3 )	( 0 )	( 0 )	( 17 )	( 10 )	( 0 )	( 0 )	( 17 )	( 10 )	( 0 )	( 0 )
	hyperplasia:medulla	0	0	0	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 )

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe  
< a > a : Number of animals examined at the site  
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. : 0243  
ANIMAL : MOUSE Crj: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 41				3200 ppm 41				8000 ppm 37				20000 ppm 42			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Reproductive system]																					
testis		<41>				<41>				<37>				<42>							
	atrophy	0	0	0	0	0	0	0	0	1	2	0	0	1	0	0	0	1	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 5 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )
	mineralization	12	0	0	0	6	0	0	0	6	1	0	0	8	0	0	0	19	0	0	0
		( 29 )	( 0 )	( 0 )	( 0 )	( 15 )	( 0 )	( 0 )	( 0 )	( 16 )	( 3 )	( 0 )	( 0 )	( 19 )	( 0 )	( 0 )	( 0 )	( 19 )	( 0 )	( 0 )	( 0 )
epididymis		<41>				<41>				<37>				<42>							
	lymphocytic infiltration	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 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	spermatogenic granuloma	0	2	0	0	1	0	0	0	0	2	0	0	1	0	0	0	2	0	0	0
		( 0 )	( 5 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )	( 2 )	( 0 )	( 0 )	( 0 )
prep/cli gl		<41>				<41>				<37>				<42>							
	duct ectasia	0	5	0	0	0	2	0	0	0	1	0	0	0	2	0	0	0	2	0	0
		( 0 )	( 12 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )	( 0 )	( 5 )	( 0 )	( 0 )
	inflammation	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 )	( 2 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
[Nervous system]																					
brain		<41>				<41>				<37>				<42>							
	mineralization	14	15	0	0	15	21	0	0	7	21	0	0	9	28	0	0 *	21	28	0	0 *
		( 34 )	( 37 )	( 0 )	( 0 )	( 37 )	( 51 )	( 0 )	( 0 )	( 19 )	( 57 )	( 0 )	( 0 )	( 21 )	( 67 )	( 0 )	( 0 )	( 21 )	( 67 )	( 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. : 0243  
 ANIMAL : MOUSE Crj:BDF1  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 8

Organ	Findings	Group Name No. of Animals on Study				Control 41				3200 ppm 41				8000 ppm 37				20000 ppm 42			
		Grade				1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)				(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

[Special sense organs/appandage]

Harder gl	degeneration	<41>				<41>				<37>				<42>			
		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 )
	hyperplasia	<41>				<41>				<37>				<42>			
		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 )	( 2 )	( 0 )	( 0 )

[Body cavities]

adipose	hemorrhage	<41>				<41>				<37>				<42>			
		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )

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

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

b b : Number of animals with lesion

( c ) c : b / a \* 100

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

(HPT150)

BAIS3

## APPENDIX K 8

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (2-YEAR STUDY: SUMMARY)

MOSUE : FEMALE : SACRIFICED ANIMALS

STUDY NO. : 0243  
ANIMAL : MOUSE Crj:BDF1  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 9

		Group Name	Control				8000 ppm				20000 ppm				50000 ppm			
		No. of Animals on Study	35				31				34				34			
Organ	Findings	Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
nasal cavit			<35>				<31>				<34>				<34>			
	atrophy		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	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 )
	eosinophilic change:olfactory epithelium		2	0	0	0	1	1	0	0	1	0	0	0	2	1	0	0
			( 6 )	( 0 )	( 0 )	( 0 )	( 3 )	( 3 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 6 )	( 3 )	( 0 )	( 0 )
eosinophilic change:respiratory epithelium		8	3	0	0	9	5	0	0	10	8	2	0	12	9	2	0 *	
		( 23 )	( 9 )	( 0 )	( 0 )	( 29 )	( 16 )	( 0 )	( 0 )	( 29 )	( 24 )	( 6 )	( 0 )	( 35 )	( 26 )	( 6 )	( 0 )	
disarrangement:olfactory epithelium		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	
respiratory metaplasia:olfactory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	
respiratory metaplasia:gland		4	2	0	0	3	4	0	0	2	2	0	0	5	2	0	0	
		( 11 )	( 6 )	( 0 )	( 0 )	( 10 )	( 13 )	( 0 )	( 0 )	( 6 )	( 6 )	( 0 )	( 0 )	( 15 )	( 6 )	( 0 )	( 0 )	
lung			<35>				<31>				<34>				<34>			
	inflammatory infiltration		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	

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

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

PAGE : 10

Organ	Findings	Group Name No. of Animals on Study Grade	Control 35				8000 ppm 31				20000 ppm 34				50000 ppm 34			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
Lung	Lymphocytic infiltration		<35>				<31>				<34>				<34>			
			0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )
	bronchiolar-alveolar cell hyperplasia		<35>				<31>				<34>				<34>			
			0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
[Hematopoietic system]																		
bone marrow	granulation		<35>				<31>				<34>				<34>			
			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 )
spleen	deposit of melanin		<35>				<31>				<34>				<33>			
			1	1	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 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	extramedullary hematopoiesis		<35>				<31>				<34>				<33>			
			0	0	0	0	2	1	1	0	0	1	0	0	2	2	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 6 )	( 3 )	( 3 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 6 )	( 6 )	( 0 )	( 0 )
	follicular hyperplasia		<35>				<31>				<34>				<33>			
			5	1	1	0	0	3	0	0	2	1	2	0	1	1	1	0
			( 14 )	( 3 )	( 3 )	( 0 )	( 0 )	( 10 )	( 0 )	( 0 )	( 6 )	( 3 )	( 6 )	( 0 )	( 3 )	( 3 )	( 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

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

PAGE : 11

		Group Name No. of Animals on Study Grade	Control 35				8000 ppm 31				20000 ppm 34				50000 ppm 34			
Organ	Findings		1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Circulatory system]																		
heart			<35>				<31>				<34>				<34>			
	thrombus		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 )
	mineralization		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 )
[Digestive system]																		
tooth			<35>				<31>				<34>				<34>			
	cyst		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 )
	inflammation		2 ( 6 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 3 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	2 ( 6 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
	foreign body granuloma		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 )
	dysplasia		1 ( 3 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 3 )	0 ( 0 )	1 ( 3 )	0 ( 0 )	1 ( 3 )	2 ( 6 )	2 ( 6 )	0 ( 0 )
stomach			<35>				<31>				<34>				<34>			
	hyperplasia:forestomach		0 ( 0 )	1 ( 3 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	2 ( 6 )	1 ( 3 )	0 ( 0 )	0 ( 0 )

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SACRIFICED ANIMALS (105W)

PAGE : 12

Organ	Findings	Group Name No. of Animals on Study Grade	Control 35				8000 ppm 31				20000 ppm 34				50000 ppm 34			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
stomach			<35>				<31>				<34>				<34>			
	inflammation:forestomach		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 )
	erosion:glandular stomach		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 )
	hyperplasia:glandular stomach		2	1	0	0	4	0	0	0	4	0	0	0	1	0	0	0
			( 6 )	( 3 )	( 0 )	( 0 )	( 13 )	( 0 )	( 0 )	( 0 )	( 12 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )
liver			<35>				<31>				<34>				<34>			
	angiectasis		0	0	1	0	0	0	1	0	0	3	0	0	2	1	0	0
			( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 9 )	( 0 )	( 0 )	( 6 )	( 3 )	( 0 )	( 0 )
	necrosis		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )
	granulation		6	18	3	0	6	12	0	0	14	5	1	0	6	10	1	0
			( 17 )	( 51 )	( 9 )	( 0 )	( 19 )	( 39 )	( 0 )	( 0 )	( 41 )	( 15 )	( 3 )	( 0 )	( 18 )	( 29 )	( 3 )	( 0 )
	extramedullary hematopoiesis		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 )
	clear cell focus		1	1	0	3	1	1	0	0	0	3	0	1	1	10	3	1
			( 3 )	( 3 )	( 0 )	( 9 )	( 3 )	( 3 )	( 0 )	( 0 )	( 0 )	( 9 )	( 0 )	( 3 )	( 3 )	( 29 )	( 9 )	( 3 )

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 SACRIFICED ANIMALS (105W)

PAGE : 13

		Group Name	Control				8000 ppm				20000 ppm				50000 ppm			
		No. of Animals on Study	35				31				34				34			
Organ_____	Findings_____	Grade	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
<hr/>																		
[Digestive system]																		
liver			<35>				<31>				<34>				<34>			
	acidophilic cell focus		0 ( 0 )	0 ( 0 )	1 ( 3 )	1 ( 3 )	1 ( 3 )	1 ( 3 )	0 ( 0 )	2 ( 6 )	0 ( 0 )	0 ( 0 )	1 ( 3 )	0 ( 0 )	0 ( 0 )	1 ( 3 )	1 ( 3 )	2 ( 6 )
	basophilic cell focus		0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 3 )	1 ( 3 )	0 ( 0 )	0 ( 0 )	2 ( 6 )	4 ( 12 )	0 ( 0 )	0 ( 0 ) *	0 ( 0 )	8 ( 24 )	3 ( 9 )	2 ( 6 ) **
pancreas			<35>				<31>				<34>				<34>			
	atrophy		0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 3 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
<hr/>																		
[Urinary system]																		
kidney			<35>				<31>				<34>				<34>			
	atrophy		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 )
	hyaline droplet		1 ( 3 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	1 ( 3 )	1 ( 3 )	0 ( 0 )	0 ( 0 )	1 ( 3 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )	0 ( 0 )
	deposit of amyloid		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 )

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 < a > a : Number of animals examined at the site  
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SACRIFICED ANIMALS (105W)

PAGE : 14

Organ	Findings	Group Name No. of Animals on Study Grade	Control 35				8000 ppm 31				20000 ppm 34				50000 ppm 34			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																		
kidney			<35>				<31>				<34>				<34>			
	hyaline cast		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 )
	lymphocytic infiltration		1	0	0	0	2	0	0	0	2	0	0	0	0	1	0	0
			( 3 )	( 0 )	( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )
	hydronephrosis		0	2	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			( 0 )	( 6 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	mineralization:papilla		2	0	0	0	2	0	0	0	0	0	0	0	2	0	0	0
			( 6 )	( 0 )	( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 6 )	( 0 )	( 0 )	( 0 )
	mineralization:pelvis		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
urin bladd			<35>				<31>				<34>				<33>			
	lymphocytic infiltration		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	hyaline droplet degeneration:superficial cell of transitional epithelium		0	0	0	0	3	0	0	0	11	0	0	0 **	20	0	0	0 **
			( 0 )	( 0 )	( 0 )	( 0 )	( 10 )	( 0 )	( 0 )	( 0 )	( 32 )	( 0 )	( 0 )	( 0 )	( 61 )	( 0 )	( 0 )	( 0 )
[Endocrine system]																		
pituitary			<35>				<31>				<34>				<34>			
	cyst		4	0	0	0	5	0	0	0	6	0	0	0	5	0	0	0
			( 11 )	( 0 )	( 0 )	( 0 )	( 16 )	( 0 )	( 0 )	( 0 )	( 18 )	( 0 )	( 0 )	( 0 )	( 15 )	( 0 )	( 0 )	( 0 )

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PAGE : 15

Organ_____	Findings_____	Group Name	Control				8000 ppm				20000 ppm				50000 ppm			
		No. of Animals on Study	35				31				34				34			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

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[Endocrine system]																		
pituitary			<35>				<31>				<34>				<34>			
	hyperplasia		1	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			( 3 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	Rathke pouch		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
adrenal			<35>				<31>				<34>				<34>			
	hyperplasia:cortical cell		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 )	( 0 )	( 0 )	( 0 )	( 0 )
	focal fatty change:cortex		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
[Reproductive system]																		
ovary			<35>				<31>				<34>				<34>			
	angiectasis		0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	cyst		4	0	0	0	5	0	0	0	7	0	0	0	3	0	0	0
			( 11 )	( 0 )	( 0 )	( 0 )	( 16 )	( 0 )	( 0 )	( 0 )	( 21 )	( 0 )	( 0 )	( 0 )	( 9 )	( 0 )	( 0 )	( 0 )

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SACRIFICED ANIMALS (105W)

PAGE : 16

Organ	Findings	Group Name No. of Animals on Study Grade				Control 35				8000 ppm 31				20000 ppm 34				50000 ppm 34			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Reproductive system]																					
ovary	mineralization	<35>				<31>				<34>				<34>							
		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 )	( 0 )	( 0 )	( 0 )
uterus	dilatation	<35>				<31>				<34>				<34>							
		0	1	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0	1	0	0
		( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )
	cystic endometrial hyperplasia	11	14	0	0	12	10	0	0	15	11	0	0	9	15	0	0	26	15	0	0
		( 31 )	( 40 )	( 0 )	( 0 )	( 39 )	( 32 )	( 0 )	( 0 )	( 44 )	( 32 )	( 0 )	( 0 )	( 26 )	( 44 )	( 0 )	( 0 )	( 61 )	( 40 )	( 0 )	( 0 )
	xanthogranuloma	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 )	( 0 )	( 0 )	( 0 )
[Nervous system]																					
brain	mineralization	<35>				<31>				<34>				<34>							
		2	10	0	0	6	10	0	0	10	7	0	0 *	6	11	0	0	18	11	0	0
		( 6 )	( 29 )	( 0 )	( 0 )	( 19 )	( 32 )	( 0 )	( 0 )	( 29 )	( 21 )	( 0 )	( 0 )	( 18 )	( 32 )	( 0 )	( 0 )	( 51 )	( 32 )	( 0 )	( 0 )
[Special sense organs/appandage]																					
Harder gl	degeneration	<35>				<31>				<34>				<34>							
		1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	3	0	0	0
		( 3 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 3 )	( 0 )	( 0 )	( 0 )	( 9 )	( 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. : 0243  
 ANIMAL : MOUSE Crj:BDF1  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 17

Organ	Findings	Group Name No. of Animals on Study Grade	Control 35				8000 ppm 31				20000 ppm 34				50000 ppm 34			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

[Special sense organs/appandage]

Harder gl	hyperplasia	<35>				<31>				<34>				<34>			
		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	fracture	<35>				<31>				<34>				<34>			
		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 )

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

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

RAT : MALE

STUDY NO. : 0242  
 ANIMAL : RAT F344/DuCrj  
 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	8000 ppm	20000 ppm	50000 ppm
0 - 52	NO. OF EXAMINED ANIMALS		0	0	1	0
	NO. OF ANIMALS WITH TUMORS		0	0	0	0
	NO. OF ANIMALS WITH SINGLE TUMORS		0	0	0	0
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	0	0	0
	NO. OF BENIGN TUMORS		0	0	0	0
	NO. OF MALIGNANT TUMORS		0	0	0	0
	NO. OF TOTAL TUMORS		0	0	0	0
53 - 78	NO. OF EXAMINED ANIMALS		3	1	1	2
	NO. OF ANIMALS WITH TUMORS		3	1	1	2
	NO. OF ANIMALS WITH SINGLE TUMORS		1	1	1	0
	NO. OF ANIMALS WITH MULTIPLE TUMORS		2	0	0	2
	NO. OF BENIGN TUMORS		4	0	0	3
	NO. OF MALIGNANT TUMORS		1	1	1	1
	NO. OF TOTAL TUMORS		5	1	1	4
79 - 104	NO. OF EXAMINED ANIMALS		14	6	5	10
	NO. OF ANIMALS WITH TUMORS		14	6	5	10
	NO. OF ANIMALS WITH SINGLE TUMORS		4	1	0	1
	NO. OF ANIMALS WITH MULTIPLE TUMORS		10	5	5	9
	NO. OF BENIGN TUMORS		24	7	10	19
	NO. OF MALIGNANT TUMORS		7	4	5	5
	NO. OF TOTAL TUMORS		31	11	15	24
105 - 105	NO. OF EXAMINED ANIMALS		33	43	43	38
	NO. OF ANIMALS WITH TUMORS		33	42	43	38
	NO. OF ANIMALS WITH SINGLE TUMORS		14	8	8	8
	NO. OF ANIMALS WITH MULTIPLE TUMORS		19	34	35	30
	NO. OF BENIGN TUMORS		56	90	93	69
	NO. OF MALIGNANT TUMORS		10	11	13	20
	NO. OF TOTAL TUMORS		66	101	106	89

STUDY NO. : 0242  
ANIMAL : RAT F344/DuCrj  
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	8000 ppm	20000 ppm	50000 ppm
0 - 105	NO. OF EXAMINED ANIMALS		50	50	50	50
	NO. OF ANIMALS WITH TUMORS		50	49	49	50
	NO. OF ANIMALS WITH SINGLE TUMORS		19	10	9	9
	NO. OF ANIMALS WITH MULTIPLE TUMORS		31	39	40	41
	NO. OF BENIGN TUMORS		84	97	103	91
	NO. OF MALIGNANT TUMORS		18	16	19	26
	NO. OF TOTAL TUMORS		102	113	122	117

(HPT070)

BAIS3

APPENDIX L 2

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

RAT : FEMALE



STUDY NO. : 0242  
 ANIMAL : RAT F344/DuCrj  
 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	8000 ppm	20000 ppm	50000 ppm
0 - 52	NO. OF EXAMINED ANIMALS		0	0	1	1
	NO. OF ANIMALS WITH TUMORS		0	0	1	1
	NO. OF ANIMALS WITH SINGLE TUMORS		0	0	1	1
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	0	0	0
	NO. OF BENIGN TUMORS		0	0	1	0
	NO. OF MALIGNANT TUMORS		0	0	0	1
	NO. OF TOTAL TUMORS		0	0	1	1
53 - 78	NO. OF EXAMINED ANIMALS		2	4	2	1
	NO. OF ANIMALS WITH TUMORS		1	4	2	1
	NO. OF ANIMALS WITH SINGLE TUMORS		1	3	2	1
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	1	0	0
	NO. OF BENIGN TUMORS		1	1	1	0
	NO. OF MALIGNANT TUMORS		0	4	1	1
	NO. OF TOTAL TUMORS		1	5	2	1
79 - 104	NO. OF EXAMINED ANIMALS		8	6	7	11
	NO. OF ANIMALS WITH TUMORS		7	6	7	10
	NO. OF ANIMALS WITH SINGLE TUMORS		3	5	5	6
	NO. OF ANIMALS WITH MULTIPLE TUMORS		4	1	2	4
	NO. OF BENIGN TUMORS		6	4	7	12
	NO. OF MALIGNANT TUMORS		7	3	3	6
	NO. OF TOTAL TUMORS		13	7	10	18
105 - 105	NO. OF EXAMINED ANIMALS		40	40	40	37
	NO. OF ANIMALS WITH TUMORS		24	23	26	25
	NO. OF ANIMALS WITH SINGLE TUMORS		18	11	9	18
	NO. OF ANIMALS WITH MULTIPLE TUMORS		6	12	17	7
	NO. OF BENIGN TUMORS		28	32	42	29
	NO. OF MALIGNANT TUMORS		6	5	11	7
	NO. OF TOTAL TUMORS		34	37	53	36

STUDY NO. : 0242  
ANIMAL : RAT F344/DuCrj  
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	8000 ppm	20000 ppm	50000 ppm
0 - 105	NO. OF EXAMINED ANIMALS		50	50	50	50
	NO. OF ANIMALS WITH TUMORS		32	33	36	37
	NO. OF ANIMALS WITH SINGLE TUMORS		22	19	17	26
	NO. OF ANIMALS WITH MULTIPLE TUMORS		10	14	19	11
	NO. OF BENIGN TUMORS		35	37	51	41
	NO. OF MALIGNANT TUMORS		13	12	15	15
	NO. OF TOTAL TUMORS		48	49	66	56

(HPT070)

BAIS3

APPENDIX L 3

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

MOUSE : MALE

STUDY NO. : 0243  
ANIMAL : MOUSE Crj: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	3200 ppm	8000 ppm	20000 ppm
0 - 52	NO. OF EXAMINED ANIMALS		1	2	1	0
	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		2	0	5	1
	NO. OF ANIMALS WITH TUMORS		1	0	3	1
	NO. OF ANIMALS WITH SINGLE TUMORS		1	0	2	1
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	0	1	0
	NO. OF BENIGN TUMORS		0	0	0	0
	NO. OF MALIGNANT TUMORS		1	0	4	1
	NO. OF TOTAL TUMORS		1	0	4	1
79 - 104	NO. OF EXAMINED ANIMALS		5	7	7	7
	NO. OF ANIMALS WITH TUMORS		2	5	4	7
	NO. OF ANIMALS WITH SINGLE TUMORS		1	4	4	7
	NO. OF ANIMALS WITH MULTIPLE TUMORS		1	1	0	0
	NO. OF BENIGN TUMORS		0	1	0	0
	NO. OF MALIGNANT TUMORS		3	5	4	7
	NO. OF TOTAL TUMORS		3	6	4	7
105 - 105	NO. OF EXAMINED ANIMALS		41	41	37	42
	NO. OF ANIMALS WITH TUMORS		17	21	13	15
	NO. OF ANIMALS WITH SINGLE TUMORS		16	18	10	13
	NO. OF ANIMALS WITH MULTIPLE TUMORS		1	3	3	2
	NO. OF BENIGN TUMORS		8	12	9	9
	NO. OF MALIGNANT TUMORS		10	12	7	8
	NO. OF TOTAL TUMORS		18	24	16	17

STUDY NO. : 0243  
ANIMAL : MOUSE Crj: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	3200 ppm	8000 ppm	20000 ppm
0 - 105	NO. OF EXAMINED ANIMALS		49	50	50	50
	NO. OF ANIMALS WITH TUMORS		20	27	20	23
	NO. OF ANIMALS WITH SINGLE TUMORS		18	23	16	21
	NO. OF ANIMALS WITH MULTIPLE TUMORS		2	4	4	2
	NO. OF BENIGN TUMORS		8	13	9	9
	NO. OF MALIGNANT TUMORS		14	18	15	16
	NO. OF TOTAL TUMORS		22	31	24	25

(HPT070)

BAIS3

## APPENDIX L4

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

MOUSE: FEMALE

STUDY NO. : 0243  
ANIMAL : MOUSE Crj: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	8000 ppm	20000 ppm	50000 ppm
0 - 52	NO. OF EXAMINED ANIMALS		0	0	1	0
	NO. OF ANIMALS WITH TUMORS		0	0	1	0
	NO. OF ANIMALS WITH SINGLE TUMORS		0	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		0	0	1	0
	NO. OF TOTAL TUMORS		0	0	1	0
53 - 78	NO. OF EXAMINED ANIMALS		4	2	2	4
	NO. OF ANIMALS WITH TUMORS		3	2	2	3
	NO. OF ANIMALS WITH SINGLE TUMORS		2	2	2	1
	NO. OF ANIMALS WITH MULTIPLE TUMORS		1	0	0	2
	NO. OF BENIGN TUMORS		2	0	0	1
	NO. OF MALIGNANT TUMORS		2	2	2	4
	NO. OF TOTAL TUMORS		4	2	2	5
79 - 104	NO. OF EXAMINED ANIMALS		11	17	13	12
	NO. OF ANIMALS WITH TUMORS		9	17	13	11
	NO. OF ANIMALS WITH SINGLE TUMORS		9	14	9	7
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	3	4	4
	NO. OF BENIGN TUMORS		0	3	3	2
	NO. OF MALIGNANT TUMORS		9	18	15	13
	NO. OF TOTAL TUMORS		9	21	18	15
105 - 105	NO. OF EXAMINED ANIMALS		35	31	34	34
	NO. OF ANIMALS WITH TUMORS		21	21	23	25
	NO. OF ANIMALS WITH SINGLE TUMORS		16	13	19	12
	NO. OF ANIMALS WITH MULTIPLE TUMORS		5	8	4	13
	NO. OF BENIGN TUMORS		10	10	14	25
	NO. OF MALIGNANT TUMORS		18	21	13	17
	NO. OF TOTAL TUMORS		28	31	27	42

STUDY NO. : 0243  
ANIMAL : MOUSE Crj: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	8000 ppm	20000 ppm	50000 ppm
0 - 105	NO. OF EXAMINED ANIMALS		50	50	50	50
	NO. OF ANIMALS WITH TUMORS		33	40	39	39
	NO. OF ANIMALS WITH SINGLE TUMORS		27	29	31	20
	NO. OF ANIMALS WITH MULTIPLE TUMORS		6	11	8	19
	NO. OF BENIGN TUMORS		12	13	17	28
	NO. OF MALIGNANT TUMORS		29	41	31	34
	NO. OF TOTAL TUMORS		41	54	48	62

(HPT070)

BAIS3



APPENDIX M 1

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (2-YEAR STUDY: SUMMARY)

RAT : MALE :

STUDY NO. : 0242  
 ANIMAL : RAT F344/DuCrj  
 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	8000 ppm 50	20000 ppm 50	50000 ppm 50
[Integumentary system/appandage]						
skin/app			<50>	<50>	<50>	<50>
	squamous cell papilloma		1 ( 2%)	0 ( 0%)	1 ( 2%)	1 ( 2%)
	trichoepithelioma		0 ( 0%)	0 ( 0%)	1 ( 2%)	0 ( 0%)
	keratoacanthoma		4 ( 8%)	3 ( 6%)	2 ( 4%)	4 ( 8%)
	sebaceous adenoma		0 ( 0%)	1 ( 2%)	1 ( 2%)	0 ( 0%)
	squamous cell carcinoma		1 ( 2%)	0 ( 0%)	0 ( 0%)	0 ( 0%)
subcutis			<50>	<50>	<50>	<50>
	fibroma		2 ( 4%)	4 ( 8%)	1 ( 2%)	4 ( 8%)
	lipoma		0 ( 0%)	1 ( 2%)	0 ( 0%)	0 ( 0%)
	fibrosarcoma		0 ( 0%)	0 ( 0%)	1 ( 2%)	0 ( 0%)
	schwannoma:malignant		1 ( 2%)	0 ( 0%)	1 ( 2%)	0 ( 0%)
[Respiratory system]						
lung			<50>	<50>	<50>	<50>
	bronchiolar-alveolar adenoma		0 ( 0%)	3 ( 6%)	3 ( 6%)	2 ( 4%)
	osteosarcoma		0 ( 0%)	1 ( 2%)	0 ( 0%)	0 ( 0%)
[Hematopoietic system]						
bone marrow			<50>	<50>	<50>	<50>
	histiocytic sarcoma		0 ( 0%)	1 ( 2%)	0 ( 0%)	0 ( 0%)

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

STUDY NO. : 0242  
 ANIMAL : RAT F344/DuCrj  
 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	8000 ppm 50	20000 ppm 50	50000 ppm 50
[Hematopoietic system]						
spleen			<50>	<50>	<50>	<50>
	sarcoma:NOS		0 ( 0%)	1 ( 2%)	0 ( 0%)	0 ( 0%)
	mononuclear cell leukemia		8 ( 16%)	1 ( 2%)	1 ( 2%)	1 ( 2%)
	hemangiosarcoma		0 ( 0%)	1 ( 2%)	0 ( 0%)	2 ( 4%)
[Digestive system]						
oral cavity			<50>	<50>	<50>	<50>
	squamous cell papilloma		1 ( 2%)	0 ( 0%)	1 ( 2%)	0 ( 0%)
small intes			<50>	<50>	<50>	<50>
	adenoma		0 ( 0%)	0 ( 0%)	1 ( 2%)	0 ( 0%)
liver			<50>	<50>	<50>	<50>
	hepatocellular adenoma		0 ( 0%)	4 ( 8%)	9 ( 18%)	9 ( 18%)
	hepatocellular carcinoma		0 ( 0%)	0 ( 0%)	5 ( 10%)	5 ( 10%)
pancreas			<50>	<50>	<50>	<50>
	islet cell adenoma		3 ( 6%)	2 ( 4%)	0 ( 0%)	2 ( 4%)
	acinar cell adenocarcinoma		0 ( 0%)	0 ( 0%)	0 ( 0%)	1 ( 2%)
[Urinary system]						
kidney			<50>	<50>	<50>	<50>
	renal cell adenoma		0 ( 0%)	0 ( 0%)	1 ( 2%)	0 ( 0%)
	liposarcoma		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)

BAIS3

STUDY NO. : 0242  
 ANIMAL : RAT F344/DuCrj  
 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	8000 ppm 50	20000 ppm 50	50000 ppm 50
[Urinary system]						
urin bladd	transitional cell papilloma		<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 2 ( 4%)	<50> 0 ( 0%)
	mastcytoma:benign		0 ( 0%)	1 ( 2%)	0 ( 0%)	0 ( 0%)
	transitional cell carcinoma		0 ( 0%)	1 ( 2%)	4 ( 8%)	3 ( 6%)
[Endocrine system]						
pituitary	adenoma		<49> 15 ( 31%)	<50> 10 ( 20%)	<50> 10 ( 20%)	<50> 10 ( 20%)
thyroid	C-cell adenoma		<50> 3 ( 6%)	<50> 5 ( 10%)	<50> 5 ( 10%)	<50> 2 ( 4%)
	follicular adenoma		0 ( 0%)	0 ( 0%)	0 ( 0%)	1 ( 2%)
	C-cell carcinoma		0 ( 0%)	2 ( 4%)	1 ( 2%)	0 ( 0%)
	follicular adenocarcinoma		4 ( 8%)	3 ( 6%)	1 ( 2%)	5 ( 10%)
adrenal	pheochromocytoma		<50> 6 ( 12%)	<50> 10 ( 20%)	<50> 12 ( 24%)	<50> 3 ( 6%)
	ganglioneuroma		0 ( 0%)	0 ( 0%)	0 ( 0%)	1 ( 2%)
	pheochromocytoma:malignant		2 ( 4%)	2 ( 4%)	2 ( 4%)	2 ( 4%)
[Reproductive system]						
testis	interstitial cell tumor		<50> 43 ( 86%)	<50> 46 ( 92%)	<50> 47 ( 94%)	<50> 47 ( 94%)

< 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. : 0242  
ANIMAL : RAT F344/DuCrj  
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	8000 ppm 50	20000 ppm 50	50000 ppm 50
[Reproductive system]						
mammary gl	adenoma		<50> 0 ( 0%)	<50> 1 ( 2%)	<50> 0 ( 0%)	<50> 1 ( 2%)
	fibroadenoma		2 ( 4%)	0 ( 0%)	3 ( 6%)	2 ( 4%)
prep/cli gl	adenoma		<50> 4 ( 8%)	<50> 4 ( 8%)	<50> 2 ( 4%)	<50> 0 ( 0%)
	keratinocanthoma		0 ( 0%)	2 ( 4%)	0 ( 0%)	0 ( 0%)
	squamous cell carcinoma		1 ( 2%)	0 ( 0%)	0 ( 0%)	0 ( 0%)
[Nervous system]						
brain	malignant reticulosis		<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 2 ( 4%)
	glioma		0 ( 0%)	0 ( 0%)	0 ( 0%)	1 ( 2%)
[Special sense organs/appandage]						
Zymbal gl	adenoma		<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 1 ( 2%)	<50> 2 ( 4%)
	squamous cell carcinoma		0 ( 0%)	0 ( 0%)	0 ( 0%)	1 ( 2%)
[Musculoskeletal system]						
bone	osteosarcoma		<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 1 ( 2%)	<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)

BAIS3

STUDY NO. : 0242  
ANIMAL : RAT F344/DuCrj  
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	8000 ppm 50	20000 ppm 50	50000 ppm 50
[Body cavities]						
peritoneum	mesothelioma		<50> 0 ( 0%)	<50> 3 ( 6%)	<50> 2 ( 4%)	<50> 1 ( 2%)
retroperit	paraganglioma:malignant		<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

(IPT085)

BAIS3

## APPENDIX M 2

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (2-YEAR STUDY: SUMMARY)

RAT : FEMALE :

STUDY NO. : 0242  
 ANIMAL : RAT F344/DuCrj  
 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	8000 ppm 50	20000 ppm 50	50000 ppm 50
[Integumentary system/appendage]						
subcutis			<50>	<50>	<50>	<50>
	fibroma		1 ( 2%)	1 ( 2%)	0 ( 0%)	0 ( 0%)
	lipoma		1 ( 2%)	0 ( 0%)	0 ( 0%)	0 ( 0%)
	schwannoma		0 ( 0%)	0 ( 0%)	0 ( 0%)	1 ( 2%)
	sarcoma:NOS		0 ( 0%)	1 ( 2%)	0 ( 0%)	0 ( 0%)
[Respiratory system]						
lung			<50>	<50>	<50>	<50>
	bronchiolar-alveolar adenoma		1 ( 2%)	0 ( 0%)	3 ( 6%)	0 ( 0%)
[Hematopoietic system]						
bone marrow			<50>	<50>	<50>	<50>
	histiocytic sarcoma		2 ( 4%)	0 ( 0%)	0 ( 0%)	0 ( 0%)
thymus			<50>	<50>	<50>	<49>
	thymoma:benign		1 ( 2%)	0 ( 0%)	0 ( 0%)	0 ( 0%)
spleen			<50>	<50>	<50>	<50>
	mononuclear cell leukemia		6 ( 12%)	7 ( 14%)	2 ( 4%)	6 ( 12%)
[Digestive system]						
esophagus			<50>	<50>	<50>	<49>
	squamous cell papilloma		1 ( 2%)	0 ( 0%)	0 ( 0%)	0 ( 0%)
large intes			<50>	<50>	<50>	<50>
	adenoma		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)

BAIS3



STUDY NO. : 0242  
 ANIMAL : RAT F344/DuCrj  
 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	8000 ppm 50	20000 ppm 50	50000 ppm 50
[Digestive system]						
liver	hepatocellular adenoma		<50> 1 ( 2%)	<50> 3 ( 6%)	<50> 3 ( 6%)	<50> 2 ( 4%)
	cholangiocellular adenoma		0 ( 0%)	0 ( 0%)	1 ( 2%)	0 ( 0%)
	hemangiosarcoma		0 ( 0%)	0 ( 0%)	0 ( 0%)	1 ( 2%)
	hepatocellular carcinoma		0 ( 0%)	0 ( 0%)	1 ( 2%)	0 ( 0%)
pancreas	islet cell adenoma		<50> 1 ( 2%)	<50> 0 ( 0%)	<50> 1 ( 2%)	<50> 1 ( 2%)
[Urinary system]						
kidney	mesenchymoma		<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 1 ( 2%)	<50> 0 ( 0%)
	renal cell adenoma		0 ( 0%)	3 ( 6%)	6 ( 12%)	4 ( 8%)
	renal cell carcinoma		0 ( 0%)	0 ( 0%)	0 ( 0%)	1 ( 2%)
urin bladd	mastcytoma:benign		<50> 1 ( 2%)	<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 0 ( 0%)
	transitional cell carcinoma		0 ( 0%)	2 ( 4%)	3 ( 6%)	2 ( 4%)
[Endocrine system]						
pituitary	adenoma		<50> 11 ( 22%)	<50> 12 ( 24%)	<50> 16 ( 32%)	<50> 11 ( 22%)

< 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. : 0242  
 ANIMAL : RAT F344/DuCrj  
 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	8000 ppm 50	20000 ppm 50	50000 ppm 50
[Endocrine system]						
pituitary			<50>	<50>	<50>	<50>
	adenocarcinoma		0 ( 0%)	0 ( 0%)	1 ( 2%)	0 ( 0%)
thyroid			<50>	<50>	<50>	<49>
	C-cell adenoma		5 ( 10%)	2 ( 4%)	5 ( 10%)	1 ( 2%)
	follicular adenocarcinoma		2 ( 4%)	0 ( 0%)	1 ( 2%)	0 ( 0%)
adrenal			<50>	<50>	<50>	<50>
	pheochromocytoma		0 ( 0%)	3 ( 6%)	2 ( 4%)	3 ( 6%)
	cortical adenoma		1 ( 2%)	0 ( 0%)	0 ( 0%)	0 ( 0%)
	pheochromocytoma:malignant		1 ( 2%)	0 ( 0%)	0 ( 0%)	1 ( 2%)
	cortical adenocarcinoma		0 ( 0%)	0 ( 0%)	1 ( 2%)	0 ( 0%)
[Reproductive system]						
ovary			<50>	<50>	<50>	<50>
	granulosa-theca cell tumor:malignant		0 ( 0%)	1 ( 2%)	0 ( 0%)	0 ( 0%)
uterus			<50>	<50>	<50>	<50>
	leiomyoma		0 ( 0%)	0 ( 0%)	0 ( 0%)	1 ( 2%)
	endometrial stromal polyp		4 ( 8%)	9 ( 18%)	8 ( 16%)	5 ( 10%)
	adenocarcinoma		0 ( 0%)	0 ( 0%)	2 ( 4%)	0 ( 0%)
	endometrial stromal sarcoma		0 ( 0%)	0 ( 0%)	0 ( 0%)	3 ( 6%)

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

(HPT085)

BAIS3

STUDY NO. : 0242  
 ANIMAL : RAT F344/DuCrj  
 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	8000 ppm 50	20000 ppm 50	50000 ppm 50
[Reproductive system]						
mammary gl	adenoma		<50> 0 ( 0%)	<50> 2 ( 4%)	<50> 0 ( 0%)	<50> 1 ( 2%)
	fibroadenoma		3 ( 6%)	2 ( 4%)	3 ( 6%)	9 ( 18%)
	adenocarcinoma		0 ( 0%)	0 ( 0%)	2 ( 4%)	0 ( 0%)
prep/cli gl	adenoma		<50> 2 ( 4%)	<50> 0 ( 0%)	<50> 1 ( 2%)	<50> 0 ( 0%)
	keratoacanthoma		1 ( 2%)	0 ( 0%)	0 ( 0%)	0 ( 0%)
[Nervous system]						
brain	glioma		<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 1 ( 2%)	<50> 1 ( 2%)
[Special sense organs/appandage]						
Zymbal gl	squamous cell carcinoma		<50> 0 ( 0%)	<50> 1 ( 2%)	<50> 0 ( 0%)	<50> 0 ( 0%)
[Musculoskeletal system]						
bone	osteosarcoma		<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 1 ( 2%)	<50> 0 ( 0%)
[Body cavities]						
mediastinum	carcinoid tumor:malignant		<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

STUDY NO. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 10

Organ	Findings	Group Name No. of animals on Study	Control 50	8000 ppm 50	20000 ppm 50	50000 ppm 50
[Body cavities]						
mediastinum	sarcoma:NOS		<50> 1 ( 2%)	<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 0 ( 0%)
mesenterium	fibroma		<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 1 ( 2%)	<50> 0 ( 0%)
adipose	lipoma		<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 1 ( 2%)
<hr/>						
< a >	a : Number of animals examined at the site					
b ( c )	b : Number of animals with neoplasm					
	c : b / a * 100					

(HPT085)

BAIS3

## APPENDIX M 3

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (2-YEAR STUDY: SUMMARY)

MOUSE: MALE

STUDY NO. : 0243  
 ANIMAL : MOUSE Crj: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 49	3200 ppm 50	8000 ppm 50	20000 ppm 50
[Integumentary system/appandage]						
subcutis	xanthoma		<49> 1 ( 2%)	<50> 1 ( 2%)	<50> 1 ( 2%)	<50> 0 ( 0%)
	histiocytic sarcoma		1 ( 2%)	1 ( 2%)	1 ( 2%)	0 ( 0%)
[Respiratory system]						
nasal cavit	chondroma		<49> 0 ( 0%)	<50> 0 ( 0%)	<50> 1 ( 2%)	<50> 0 ( 0%)
lung	bronchiolar-alveolar adenoma		<49> 1 ( 2%)	<50> 3 ( 6%)	<50> 2 ( 4%)	<50> 1 ( 2%)
	bronchiolar-alveolar carcinoma		1 ( 2%)	1 ( 2%)	2 ( 4%)	0 ( 0%)
[Hematopoietic system]						
lymph node	malignant lymphoma		<49> 2 ( 4%)	<50> 4 ( 8%)	<50> 4 ( 8%)	<50> 3 ( 6%)
	mastcytoma:malignant		2 ( 4%)	1 ( 2%)	1 ( 2%)	2 ( 4%)
spleen	hemangioma		<49> 0 ( 0%)	<50> 0 ( 0%)	<50> 1 ( 2%)	<50> 0 ( 0%)
	malignant lymphoma		1 ( 2%)	2 ( 4%)	0 ( 0%)	2 ( 4%)
	mastcytoma:malignant		0 ( 0%)	0 ( 0%)	0 ( 0%)	1 ( 2%)
[Circulatory system]						
heart	hemangioma		<49> 0 ( 0%)	<50> 0 ( 0%)	<50> 1 ( 2%)	<50> 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. : 0243  
 ANIMAL : MOUSE Crj:BDF1  
 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 49	3200 ppm 50	8000 ppm 50	20000 ppm 50
[Digestive system]						
salivary gl			<49>	<50>	<50>	<50>
	histiocytic sarcoma		0 ( 0%)	1 ( 2%)	0 ( 0%)	1 ( 2%)
liver			<49>	<50>	<50>	<50>
	hepatocellular adenoma		4 ( 8%)	6 ( 12%)	1 ( 2%)	5 ( 10%)
	histiocytic sarcoma		2 ( 4%)	4 ( 8%)	5 ( 10%)	3 ( 6%)
	hemangiosarcoma		2 ( 4%)	0 ( 0%)	1 ( 2%)	0 ( 0%)
	hepatocellular carcinoma		1 ( 2%)	3 ( 6%)	0 ( 0%)	0 ( 0%)
[Urinary system]						
kidney			<49>	<50>	<50>	<50>
	transitional cell carcinoma		0 ( 0%)	0 ( 0%)	0 ( 0%)	1 ( 2%)
urin bladd			<49>	<50>	<50>	<50>
	xanthoma		0 ( 0%)	2 ( 4%)	0 ( 0%)	0 ( 0%)
	histiocytic sarcoma		0 ( 0%)	0 ( 0%)	0 ( 0%)	2 ( 4%)
[Endocrine system]						
adrenal			<49>	<50>	<50>	<50>
	cortical adenoma		1 ( 2%)	0 ( 0%)	0 ( 0%)	0 ( 0%)
[Reproductive system]						
testis			<49>	<50>	<50>	<50>
	interstitial cell tumor		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

(HPT085)

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STUDY NO. : 0243  
ANIMAL : MOUSE Crj: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 49	3200 ppm 50	8000 ppm 50	20000 ppm 50
[Reproductive system]						
testis			<49>	<50>	<50>	<50>
	histiocytic sarcoma		1 ( 2%)	0 ( 0%)	0 ( 0%)	0 ( 0%)
epididymis			<49>	<50>	<50>	<50>
	histiocytic sarcoma		1 ( 2%)	1 ( 2%)	1 ( 2%)	1 ( 2%)
[Special sense organs/appandage]						
Harder gl			<49>	<50>	<50>	<50>
	adenoma		0 ( 0%)	1 ( 2%)	2 ( 4%)	3 ( 6%)

< 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 M 4

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (2-YEAR STUDY: SUMMARY)

MOUSE: FEMALE

STUDY NO. : 0243  
 ANIMAL : MOUSE Crj:BDF1  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 4

Organ	Findings	Group Name No. of animals on Study	Control 50	8000 ppm 50	20000 ppm 50	50000 ppm 50
[Integumentary system/appandage]						
skin/app			<50>	<50>	<50>	<50>
	trichoepithelioma		1 ( 2%)	0 ( 0%)	0 ( 0%)	0 ( 0%)
subcutis			<50>	<50>	<50>	<50>
	xanthoma		0 ( 0%)	1 ( 2%)	0 ( 0%)	0 ( 0%)
	histiocytic sarcoma		0 ( 0%)	1 ( 2%)	0 ( 0%)	1 ( 2%)
	hemangiosarcoma		1 ( 2%)	0 ( 0%)	0 ( 0%)	0 ( 0%)
[Respiratory system]						
lung			<50>	<50>	<50>	<50>
	bronchiolar-alveolar adenoma		1 ( 2%)	2 ( 4%)	4 ( 8%)	0 ( 0%)
	bronchiolar-alveolar carcinoma		2 ( 4%)	2 ( 4%)	2 ( 4%)	1 ( 2%)
[Hematopoietic system]						
lymph node			<50>	<50>	<50>	<50>
	malignant lymphoma		11 ( 22%)	13 ( 26%)	7 ( 14%)	7 ( 14%)
	mastcytoma:malignant		0 ( 0%)	0 ( 0%)	1 ( 2%)	0 ( 0%)
spleen			<50>	<50>	<50>	<49>
	hemangioma		0 ( 0%)	1 ( 2%)	0 ( 0%)	0 ( 0%)
	malignant lymphoma		4 ( 8%)	1 ( 2%)	4 ( 8%)	0 ( 0%)
[Digestive system]						
oral cavity			<50>	<50>	<50>	<50>
	squamous cell papilloma		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

(HPT085)

BAIS3

STUDY NO. : 0243  
 ANIMAL : MOUSE Crj: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	8000 ppm 50	20000 ppm 50	50000 ppm 50
[Digestive system]						
salivary gl	histiocytic sarcoma		<50> 0 ( 0%)	<50> 1 ( 2%)	<50> 0 ( 0%)	<50> 0 ( 0%)
stomach	mastcytoma:malignant		<49> 0 ( 0%)	<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 1 ( 2%)
large intes	leiomyosarcoma		<50> 0 ( 0%)	<50> 1 ( 2%)	<50> 0 ( 0%)	<50> 0 ( 0%)
liver	hepatocellular adenoma		<50> 2 ( 4%)	<50> 3 ( 6%)	<50> 6 ( 12%)	<50> 20 ( 40%)
	hepatocholangiocellular adenoma		0 ( 0%)	0 ( 0%)	0 ( 0%)	1 ( 2%)
	histiocytic sarcoma		0 ( 0%)	3 ( 6%)	4 ( 8%)	3 ( 6%)
	hemangiosarcoma		3 ( 6%)	1 ( 2%)	1 ( 2%)	1 ( 2%)
	hepatocellular carcinoma		0 ( 0%)	2 ( 4%)	5 ( 10%)	12 ( 24%)
[Urinary system]						
urin bladd	histiocytic sarcoma		<50> 0 ( 0%)	<50> 1 ( 2%)	<50> 0 ( 0%)	<49> 0 ( 0%)
[Endocrine system]						
pituitary	adenoma		<50> 1 ( 2%)	<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 1 ( 2%)
thyroid	C-cell carcinoma		<49> 0 ( 0%)	<50> 1 ( 2%)	<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)

BAIS3

STUDY NO. : 0243  
 ANIMAL : MOUSE Crj: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	8000 ppm 50	20000 ppm 50	50000 ppm 50
[Endocrine system]						
adrenal	pheochromocytoma		<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 1 ( 2%)	<50> 0 ( 0%)
	A-B cell tumor		0 ( 0%)	0 ( 0%)	0 ( 0%)	1 ( 2%)
[Reproductive system]						
ovary	cystadenoma		<50> 0 ( 0%)	<50> 1 ( 2%)	<50> 2 ( 4%)	<50> 0 ( 0%)
	hemangioma		2 ( 4%)	2 ( 4%)	0 ( 0%)	0 ( 0%)
uterus	leiomyoma		<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 1 ( 2%)	<50> 0 ( 0%)
	xanthoma		0 ( 0%)	0 ( 0%)	0 ( 0%)	1 ( 2%)
	endometrial stromal polyp		2 ( 4%)	1 ( 2%)	0 ( 0%)	0 ( 0%)
	leiomyosarcoma		1 ( 2%)	0 ( 0%)	0 ( 0%)	0 ( 0%)
	histiocytic sarcoma		6 ( 12%)	12 ( 24%)	7 ( 14%)	7 ( 14%)
mammary gl	adenocarcinoma		<50> 0 ( 0%)	<50> 2 ( 4%)	<50> 0 ( 0%)	<50> 0 ( 0%)
[Special sense organs/appandage]						
Harder gl	adenoma		<50> 1 ( 2%)	<50> 2 ( 4%)	<50> 3 ( 6%)	<50> 3 ( 6%)

< 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. : 0243  
ANIMAL : MOUSE Crj: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	8000 ppm 50	20000 ppm 50	50000 ppm 50
[Musculoskeletal system]						
muscle			<50>	<50>	<50>	<50>
	hemangioma		0 ( 0%)	0 ( 0%)	0 ( 0%)	1 ( 2%)
bone			<50>	<50>	<50>	<50>
	osteoma		1 ( 2%)	0 ( 0%)	0 ( 0%)	0 ( 0%)
	osteosarcoma		1 ( 2%)	0 ( 0%)	0 ( 0%)	0 ( 0%)

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

(HPT085)

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## APPENDIX N 1

### NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

RAT : MALE

STUDY No. : 0242  
 ANIMAL : RAT F344/DuCrj  
 SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 1

Group Name	Control	8000 ppm	20000 ppm	50000 ppm
SITE : skin/appendage TUMOR : keratoacanthoma				
Tumor rate				
Overall rates(a)	4/50( 8.0)	3/50( 6.0)	2/50( 4.0)	4/50( 8.0)
Adjusted rates(b)	9.09	6.98	4.65	9.09
Terminal rates(c)	3/33( 9.1)	3/43( 7.0)	2/43( 4.7)	3/38( 7.9)
Statistical analysis				
Peto test				
Standard method(d)	P = -----			
Prevalence method(d)	P = 0.4130			
Combined analysis(d)	P = -----			
Cochran-Armitage test(e)	P = 0.8740			
Fisher Exact test(e)		P = 0.4895	P = 0.3574	P = 0.3579
SITE : skin/appendage TUMOR : squamous cell papilloma,squamous cell carcinoma,keratoacanthoma				
Tumor rate				
Overall rates(a)	6/50( 12.0)	3/50( 6.0)	3/50( 6.0)	5/50( 10.0)
Adjusted rates(b)	15.15	6.98	6.98	11.36
Terminal rates(c)	5/33( 15.2)	3/43( 7.0)	3/43( 7.0)	4/38( 10.5)
Statistical analysis				
Peto test				
Standard method(d)	P = -----			
Prevalence method(d)	P = 0.4670			
Combined analysis(d)	P = -----			
Cochran-Armitage test(e)	P = 0.9734			
Fisher Exact test(e)		P = 0.2728	P = 0.2728	P = 0.4872
SITE : subcutis TUMOR : fibroma				
Tumor rate				
Overall rates(a)	2/50( 4.0)	4/50( 8.0)	1/50( 2.0)	4/50( 8.0)
Adjusted rates(b)	3.03	9.30	2.33	7.32
Terminal rates(c)	1/33( 3.0)	4/43( 9.3)	1/43( 2.3)	2/38( 5.3)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3261			
Prevalence method(d)	P = 0.2803			
Combined analysis(d)	P = 0.2432			
Cochran-Armitage test(e)	P = 0.5403			
Fisher Exact test(e)		P = 0.3574	P = 0.4926	P = 0.3574

STUDY No. : 0242  
ANIMAL : RAT F344/DuCrj  
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 2

Group Name	Control	8000 ppm	20000 ppm	50000 ppm
SITE : subcutis TUMOR : fibroma,fibrosarcoma				
Tumor rate				
Overall rates(a)	2/50( 4.0)	4/50( 8.0)	2/50( 4.0)	4/50( 8.0)
Adjusted rates(b)	3.03	9.30	2.33	7.32
Terminal rates(c)	1/33( 3.0)	4/43( 9.3)	1/43( 2.3)	2/38( 5.3)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3469			
Prevalence method(d)	P = 0.2803			
Combined analysis(d)	P = 0.2502			
Cochran-Armitage test(e)	P = 0.5514			
Fisher Exact test(e)		P = 0.3574	P = 0.3088	P = 0.3574
SITE : lung TUMOR : bronchiolar-alveolar adenoma				
Tumor rate				
Overall rates(a)	0/50( 0.0)	3/50( 6.0)	3/50( 6.0)	2/50( 4.0)
Adjusted rates(b)	0.0	6.98	6.98	5.26
Terminal rates(c)	0/33( 0.0)	3/43( 7.0)	3/43( 7.0)	2/38( 5.3)
Statistical analysis				
Peto test				
Standard method(d)	P = -----			
Prevalence method(d)	P = 0.2996			
Combined analysis(d)	P = -----			
Cochran-Armitage test(e)	P = 0.5948			
Fisher Exact test(e)		P = 0.1325	P = 0.1325	P = 0.2574
SITE : spleen TUMOR : mononuclear cell leukemia				
Tumor rate				
Overall rates(a)	8/50( 16.0)	1/50( 2.0)	1/50( 2.0)	1/50( 2.0)
Adjusted rates(b)	10.26	0.0	0.0	2.63
Terminal rates(c)	3/33( 9.1)	0/43( 0.0)	0/43( 0.0)	1/38( 2.6)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.9857			
Prevalence method(d)	P = 0.8720			
Combined analysis(d)	P = 0.9924			
Cochran-Armitage test(e)	P = 0.0258*			
Fisher Exact test(e)		P = 0.0254*	P = 0.0254*	P = 0.0254*



STUDY No. : 0242  
 ANIMAL : RAT F344/DuCrj  
 SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 3

Group Name	Control	8000 ppm	20000 ppm	50000 ppm
SITE : liver TUMOR : hepatocellular adenoma				
Tumor rate				
Overall rates(a)	0/50( 0.0)	4/50( 8.0)	9/50( 18.0)	9/50( 18.0)
Adjusted rates(b)	0.0	9.30	20.93	21.05
Terminal rates(c)	0/33( 0.0)	4/43( 9.3)	9/43( 20.9)	8/38( 21.1)
Statistical analysis				
Peto test				
Standard method(d)	P = -----			
Prevalence method(d)	P = 0.0032**			
Combined analysis(d)	P = -----			
Cochran-Armitage test(e)	P = 0.0056**			
Fisher Exact test(e)		P = 0.0688	P = 0.0029**	P = 0.0029**
SITE : liver TUMOR : hepatocellular carcinoma				
Tumor rate				
Overall rates(a)	0/50( 0.0)	0/50( 0.0)	5/50( 10.0)	5/50( 10.0)
Adjusted rates(b)	0.0	0.0	11.63	10.53
Terminal rates(c)	0/33( 0.0)	0/43( 0.0)	5/43( 11.6)	4/38( 10.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1138			
Prevalence method(d)	P = 0.0158*			
Combined analysis(d)	P = 0.0056**			
Cochran-Armitage test(e)	P = 0.0081**			
Fisher Exact test(e)		P = 0.5000	P = 0.0360*	P = 0.0360*
SITE : liver TUMOR : hepatocellular adenoma,hepatocellular carcinoma				
Tumor rate				
Overall rates(a)	0/50( 0.0)	4/50( 8.0)	13/50( 26.0)	13/50( 26.0)
Adjusted rates(b)	0.0	9.30	30.23	31.58
Terminal rates(c)	0/33( 0.0)	4/43( 9.3)	13/43( 30.2)	12/38( 31.6)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1138			
Prevalence method(d)	P = 0.0003**			
Combined analysis(d)	P = 0.0001**			
Cochran-Armitage test(e)	P = 0.0002**			
Fisher Exact test(e)		P = 0.0688	P = 0.0003**	P = 0.0003**

(HPT360A)

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STUDY No. : 0242  
ANIMAL : RAT F344/DuCrj  
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 4

Group Name	Control	8000 ppm	20000 ppm	50000 ppm
SITE : pancreas TUMOR : islet cell adenoma				
Tumor rate				
Overall rates(a)	3/50( 6.0)	2/50( 4.0)	0/50( 0.0)	2/50( 4.0)
Adjusted rates(b)	8.33	4.65	0.0	4.26
Terminal rates(c)	2/33( 6.1)	2/43( 4.7)	0/43( 0.0)	1/38( 2.6)
Statistical analysis				
Peto test				
Standard method(d)	P = -----			
Prevalence method(d)	P = 0.6405			
Combined analysis(d)	P = -----			
Cochran-Armitage test(e)	P = 0.6779			
Fisher Exact test(e)		P = 0.4909	P = 0.1325	P = 0.4909
SITE : urinary bladder TUMOR : transitional cell carcinoma				
Tumor rate				
Overall rates(a)	0/50( 0.0)	1/50( 2.0)	4/50( 8.0)	3/50( 6.0)
Adjusted rates(b)	0.0	2.33	8.33	7.89
Terminal rates(c)	0/33( 0.0)	1/43( 2.3)	3/43( 7.0)	3/38( 7.9)
Statistical analysis				
Peto test				
Standard method(d)	P = -----			
Prevalence method(d)	P = 0.0552			
Combined analysis(d)	P = -----			
Cochran-Armitage test(e)	P = 0.1193			
Fisher Exact test(e)		P = 0.4950	P = 0.0688	P = 0.1325
SITE : urinary bladder TUMOR : transitional cell papilloma,transitional cell carcinoma				
Tumor rate				
Overall rates(a)	0/50( 0.0)	1/50( 2.0)	6/50( 12.0)	3/50( 6.0)
Adjusted rates(b)	0.0	2.33	12.50	7.89
Terminal rates(c)	0/33( 0.0)	1/43( 2.3)	4/43( 9.3)	3/38( 7.9)
Statistical analysis				
Peto test				
Standard method(d)	P = -----			
Prevalence method(d)	P = 0.0689			
Combined analysis(d)	P = -----			
Cochran-Armitage test(e)	P = 0.1563			
Fisher Exact test(e)		P = 0.4950	P = 0.0190*	P = 0.1325

STUDY No. : 0242  
 ANIMAL : RAT F344/DuCrj  
 SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 5

Group Name	Control	8000 ppm	20000 ppm	50000 ppm
SITE : pituitary gland TUMOR : adenoma				
Tumor rate				
Overall rates(a)	15/49( 30.6)	10/50( 20.0)	10/50( 20.0)	10/50( 20.0)
Adjusted rates(b)	21.88	18.60	20.00	21.05
Terminal rates(c)	7/32( 21.9)	8/43( 18.6)	8/43( 18.6)	8/38( 21.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.9390			
Prevalence method(d)	P = 0.5542			
Combined analysis(d)	P = 0.8294			
Cochran-Armitage test(e)	P = 0.3632			
Fisher Exact test(e)		P = 0.2377	P = 0.2377	P = 0.2377
SITE : thyroid TUMOR : C-cell adenoma				
Tumor rate				
Overall rates(a)	3/50( 6.0)	5/50( 10.0)	5/50( 10.0)	2/50( 4.0)
Adjusted rates(b)	7.50	11.63	11.63	5.00
Terminal rates(c)	1/33( 3.0)	5/43( 11.6)	5/43( 11.6)	1/38( 2.6)
Statistical analysis				
Peto test				
Standard method(d)	P = -----			
Prevalence method(d)	P = 0.7529			
Combined analysis(d)	P = -----			
Cochran-Armitage test(e)	P = 0.4581			
Fisher Exact test(e)		P = 0.3790	P = 0.3790	P = 0.4909
SITE : thyroid TUMOR : follicular adenocarcinoma				
Tumor rate				
Overall rates(a)	4/50( 8.0)	3/50( 6.0)	1/50( 2.0)	5/50( 10.0)
Adjusted rates(b)	12.12	6.98	2.33	13.16
Terminal rates(c)	4/33( 12.1)	3/43( 7.0)	1/43( 2.3)	5/38( 13.2)
Statistical analysis				
Peto test				
Standard method(d)	P = -----			
Prevalence method(d)	P = 0.2775			
Combined analysis(d)	P = -----			
Cochran-Armitage test(e)	P = 0.5408			
Fisher Exact test(e)		P = 0.4895	P = 0.1998	P = 0.4883

STUDY No. : 0242  
ANIMAL : RAT F344/DuCrj  
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 6

Group Name	Control	8000 ppm	20000 ppm	50000 ppm
SITE : thyroid TUMOR : C-cell adenoma,C-cell carcinoma				
Tumor rate				
Overall rates(a)	3/50( 6.0)	7/50( 14.0)	6/50( 12.0)	2/50( 4.0)
Adjusted rates(b)	7.50	16.28	13.85	5.00
Terminal rates(c)	1/33( 3.0)	7/43( 16.3)	6/43( 14.0)	1/38( 2.6)
Statistical analysis				
Peto test				
Standard method(d)	P = -----			
Prevalence method(d)	P = 0.8244			
Combined analysis(d)	P = -----			
Cochran-Armitage test(e)	P = 0.3292			
Fisher Exact test(e)		P = 0.1917	P = 0.2728	P = 0.4909
SITE : thyroid TUMOR : follicular adenoma,follicular adenocarcinoma				
Tumor rate				
Overall rates(a)	4/50( 8.0)	3/50( 6.0)	1/50( 2.0)	6/50( 12.0)
Adjusted rates(b)	12.12	6.98	2.33	14.63
Terminal rates(c)	4/33( 12.1)	3/43( 7.0)	1/43( 2.3)	5/38( 13.2)
Statistical analysis				
Peto test				
Standard method(d)	P = -----			
Prevalence method(d)	P = 0.1360			
Combined analysis(d)	P = -----			
Cochran-Armitage test(e)	P = 0.3002			
Fisher Exact test(e)		P = 0.4895	P = 0.1998	P = 0.3944
SITE : adrenal gland TUMOR : pheochromocytoma				
Tumor rate				
Overall rates(a)	6/50( 12.0)	10/50( 20.0)	12/50( 24.0)	3/50( 6.0)
Adjusted rates(b)	16.22	23.26	26.67	7.89
Terminal rates(c)	4/33( 12.1)	10/43( 23.3)	11/43( 25.6)	3/38( 7.9)
Statistical analysis				
Peto test				
Standard method(d)	P = -----			
Prevalence method(d)	P = 0.9270			
Combined analysis(d)	P = -----			
Cochran-Armitage test(e)	P = 0.1665			
Fisher Exact test(e)		P = 0.2557	P = 0.1474	P = 0.2728

STUDY No. : 0242  
ANIMAL : RAT F344/DuCrj  
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 7

Group Name	Control	8000 ppm	20000 ppm	50000 ppm
SITE : adrenal gland TUMOR : pheochromocytoma,pheochromocytoma:malignant				
Tumor rate				
Overall rates(a)	6/50( 12.0)	12/50( 24.0)	14/50( 28.0)	5/50( 10.0)
Adjusted rates(b)	16.22	25.58	28.89	13.16
Terminal rates(c)	4/33( 12.1)	11/43( 25.6)	12/43( 27.9)	5/38( 13.2)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5873			
Prevalence method(d)	P = 0.8030			
Combined analysis(d)	P = 0.8226			
Cochran-Armitage test(e)	P = 0.3599			
Fisher Exact test(e)		P = 0.1474	P = 0.0810	P = 0.4872
SITE : testis TUMOR : interstitial cell tumor				
Tumor rate				
Overall rates(a)	43/50( 86.0)	46/50( 92.0)	47/50( 94.0)	47/50( 94.0)
Adjusted rates(b)	97.14	95.74	97.92	97.44
Terminal rates(c)	32/33( 97.0)	41/43( 95.3)	42/43( 97.7)	37/38( 97.4)
Statistical analysis				
Peto test				
Standard method(d)	P = -----			
Prevalence method(d)	P = 0.0876			
Combined analysis(d)	P = -----			
Cochran-Armitage test(e)	P = 0.2322			
Fisher Exact test(e)		P = 0.4659	P = 0.4362	P = 0.4362
SITE : mammary gland TUMOR : fibroadenoma				
Tumor rate				
Overall rates(a)	2/50( 4.0)	0/50( 0.0)	3/50( 6.0)	2/50( 4.0)
Adjusted rates(b)	6.06	0.0	6.98	4.35
Terminal rates(c)	2/33( 6.1)	0/43( 0.0)	3/43( 7.0)	1/38( 2.6)
Statistical analysis				
Peto test				
Standard method(d)	P = -----			
Prevalence method(d)	P = 0.3144			
Combined analysis(d)	P = -----			
Cochran-Armitage test(e)	P = 0.6340			
Fisher Exact test(e)		P = 0.2574	P = 0.4909	P = 0.3088

STUDY No. : 0242  
ANIMAL : RAT F344/DuCrj  
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 8

Group Name	Control	8000 ppm	20000 ppm	50000 ppm
SITE : mammary gland TUMOR : adenoma,fibroadenoma				
Tumor rate				
Overall rates(a)	2/50( 4.0)	1/50( 2.0)	3/50( 6.0)	3/50( 6.0)
Adjusted rates(b)	6.06	2.33	6.98	6.52
Terminal rates(c)	2/33( 6.1)	1/43( 2.3)	3/43( 7.0)	2/38( 5.3)
Statistical analysis				
Peto test				
Standard method(d)	P = -----			
Prevalence method(d)	P = 0.2273			
Combined analysis(d)	P = -----			
Cochran-Armitage test(e)	P = 0.4453			
Fisher Exact test(e)		P = 0.4926	P = 0.4909	P = 0.4909
SITE : preputial/clitoral gland TUMOR : adenoma				
Tumor rate				
Overall rates(a)	4/50( 8.0)	4/50( 8.0)	2/50( 4.0)	0/50( 0.0)
Adjusted rates(b)	9.09	9.30	4.65	0.0
Terminal rates(c)	3/33( 9.1)	4/43( 9.3)	2/43( 4.7)	0/38( 0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 1.0000 ?			
Prevalence method(d)	P = 0.9836			
Combined analysis(d)	P = 0.9925			
Cochran-Armitage test(e)	P = 0.0356*			
Fisher Exact test(e)		P = 0.3579	P = 0.3574	P = 0.0688

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STUDY No. : 0242  
 ANIMAL : RAT F344/DuCrj  
 SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 9

Group Name	Control	8000 ppm	20000 ppm	50000 ppm
SITE : peritoneum TUMOR : mesothelioma				
Tumor rate				
Overall rates(a)	0/50( 0.0)	3/50( 6.0)	2/50( 4.0)	1/50( 2.0)
Adjusted rates(b)	0.0	4.65	4.65	2.38
Terminal rates(c)	0/33( 0.0)	2/43( 4.7)	2/43( 4.7)	0/38( 0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5618			
Prevalence method(d)	P = 0.3815			
Combined analysis(d)	P = 0.4870			
Cochran-Armitage test(e)	P = 0.9478			
Fisher Exact test(e)		P = 0.1325	P = 0.2574	P = 0.4950

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- (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 N 2

### NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

RAT : FEMALE



STUDY No. : 0242  
ANIMAL : RAT F344/DuCrJ  
SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 10

Group Name	Control	8000 ppm	20000 ppm	50000 ppm
SITE : lung TUMOR : bronchiolar-alveolar adenoma				
Tumor rate				
Overall rates(a)	1/50( 2.0)	0/50( 0.0)	3/50( 6.0)	0/50( 0.0)
Adjusted rates(b)	2.50	0.0	7.50	0.0
Terminal rates(c)	1/40( 2.5)	0/40( 0.0)	3/40( 7.5)	0/37( 0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = -----			
Prevalence method(d)	P = 0.6319			
Combined analysis(d)	P = -----			
Cochran-Armitage test(e)	P = 0.6322			
Fisher Exact test(e)		P = 0.4950	P = 0.3235	P = 0.4950
SITE : spleen TUMOR : mononuclear cell leukemia				
Tumor rate				
Overall rates(a)	6/50( 12.0)	7/50( 14.0)	2/50( 4.0)	6/50( 12.0)
Adjusted rates(b)	7.50	5.00	5.00	8.11
Terminal rates(c)	3/40( 7.5)	2/40( 5.0)	2/40( 5.0)	3/37( 8.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.6283			
Prevalence method(d)	P = 0.3734			
Combined analysis(d)	P = 0.5188			
Cochran-Armitage test(e)	P = 0.8698			
Fisher Exact test(e)		P = 0.4863	P = 0.1606	P = 0.3807
SITE : liver TUMOR : hepatocellular adenoma				
Tumor rate				
Overall rates(a)	1/50( 2.0)	3/50( 6.0)	3/50( 6.0)	2/50( 4.0)
Adjusted rates(b)	2.17	7.50	7.50	5.41
Terminal rates(c)	0/40( 0.0)	3/40( 7.5)	3/40( 7.5)	2/37( 5.4)
Statistical analysis				
Peto test				
Standard method(d)	P = -----			
Prevalence method(d)	P = 0.4239			
Combined analysis(d)	P = -----			
Cochran-Armitage test(e)	P = 0.8787			
Fisher Exact test(e)		P = 0.3235	P = 0.3235	P = 0.4926

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STUDY No. : 0242  
ANIMAL : RAT F344/DuGrj  
SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 11

Group Name	Control	8000 ppm	20000 ppm	50000 ppm
SITE : liver TUMOR : hepatocellular adenoma,hepatocellular carcinoma				
Tumor rate				
Overall rates(a)	1/50( 2.0)	3/50( 6.0)	4/50( 8.0)	2/50( 4.0)
Adjusted rates(b)	2.17	7.50	10.00	5.41
Terminal rates(c)	0/40( 0.0)	3/40( 7.5)	4/40( 10.0)	2/37( 5.4)
Statistical analysis				
Peto test				
Standard method(d)	P = -----			
Prevalence method(d)	P = 0.4204			
Combined analysis(d)	P = -----			
Cochran-Armitage test(e)	P = 0.8778			
Fisher Exact test(e)		P = 0.3235	P = 0.1998	P = 0.4926
SITE : kidney TUMOR : renal cell adenoma				
Tumor rate				
Overall rates(a)	0/50( 0.0)	3/50( 6.0)	6/50( 12.0)	4/50( 8.0)
Adjusted rates(b)	0.0	7.50	14.63	8.89
Terminal rates(c)	0/40( 0.0)	3/40( 7.5)	5/40( 12.5)	3/37( 8.1)
Statistical analysis				
Peto test				
Standard method(d)	P = -----			
Prevalence method(d)	P = 0.0937			
Combined analysis(d)	P = -----			
Cochran-Armitage test(e)	P = 0.1717			
Fisher Exact test(e)		P = 0.1325	P = 0.0190*	P = 0.0688
SITE : kidney TUMOR : renal cell adenoma,renal cell carcinoma				
Tumor rate				
Overall rates(a)	0/50( 0.0)	3/50( 6.0)	6/50( 12.0)	5/50( 10.0)
Adjusted rates(b)	0.0	7.50	14.63	9.09
Terminal rates(c)	0/40( 0.0)	3/40( 7.5)	5/40( 12.5)	3/37( 8.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1225			
Prevalence method(d)	P = 0.0899			
Combined analysis(d)	P = 0.0441*			
Cochran-Armitage test(e)	P = 0.0775			
Fisher Exact test(e)		P = 0.1325	P = 0.0190*	P = 0.0360*

(HPT360A)

BAIS3

STUDY No. : 0242  
ANIMAL : RAT F344/DuCrj  
SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 12

Group Name	Control	8000 ppm	20000 ppm	50000 ppm
SITE : urinary bladder TUMOR : transitional cell carcinoma				
Tumor rate				
Overall rates(a)	0/50( 0.0)	2/50( 4.0)	3/50( 6.0)	2/50( 4.0)
Adjusted rates(b)	0.0	5.00	7.50	5.41
Terminal rates(c)	0/40( 0.0)	2/40( 5.0)	3/40( 7.5)	2/37( 5.4)
Statistical analysis				
Peto test				
Standard method(d)	P = -----			
Prevalence method(d)	P = 0.1871			
Combined analysis(d)	P = -----			
Cochran-Armitage test(e)	P = 0.4236			
Fisher Exact test(e)		P = 0.2574	P = 0.1325	P = 0.2574
SITE : pituitary gland TUMOR : adenoma				
Tumor rate				
Overall rates(a)	11/50( 22.0)	12/50( 24.0)	16/50( 32.0)	11/50( 22.0)
Adjusted rates(b)	22.50	26.19	32.50	21.43
Terminal rates(c)	9/40( 22.5)	9/40( 22.5)	13/40( 32.5)	6/37( 16.2)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3824			
Prevalence method(d)	P = 0.5781			
Combined analysis(d)	P = 0.5235			
Cochran-Armitage test(e)	P = 0.9383			
Fisher Exact test(e)		P = 0.4826	P = 0.2625	P = 0.4072
SITE : pituitary gland TUMOR : adenoma,adenocarcinoma				
Tumor rate				
Overall rates(a)	11/50( 22.0)	12/50( 24.0)	17/50( 34.0)	11/50( 22.0)
Adjusted rates(b)	22.50	26.19	32.50	21.43
Terminal rates(c)	9/40( 22.5)	9/40( 22.5)	13/40( 32.5)	6/37( 16.2)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3869			
Prevalence method(d)	P = 0.5771			
Combined analysis(d)	P = 0.5214			
Cochran-Armitage test(e)	P = 0.9421			
Fisher Exact test(e)		P = 0.4826	P = 0.2154	P = 0.4072

STUDY No. : 0242  
ANIMAL : RAT F344/DuCrj  
SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 13

Group Name	Control	8000 ppm	20000 ppm	50000 ppm
SITE : thyroid TUMOR : C-cell adenoma				
Tumor rate				
Overall rates(a)	5/50( 10.0)	2/50( 4.0)	5/50( 10.0)	1/49( 2.0)
Adjusted rates(b)	10.42	5.00	10.00	2.70
Terminal rates(c)	4/40( 10.0)	2/40( 5.0)	4/40( 10.0)	1/37( 2.7)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3825			
Prevalence method(d)	P = 0.9078			
Combined analysis(d)	P = 0.8951			
Cochran-Armitage test(e)	P = 0.1947			
Fisher Exact test(e)		P = 0.2425	P = 0.3710	P = 0.1261
SITE : adrenal gland TUMOR : pheochromocytoma				
Tumor rate				
Overall rates(a)	0/50( 0.0)	3/50( 6.0)	2/50( 4.0)	3/50( 6.0)
Adjusted rates(b)	0.0	7.50	4.55	8.11
Terminal rates(c)	0/40( 0.0)	3/40( 7.5)	1/40( 2.5)	3/37( 8.1)
Statistical analysis				
Peto test				
Standard method(d)	P = -----			
Prevalence method(d)	P = 0.1426			
Combined analysis(d)	P = -----			
Cochran-Armitage test(e)	P = 0.2705			
Fisher Exact test(e)		P = 0.1325	P = 0.2574	P = 0.1325
SITE : adrenal gland TUMOR : pheochromocytoma,pheochromocytoma:malignant				
Tumor rate				
Overall rates(a)	1/50( 2.0)	3/50( 6.0)	2/50( 4.0)	4/50( 8.0)
Adjusted rates(b)	0.0	7.50	4.55	10.81
Terminal rates(c)	0/40( 0.0)	3/40( 7.5)	1/40( 2.5)	4/37( 10.8)
Statistical analysis				
Peto test				
Standard method(d)	P = 1.0000 ?			
Prevalence method(d)	P = 0.0640			
Combined analysis(d)	P = 0.1268			
Cochran-Armitage test(e)	P = 0.2385			
Fisher Exact test(e)		P = 0.3235	P = 0.4926	P = 0.1998

STUDY No. : 0242  
ANIMAL : RAT F344/DuCrj  
SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 14

Group Name	Control	8000 ppm	20000 ppm	50000 ppm
SITE : uterus TUMOR : endometrial stromal polyp				
Tumor rate				
Overall rates(a)	4/50( 8.0)	9/50( 18.0)	8/50( 16.0)	5/50( 10.0)
Adjusted rates(b)	9.30	20.00	17.07	13.51
Terminal rates(c)	3/40( 7.5)	8/40( 20.0)	6/40( 15.0)	5/37( 13.5)
Statistical analysis				
Peto test				
Standard method(d)	P = -----			
Prevalence method(d)	P = 0.5848			
Combined analysis(d)	P = -----			
Cochran-Armitage test(e)	P = 0.7820			
Fisher Exact test(e)		P = 0.1562	P = 0.2169	P = 0.4883
SITE : uterus TUMOR : endometrial stromal sarcoma				
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	2.63
Terminal rates(c)	0/40( 0.0)	0/40( 0.0)	0/40( 0.0)	0/37( 0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.0164* ?			
Prevalence method(d)	P = 0.1137			
Combined analysis(d)	P = 0.0032**?			
Cochran-Armitage test(e)	P = 0.0051**			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.1325
SITE : mammary gland TUMOR : fibroadenoma				
Tumor rate				
Overall rates(a)	3/50( 6.0)	2/50( 4.0)	3/50( 6.0)	9/50( 18.0)
Adjusted rates(b)	7.50	5.00	7.50	17.07
Terminal rates(c)	3/40( 7.5)	2/40( 5.0)	3/40( 7.5)	6/37( 16.2)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.0172* ?			
Prevalence method(d)	P = 0.0299*			
Combined analysis(d)	P = 0.0057**			
Cochran-Armitage test(e)	P = 0.0094**			
Fisher Exact test(e)		P = 0.4909	P = 0.3392	P = 0.0899

STUDY No. : 0242  
ANIMAL : RAT F344/DuCrJ  
SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 15

Group Name	Control	8000 ppm	20000 ppm	50000 ppm
SITE : mammary gland TUMOR : adenoma,fibroadenoma				
Tumor rate				
Overall rates(a)	3/50( 6.0)	4/50( 8.0)	3/50( 6.0)	10/50( 20.0)
Adjusted rates(b)	7.50	7.50	7.50	18.60
Terminal rates(c)	3/40( 7.5)	3/40( 7.5)	3/40( 7.5)	6/37( 16.2)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.0822			
Prevalence method(d)	P = 0.0221*			
Combined analysis(d)	P = 0.0077**			
Cochran-Armitage test(e)	P = 0.0122*			
Fisher Exact test(e)		P = 0.4895	P = 0.3392	P = 0.0604
SITE : mammary gland TUMOR : adenoma,fibroadenoma,adenocarcinoma				
Tumor rate				
Overall rates(a)	3/50( 6.0)	4/50( 8.0)	5/50( 10.0)	10/50( 20.0)
Adjusted rates(b)	7.50	7.50	10.00	18.60
Terminal rates(c)	3/40( 7.5)	3/40( 7.5)	4/40( 10.0)	6/37( 16.2)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1061			
Prevalence method(d)	P = 0.0242*			
Combined analysis(d)	P = 0.0098**			
Cochran-Armitage test(e)	P = 0.0157*			
Fisher Exact test(e)		P = 0.4895	P = 0.3790	P = 0.0604

(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 N 3

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

MOSUE : MALE

STUDY No. : 0243  
ANIMAL : MOUSE Crj:BDF1  
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 1

Group Name	Control	3200 ppm	8000 ppm	20000 ppm
SITE : lung TUMOR : bronchiolar-alveolar adenoma				
Tumor rate				
Overall rates(a)	1/49( 2.0)	3/50( 6.0)	2/50( 4.0)	1/50( 2.0)
Adjusted rates(b)	2.44	7.14	5.41	2.38
Terminal rates(c)	1/41( 2.4)	2/41( 4.9)	2/37( 5.4)	1/42( 2.4)
Statistical analysis				
Peto test				
Standard method(d)	P = -----			
Prevalence method(d)	P = 0.6489			
Combined analysis(d)	P = -----			
Cochran-Armitage test(e)	P = 0.6385			
Fisher Exact test(e)		P = 0.3312	P = 0.4851	P = 0.2426
SITE : lung TUMOR : bronchiolar-alveolar adenoma,bronchiolar-alveolar carcinoma				
Tumor rate				
Overall rates(a)	2/49( 4.1)	4/50( 8.0)	4/50( 8.0)	1/50( 2.0)
Adjusted rates(b)	4.65	9.52	8.11	2.38
Terminal rates(c)	1/41( 2.4)	3/41( 7.3)	3/37( 8.1)	1/42( 2.4)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3941			
Prevalence method(d)	P = 0.8039			
Combined analysis(d)	P = 0.7909			
Cochran-Armitage test(e)	P = 0.3815			
Fisher Exact test(e)		P = 0.3668	P = 0.3668	P = 0.5000
SITE : lymph node TUMOR : malignant lymphoma				
Tumor rate				
Overall rates(a)	2/49( 4.1)	4/50( 8.0)	4/50( 8.0)	3/50( 6.0)
Adjusted rates(b)	4.88	4.88	8.11	4.76
Terminal rates(c)	2/41( 4.9)	2/41( 4.9)	3/37( 8.1)	2/42( 4.8)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.4018			
Prevalence method(d)	P = 0.4925			
Combined analysis(d)	P = 0.4509			
Cochran-Armitage test(e)	P = 0.9131			
Fisher Exact test(e)		P = 0.3668	P = 0.3668	P = 0.4816



STUDY No. : 0243  
 ANIMAL : MOUSE Crj:BDF1  
 SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 2

Group Name	Control	3200 ppm	8000 ppm	20000 ppm
SITE : liver TUMOR : hepatocellular adenoma				
Tumor rate				
Overall rates(a)	4/49( 8.2)	6/50( 12.0)	1/50( 2.0)	5/50( 10.0)
Adjusted rates(b)	9.76	14.63	2.70	11.90
Terminal rates(c)	4/41( 9.8)	6/41( 14.6)	1/37( 2.7)	5/42( 11.9)
Statistical analysis				
Peto test				
Standard method(d)	P = -----			
Prevalence method(d)	P = 0.4730			
Combined analysis(d)	P = -----			
Cochran-Armitage test(e)	P = 0.9515			
Fisher Exact test(e)		P = 0.4066	P = 0.1936	P = 0.4763
SITE : liver TUMOR : histiocytic sarcoma				
Tumor rate				
Overall rates(a)	2/49( 4.1)	4/50( 8.0)	5/50( 10.0)	3/50( 6.0)
Adjusted rates(b)	0.0	2.44	0.0	0.0
Terminal rates(c)	0/41( 0.0)	1/41( 2.4)	0/37( 0.0)	0/42( 0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.4006			
Prevalence method(d)	P = 0.5459			
Combined analysis(d)	P = 0.4660			
Cochran-Armitage test(e)	P = 0.9113			
Fisher Exact test(e)		P = 0.3668	P = 0.2510	P = 0.4816
SITE : liver TUMOR : hepatocellular carcinoma				
Tumor rate				
Overall rates(a)	1/49( 2.0)	3/50( 6.0)	0/50( 0.0)	0/50( 0.0)
Adjusted rates(b)	2.44	4.88	0.0	0.0
Terminal rates(c)	1/41( 2.4)	2/41( 4.9)	0/37( 0.0)	0/42( 0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5565			
Prevalence method(d)	P = 0.9107			
Combined analysis(d)	P = 0.9354			
Cochran-Armitage test(e)	P = 0.1480			
Fisher Exact test(e)		P = 0.3312	P = 0.5000	P = 0.5000

(HPT360A)

BAIS3

STUDY No. : 0243  
ANIMAL : MOUSE Crj:BDF1  
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 3

Group Name	Control	3200 ppm	8000 ppm	20000 ppm
SITE : liver TUMOR : hepatocellular adenoma,hepatocellular carcinoma				
Tumor rate				
Overall rates(a)	5/49( 10.2)	9/50( 18.0)	1/50( 2.0)	5/50( 10.0)
Adjusted rates(b)	12.20	19.51	2.70	11.90
Terminal rates(c)	5/41( 12.2)	8/41( 19.5)	1/37( 2.7)	5/42( 11.9)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5565			
Prevalence method(d)	P = 0.6847			
Combined analysis(d)	P = 0.7323			
Cochran-Armitage test(e)	P = 0.5351			
Fisher Exact test(e)		P = 0.2494	P = 0.1163	P = 0.3592
SITE : Harderian gland TUMOR : adenoma				
Tumor rate				
Overall rates(a)	0/49( 0.0)	1/50( 2.0)	2/50( 4.0)	3/50( 6.0)
Adjusted rates(b)	0.0	2.44	5.41	7.14
Terminal rates(c)	0/41( 0.0)	1/41( 2.4)	2/37( 5.4)	3/42( 7.1)
Statistical analysis				
Peto test				
Standard method(d)	P = -----			
Prevalence method(d)	P = 0.0517			
Combined analysis(d)	P = -----			
Cochran-Armitage test(e)	P = 0.0792			
Fisher Exact test(e)		P = 0.4900	P = 0.2626	P = 0.1364

(IPT360A)

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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

STUDY No. : 0243  
ANIMAL : MOUSE Crj:BDF1  
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 1

Group Name	Control	3200 ppm	8000 ppm	20000 ppm
SITE : ALL SITE TUMOR : histiocytic sarcoma				
Tumor rate				
Overall rates(a)	5/49( 10.2)	7/50( 14.0)	7/50( 14.0)	7/50( 14.0)
Adjusted rates(b)	7.32	9.78	2.70	4.76
Terminal rates(c)	3/41( 7.3)	4/41( 9.8)	1/37( 2.7)	2/42( 4.8)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1637			
Prevalence method(d)	P = 0.7660			
Combined analysis(d)	P = 0.3667			
Cochran-Armitage test(e)	P = 0.6864			
Fisher Exact test(e)		P = 0.4195	P = 0.4195	P = 0.4195
SITE : ALL SITE TUMOR : malignant lymphoma				
Tumor rate				
Overall rates(a)	3/49( 6.1)	6/50( 12.0)	4/50( 8.0)	5/50( 10.0)
Adjusted rates(b)	7.32	9.76	8.11	9.52
Terminal rates(c)	3/41( 7.3)	4/41( 9.8)	3/37( 8.1)	4/42( 9.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.4018			
Prevalence method(d)	P = 0.3970			
Combined analysis(d)	P = 0.3735			
Cochran-Armitage test(e)	P = 0.7426			
Fisher Exact test(e)		P = 0.2829	P = 0.4788	P = 0.3899

(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 N 4

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

MOSUE :FEMALE

STUDY No. : 0243  
 ANIMAL : MOUSE Crj:BDF1  
 SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 4

Group Name	Control	8000 ppm	20000 ppm	50000 ppm
SITE : lung TUMOR : bronchiolar-alveolar adenoma				
Tumor rate				
Overall rates(a)	1/50( 2.0)	2/50( 4.0)	4/50( 8.0)	0/50( 0.0)
Adjusted rates(b)	2.86	6.25	10.53	0.0
Terminal rates(c)	1/35( 2.9)	1/31( 3.2)	3/34( 8.8)	0/34( 0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = -----			
Prevalence method(d)	P = 0.7895			
Combined analysis(d)	P = -----			
Cochran-Armitage test(e)	P = 0.4120			
Fisher Exact test(e)		P = 0.4926	P = 0.1998	P = 0.4950
SITE : lung TUMOR : bronchiolar-alveolar adenoma,bronchiolar-alveolar carcinoma				
Tumor rate				
Overall rates(a)	3/50( 6.0)	4/50( 8.0)	6/50( 12.0)	1/50( 2.0)
Adjusted rates(b)	8.57	9.38	15.79	0.0
Terminal rates(c)	3/35( 8.6)	2/31( 6.5)	4/34( 11.8)	0/34( 0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.2547			
Prevalence method(d)	P = 0.9307			
Combined analysis(d)	P = 0.8548			
Cochran-Armitage test(e)	P = 0.3002			
Fisher Exact test(e)		P = 0.4895	P = 0.2728	P = 0.3235
SITE : Lymph node TUMOR : malignant lymphoma				
Tumor rate				
Overall rates(a)	11/50( 22.0)	13/50( 26.0)	7/50( 14.0)	7/50( 14.0)
Adjusted rates(b)	20.00	16.13	8.82	5.88
Terminal rates(c)	7/35( 20.0)	5/31( 16.1)	3/34( 8.8)	2/34( 5.9)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5802			
Prevalence method(d)	P = 0.9690			
Combined analysis(d)	P = 0.9127			
Cochran-Armitage test(e)	P = 0.1630			
Fisher Exact test(e)		P = 0.4450	P = 0.2711	P = 0.2711

STUDY No. : 0243  
ANIMAL : MOUSE Crj:BDF1  
SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 5

Group Name	Control	8000 ppm	20000 ppm	50000 ppm
SITE : spleen TUMOR : malignant Lymphoma				
Tumor rate				
Overall rates(a)	4/50( 8.0)	1/50( 2.0)	4/50( 8.0)	0/49( 0.0)
Adjusted rates(b)	11.43	3.23	8.82	0.0
Terminal rates(c)	4/35( 11.4)	1/31( 3.2)	3/34( 8.8)	0/33( 0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3828			
Prevalence method(d)	P = 0.9606			
Combined analysis(d)	P = 0.9471			
Cochran-Armitage test(e)	P = 0.1204			
Fisher Exact test(e)		P = 0.1998	P = 0.3579	P = 0.0715
SITE : liver TUMOR : hepatocellular adenoma				
Tumor rate				
Overall rates(a)	2/50( 4.0)	3/50( 6.0)	6/50( 12.0)	20/50( 40.0)
Adjusted rates(b)	5.71	9.68	15.79	58.82
Terminal rates(c)	2/35( 5.7)	3/31( 9.7)	5/34( 14.7)	20/34( 58.8)
Statistical analysis				
Peto test				
Standard method(d)	P = -----			
Prevalence method(d)	P < 0.0001**			
Combined analysis(d)	P = -----			
Cochran-Armitage test(e)	P < 0.0001**			
Fisher Exact test(e)		P = 0.4909	P = 0.1606	P = 0.0003**
SITE : liver TUMOR : histiocytic sarcoma				
Tumor rate				
Overall rates(a)	0/50( 0.0)	3/50( 6.0)	4/50( 8.0)	3/50( 6.0)
Adjusted rates(b)	0.0	0.0	2.56	0.0
Terminal rates(c)	0/35( 0.0)	0/31( 0.0)	0/34( 0.0)	0/34( 0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1645			
Prevalence method(d)	P = 0.4029			
Combined analysis(d)	P = 0.1764			
Cochran-Armitage test(e)	P = 0.3135			
Fisher Exact test(e)		P = 0.1325	P = 0.0688	P = 0.1325

(HPT360A)

BAIS3

STUDY No. : 0243  
 ANIMAL : MOUSE Grj:BDF1  
 SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 6

Group Name	Control	8000 ppm	20000 ppm	50000 ppm
SITE : Liver TUMOR : hemangiosarcoma				
Tumor rate				
Overall rates(a)	3/50( 6.0)	1/50( 2.0)	1/50( 2.0)	1/50( 2.0)
Adjusted rates(b)	5.71	3.23	0.0	2.94
Terminal rates(c)	2/35( 5.7)	1/31( 3.2)	0/34( 0.0)	1/34( 2.9)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.7236			
Prevalence method(d)	P = 0.6784			
Combined analysis(d)	P = 0.7963			
Cochran-Armitage test(e)	P = 0.3947			
Fisher Exact test(e)		P = 0.3235	P = 0.3235	P = 0.3235
SITE : Liver TUMOR : hepatocellular carcinoma				
Tumor rate				
Overall rates(a)	0/50( 0.0)	2/50( 4.0)	5/50( 10.0)	12/50( 24.0)
Adjusted rates(b)	0.0	6.45	8.82	29.41
Terminal rates(c)	0/35( 0.0)	2/31( 6.5)	3/34( 8.8)	10/34( 29.4)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1852			
Prevalence method(d)	P < 0.0001**			
Combined analysis(d)	P < 0.0001**			
Cochran-Armitage test(e)	P < 0.0001**			
Fisher Exact test(e)		P = 0.2574	P = 0.0360*	P = 0.0005**
SITE : Liver TUMOR : hepatocellular adenoma,hepatocellular carcinoma				
Tumor rate				
Overall rates(a)	2/50( 4.0)	5/50( 10.0)	11/50( 22.0)	26/50( 52.0)
Adjusted rates(b)	5.71	16.13	25.00	70.59
Terminal rates(c)	2/35( 5.7)	5/31( 16.1)	8/34( 23.5)	24/34( 70.6)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1852			
Prevalence method(d)	P < 0.0001**?			
Combined analysis(d)	P < 0.0001**?			
Cochran-Armitage test(e)	P < 0.0001**			
Fisher Exact test(e)		P = 0.2425	P = 0.0170*	P < 0.0001**

(HPT360A)

BAIS3

STUDY No. : 0243  
ANIMAL : MOUSE Crj:BDF1  
SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 7

Group Name	Control	8000 ppm	20000 ppm	50000 ppm
SITE : uterus TUMOR : histiocytic sarcoma				
Tumor rate				
Overall rates(a)	6/50( 12.0)	12/50( 24.0)	7/50( 14.0)	7/50( 14.0)
Adjusted rates(b)	2.86	19.35	5.88	11.63
Terminal rates(c)	1/35( 2.9)	6/31( 19.4)	2/34( 5.9)	3/34( 8.8)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8854			
Prevalence method(d)	P = 0.2838			
Combined analysis(d)	P = 0.6873			
Cochran-Armitage test(e)	P = 0.6996			
Fisher Exact test(e)		P = 0.1474	P = 0.4863	P = 0.4863
SITE : Harderian gland TUMOR : adenoma				
Tumor rate				
Overall rates(a)	1/50( 2.0)	2/50( 4.0)	3/50( 6.0)	3/50( 6.0)
Adjusted rates(b)	2.86	5.13	7.32	8.33
Terminal rates(c)	1/35( 2.9)	1/31( 3.2)	2/34( 5.9)	2/34( 5.9)
Statistical analysis				
Peto test				
Standard method(d)	P = -----			
Prevalence method(d)	P = 0.1766			
Combined analysis(d)	P = -----			
Cochran-Armitage test(e)	P = 0.3645			
Fisher Exact test(e)		P = 0.4926	P = 0.3235	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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$



STUDY No. : 0243  
ANIMAL : MOUSE Crj:BDF1  
SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 2

Group Name	Control	8000 ppm	20000 ppm	50000 ppm
SITE : ALL SITE TUMOR : histiocytic sarcoma				
Tumor rate				
Overall rates(a)	6/50( 12.0)	18/50( 36.0)	11/50( 22.0)	11/50( 22.0)
Adjusted rates(b)	2.86	25.81	7.69	14.63
Terminal rates(c)	1/35( 2.9)	8/31( 25.8)	2/34( 5.9)	4/34( 11.8)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.6823			
Prevalence method(d)	P = 0.2553			
Combined analysis(d)	P = 0.4854			
Cochran-Armitage test(e)	P = 0.8805			
Fisher Exact test(e)		P = 0.0222*	P = 0.1955	P = 0.1955
SITE : ALL SITE TUMOR : malignant lymphoma				
Tumor rate				
Overall rates(a)	15/50( 30.0)	14/50( 28.0)	11/50( 22.0)	7/50( 14.0)
Adjusted rates(b)	31.43	19.35	17.65	5.88
Terminal rates(c)	11/35( 31.4)	6/31( 19.4)	6/34( 17.6)	2/34( 5.9)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5762			
Prevalence method(d)	P = 0.9965			
Combined analysis(d)	P = 0.9770			
Cochran-Armitage test(e)	P = 0.0395*			
Fisher Exact test(e)		P = 0.4810	P = 0.3167	P = 0.0941

(HPT360A)

BAISS

- (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 1

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR (2-YEAR STUDY: SUMMARY)

RAT: MALE : ALL ANIMALS

STUDY NO. : 0242  
 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1  
 SEX : MALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 1

Group Name		Control	8000 ppm	20000 ppm	50000 ppm
No. of Animals on Study		50	50	50	50
Organ	Findings				
[Respiratory system]					
nasal cavit	leukemic cell infiltration	<50> 1	<50> 0	<50> 0	<50> 0
	metastasis:pancreas tumor	0	0	0	1
lung	leukemic cell infiltration	<50> 4	<50> 1	<50> 1	<50> 0
	metastasis:thyroid tumor	1	1	0	0
	metastasis:pancreas tumor	0	0	0	1
	metastasis:bone tumor	0	0	1	1
	metastasis:preputial/clitoral gland tumor	1	0	0	0
[Hematopoietic system]					
bone marrow	leukemic cell infiltration	<50> 4	<50> 1	<50> 1	<50> 1
lymph node	leukemic cell infiltration	<50> 3	<50> 0	<50> 0	<50> 0
[Circulatory system]					
heart	leukemic cell infiltration	<50> 1	<50> 0	<50> 0	<50> 1
	metastasis:thyroid tumor	1	0	0	0
[Digestive system]					
salivary gl	leukemic cell infiltration	<50> 1	<50> 0	<50> 0	<50> 0
< a >	a : Number of animals examined at the site				
b	b : Number of animals with lesion				

STUDY NO. : 0242  
 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1  
 SEX : MALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 2

Organ	Findings	Group Name No. of Animals on Study	Control 50	8000 ppm 50	20000 ppm 50	50000 ppm 50
[Digestive system]						
stomach			<50>	<50>	<50>	<50>
	leukemic cell infiltration		1	0	0	0
small intes			<50>	<50>	<50>	<50>
	leukemic cell infiltration		1	0	0	0
large intes			<50>	<50>	<50>	<50>
	leukemic cell infiltration		1	0	0	0
liver			<50>	<50>	<50>	<50>
	leukemic cell infiltration		5	1	1	1
pancreas			<50>	<50>	<50>	<50>
	leukemic cell infiltration		2	0	0	0
[Urinary system]						
kidney			<50>	<50>	<50>	<50>
	leukemic cell infiltration		3	1	1	0
	metastasis:pancreas tumor		0	0	0	1
urin bladd			<50>	<50>	<50>	<50>
	leukemic cell infiltration		1	0	0	0
[Endocrine system]						
pituitary			<49>	<50>	<50>	<50>
	leukemic cell infiltration		1	0	0	0
	metastasis:pancreas tumor		0	0	0	1
thyroid			<50>	<50>	<50>	<50>
	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. : 0242  
 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1  
 SEX : MALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 3

Organ	Findings	Group Name No. of Animals on Study	Control 50	8000 ppm 50	20000 ppm 50	50000 ppm 50
[Endocrine system]						
adrenal	leukemic cell infiltration		<50> 2	<50> 1	<50> 1	<50> 1
	metastasis:pancreas tumor		0	0	0	1
[Reproductive system]						
prostate	leukemic cell infiltration		<50> 1	<50> 0	<50> 0	<50> 0
[Nervous system]						
brain	leukemic cell infiltration		<50> 2	<50> 1	<50> 1	<50> 0
[Musculoskeletal system]						
muscle	leukemic cell infiltration		<50> 0	<50> 1	<50> 0	<50> 0
	metastasis:pancreas tumor		0	0	0	1
[Body cavities]						
pleura	metastasis:bone tumor		<50> 0	<50> 0	<50> 0	<50> 1
retroperit	metastasis:preputial/clitoral gland tumor		<50> 1	<50> 0	<50> 0	<50> 0

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

## APPENDIX O 2

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR (2-YEAR STUDY: SUMMARY)

RAT: FEMALE : ALL ANIMALS

STUDY NO. : 0242  
 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 1

Group Name No. of Animals on Study		Control 50	8000 ppm 50	20000 ppm 50	50000 ppm 50
Organ	Findings				
[Respiratory system]					
nasal cavit		<50>	<50>	<50>	<50>
	leukemic cell infiltration	0	0	0	1
lung		<50>	<50>	<50>	<50>
	leukemic cell infiltration	4	6	1	4
	metastasis:bone tumor	0	0	1	0
	metastasis:mammary gland tumor	0	0	1	0
	metastasis:mediastinum tumor	1	0	0	0
[Hematopoietic system]					
bone marrow		<50>	<50>	<50>	<50>
	leukemic cell infiltration	0	3	0	3
lymph node		<50>	<50>	<50>	<50>
	leukemic cell infiltration	3	0	0	3
	metastasis:uterus tumor	0	0	0	1
[Circulatory system]					
heart		<50>	<50>	<50>	<50>
	leukemic cell infiltration	0	1	0	1
	metastasis:mediastinum tumor	1	0	0	0
[Digestive system]					
tongue		<50>	<50>	<50>	<50>
	metastasis:subcutis tumor	0	1	0	0

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

STUDY NO. : 0242  
 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 2

Organ	Findings	Group Name No. of Animals on Study	Control 50	8000 ppm 50	20000 ppm 50	50000 ppm 50
[Digestive system]						
salivary gl	leukemic cell infiltration		<50> 1	<50> 0	<50> 0	<50> 0
stomach	leukemic cell infiltration		<50> 1	<50> 0	<50> 0	<50> 0
	metastasis:uterus tumor		0	0	1	0
small intes	leukemic cell infiltration		<50> 1	<50> 0	<50> 0	<50> 0
large intes	leukemic cell infiltration		<50> 1	<50> 0	<50> 0	<50> 0
liver	leukemic cell infiltration		<50> 5	<50> 7	<50> 1	<50> 6
	metastasis:uterus tumor		0	0	1	1
pancreas	leukemic cell infiltration		<50> 2	<50> 0	<50> 0	<50> 1
[Urinary system]						
kidney	leukemic cell infiltration		<50> 1	<50> 3	<50> 2	<50> 3
	metastasis:mediastinum tumor		1	0	0	0
[Endocrine system]						
pituitary	leukemic cell infiltration		<50> 1	<50> 0	<50> 0	<50> 1

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



STUDY NO. : 0242  
 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 3

Organ	Findings	Group Name No. of Animals on Study	Control 50	8000 ppm 50	20000 ppm 50	50000 ppm 50
[Endocrine system]						
adrenal	leukemic cell infiltration		<50> 3	<50> 3	<50> 1	<50> 3
[Reproductive system]						
ovary	leukemic cell infiltration		<50> 0	<50> 2	<50> 0	<50> 0
[Nervous system]						
brain	leukemic cell infiltration		<50> 1	<50> 3	<50> 0	<50> 2
	metastasis:pituitary tumor		0	0	1	0
spinal cord	leukemic cell infiltration		<50> 0	<50> 3	<50> 0	<50> 1
[Musculoskeletal system]						
muscle	leukemic cell infiltration		<50> 1	<50> 0	<50> 0	<50> 1
[Body cavities]						
pleura	metastasis:mediastinum tumor		<50> 1	<50> 0	<50> 0	<50> 0
peritoneum	metastasis:uterus tumor		<50> 0	<50> 0	<50> 0	<50> 1
retroperit	metastasis:uterus tumor		<50> 0	<50> 0	<50> 1	<50> 0

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

## APPENDIX O 3

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR (2-YEAR STUDY: SUMMARY)

RAT: MALE : SACRIFICED ANIMALS

STUDY NO. : 0242  
 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 1

Group Name No. of Animals on Study		Control 40	8000 ppm 40	20000 ppm 40	50000 ppm 37
Organ	Findings				
[Respiratory system]					
lung	leukemic cell infiltration	<40> 2	<40> 1	<40> 1	<37> 2
[Hematopoietic system]					
bone marrow	leukemic cell infiltration	<40> 0	<40> 0	<40> 0	<37> 1
lymph node	leukemic cell infiltration	<40> 1	<40> 0	<40> 0	<37> 1
[Digestive system]					
salivary gl	leukemic cell infiltration	<40> 1	<40> 0	<40> 0	<37> 0
stomach	leukemic cell infiltration	<40> 1	<40> 0	<40> 0	<37> 0
small intes	leukemic cell infiltration	<40> 1	<40> 0	<40> 0	<37> 0
large intes	leukemic cell infiltration	<40> 1	<40> 0	<40> 0	<37> 0
liver	leukemic cell infiltration	<40> 3	<40> 2	<40> 1	<37> 3
pancreas	leukemic cell infiltration	<40> 1	<40> 0	<40> 0	<37> 0
[Urinary system]					
kidney	leukemic cell infiltration	<40> 0	<40> 0	<40> 2	<37> 0

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

STUDY NO. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 2

		Group Name	Control	8000 ppm	20000 ppm	50000 ppm
		No. of Animals on Study	40	40	40	37
Organ	Findings					
[Endocrine system]						
pituitary			<40>	<40>	<40>	<37>
	leukemic cell infiltration		1	0	0	0
adrenal			<40>	<40>	<40>	<37>
	leukemic cell infiltration		1	0	1	1
[Nervous system]						
brain			<40>	<40>	<40>	<37>
	leukemic cell infiltration		1	0	0	0
< a >	a : Number of animals examined at the site					
b	b : Number of animals with lesion					

(JPT150)

BAIS3

## APPENDIX O 4

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR (2-YEAR STUDY: SUMMARY)

RAT: FEMALE : SACRIFICED ANIMALS

STUDY NO. : 0242  
 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 1

Group Name		Control	8000 ppm	20000 ppm	50000 ppm
No. of Animals on Study		33	43	43	38
Organ	Findings				
[Respiratory system]					
nasal cavit		<33>	<43>	<43>	<38>
	metastasis:pancreas tumor	0	0	0	1
lung		<33>	<43>	<43>	<38>
	metastasis:thyroid tumor	1	1	0	0
	metastasis:pancreas tumor	0	0	0	1
[Hematopoietic system]					
bone marrow		<33>	<43>	<43>	<38>
	leukemic cell infiltration	0	0	0	1
[Circulatory system]					
heart		<33>	<43>	<43>	<38>
	leukemic cell infiltration	0	0	0	1
	metastasis:thyroid tumor	1	0	0	0
[Digestive system]					
liver		<33>	<43>	<43>	<38>
	leukemic cell infiltration	0	0	0	1
[Urinary system]					
kidney		<33>	<43>	<43>	<38>
	metastasis:pancreas tumor	0	0	0	1
[Endocrine system]					
pituitary		<32>	<43>	<43>	<38>
	metastasis:pancreas tumor	0	0	0	1

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

STUDY NO. : 0242  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 2

Organ	Findings	Group Name No. of Animals on Study	Control 33	8000 ppm 43	20000 ppm 43	50000 ppm 38
-------	----------	---------------------------------------	---------------	----------------	-----------------	-----------------

[Endocrine system]

adrenal			<33>	<43>	<43>	<38>
	leukemic cell infiltration		0	0	0	1
	metastasis:pancreas tumor		0	0	0	1

[Musculoskeletal system]

muscle			<33>	<43>	<43>	<38>
	metastasis:pancreas tumor		0	0	0	1

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

(JPT150)

BAIS3

## APPENDIX O 5

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR (2-YEAR STUDY: SUMMARY)

MOUSE: MALE : ALL ANIMALS



STUDY NO. : 0243  
 ANIMAL : MOUSE Crj:BDF1  
 REPORT TYPE : A1  
 SEX : MALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 1

Organ	Findings	Group Name No. of Animals on Study	Control 49	3200 ppm 50	8000 ppm 50	20000 ppm 50
[Respiratory system]						
nasal cavit	metastasis:liver tumor		<49> 0	<50> 0	<50> 0	<50> 1
	metastasis:subcutis tumor		0	0	1	0
	metastasis:spleen tumor		0	0	0	1
	metastasis:urinary bladder tumor		0	0	0	1
lung	leukemic cell infiltration		<49> 1	<50> 2	<50> 1	<50> 1
	metastasis:liver tumor		1	1	2	1
	metastasis:spleen tumor		0	0	0	1
	metastasis:urinary bladder tumor		0	0	0	1
[Hematopoietic system]						
bone marrow	leukemic cell infiltration		<49> 0	<50> 1	<50> 0	<50> 0
	metastasis:subcutis tumor		0	0	1	0
lymph node	metastasis:liver tumor		<49> 0	<50> 0	<50> 0	<50> 1
	metastasis:subcutis tumor		0	1	0	0
spleen	leukemic cell infiltration		<49> 2	<50> 3	<50> 2	<50> 2
	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. : 0243  
 ANIMAL : MOUSE Crj:BDF1  
 REPORT TYPE : A1  
 SEX : MALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 2

Organ	Findings	Group Name No. of Animals on Study	Control 49	3200 ppm 50	8000 ppm 50	20000 ppm 50
[Hematopoietic system]						
spleen	metastasis:lympho node tumor		<49> 1	<50> 0	<50> 0	<50> 0
[Circulatory system]						
heart	leukemic cell infiltration		<49> 0	<50> 1	<50> 1	<50> 1
	metastasis:liver tumor		0	1	2	0
[Digestive system]						
tongue	leukemic cell infiltration		<49> 0	<50> 1	<50> 0	<50> 0
salivary gl	leukemic cell infiltration		<49> 0	<50> 1	<50> 1	<50> 0
	metastasis:liver tumor		0	1	1	0
	metastasis:subcutis tumor		0	1	0	0
stomach	leukemic cell infiltration		<49> 0	<50> 0	<50> 1	<50> 0
	metastasis:liver tumor		1	0	1	0
	metastasis:lympho node tumor		1	0	0	0
small intes	metastasis:liver tumor		<49> 1	<50> 0	<50> 0	<50> 0
	metastasis:epididymis tumor		0	0	0	1
< a > b	a : Number of animals examined at the site b : Number of animals with lesion					

STUDY NO. : 0243  
 ANIMAL : MOUSE Crj:BDF1  
 REPORT TYPE : A1  
 SEX : MALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 3

Group Name No. of Animals on Study		Control 49	3200 ppm 50	8000 ppm 50	20000 ppm 50
Organ	Findings				
[Digestive system]					
large intes	metastasis:epididymis tumor	<49> 0	<50> 0	<50> 0	<50> 1
liver	leukemic cell infiltration	<49> 1	<50> 1	<50> 2	<50> 1
	metastasis:subcutis tumor	0	0	1	0
	metastasis:spleen tumor	0	0	0	1
	metastasis:urinary bladder tumor	0	0	0	1
	metastasis:epididymis tumor	0	0	0	1
	metastasis:lympho node tumor	1	0	0	1
pancreas	leukemic cell infiltration	<49> 1	<50> 2	<50> 0	<50> 0
	metastasis:liver tumor	1	0	0	0
	metastasis:urinary bladder tumor	0	0	0	1
[Urinary system]					
kidney	leukemic cell infiltration	<49> 1	<50> 1	<50> 2	<50> 1
	metastasis:liver tumor	1	1	1	2
	metastasis:spleen tumor	0	0	0	1
	metastasis:salivary gland tumor	0	0	0	1
	metastasis:lympho node tumor	1	0	0	0

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

STUDY NO. : 0243  
 ANIMAL : MOUSE Crj:BDF1  
 REPORT TYPE : A1  
 SEX : MALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 4

		Group Name No. of Animals on Study	Control 49	3200 ppm 50	8000 ppm 50	20000 ppm 50
Organ	Findings					
[Urinary system]						
urin bladd	leukemic cell infiltration		<49> 1	<50> 0	<50> 0	<50> 0
	metastasis:epididymis tumor		1	0	0	0
[Endocrine system]						
panc islet	metastasis:lympho node tumor		<49> 1	<50> 0	<50> 0	<50> 0
adrenal	metastasis:spleen tumor		<49> 0	<50> 0	<50> 0	<50> 1
[Reproductive system]						
testis	metastasis:liver tumor		<49> 0	<50> 1	<50> 0	<50> 0
	metastasis:subcutis tumor		0	0	1	0
	metastasis:epididymis tumor		0	0	0	1
	metastasis:salivary gland tumor		0	1	0	0
epididymis	leukemic cell infiltration		<49> 1	<50> 0	<50> 1	<50> 0
	metastasis:subcutis tumor		0	0	1	0
semin ves	leukemic cell infiltration		<49> 0	<50> 1	<50> 1	<50> 0
	metastasis:liver tumor		1	0	0	0
< a >	a : Number of animals examined at the site					
b	b : Number of animals with lesion					

STUDY NO. : 0243  
ANIMAL : MOUSE Crj:BDF1  
REPORT TYPE : A1  
SEX : MALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
ALL ANIMALS (0-105W)

PAGE : 5

Group Name No. of Animals on Study		Control 49	3200 ppm 50	8000 ppm 50	20000 ppm 50
Organ	Findings				
[Reproductive system]					
prostate	leukemic cell infiltration	<49> 0	<50> 0	<50> 1	<50> 0
[Musculoskeletal system]					
muscle	metastasis:liver tumor	<49> 0	<50> 0	<50> 0	<50> 1
[Body cavities]					
mediastinum	metastasis:liver tumor	<49> 0	<50> 0	<50> 1	<50> 0
	metastasis:lung tumor	0	0	1	0
peritoneum	metastasis:liver tumor	<49> 0	<50> 0	<50> 1	<50> 0

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

(JPT150)

BA1S3

## APPENDIX O 6

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR (2-YEAR STUDY : SUMMARY)

MOUSE: FEMALE : ALL ANIMALS

STUDY NO. : 0243  
 ANIMAL : MOUSE Crj:BDF1  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 6

Group Name No. of Animals on Study		Control 50	8000 ppm 50	20000 ppm 50	50000 ppm 50
Organ	Findings				
[Integumentary system/appandage]					
skin/app	leukemic cell infiltration	<50> 0	<50> 0	<50> 0	<50> 3
[Respiratory system]					
nasal cavit	leukemic cell infiltration	<50> 0	<50> 1	<50> 1	<50> 0
	metastasis:liver tumor	0	1	0	0
	metastasis:uterus tumor	0	1	1	0
larynx	metastasis:thyroid tumor	<50> 0	<50> 1	<50> 0	<50> 0
lung	leukemic cell infiltration	<50> 4	<50> 11	<50> 7	<50> 5
	metastasis:liver tumor	0	1	4	2
	metastasis:uterus tumor	3	2	2	0
	metastasis:subcutis tumor	0	1	0	0
	metastasis:bone tumor	1	0	0	0
[Hematopoietic system]					
bone marrow	leukemic cell infiltration	<50> 0	<50> 3	<50> 2	<50> 0
	metastasis:liver tumor	0	0	0	1
	metastasis:uterus tumor	1	0	0	0
< a >	a : Number of animals examined at the site				
b	b : Number of animals with lesion				

STUDY NO. : 0243  
 ANIMAL : MOUSE Crj:BDF1  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 7

Group Name No. of Animals on Study		Control 50	8000 ppm 50	20000 ppm 50	50000 ppm 50
Organ	Findings				
[Hematopoietic system]					
bone marrow		<50>	<50>	<50>	<50>
	metastasis:lympho node tumor	0	0	1	0
lymph node		<50>	<50>	<50>	<50>
	metastasis:liver tumor	0	0	1	0
spleen		<50>	<50>	<50>	<50>
	leukemic cell infiltration	6	9	5	7
	metastasis:liver tumor	0	0	1	2
	metastasis:lympho node tumor	0	0	1	0
[Circulatory system]					
heart		<50>	<50>	<50>	<50>
	leukemic cell infiltration	0	3	2	3
	metastasis:liver tumor	0	1	0	0
[Digestive system]					
tongue		<50>	<50>	<50>	<50>
	leukemic cell infiltration	0	1	0	0
salivary gl		<50>	<50>	<50>	<50>
	leukemic cell infiltration	2	5	3	2
stomach		<50>	<50>	<50>	<50>
	leukemic cell infiltration	2	3	2	1
	metastasis:liver tumor	0	1	0	0
	metastasis:uterus tumor	1	2	2	0
< a >	a : Number of animals examined at the site				
b	b : Number of animals with lesion				



STUDY NO. : 0243  
 ANIMAL : MOUSE Crj:BDF1  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 8

Organ	Findings	Group Name No. of Animals on Study	Control 50	8000 ppm 50	20000 ppm 50	50000 ppm 50
[Digestive system]						
small intes	leukemic cell infiltration		<50> 0	<50> 0	<50> 1	<50> 0
	metastasis:uterus tumor		0	1	0	0
large intes	leukemic cell infiltration		<50> 0	<50> 0	<50> 1	<50> 0
	leukemic cell infiltration		<50> 8	<50> 10	<50> 6	<50> 5
liver	metastasis:uterus tumor		6	6	5	2
	metastasis:subcutis tumor		0	1	0	0
	metastasis:bone tumor		1	0	0	0
	metastasis:lympho node tumor		0	0	1	0
	metastasis:lympho node tumor		0	0	1	0
pancreas	leukemic cell infiltration		<50> 0	<50> 2	<50> 2	<50> 0
	metastasis:uterus tumor		1	0	1	0
[Urinary system]						
kidney	leukemic cell infiltration		<50> 4	<50> 8	<50> 6	<50> 3
	metastasis:liver tumor		0	0	1	1
	metastasis:uterus tumor		1	1	2	0
	metastasis:subcutis tumor		0	1	0	0
< a >	a : Number of animals examined at the site					
b	b : Number of animals with lesion					

STUDY NO. : 0243  
 ANIMAL : MOUSE Crj:BDF1  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 9

Organ	Findings	Group Name No. of Animals on Study	Control 50	8000 ppm 50	20000 ppm 50	50000 ppm 50
[Urinary system]						
kidney	metastasis:stomach tumor		<50> 0	<50> 0	<50> 0	<50> 1
	metastasis:urinary bladder tumor		0	1	0	0
	metastasis:lympho node tumor		0	0	1	0
urin bladd	leukemic cell infiltration		<50> 3	<50> 7	<50> 4	<50> 1
	metastasis:liver tumor		0	1	0	0
	metastasis:subcutis tumor		0	1	0	0
[Endocrine system]						
thyroid	leukemic cell infiltration		<50> 0	<50> 0	<50> 0	<50> 1
adrenal	leukemic cell infiltration		<50> 1	<50> 3	<50> 1	<50> 1
[Reproductive system]						
ovary	leukemic cell infiltration		<50> 4	<50> 10	<50> 2	<50> 4
	metastasis:liver tumor		0	1	1	0
	metastasis:uterus tumor		3	3	5	2
	metastasis:subcutis tumor		0	1	0	0
uterus	leukemic cell infiltration		<50> 1	<50> 5	<50> 2	<50> 0
< a > b	a : Number of animals examined at the site b : Number of animals with lesion					

STUDY NO. : 0243  
 ANIMAL : MOUSE Crj:BDF1  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 10

Group Name No. of Animals on Study		Control 50	8000 ppm 50	20000 ppm 50	50000 ppm 50
Organ	Findings				
[Reproductive system]					
vagina	leukemic cell infiltration	<50> 0	<50> 4	<50> 0	<50> 0
	metastasis:subcutis tumor	0	1	0	1
[Nervous system]					
brain	leukemic cell infiltration	<50> 0	<50> 3	<50> 1	<50> 0
	metastasis:liver tumor	0	1	0	0
periph nerv	metastasis:liver tumor	<50> 0	<50> 1	<50> 0	<50> 0
[Special sense organs/appandage]					
eye	leukemic cell infiltration	<50> 0	<50> 0	<50> 1	<50> 0
Harder gl	leukemic cell infiltration	<50> 0	<50> 1	<50> 1	<50> 1
[Musculoskeletal system]					
muscle	leukemic cell infiltration	<50> 0	<50> 0	<50> 2	<50> 0
[Body cavities]					
mediastinum	metastasis:bone tumor	<50> 1	<50> 0	<50> 0	<50> 0

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

STUDY NO. : 0243  
ANIMAL : MOUSE C-1:BDF1  
REPORT TYPE : A1  
SEX : FEMALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
ALL ANIMALS (0-105W)

PAGE : 11

		Group Name	Control	8000 ppm	20000 ppm	50000 ppm
		No. of Animals on Study	50	50	50	50
Organ	Findings					
[Body cavities]						
mediastinum			<50>	<50>	<50>	<50>
	metastasis:lympho node tumor		0	0	1	0
peritoneum			<50>	<50>	<50>	<50>
	leukemic cell infiltration		4	5	1	2
	metastasis:liver tumor		0	0	1	0
< a >		a : Number of animals examined at the site				
b		b : Number of animals with lesion				

(JPT150)

BAIS3

## APPENDIX O 7

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR (2-YEAR STUDY: SUMMARY)

MOUSE: MALE : SACRIFICED ANIMALS

STUDY NO. : 0243  
 ANIMAL : MOUSE Crj:BDF1  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 1

Organ	Findings	Group Name No. of Animals on Study	Control 41	3200 ppm 41	8000 ppm 37	20000 ppm 42
[Respiratory system]						
nasal cavity			<41>	<41>	<37>	<42>
	metastasis:spleen tumor		0	0	0	1
lung			<41>	<41>	<37>	<42>
	leukemic cell infiltration		1	1	1	0
	metastasis:spleen tumor		0	0	0	1
[Hematopoietic system]						
bone marrow			<41>	<41>	<37>	<42>
	leukemic cell infiltration		0	1	0	0
lymph node			<41>	<41>	<37>	<42>
	metastasis:subcutis tumor		0	1	0	0
spleen			<41>	<41>	<37>	<42>
	leukemic cell infiltration		2	2	2	2
	metastasis:lymph node tumor		1	0	0	0
[Circulatory system]						
heart			<41>	<41>	<37>	<42>
	leukemic cell infiltration		0	1	1	0
	metastasis:liver tumor		0	1	0	0
[Digestive system]						
tongue			<41>	<41>	<37>	<42>
	leukemic cell infiltration		0	1	0	0

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

STUDY NO. : 0243  
ANIMAL : MOUSE Crj:BDF1  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 2

Organ	Findings	Group Name No. of Animals on Study	Control 41	3200 ppm 41	8000 ppm 37	20000 ppm 42
[Digestive system]						
salivary gl			<41>	<41>	<37>	<42>
	leukemic cell infiltration		0	1	1	0
	metastasis:subcutis tumor		0	1	0	0
stomach			<41>	<41>	<37>	<42>
	leukemic cell infiltration		0	0	1	0
	metastasis:lympho node tumor		1	0	0	0
liver			<41>	<41>	<37>	<42>
	leukemic cell infiltration		1	1	1	0
	metastasis:spleen tumor		0	0	0	1
	metastasis:lympho node tumor		1	0	0	0
pancreas			<41>	<41>	<37>	<42>
	leukemic cell infiltration		1	1	0	0
[Urinary system]						
kidney			<41>	<41>	<37>	<42>
	leukemic cell infiltration		1	1	1	0
	metastasis:spleen tumor		0	0	0	1
	metastasis:salivary gland tumor		0	0	0	1
	metastasis:lympho node tumor		1	0	0	0
urin bladd			<41>	<41>	<37>	<42>
	leukemic cell infiltration		1	0	0	0
	metastasis:epididymis tumor		1	0	0	0
< a >	a : Number of animals examined at the site					
b	b : Number of animals with lesion					

STUDY NO. : 0243  
ANIMAL : MOUSE Crj:BDF1  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 3

Group Name No. of Animals on Study		Control 41	3200 ppm 41	8000 ppm 37	20000 ppm 42
Organ	Findings				
[Endocrine system]					
panc islet	metastasis:lympho node tumor	<41> 1	<41> 0	<37> 0	<42> 0
adrenal	metastasis:spleen tumor	<41> 0	<41> 0	<37> 0	<42> 1
[Reproductive system]					
testis	metastasis:salivary gland tumor	<41> 0	<41> 1	<37> 0	<42> 0
epididymis	leukemic cell infiltration	<41> 1	<41> 0	<37> 1	<42> 0
semin ves	leukemic cell infiltration	<41> 0	<41> 1	<37> 1	<42> 0
prostate	leukemic cell infiltration	<41> 0	<41> 0	<37> 1	<42> 0

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

(JPT150)

BAIS3



## APPENDIX O 8

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR (2-YEAR STUDY: SUMMARY)

MOUSE: FEMALE : SACRIFICED ANIMALS

STUDY NO. : 0243  
 ANIMAL : MOUSE Crj:BDF1  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 4

Organ	Findings	Group Name No. of Animals on Study	Control 35	8000 ppm 31	20000 ppm 34	50000 ppm 34
[Respiratory system]						
nasal cavit	metastasis:uterus tumor		<35> 0	<31> 1	<34> 0	<34> 0
lung	leukemic cell infiltration		<35> 1	<31> 6	<34> 3	<34> 0
	metastasis:liver tumor		0	0	1	0
[Hematopoietic system]						
bone marrow	leukemic cell infiltration		<35> 0	<31> 2	<34> 0	<34> 0
	metastasis:lympho node tumor		0	0	1	0
spleen	leukemic cell infiltration		<35> 4	<31> 5	<34> 3	<34> 2
	metastasis:lympho node tumor		0	0	1	0
[Circulatory system]						
heart	leukemic cell infiltration		<35> 0	<31> 1	<34> 1	<34> 0
[Digestive system]						
salivary gl	leukemic cell infiltration		<35> 1	<31> 2	<34> 2	<34> 0
stomach	leukemic cell infiltration		<35> 0	<31> 1	<34> 1	<34> 0
< a > a : Number of animals examined at the site b b : Number of animals with lesion						

STUDY NO. : 0243  
 ANIMAL : MOUSE Crj:BDF1  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 5

Organ	Findings	Group Name No. of Animals on Study	Control 35	8000 ppm 31	20000 ppm 34	50000 ppm 34
[Digestive system]						
stomach	metastasis:uterus tumor		<35> 1	<31> 0	<34> 0	<34> 0
liver	leukemic cell infiltration		<35> 5	<31> 5	<34> 3	<34> 1
	metastasis:uterus tumor		1	2	0	0
	metastasis:lympho node tumor		0	0	1	0
pancreas	leukemic cell infiltration		<35> 0	<31> 1	<34> 1	<34> 0
	metastasis:uterus tumor		1	0	0	0
[Urinary system]						
kidney	leukemic cell infiltration		<35> 3	<31> 5	<34> 3	<34> 1
	metastasis:uterus tumor		0	1	0	0
	metastasis:urinary bladder tumor		0	1	0	0
	metastasis:lympho node tumor		0	0	1	0
urin bladd	leukemic cell infiltration		<35> 2	<31> 4	<34> 3	<34> 0
[Endocrine system]						
adrenal	leukemic cell infiltration		<35> 0	<31> 1	<34> 1	<34> 0
< a > a : Number of animals examined at the site b b : Number of animals with lesion						

STUDY NO. : 0243  
 ANIMAL : MOUSE Crj:BDF1  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 6

Organ	Findings	Group Name No. of Animals on Study	Control 35	8000 ppm 31	20000 ppm 34	50000 ppm 34
[Reproductive system]						
ovary	leukemic cell infiltration		<35> 2	<31> 2	<34> 0	<34> 0
	metastasis:uterus tumor		1	1	0	0
uterus	leukemic cell infiltration		<35> 1	<31> 2	<34> 0	<34> 0
	metastasis:subcutis tumor		0	0	0	1
vagina	leukemic cell infiltration		<35> 0	<31> 2	<34> 0	<34> 0
	metastasis:subcutis tumor		0	0	0	1
[Nervous system]						
brain	leukemic cell infiltration		<35> 0	<31> 1	<34> 0	<34> 0
[Musculoskeletal system]						
muscle	leukemic cell infiltration		<35> 0	<31> 0	<34> 2	<34> 0
[Body cavities]						
mediastinum	metastasis:lympho node tumor		<35> 0	<31> 0	<34> 1	<34> 0
peritoneum	leukemic cell infiltration		<35> 1	<31> 1	<34> 0	<34> 0
< a >	a : Number of animals examined at the site					
b	b : Number of animals with lesion					

(JPT150)

BAIS3

## APPENDIX P 1

### IDENTITY AND IMPURITY OF ANTHRACENE IN THE 2-YEAR FEED STUDIES

## Identity and Impurity of Anthracene in the 2-Year Feed Studies

A.Lot No.507E4208

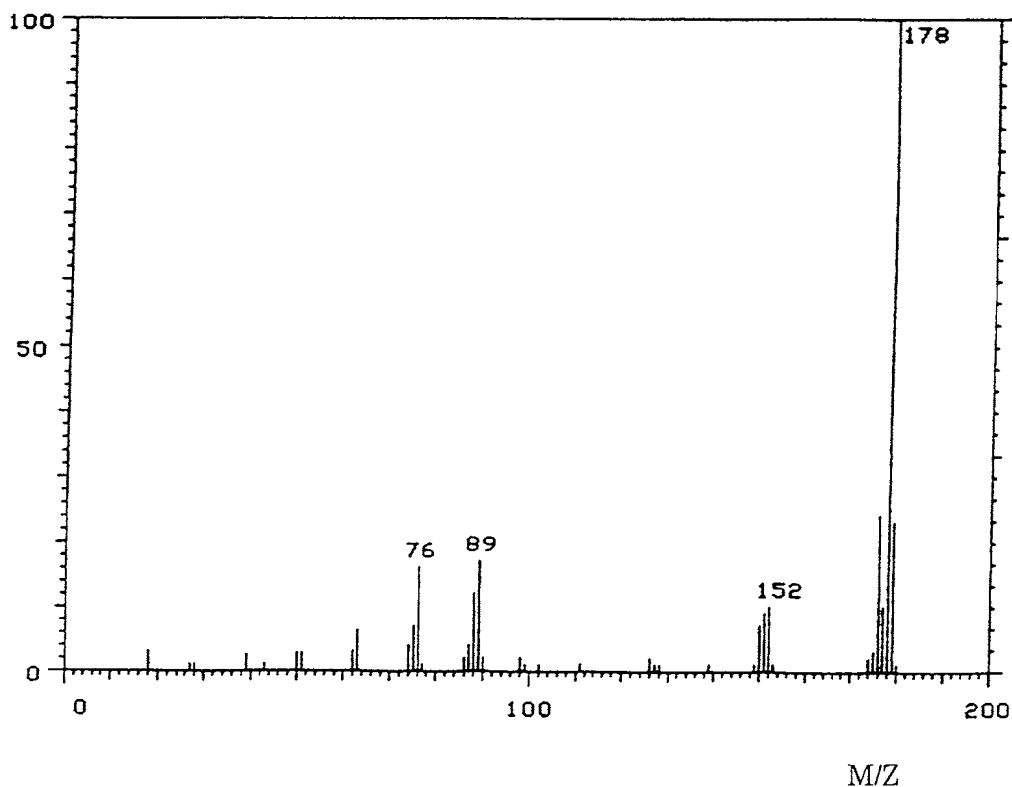
## 1. Identity(Spectral data)

## (1) Mass Spectrometry

Instrument ; Hitachi M-80B Mass Spectrometer

Ionization ; EI(Electron Ionization)

Ionization Voltage ; 70eV



Mass Spectrum of Test Substance

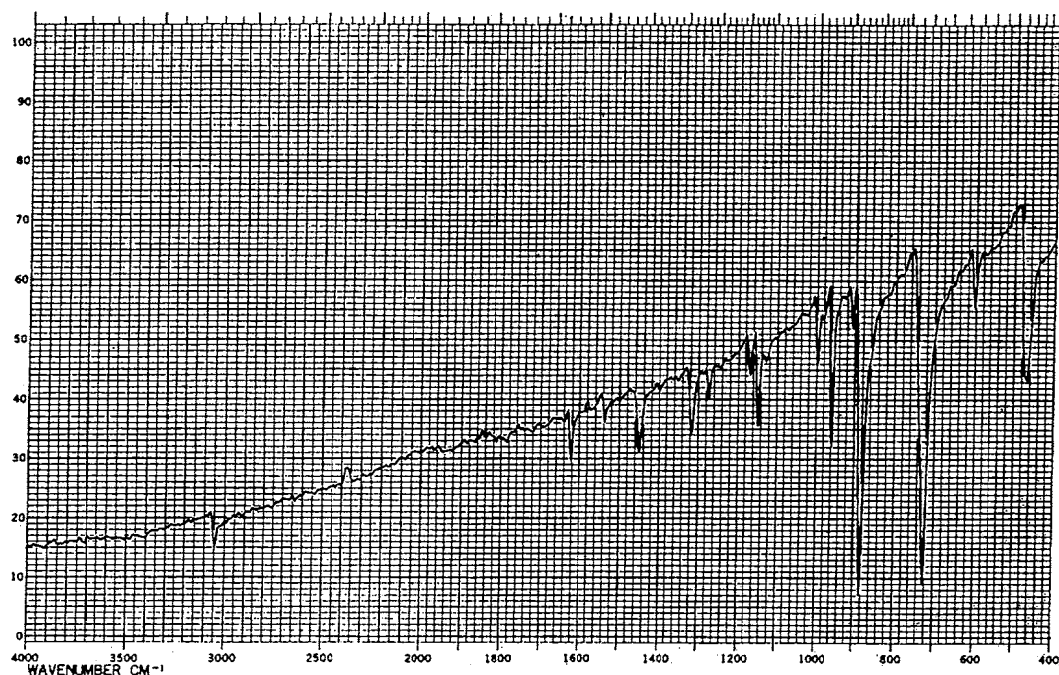
Results; The mass spectrum was consistent with literature spectrum.

<u>Determined</u>	<u>Literature Value*</u>
Molecular and Fragment Peak(M/Z)	Molecular and Fragment Peak(M/Z)
178[M] <sup>+</sup>	178[M] <sup>+</sup>
152	152
89	89
76	76

(\* EPA/NIH Mass Spectral  
Data Base(1978) Vol.1,  
p. 882.)

## (2) 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>Determines</u>	<u>Literature Values*</u>
Wave Number( $\text{cm}^{-1}$ )	Wave Number( $\text{cm}^{-1}$ )
460~ 490	460~ 490
700~ 750	700~ 750
860~ 900	860~ 900
940~ 970	940~ 970
990~1010	990~1010
1130~1160	1130~1160
1300~1330	1300~1330
1440~1470	1440~1470
	1530~1550
1610~1640	1610~1640
3030~3080	3010~3050

(Sadtler Handbook  
 by Sadtler Research  
 Laboratories, Inc.  
 (1978) p. 78.)

## 2. Impurity(Gas Chromatography)

Instrument ; Hewlett Packard 5890A Gas Chromatograph

Column ; METHYL SILICONE(0.2mm  $\phi$   $\times$  30m)

Column Temperature ; 170°C

Flow Rate ; 1 ml/min

Detector ; FID(Flame Ionization Detector)

Injection Volume ; 1  $\mu$ l

Results; Gas chromatography indicated one major peak(peak No.1) and two impurities. It was identified only by comparing its gas chromatograph with that of the Carbazole(peak No.3) in the Anthracene,the amount in the test substance was 0.0857% by standard sample(Carbazole).

Sample Name	Peak No.	Retention Time(min)	Peak Name
Test substance	1	16.477	Anthracene
	2	16.9	Not Identity
	3	17.867	Carbazole
Carbazole (standard sample)		17.925	

3. Conclusions; The result of the mass spectrum and the infrared spectrum agreed with the literature values. Consequently, the test substance was identified as Anthracene.
- Gas chromatography indicated one major peak and two impurities, it was identified only by comparing its gas chromatograph with that of the Carbazole, the amount in the test substance was 0.0857%.



B.Lot No.507E4209

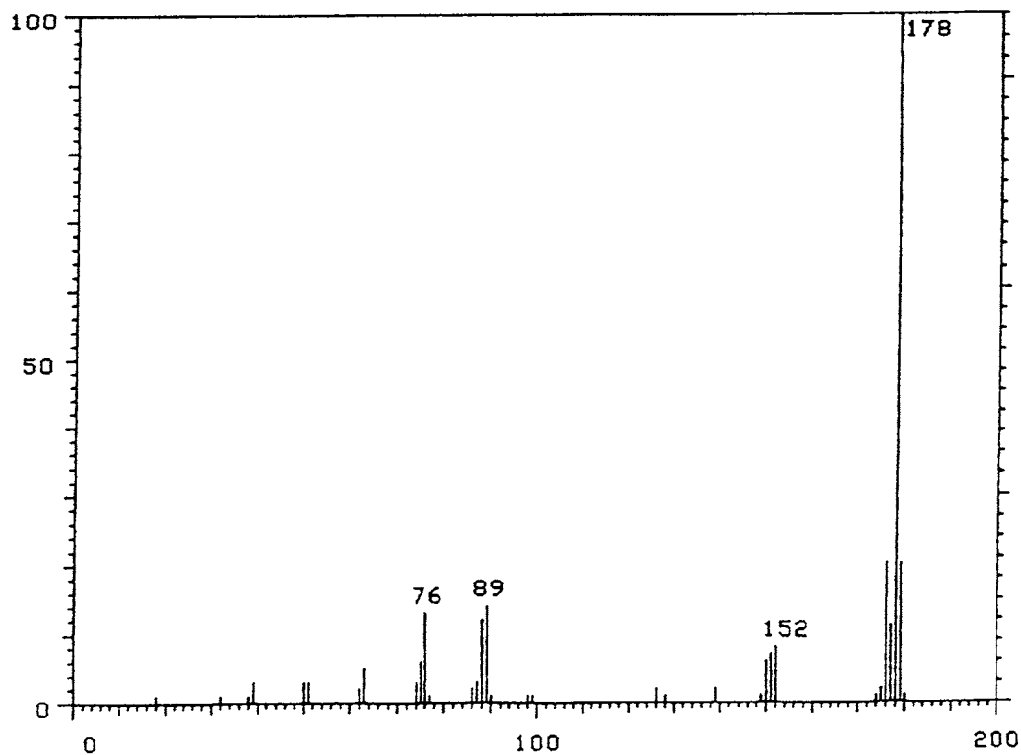
## 1. Identity(Spectral data)

## (1) Mass Spectrometry

Instrument ; Hitachi M-80B Mass Spectrometer

Ionization ; EI(Electron Ionization)

Ionization Voltage ; 70eV



Mass Spectrum of Test Substance

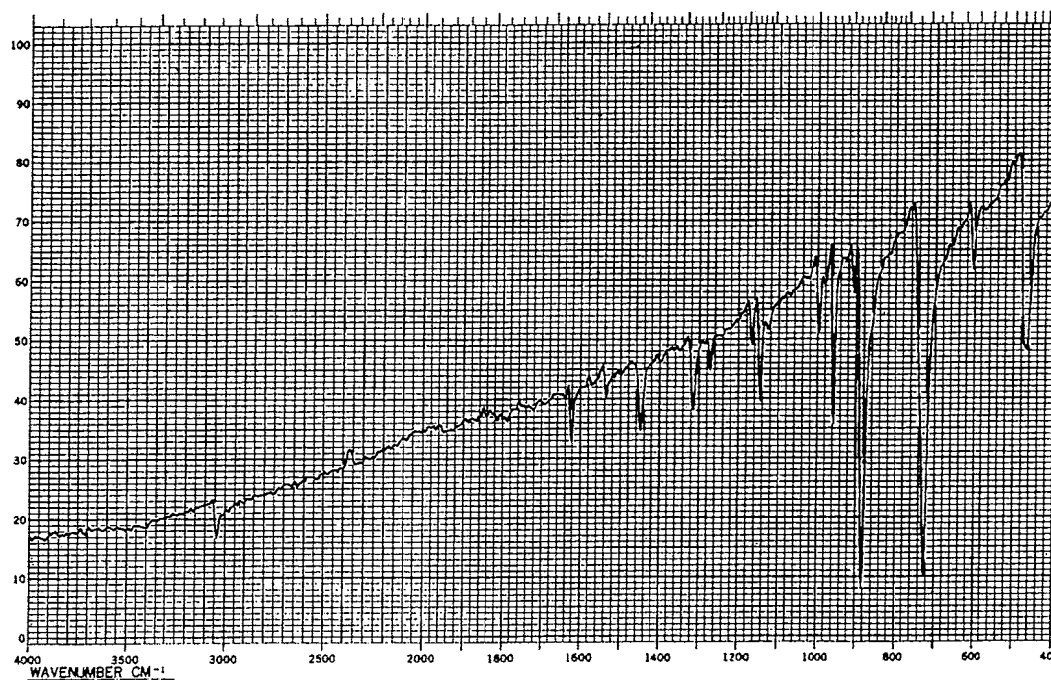
Results; The mass spectrum was consistent with literature spectrum.

<u>Determined</u>	<u>Literature Value*</u>
Molecular and Fragment Peak(M/Z)	Molecular and Fragment Peak(M/Z)
178[M] <sup>+</sup>	178[M] <sup>+</sup>
152	152
89	89
76	76

(\* EPA/NIH Mass Spectral  
Data Base(1978) Vol.1,  
p. 882.)

## (2) 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>Determines</u>	<u>Literature Values*</u>
Wave Number( $\text{cm}^{-1}$ )	Wave Number( $\text{cm}^{-1}$ )
460~ 490	460~ 490
700~ 750	700~ 750
860~ 900	860~ 900
940~ 970	940~ 970
990~1010	990~1010
1130~1160	1130~1160
1300~1330	1300~1330
1440~1470	1440~1470
	1530~1550
1610~1640	1610~1640
3030~3080	3010~3050

(Sadtler Handbook  
 by Sadtler Research  
 Laboratories, Inc.  
 (1978) p. 78.)

## 2. Impurity(Gas Chromatography)

Instrument ; Hewlett Packard 5890A Gas Chromatograph

Column ; METHYL SILICONE(0.2mm  $\phi$   $\times$  30m)

Column Temperature ; 170°C

Flow Rate ; 1 ml/min

Detector ; FID(Flame Ionization Detector)

Injection Volume ; 1  $\mu$ l

Results; Gas chromatography indicated one major peak(peak No.1) and two impurities. It was identified only by comparing its gas chromatograph with that of the Carbazole(peak No.3) in the Anthracene,the amount in the test substance was 0.0841% by standard sample(Carbazole).

Sample Name	Peak No.	Retention Time(min)	Peak Name
Test substance	1	16.472	Anthracene
	2	16.89	Not Identity
	3	17.848	Carbazole
Carbazole (standard sample)		17.925	

3. Conclusions; The result of the mass spectrum and the infrared spectrum agreed with the literature values. Consequently, the test substance was identified as Anthracene.
- Gas chromatography indicated one major peak and two impurities, it was identified only by comparing its gas chromatograph with that of the Carbazole, the amount in the test substance was 0.0841%.

C.Lot No.507E4210

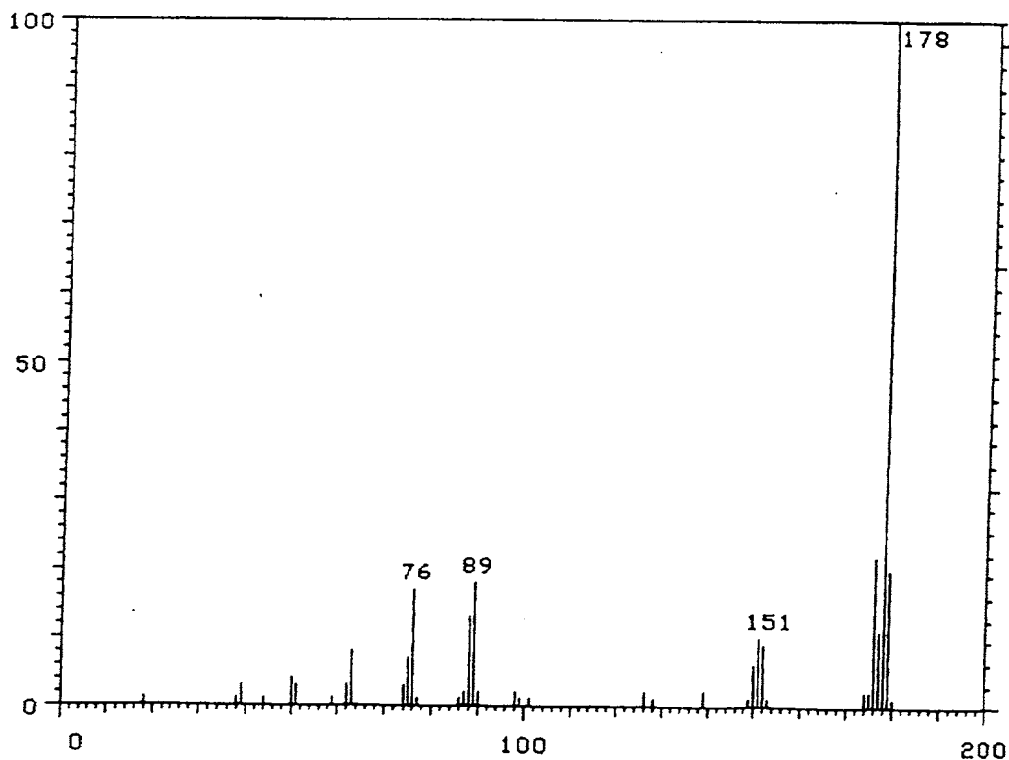
## 1. Identity(Spectral data)

## (1) Mass Spectrometry

Instrument ; Hitachi M-80B Mass Spectrometer

Ionization ; EI(Electron Ionization)

Ionization Voltage ; 70eV



Mass Spectrum of Test Substance

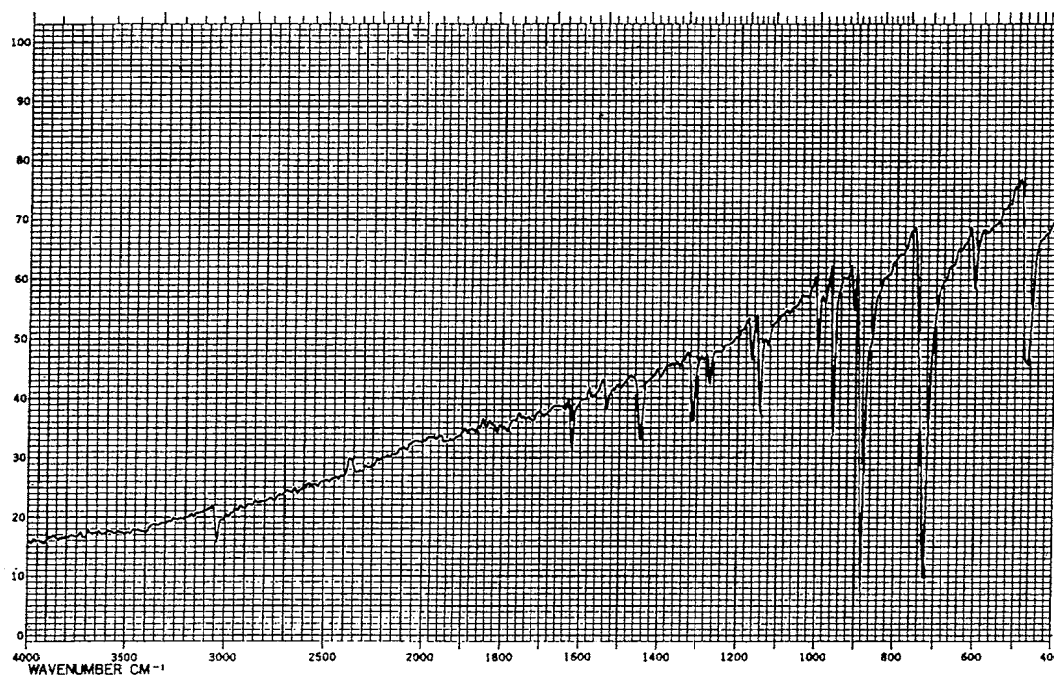
Results; The mass spectrum was consistent with literature spectrum.

Determined	Literature Value*
Molecular and Fragment Peak(M/Z)	Molecular and Fragment Peak(M/Z)
178[M] <sup>+</sup>	178[M] <sup>+</sup>
152	152
89	89
76	76

(\* EPA/NIH Mass Spectral  
Data Base(1978) Vol.1,  
p. 882.)

## (2) 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.

Determines	Literature Values*
Wave Number( $\text{cm}^{-1}$ )	Wave Number( $\text{cm}^{-1}$ )
460~ 490	460~ 490
700~ 750	700~ 750
860~ 900	860~ 900
940~ 970	940~ 970
990~1010	990~1010
1130~1160	1130~1160
1300~1330	1300~1330
1440~1470	1440~1470
	1530~1550
1610~1640	1610~1640
3030~3080	3010~3050

(Sadtler Handbook  
 by Sadtler Research  
 Laboratories, Inc.  
 (1978) p. 78.)

## 2. Impurity(Gas Chromatography)

Instrument ; Hewlett Packard 5890A Gas Chromatograph

Column ; METHYL SILICONE(0.2mm  $\phi$   $\times$  30m)

Column Temperature ; 170°C

Flow Rate ; 1 ml/min

Detector ; FID(Flame Ionization Detector)

Injection Volume ; 1  $\mu$ l

Results; Gas chromatography indicated one major peak(peak No.1) and two impurities. It was identified only by comparing its gas chromatograph with that of the Carbazole(peak No.3) in the Anthracene,the amount in the test substance was 0.0594% by standard sample(Carbazole).

Sample Name	Peak No.	Retention Time(min)	Peak Name
Test substance	1	16.458	Anthracene
	2	16.882	Not Identity
	3	17.842	Carbazole
Carbazole (standard sample)		17.925	

3. Conclusions; The result of the mass spectrum and the infrared spectrum agreed with the literature values. Consequently, the test substance was identified as Anthracene.
- Gas chromatography indicated one major peak and two impurities, it was identified only by comparing its gas chromatograph with that of the Carbazole, the amount in the test substance was 0.0594%.

## APPENDIX P 2

### STABILITY OF ANTHRACENE IN THE 2-YEAR FEED STUDIES

## Stability of Anthracene in the 2-Year Feed Studies

A.Lot No.507E4208

1. Sample storage; This lot was used from 1993.9.9 to 1994.6.16. Test substance was stored at room temperature.

## 2. Infrared Spectrometry

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

Results; The result of infrared spectrum did not change when the term of administration.

<u>1993.08.04.</u>	<u>1994.06.23.</u>
Wave Number( $\text{cm}^{-1}$ )	Wave Number( $\text{cm}^{-1}$ )
460~ 490	460~ 490
700~ 750	700~ 750
860~ 900	860~ 900
940~ 970	940~ 970
990~1010	990~1010
1130~1160	1130~1160
1300~1330	1300~1330
1440~1470	1440~1470
1610~1640	1610~1640
3030~3080	3030~3080

## 3. Gas Chromatography

Instrument ; Hewlett Packard 5890A Gas Chromatograph  
 Column ; METHYL SILICONE(0.2mm  $\phi$   $\times$  30m)  
 Column Temperature ; 170°C  
 Flow Rate ; 1 ml/min  
 Detector ; FID(Flame Ionization Detector)  
 Injection Volume ; 1  $\mu$ l

Results; Gas chromatography indicated one major peak(peak No.1) and two impurities(peak No.2,3 < 0.3% of total area) analyzed at 1993.8.4 and one major peak(peak No.1) and two impurities(peak No.2,3 < 0.3% of total area) analyzed at 1994.6.23. No new trace impurity peak in the test substance analyzed at 1994.6.23 was detected.



Date	Peak No.	Retention Time(min)	(percent of total peak)
1993.08.04	1	16.477	99.7771
(date analyzed)	2	16.9	0.1414
	3	17.867	0.0816
1994.06.23	1	16.458	99.7837
(date analyzed)	2	16.882	0.1345
	3	17.84	0.0818

4. 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).

B.Lot No.507E4209

1. Sample storage; This lot was used from 1994.6.16 to 1995.6.1. Test substance was stored at room temperature.

## 2. Infrared Spectrometry

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

Results; The result of infrared spectrum did not change when the term of administration.

<u>1993.08.04.</u>	<u>1995.06.08.</u>
Wave Number( $\text{cm}^{-1}$ )	Wave Number( $\text{cm}^{-1}$ )
460~ 490	460~ 490
700~ 750	700~ 750
860~ 900	860~ 900
940~ 970	940~ 970
990~1010	990~1010
1130~1160	1130~1160
1300~1330	1300~1330
1440~1470	1440~1470
1610~1640	1610~1640
3030~3080	3030~3080

## 3. Gas Chromatography

Instrument ; Hewlett Packard 5890A Gas Chromatograph  
 Column ; METHYL SILICONE(0.2mm  $\phi$   $\times$  30m)  
 Column Temperature ; 170°C  
 Flow Rate ; 1 ml/min  
 Detector ; FID(Flame Ionization Detector)  
 Injection Volume ; 1  $\mu$ l

Results; Gas chromatography indicated one major peak(peak No.1) and two impurities(peak No.2,3 < 0.3% of total area) analyzed at 1993.8.4 and one major peak(peak No.1) and two impurities(peak No.2,3 < 0.3% of total area) analyzed at 1995.6.8. No new treace impurity peak in the test substance analyzed at 1995.6.8 was detected.

Date	Peak No.	Retention Time(min)	(percent of total peak)
1993.08.04	1	16.472	99.7795
(date analyzed)	2	16.89	0.1345
	3	17.848	0.0860
1995.06.08	1	16.447	99.7854
(date analyzed)	2	16.877	0.1358
	3	17.832	0.0788

4. Conclusions; The results indicated that the test substance did not change when stored in the dark at room temperature during this period(for about 22 months).

C.Lot No.507E4210

1. Sample storage; This lot was used from 1995.2.2 to 1995.10.5. Test substance was stored at room temperature.

## 2. Infrared Spectrometry

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

Results; The result of infrared spectrum did not change when the term of administration.

<u>1993.08.04.</u>	<u>1995.10.12.</u>
Wave Number( $\text{cm}^{-1}$ )	Wave Number( $\text{cm}^{-1}$ )
460~ 490	460~ 490
700~ 750	700~ 750
860~ 900	860~ 900
940~ 970	940~ 970
990~1010	990~1010
1130~1160	1130~1160
1300~1330	1300~1330
1440~1470	1440~1470
1610~1640	1610~1640
3030~3080	3030~3080

## 3. Gas Chromatography

Instrument ; Hewlett Packard 5890A Gas Chromatograph  
 Column ; METHYL SILICONE(0.2mm  $\phi$   $\times$  30m)  
 Column Temperature ; 170°C  
 Flow Rate ; 1 ml/min  
 Detector ; FID(Flame Ionization Detector)  
 Injection Volume ; 1  $\mu$ l

Results; Gas chromatography indicated one major peak(peak No.1) and two impurities(peak No.2,3 < 0.2% of total area) analyzed at 1993.8.4 and one major peak(peak No.1) and two impurities(peak No.2,3 < 0.2% of total area) analyzed at 1995.10.12. No new treace impurity peak in the test substance analyzed at 1995.10.12 was detected.

Date	Peak No.	Retention Time(min)	(percent of total peak)
1993.08.04	1	16.458	99.8018
(date analyzed)	2	16.882	0.1388
	3	17.842	0.0595
1995.10.12	1	16.457	99.8043
(date analyzed)	2	16.875	0.1397
	3	17.833	0.0560

4. Conclusions; The results indicated that the test substance did not change when stored in the dark at room temperature during this period(for about 26 months).

APPENDIX P 3

CONCENTRATION OF ANTHRACENE IN FORMULATED DIETS OF RATS  
IN THE 2-YEAR FEED STUDY

CONCENTRATION OF ANTHRACENE IN FORMULATED DIETS OF RATS IN THE 2-YEAR FEED STUDY  
(Male)(Female)

Date analyzed	Target Concentration(ppm)		
	8000(*)	20000(*)	50000(*)
1993.09.08	7703( 96.3)	21258(106.3)	50349(100.7)
1993.12.08	8138(101.7)	19846( 99.2)	49275( 98.5)
1994.03.09	7400( 92.5)	22353(111.8)	49948( 99.9)
1994.06.15	7438( 93.0)	19992(100.0)	49721( 99.4)
1994.08.22	7947( 99.3)	21186(105.9)	51419(102.8)
1994.10.17	7811( 97.6)	20300(101.5)	49976(100.0)
1995.02.01	7070( 98.4)	22004(110.0)	52563(105.1)
1995.05.08	7816( 97.7)	21068(105.3)	52609(105.2)
1995.08.02	7690( 96.1)	21998(110.0)	52678(105.4)

(\*) % of target concentration

Analytical method: The sample were analyzed by the GC.

Instrument	: Hewlett Packard 5890A	Flow Rate	: 1ml/min
Column	: METHYL SILICONE(0.2mm $\phi$ $\times$ 30m)	Detector	: FID(Flame Ionization Detector)
Column Temperature:	260°C	Injection Volume	: 1 $\mu$ l
Carrier	: He		

APPENDIX P 4

CONCENTRATION OF ANTHRACENE IN FORMULATED DIETS IN MICE  
IN THE 2-YEAR FEED STUDY



## CONCENTRATION OF ANTHRACENE IN FORMULATED DIETS OF MALE MICE IN THE 2-YEAR FEED STUDY

(Male)

Date analyzed	Target Concentration(ppm)		
	3200(*)	8000	20000
1993.09.29	3052( 95.4)	7291( 91.1)	20321( 97.1)
1993.12.08	3267(102.1)	8138(101.7)	19846( 99.2)
1994.03.09	3154( 98.6)	7400( 92.5)	22353(111.8)
1994.06.15	2959( 92.5)	7438( 93.0)	19992(100.0)
1994.08.22	3129( 97.8)	7947( 99.3)	21186(105.9)
1994.10.17	3012( 94.1)	7811( 97.6)	20300(101.5)
1995.02.01	3328(104.0)	7870( 98.4)	22004(110.0)
1995.05.08	3209(100.3)	7816( 97.7)	21068(105.3)
1995.08.02	3235(101.1)	7690( 96.1)	21998(110.0)

(\*) % of target concentration

Analytical method: The sample were analyzed by the GC.

Instrument : Hewlett Packard 5890A  
 Column : METHYL SILICONE(0.2mm $\phi$   $\times$  30m)  
 Column Temperature: 260°C  
 Carrier : He

Flow Rate : 1ml/min  
 Detector : FID(Flame Ionization Detector)  
 Injection Volume : 1 $\mu$ l

## CONCENTRATION OF ANTHRACENE IN FORMULATED DIETS OF FEMALE MICE IN THE 2-YEAR FEED STUDY

(Female)

Date analyzed	Target Concentration(ppm)		
	8000	20000	50000
1993.09.29	7291( 91.1)*	20321(101.6)	48526( 97.1)
1993.12.08	8138(101.7)	19846( 99.2)	49275( 98.5)
1994.03.09	7400( 92.5)	22353(111.8)	44948( 99.9)
1994.06.15	7438( 93.0)	19992(100.0)	49721( 99.4)
1994.08.22	7947( 99.3)	21186(105.9)	51419(102.8)
1994.10.17	7811( 97.6)	20300(101.5)	49976(100.0)
1995.02.01	7870( 98.4)	22004(110.0)	52563(105.1)
1995.05.08	7816( 97.7)	21068(105.3)	52609(105.2)
1995.08.02	7690( 96.1)	21998(110.0)	52678(105.4)

(\*) % of target concentration

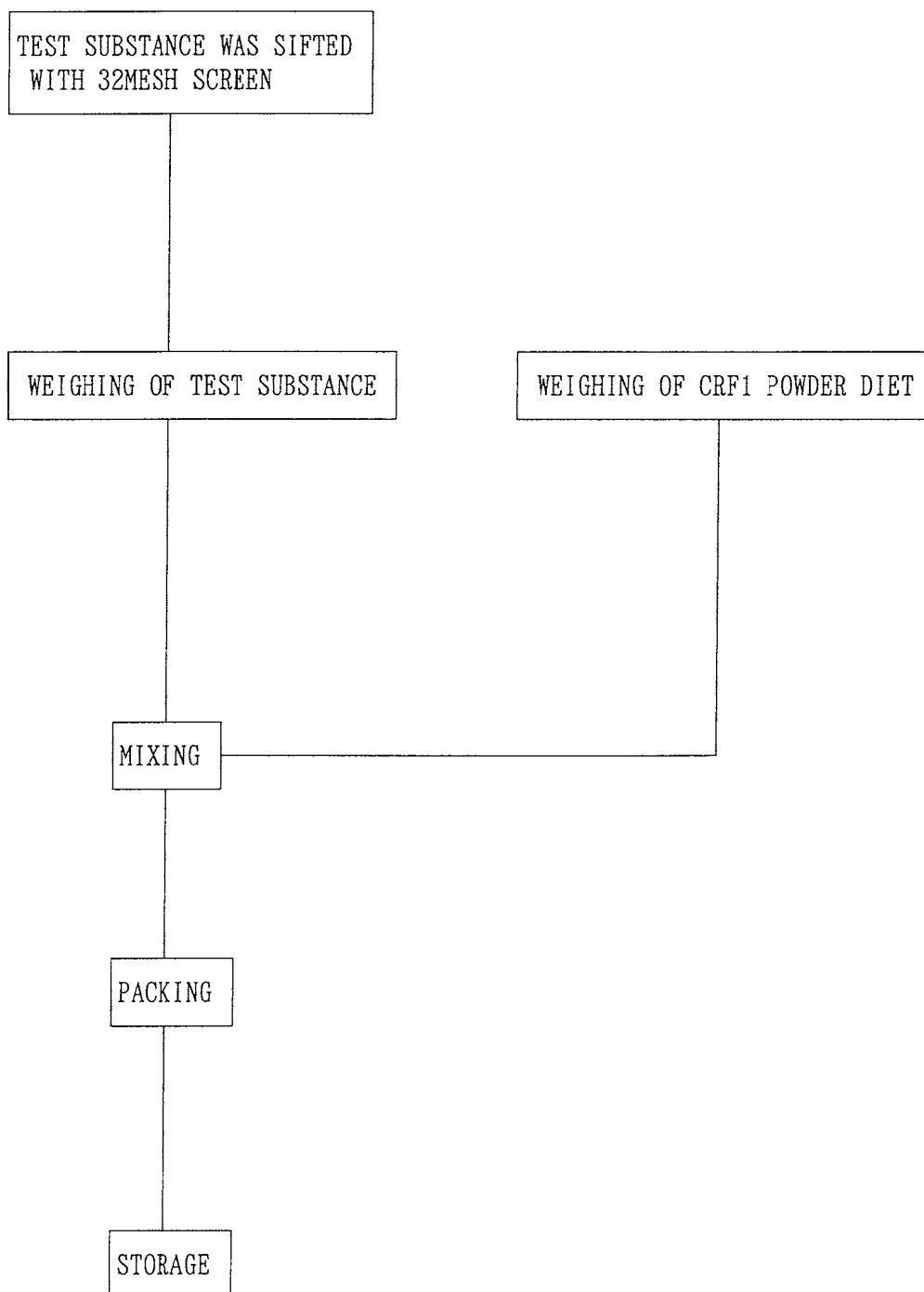
Analytical method: The sample were analyzed by the GC.

Instrument	: Hewlett Packard 5890A	Flow Rate	: 1ml/min
Column	: METHYL SILICONE(0.2mm $\phi$ ×30m)	Detector	: FID(Flame Ionization Detector)
Column Temperature:	260°C	Injection Volume	: 1 $\mu$ l
Carrier	: He		

APPENDIX P 5

STABILITY OF ANTHRACENE IN FORMULATED DIETS  
IN THE 2-YEAR FEED STUDY

Dose Formulations of Anthracene in the 2-Year Studies  
(Prepared in Japan Bioassay Research Center)



APPENDIX Q 1

DOSE FORMULATIONS OF ANTHRACENE IN THE 2-YEAR FEED STUDIES

(PREPARED IN JAPAN BIOASSAY RESEARCH CENTER)

## Stability of Anthracene in Formulated Diets in 2-Years Feed Studies

Term of stability	Target Concentration(ppm)	
	3200	50000
1993.08.12(a)	3178	49043
1993.08.27(b)	2879	49389
1993.09.08(c)	3150	49960
1993.10.13(d)	3222	49910
1993.11.15(e)	3104	48090
1993.12.08(f)	3193	50070

a ; Date of preparation

b ; The stability of Anthracene in formulated diets were established for 15 days when stored at animal room( $24\pm 2^{\circ}\text{C}$ ).

c ; The stability of Anthracene in formulated diets were established for about 1 months when stored at diet storage room(room temperature).

d ; The stability of Anthracene in formulated diets were established for about 2 months when stored at diet storage room(room temperature).

e ; The stability of Anthracene in formulated diets were established for about 3 months when stored at diet storage room(room temperature).

f ; The stability of Anthracene in formulated diets were established for about 4 months when stored at diet storage room(room temperature).

Analytical method; The samples were analyzed by the GC.

Instrument : Hewlett Packard 5890A  
 Column : METHYL SILICONE(0.2mm $\phi$   $\times$  30m)  
 Column Temperature: 260°C  
 Carrier : He

Flow Rate : 1ml/min  
 Detector : FID(Flame Ionization Detector)  
 Injection Volume : 1 $\mu$ l

## Stability of Anthracene in Formulated Diets in 2-Years Feed Studies

Term of stability	Target Concentration(ppm)	
	3200	50000
1994.08.22(a)	3129	51419
1995.02.01(b)	3071	51804

a ; Date of preparation

b ; The stability of Anthracene in formulated diets were established for about 5 months when stored at diet storage room(room temperature).

Analytical method; The samples were analyzed by the GC.

Instrument : Hewlett Packard 5890A  
Column : METHYL SILICONE(0.2mm $\phi$   $\times$  30m)  
Column Temperature: 260°C  
Carrier : He

Flow Rate : 1ml/min  
Detector : FID(Flame Ionization Detector)  
Injection Volume : 1 $\mu$ l

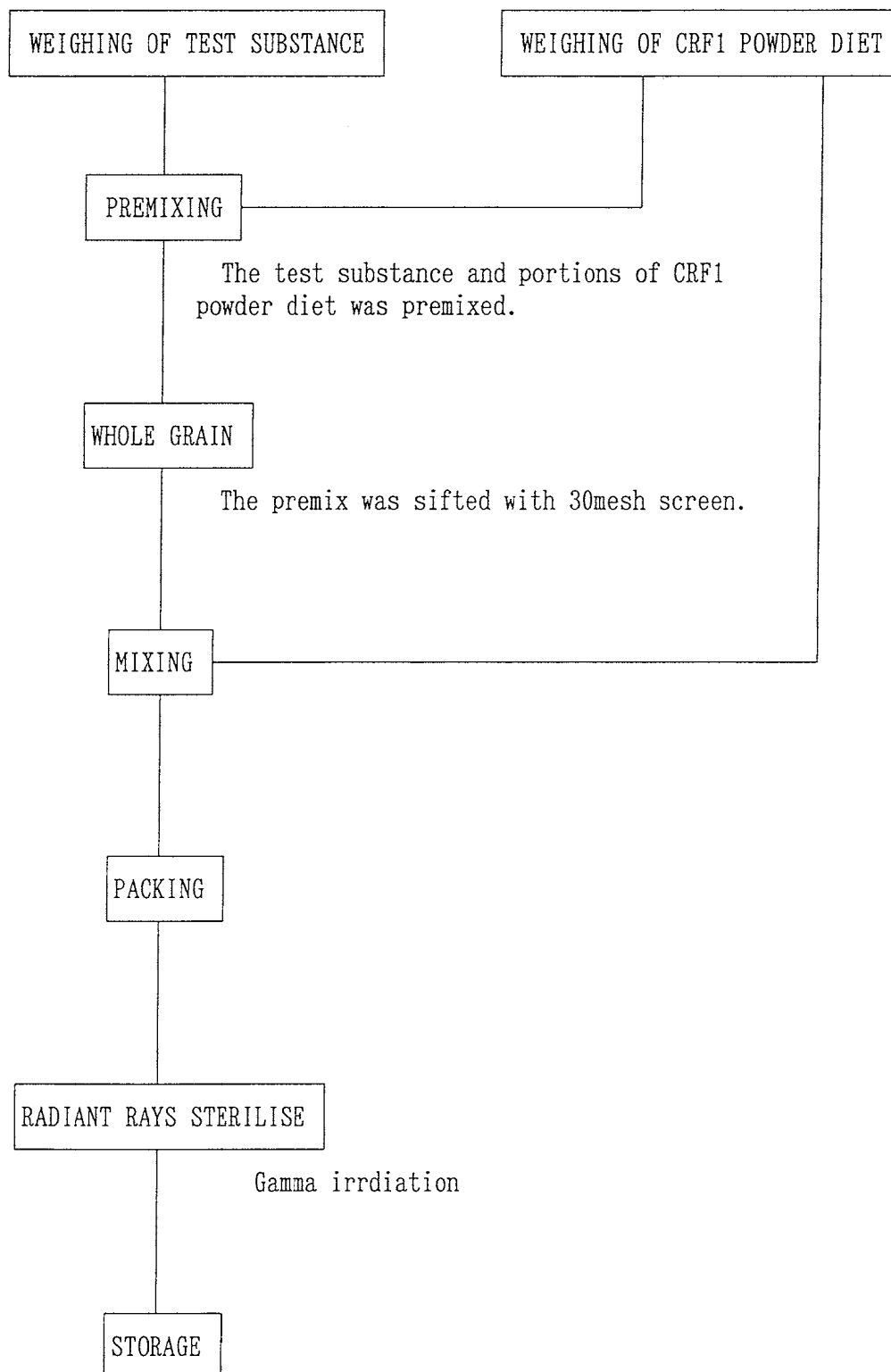
APPENDIX Q 2

DOSE FORMULATIONS OF ANTHRACENE IN THE 2-YEAR FEED STUDIES

(PREPARED BY ORIENTAL YEAST CO.,LTD.)



Dose Formulations of Anthracene in the 2-Year Studies  
(Prepared by Oriental Yeast Co. LTD)



## APPENDIX R 1

### METHODS FOR HEMATOLOGY,BIOCHEMISTRY AND URINALYSIS

# METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS

Item	Method	Unit
<b>Hematology</b>		
Red blood cell (RBC)	Light scattering method <sup>1)</sup>	$\times 10^6 / \mu\text{l}$
Hemoglobin (Hgb)	Cyanmethemoglobin method <sup>1)</sup>	g/dl
Hematocrit (Hct)	Calculated as $\text{RBC} \times \text{MCV} / 10$ <sup>1)</sup>	%
Mean corpuscular volume (MCV)	Light scattering method <sup>1)</sup>	fl
Mean corpuscular hemoglobin (MCH)	Calculated as $\text{Hgb} / \text{RBC} \times 10$ <sup>1)</sup>	pg
Mean corpuscular hemoglobin concentration (MCHC)	Calculated as $\text{Hgb} / \text{Hct} \times 100$ <sup>1)</sup>	g/dl
Platelet	Light scattering method <sup>1)</sup>	$\times 10^3 / \mu\text{l}$
White blood cell (WBC)	Light scattering method <sup>1)</sup>	$\times 10^3 / \mu\text{l}$
Differential WBC	Pattern recognition method <sup>2)</sup> (May-Grunwald-Giemsa staining)	%
Reticulocyte	Pattern recognition method <sup>2)</sup> (New methyleneblue staining)	%
Prothrombin time	Quick one stage method <sup>3)</sup>	sec
Activated partial thromboplastin time (APTT)	Ellagic acid activated method <sup>3)</sup>	sec
<b>Biochemistry</b>		
Total protein (TP)	Biuret method <sup>4)</sup>	g/dl
Albumin (Alb)	BCG method <sup>4)</sup>	g/dl
A/G ratio	Calculated as $\text{Alb} / (\text{TP} - \text{Alb})$ <sup>4)</sup>	
T-bilirubin	Michaelson method <sup>4)</sup>	mg/dl
Glucose	Enzymatic method (HK-G-6-PDH) <sup>4)</sup>	mg/dl
T-cholesterol	Enzymatic method (CEH-COD-POD) <sup>4)</sup>	mg/dl
Triglyceride	Enzymatic method (GK-GPO-POD) <sup>4)</sup>	
Phospholipid	Enzymatic method (PLD-COD-POD) <sup>4)</sup>	mg/dl
Glutamic oxaloacetic transaminase (GOT)	Karmen method <sup>4)</sup>	IU/l
Glutamic pyruvic transaminase (GPT)	Karmen method <sup>4)</sup>	IU/l
Lactate dehydrogenase (LDH)	Wroblewski-LaDue method <sup>4)</sup>	IU/l
Alkaline phosphatase (ALP)	GSCC method <sup>4)</sup>	
$\gamma$ -Glutamyl transpeptidase (G-GTP)	L- $\gamma$ -Glutamyl-p-nitroanilide substrate method <sup>4)</sup>	IU/l
Creatine phosphokinase (CPK)	GSCC method <sup>4)</sup>	IU/l
Urea nitrogen	Enzymatic method (Urease-GLDH) <sup>4)</sup>	mg/dl
Creatinine	Jaffe method <sup>4)</sup>	mg/dl
Sodium	Flame photometry <sup>5)</sup>	mEq/l
Potassium	Flame photometry <sup>5)</sup>	mEq/l
Chloride	Coulometric titration <sup>5)</sup>	mEq/l
Calcium	OCPC method <sup>4)</sup>	mg/dl
Inorganic phosphorus	Enzymatic method (SPL-PGM-G-6-PDH) <sup>4)</sup>	mg/dl
<b>Urinalysis</b>		
PH, Protein, Glucose, Ketone body, Bilirubin, Occult blood, Urobilinogen	Urinalysis reagent paper method <sup>6)</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 coagulometer (Amelung KC-10 : Heinrich Amelung GmbH, Germany)
- 4) Automatic analyzer (Hitachi 705 : Hitachi, Ltd., Japan)
- 5) Flame photometer (Hitachi 750 : Hitachi, Ltd., Japan)
- 6) Ames reagent strips for urinalysis (Multistix, Uro-Labstix : Miles Sankyo Co., Ltd., Japan)

## APPENDIX R 2

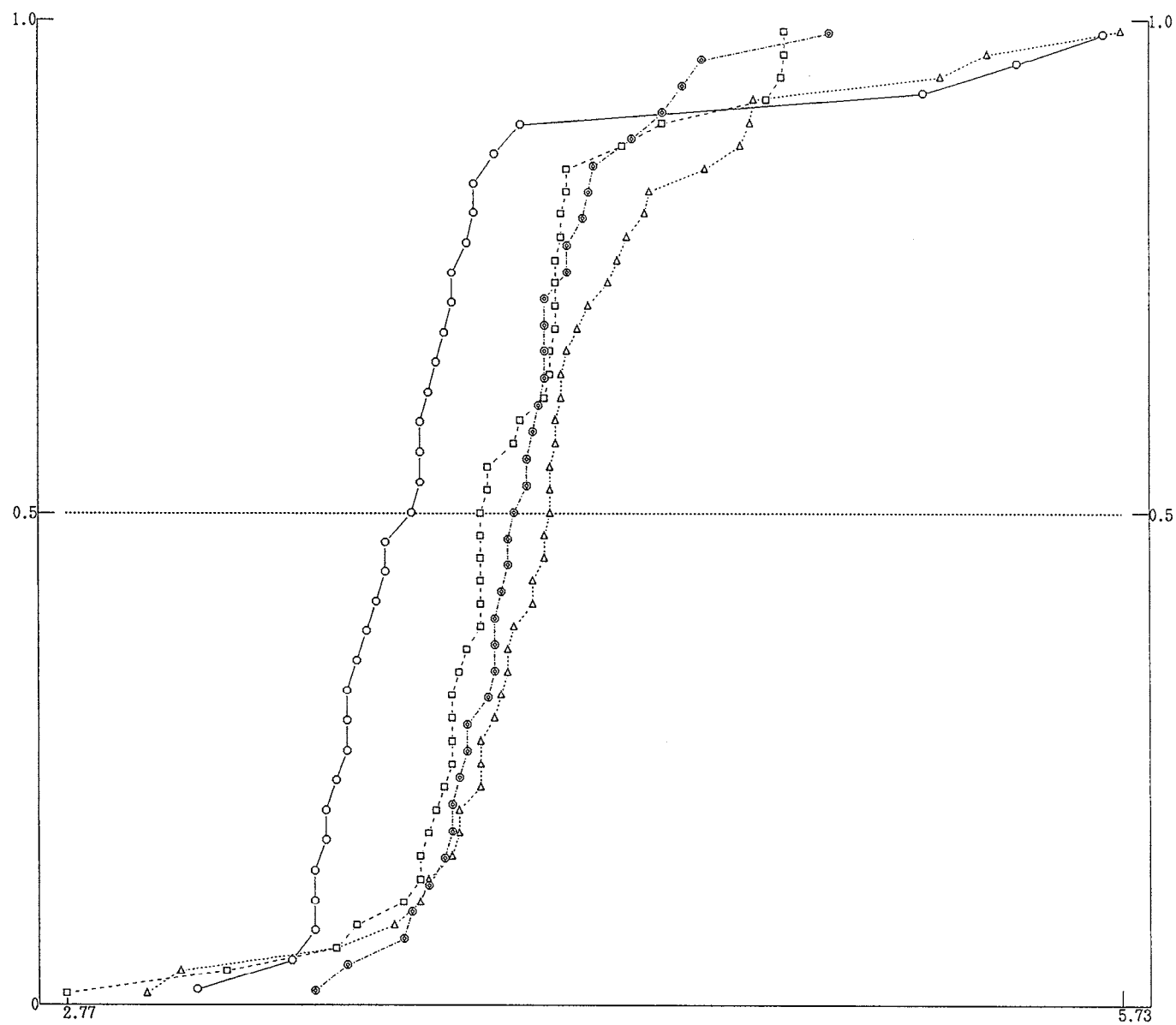
### UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

## UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

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

## APPENDIX S 1

Q PLOT GRAPH FOR RETICULOCYTE OF MALE RATS IN THE  
2-YEAR FEED STUDY OF ANTHRACENE



STUDY NO : 0242  
 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1  
 OUTPUT TYPE : SURVIVAL ANIMALS  
 SEX : MALE

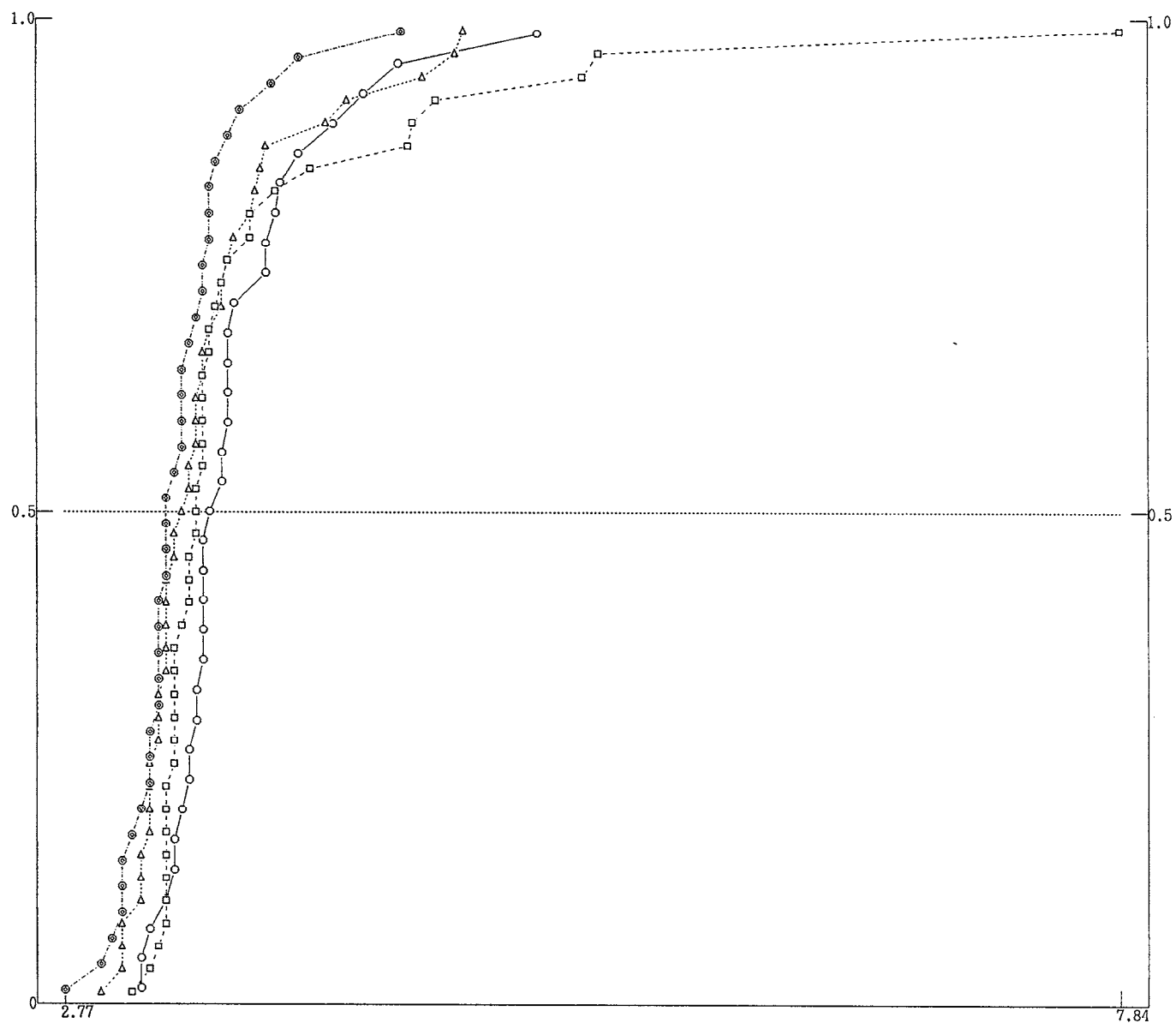
%  
 (LN)  
 RETICULOCYTE

—○— CONTROL  
 .....△..... 8000 PPM  
 - - - - □ - - - - 20000 PPM  
 - · - · - · 50000 PPM

## APPENDIX S 2

Q PLOT GRAPH FOR GLUTAMIC PYRUVIC TRANSAMINASE (GPT)  
OF MALE RATS IN THE 2-YEAR FEED STUDY OF ANTHRACENE





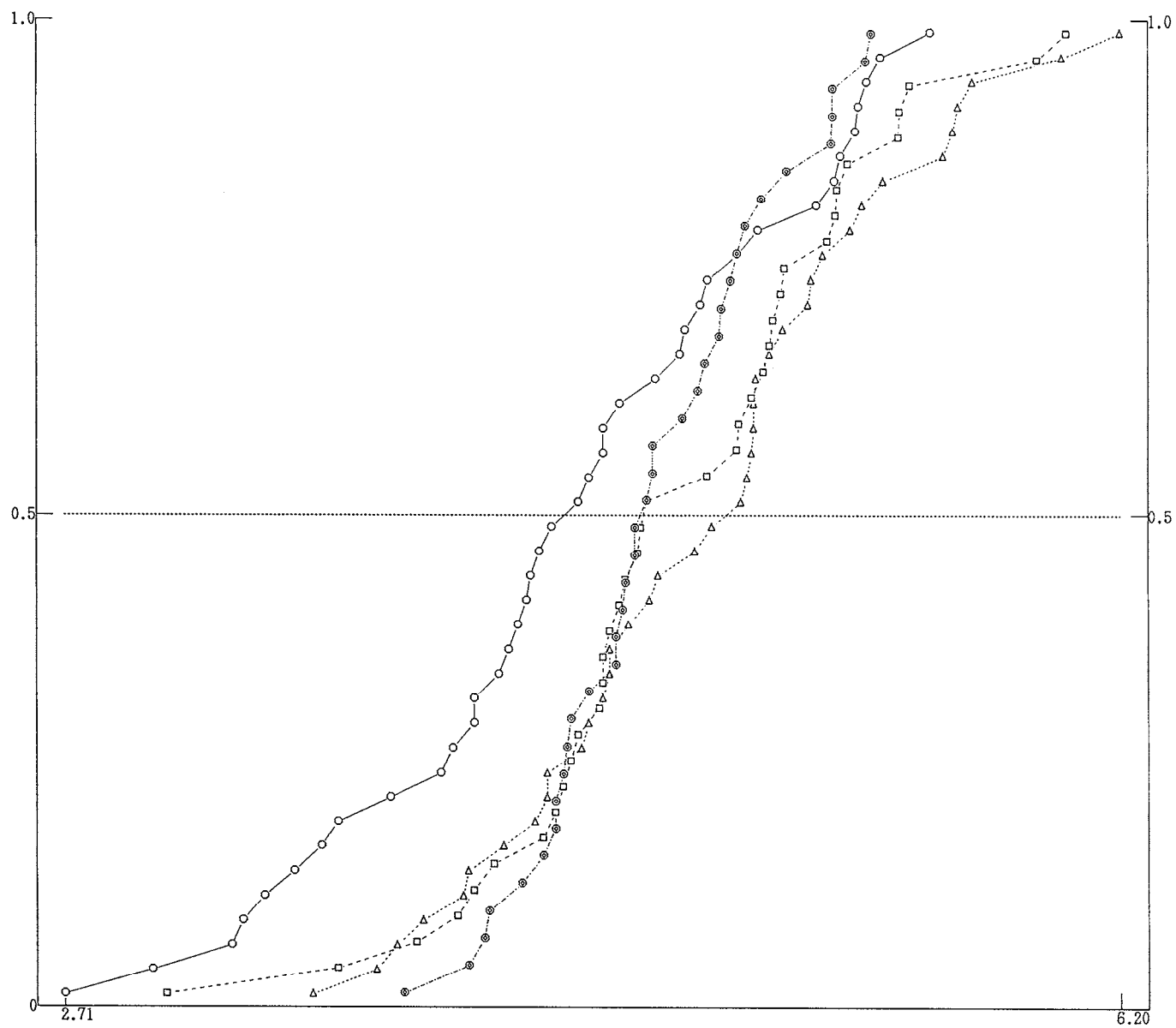
STUDY NO : 0242  
 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1  
 OUTPUT TYPE : SURVIVAL ANIMALS  
 SEX : MALE

IU/L  
 (LN)  
 GPT

—○— CONTROL  
 .....△..... 8000 PPM  
 - - - - □ - - - 20000 PPM  
 - · - · - · 50000 PPM

## APPENDIX S 3

Q PLOT GRAPH FOR TRIGLYCERIDE OF FEMALE RATS IN THE  
2-YEAR FEED STUDY OF ANTHRACENE



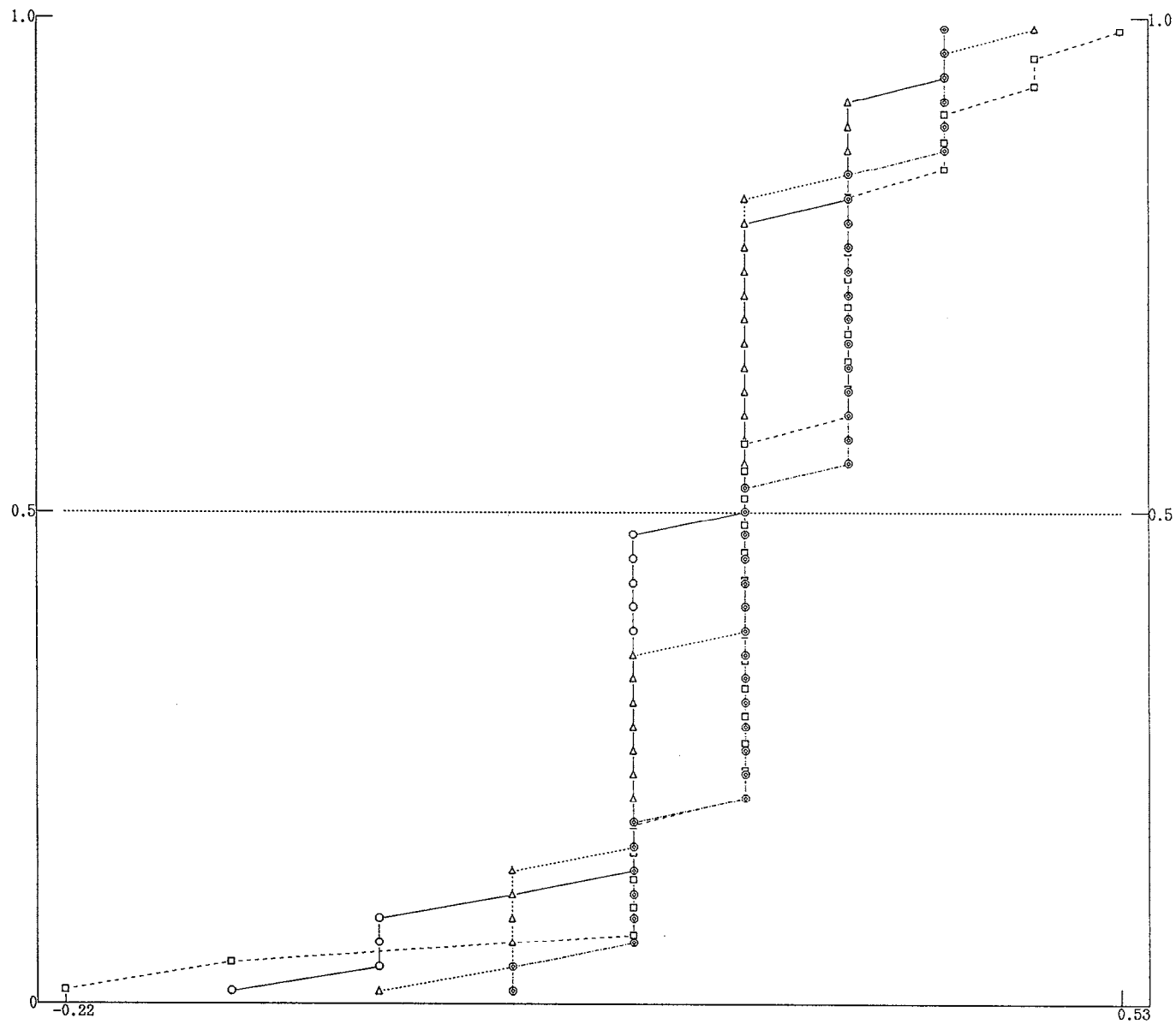
STUDY NO : 0242  
 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1  
 OUTPUT TYPE : SURVIVAL ANIMALS  
 SEX : FEMALE

mg/dL  
 (LN)  
 TRIGLYCERIDE

—○— CONTROL  
 -△- 8000 PPM  
 -□- 20000 PPM  
 -●- 50000 PPM

## APPENDIX S 4

Q PLOT GRAPH FOR A/G RATIO OF MALE MICE IN THE  
2-YEAR FEED STUDY OF ANTHRACENE



STUDY NO : 0243  
 ANIMAL : MOUSE C<sub>7</sub>j:BDF1  
 REPORT TYPE : A1  
 OUTPUT TYPE : SURVIVAL ANIMALS  
 SEX : MALE

(LN)  
 A/G RATIO

—○— CONTROL  
 .....△..... 3200 PPM  
 - - - - □ - - - - 8000 PPM  
 - · - · - · 20000 PPM