ビフェニルのラット及びマウスを用いた経口投与によるがん原性試験(混餌試験)報告書

試験番号: ラット/0205; マウス/0206

# **APPENDIX**

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

RAT: MALE: DEAD AND MORIBUND ANIMALS

SEX

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

REPORT TYPE : A1 : MALE

	Group N No. of Grade	Animals on Study 13 1 2 3 4	500ppm 9 _1 2 3 4	1500ppm 12 1 2 3 4	4500ppm 19 1 2 3 4
0rgan	Findings	(%) (%) (%)	(%) (%) (%)	1 2 3 4 (%) (%) (%)	(%) (%) (%)
[Integumentar	y system/appandage]				
skin/app	inflammation	<13> 0 0 1 0 ( 0) ( 0) ( 8) ( 0)	0 0 0 0 0 0 ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	epidermal cyst	0 0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 1 0 0 ( 0) ( 0)	0 0 0 0 0 (0) (0)
[Respiratory	system]				
nasal cavit	thrombus	0 0 1 0 ( 0) ( 0) ( 8) ( 0)	( 0) ( 0) ( 0) ( 0)	1 0 3 0 ( 8) ( 0) ( 25) ( 0)	3 3 2 0 ( 16) ( 16) ( 11) ( 0)
	mineralization	11 0 0 0 ( 85) ( 0) ( 0) ( 0)	5 0 0 0 (56) (0) (0) (0)	10 0 0 0 (83) (0) (0) (0)	10 1 0 0 (53) (5) (0) (0)
	eosinophilic change:olfactory epithelium	12 0 0 0 ( 92) ( 0) ( 0) ( 0)	8 0 0 0 0 (89) (0) (0) (0)	4 0 0 0 (33) (0) (0) (0)	5 0 0 0 (26) (0) (0) (0)
	eosinophilic change:respiratory epithelium	5 0 0 0 (38) (0) (0) (0)	5 0 0 0 (56)(0)(0)(0)	2 0 0 0 0 (17) (0) (0) (0)	2 0 0 0 0 (11) (0) (0) (0)
	inflammation:foreign body	2 0 0 0 (15) (0) (0) (0)	1 0 0 0 0 (11) (0) (0)	2 1 0 0 (17) (8) (0) (0)	8 1 0 0 (42) (5) (0) (0)
Grade <a>&gt; b (c)</a>	1: Slight 2: Moderate 3: Marke a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	ed 4 : Severe			

(HPT150)

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

REPORT TYPE : A1 SEX : MALE

Organ		up Name Control of Animals on Study 13 de 1 2 3 4 (%) (%) (%) (%)	500ppm 9 1 2 3 4 (%) (%) (%) (%)	1500ppm 12 1 2 3 4 (%) (%) (%) (%)	4500ppm 19 12 3 4 (%) (%) (%) (%)
[Respiratory	system]				
nasal cavit	respiratory metaplasia:olfactory epitheli	\( \lambda \) \(	<pre></pre>	1 0 0 0 ( 8) ( 0) ( 0) ( 0)	3 0 0 0 (16) (0) (0) (0)
	respiratory metaplasia:gland	12 0 0 0 ( 92) ( 0) ( 0) ( 0)	8 0 0 0 (89) ( 0) ( 0) ( 0)	9 0 0 0 0 (75) ( 0) ( 0) ( 0)	15 0 0 0 ( 79) ( 0) ( 0) ( 0)
lung	congestion	(13) 0 1 0 0 ( 0) ( 8) ( 0) ( 0)	<pre></pre>	<12> 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<19> 0 0 0 0 0 0 0 0 0 0 0
	inflammatory infiltration	0 0 0 0 0 ( 0) ( 0)	1 0 0 0 0 (11) (0) (0) (0)	1 0 0 0 0 ( 8) ( 0) ( 0) ( 0)	0 4 0 0 (0) (21) (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)	1 0 0 0 0 (5) (0) (0)
[Hematopoieti	c system]				
bone marrow	angiectasis	<13> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	(9) 1 0 0 0 (11) (0) (0) (0)	2 0 0 0 ( 17) ( 0) ( 0) ( 0)	2 0 0 0 (11) (0) (0) (0)
Grade < a > b ( c )	1: Slight 2: Moderate 3: a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	farked 4 ; Severe			
(HPT150)					BAISS

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

REPORT TYPE : A1 SEX

: MALE

500ppm 1500ppm 4500ppm Group Name Control 19 No. of Animals on Study 13 12 Grade (%) (%) (%) Findings (%) (%) (%) (%) Organ\_ [Hematopoietic system] < 9> bone marrow <13> 0 0 0 0 0 0 1 0 0 0 granulation (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (5)(0)(0)(0) increased hematopoiesis (0)(0)(0)(0) (5)(0)(0)(0) (15) (0) (0) (0) (22) (0) (0) (0) decreased hematopoiesis 0 0 (0)(0)(8)(0) (0)(0)(0)(0) (8)(0)(0)(0) (0)(0)(0)(0) 0 0 0 0 1 0 0 0 3 0 0 0 erythropoiesis:increased (0)(0)(0)(0) (8) (0) (0) (0) (0)(0)(0)(0) (16) (0) (0) (0) <13> < 9> <12> <19> spleen 0 0 0 0 0 0 0 0 1 0 atrophy (0)(0)(0)(0) (0)(0)(5)(0) (0)(0)(0)(0) (0)(0)(0)(0) 0 3 0 2 0 2 0 0 0 0 0 deposit of hemosiderin (0)(23)(0)(0) (0)(22)(0)(0) (25) (17) (0) (0) (0)(0)(0)(0) extramedullary hematopoiesis 0 1 1 0 1 2 0 0 1 1 0 0 ( 0) (11) (11) ( 0) (8)(8)(0)(0) (8) (17) (0) (0) (5)(5)(0)(0) [Circulatory system] heart 3 0 0 0 0 3 0 0 0 3 1 0 0 myocardial fibrosis (23) (0) (0) (0) (22) (0) (0) (0) (25) (0) (0) (0) (16) (5) (0) (0) Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe <a>></a> a: Number of animals examined at the site b b: Number of animals with lesion

(c) (IIPT150) c:b/a\*100

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

REPORT TYPE : A1

SEX : MALE

0rgan		Group Name Control No. of Animals on Study 13 Grade 1 2 3 4 (%) (%) (%) (%)	500ppm 9 1 2 3 4 (%) (%) (%) (%)	1500ppm 12 1 2 3 4 (%) (%) (%) (%)	4500ppm 19 1 2 3 4 (%) (%) (%) (%)
[Digestive s	system]				
stomach	erasion:forestomach	<pre></pre>	<pre></pre>	<12> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<19> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
	ulcer:forestomach	1 0 0 0 ( 8) ( 0) ( 0) ( 0)	1 0 0 0 (11) ( 0) ( 0) ( 0)	1 0 0 0 0 ( 8) ( 0) ( 0) ( 0)	3 0 0 0 0 (16) (0) (0)
	inflammation:forestomach	1 0 0 0 ( 8) ( 0) ( 0) ( 0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 ( 0) ( 0)
	erosion:glandular stomach	0 0 0 0 0 ( 0) ( 0)	1 0 0 0 (11) (0) (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (5) (0) (0) (0)
	ulcer:glandular stomach	0 0 0 0 0 ( 0) ( 0)	1 0 0 0 (11) (0) (0) (0)	1 0 0 0 0 ( 8) ( 0) ( 0) ( 0)	1 0 0 0 ( 5) ( 0) ( 0) ( 0)
	hemorrhage:glandular stomach	1 0 0 0 0 ( 8) ( 0) ( 0) ( 0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0)	0 0 0 0 0 (0) (0)
	mineralization:glandular stomach	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 0 ( 0) ( 0)	2 0 0 0 0 (11) (0) (0) (0)
liver	herniation	( 0) ( 0) ( 0) ( 0) 0	<pre></pre>	1 0 0 0 ( 8) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
Grade <a>&gt; b <a>c</a></a>	1: Slight 2: Moderate 3 a: Number of animals examined at the si b: Number of animals with lesion c: b / a * 100	: Marked 4 : Severe te			

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

REPORT TYPE : A1
SEX : MALE

Group Name Control 500ppm 1500ppm 4500ppm No. of Animals on Study 13 9 12 19 Grade (%) (%) (%) (%) 0rgan Findings (%) (%) (%) (%) (%) (%) (%) [Digestive system] liver <13> <12> <19> necrosis:central 0 0 0 0 0 0 0 0 1 1 0 0 1 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (8) (8) (0) (0) (5)(0)(0)(0) fatty change:peripheral 0 2 1 0 0 0 0 0 0 0 0 0 0 0 0 (0)(15)(8)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) granulation 0 (0)(0)(0)(0) (0)(0)(0)(0) (8) (8) (0) (0) (0)(0)(5)(0) acidophilic cell focus 1 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (5)(0)(0)(0) basophilic cell focus 0 1 0 0 0 (0)(8)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (5)(0)(0)(0) spongiosis hepatis 2 0 0 0 4 0 0 0 (15) (0) (0) (0) (0)(0)(0)(0) (8)(0)(0)(0) (21) (0) (0) (0) bile duct hyperplasia 0 11 (23) (69) (8) (0) (0)(78)(0)(0) (0)(92)(0)(0) (32) (47) (5) (0) biliary cyst 0 0 0 0 0 0 0 0 (8) (0) (0) (0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) Grade 1: Slight 2 : Moderate 3 : Marked 4 : Severe <a>></a> a: Number of animals examined at the site b b: Number of animals with lesion (c) c:b/a\*100

SEX

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

REPORT TYPE : A1

: MALE

Organ	Group Nam No. of An Grade Findings	ne Control nimals on Study 13	9 1 2 3 4 (%) (%) (%) (%)	1500ppm 12 12 1 2 3 4 (%) (%) (%) (%)	4500ppm 19 10 10 10 10 10 10 10 10 10 10 10 10 10
[Digestive sy	vstem]				
pancreas	atrophy	(13> 0 1 0 0 ( 0) ( 8) ( 0) ( 0)	(9) 1 1 0 0 (11) (11) (0) (0)	<12> 0 0 0 0 0 0 0 0 0 0 0 0 0 0	2 0 0 0 ( 11) ( 0) ( 0) ( 0)
[Urinary syst	tem]				
kidney	deposit of hemosiderin	(13) 0 2 0 0 (0) (15) (0) (0)	( 0) ( 0) ( 0) ( 0)	1 0 0 0 ( 8) ( 0) ( 0) ( 0)	2 1 0 0 ( 11) ( 5) ( 0) ( 0)
	squamous cell metaplasia	0 0 0 0 0 (0) (0)	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (5) (0) (0)
	chranic nephrapathy	0 3 3 3 3 (0) (23) (23)	0 4 1 0 ( 0) ( 44) ( 11) ( 0)	1 4 0 1 ( 8) ( 33) ( 0) ( 8)	3 4 1 0 (16) (21) (5) (0)
	tubular necrosis	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0)	0 1 3 0 ( 0) ( 8) ( 25) ( 0)	1 2 2 0 ( 5) ( 11) ( 11) ( 0)
	papillary necrosis	( 0) ( 0) ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0)	0 3 1 0 ( 0) ( 16) ( 5) ( 0)
	mineralization:cortico-medullary junction	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0)	2 1 0 0 (11) (5) (0) (0)
Grade (a) b (c)	1: Slight 2: Moderate 3: Marked a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	4 : Severe			

STUDY NO. : 0205 ANIMAL : RAT F344 REPORT TYPE : A1

: MALE

SEX

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

Organ		up Name Control of Animals on Study 13 de 1 2 3 4 (%) (%) (%) (%)	500ppm 9 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	4500ppm 19 19 (%) (%) (%) (%)
[Urinary sy:	stem]				
kidney	mìneralization:papilla	<13> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	(9) 1 0 0 0 (11) (0) (0) (0)	<12> 4 0 0 0 ( 33) ( 0) ( 0) ( 0)	<19> 6 2 0 0 ( 32) ( 11) ( 0) ( 0)
	mineralization:pelvis	1 0 0 0 0 ( 8) ( 0) ( 0) ( 0)	0 0 0 0 0 (0) (0)	4 0 0 0 (33) (0) (0) (0)	5 1 0 0 (26) (5) (0) (0)
	mineralization:cortex	0 0 0 0 0 (0) (0)	1 0 0 0 (11) (0) (0) (0)	0 0 0 0 0 ( 0) ( 0)	2 1 0 0 (11) (5) (0) (0)
	desquamation:pelvis	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 ( 0) ( 0)	5 0 0 0 (26) (0) (0) (0)
	simple hyperplasia:transitional epitheliu	1 0 0 0 ( 8) ( 0) ( 0) ( 0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	3 0 0 0 (16) (0) (0) (0)
	nodular hyperplasia:transitional epitheli	0 0 0 0 0 ( 0) ( 0) ( 0)	0 0 0 0 0 (0)	0 0 0 0 0 ( 0) ( 0)	4 1 0 0 (21) (5) (0) (0)
	calculus	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 0 (0)	0 0 0 0 0 0 ( 0) ( 0)	5 1 0 0 (26) (5) (0) (0)
ureter	dilatation	<pre></pre>	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	3> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<pre></pre>
Grade <a>&gt; b (c)</a>	1: Slight 2: Moderate 3: M a: Number of animals examined at the site b: Number of animals with lesion c: b/a*100	arked 4: Severe			

STUDY NO. : 0205
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

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

Organ		Group Name No. of Animals on Study Grade 1 (%)	Control 13 2 3 4 (%) (%) (%)	500ppm 9 1 2 3 4 (%) (%) (%)	1500ppm 12 1 2 3 4 (%) (%) (%) (%)	4500ppm 19 12 3 4 (%) (%) (%) (%)
[Urinary sys	tem]					
urin bladd	hemorrhage	0 ( 0) (	<13> 0 0 0 0) ( 0) ( 0)	( 0) ( 0) ( 0) ( 0)	<12> 0 0 0 0 0 0 0 0 0 0 0 0	(19) 0 4 0 0 ( 0) ( 21) ( 0) ( 0)
	squamous cell metaplasia	0 ( 0) (	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 (0) (0)	3 2 0 0 (16) (11) (0) (0)
	squamous cell hyperplasia	( 0) (	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0)	2 0 0 0 0 (11) (0) (0) (0)
	inflammatory polyp	( 0) (	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0)	0 1 3 1 ( 0) ( 5) ( 16) ( 5)
	simple hyperplasia:transitional epithe		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0)	5 1 0 0 (26) (5) (0) (0)
	nodular hyperplasia:transitional epith	nelium 0 ( 0) (	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 (0) (0)	8 6 1 0 (42) (32) (5) (0)
	papillary hyperplasia:transitional epi		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0)	2 5 0 0 (11) (26) (0) (0)
	basal cell hyperplasia:transitional ep		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 (0) (0)	0 2 1 0 ( 0) ( 11) ( 5) ( 0)
Grade <a>&gt; b (c)</a>	1: Slight 2: Moderate 3 a: Number of animals examined at the si b: Number of animals with lesion c: b/a * 100	: Marked 4 : Severe te	·			

STUDY NO. : 0205
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name         Control           No. of Animals on Study         13           Grade         1 2 3 4           (%)         (%)         (%)         (%)	500ppm 9 1 2 3 4 (%) (%) (%) (%)	1500ppm 12 1 2 3 4 (%) (%) (%) (%)	4500ppm 19 1 2 3 4 (%) (%) (%) (%)
[Endocrine s	system]				
pituitary	hyperplasi <b>a</b>	<13> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<pre></pre>	\( \lambda 12 \rangle \) \( 1  0  0  0 \) \( ( 8)  ( 0)  ( 0)  ( 0) \)	1 0 0 0 ( 5) ( 0) ( 0) ( 0)
	hyperplasia:gland	0 0 0 0 0 (0) (0)	0 1 0 0 (0) (11) (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
	Rathke pouch	0 0 0 0 0 (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 ( 8) ( 0) ( 0) ( 0)	1 0 0 0 ( 5) ( 0) ( 0) ( 0)
thyroid	C-cell hyperplasia	( 0) ( 0) ( 0) ( 0)	(9) 1 1 0 0 (11) (11) (0) (0)	(12> 0 1 0 0 ( 0) ( 8) ( 0) ( 0)	1 0 0 0 ( 5) ( 0) ( 0) ( 0)
adrena l	hypertrophy	0 1 0 0 ( 0) ( 8) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<12> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<19> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	hyperplasia:medulla	0 0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 0 ( 0) ( 0)	1 0 0 0 0 ( 8) ( 0) ( 0) ( 0)	1 0 0 0 0 ( 5) ( 0) ( 0) ( 0)
(Reproductiv	ve system]				
testis	atrophy	(13) 0 3 0 0 ( 0) ( 23) ( 0) ( 0)	( 0) ( 0) ( 0) ( 0)	(12) 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<19> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
Grade <a>&gt; b (c)</a>	1: Slight 2: Moderate 3 a: Number of animals examined at the s b: Number of animals with lesion c: b / a * 100	: Marked 4 : Severe ite			

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

REPORT TYPE : A1 SEX : MALE

Organ		Group Name         Control           No. of Animals on Study         13           Grade         1 2 3 4           (%)         (%)         (%)         (%)         (%)	500ppm 9 1 2 3 4 (%) (%) (%) (%)	1500ppm 12 1 2 3 4 (%) (%) (%) (%)	4500ppm 19 1 2 3 4 (%) (%) (%) (%)
[Reproductive	system]				
testis	arteritis	\( \lambda 13 \rangle \) \[ 1  1  0  0 \\ (8)  (8)  (0)  (0) \]	<pre></pre>	<12> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<19> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
	interstitial cell hyperplasia	4 0 0 0 (31) (0) (0) (0)	1 0 0 0 (11) (0) (0) (0)	1 0 0 0 0 ( 8) ( 0) ( 0) ( 0)	1 0 0 0 0 (5) (0) (0)
prostate	inflammation	(13) 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 ( 8) ( 0) ( 0) ( 0)	(19) 0 1 0 0 ( 0) ( 5) ( 0) ( 0)
	hyperplasia	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 ( 0) ( 0)	2 0 0 0 0 (11) (0) (0) (0)
mammary gl	hyperplasia	(13> 0 1 0 0 ( 0) ( 8) ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	galactocele	1 1 0 0 (8) (8) (0) (0)	0 0 0 0 0 (0)	1 0 0 0 0 ( 8) ( 0) ( 0) ( 0)	0 0 0 0 0 0 (0) (0)
[Nervous syst	tem]				
brain	hemorrhage	<13> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 1 0 ( 5) ( 0) ( 5) ( 0)
Grade (a) b (c)	1: Slight 2: Moderate 3 a: Number of animals examined at the si b: Number of animals with lesion c: b / a * 100	: Marked 4 : Severe te			

(HPT150)

BAIS3

STUDY NO. : 0205 ANIMAL : RAT F344 REPORT TYPE ; A1

: MALE

SEX

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

PAGE: 11

0rgan	No	roup Name Control  o. of Animals on Study 13 rade 1 2 3 4 (%) (%) (%) (%)	9 1 2 3 4 (%) (%) (%) (%)	1500ppm 12 12 (%) (%) (%) (%)	4500ppm 19 19 (%) (%) (%) (%)
[Nervous syst	tem]				
spinal cord	hemorrhage	0 0 0 0 0 0 0 0 0 0 0 0 0 0	( 0) ( 0) ( 0) ( 0)	1 0 0 0 ( 8) ( 0) ( 0) ( 0)	0 2 0 0 ( 0) ( 11) ( 0) ( 0)
[Special sens	se organs/appandage]				
өуө	retinal atrophy	<13> 8 2 0 0 (62) (15) (0) (0)	3 0 0 0 (33) (0) (0) (0)	6 1 0 0 (50) (8) (0) (0)	7 5 1 0 ( 37) ( 26) ( 5) ( 0)
	keratitis	0 1 0 0 ( 0) ( 0)	0 0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 (0) (0)	0 0 1 0 ( 0) ( 5) ( 0)
arder gl	degeneration	2 0 0 0 (15) (0) (0) (0)	0 1 0 0 ( 0) ( 11) ( 0) ( 0)	1 2 0 0 ( 8) ( 17) ( 0) ( 0)	( 0) ( 5) ( 0) ( 0)
	lymphocytic infiltration	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 1 0 0 ( 0) ( 8) ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0)
	hyperplasia	1 0 0 0 0 ( 8) ( 0) ( 0) ( 0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0)
rade a > b c )	1: Slight 2: Moderate 3: a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	Marked 4: Severe			

(HPT150)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

REPORT TYPE : A1 SEX : MALE

(HPT150)

Group Name Control 500ppm 1500ppm 4500ppm No. of Animals on Study 13 9 12 19 Grade 3 3 3 3 (%) (%) Findings\_ (%) (%) (%) (%) (%) [Special sense organs/appandage] nasolacr d <13> < 9> inflammation 0 0 0 0 0 0 0 0 0 0 1 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (8)(0)(0)(0) (5)(0)(0)(0) [Musculoskeletal system] <13> ⟨ 9⟩ muscle ⟨19⟩ mineralization 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(11)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) [Body cavities] peritoneum <13> < 9> <12> <19> peritonitis 1 0 0 0 0 0 0 0 0 0 0 0 (8)(0)(0)(0) ( 0) ( 0) ( 0) ( 0) (0)(0)(0)(0) (0)(0)(0)(0) Grade 1 : Slight 3 : Marked 2 : Moderate 4 : Severe <a>></a> a: Number of animals examined at the site b b: Number of animals with lesion (c) c : b / a \* 100

BAIS3

### APPENDIX K 2

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

RAT: FEMALE: DEAD AND MORIBUND ANIMALS

STUDY NO. : 0205 ANIMAL : RAT F344 REPORT TYPE : A1

SEX

: FEMALE

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

14 DEAD AND MORIBUND AN

Organ		of Animals on Study 6	Control 3 4 (%) (%)	500ppm 12 12 3 4 (%) (%) (%)	1500ppm 6 1 2 3 4 (%) (%) (%)	4500ppm 13 1 2 3 4 (%) (%) (%) (%)
[Respiratory	system]					
nasal cavit	thrombus	1 2 ( 17) ( 33) (	0 0	0 1 0 0 ( 0) ( 8) ( 0) ( 0)	<pre></pre>	(13) 4 0 1 0 (31) (0) (8) (0)
	necrosis	1 0 (17) (0) (	0 0	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0) (0)
	mineralization	1 0 (17) (0) (	0 0	4 0 0 0 0 (33) (0) (0) (0)	2 0 0 0 0 (33) (0) (0) (0)	5 0 0 0 (38) (0) (0) (0)
	eosinophilic change:olfactory epithelium	1 4 (17) (67) (		4 7 1 0 (33) (58) (8) (0)	2 4 0 0 (33) (67) (0) (0)	5 5 0 0 (38) (38) (0) (0)
	eosinophilic change:respiratory epitheliu	m 2 1 (33) (17) (	0 0	12 0 0 0 (100) ( 0) ( 0) ( 0)	5 0 0 0 (83) (0) (0) (0)	10 0 0 0 (77) ( 0) ( 0) ( 0)
	inflammation:foreign body	0 0 ( 0) (	0 0	1 0 0 0 (8) (0) (0) (0)	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 (0) (0)
	inflammation:olfactory epithelium	1 0 (17) (0) (	0 0	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 (0) (0)
	respiratory metaplasia:gland	4 0 ( 67) ( 0) (	0 0	10 0 0 0 (83) (0) (0) (0)	6 0 0 0 (100) ( 0) ( 0) ( 0)	10 0 0 0 (77) ( 0) ( 0) ( 0)
Grade ( a >  b ( c )	1: Slight 2: Moderate 3: Namber of animals examined at the site b: Number of animals with lesion c: b / a * 100	farked 4 : Severe				

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

REPORT TYPE : A1 SEX : FEMALE

		oup Name Control . of Animals on Study 6	500ppm 12	1500ppm 6	4500ppm 13
rgan		ade 1 2 3 4 (%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)	13 4 (%) (%) (%) (%)
Respiratory :	system]				
nasopharynx	inflammation:foreign body	<pre></pre>	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<pre></pre>	1 0 0 0 ( 8) ( 0) ( 0) ( 0)
larynx	inflammatory infiltration	0 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<pre></pre>	(13) 0 1 0 0 ( 0) ( 8) ( 0) ( 0)
Lung	cangestian	( 6) 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	(12) 1 0 0 0 ( 8) ( 0) ( 0) ( 0)	<pre></pre>	\( \lambda 13 \rangle \) \[ 1  0  0  0  (8)  (0) \q
	hemorrhage	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 1 0 0 ( 0) ( 0)
	inflammatory infiltration	0 0 0 0 0 ( 0) ( 0)	1 0 0 0 0 ( 8) ( 0) ( 0) ( 0)	1 0 0 0 (17) (0) (0) (0)	1 2 0 0 ( 8) ( 15) ( 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 ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0) ( 0)	0 1 0 0 ( 0) ( 0)
[Hematopoieti	c system]				
oone marrow	increased hematopoiesis	(6) 1 0 0 0 (17) (0) (0) (0)	1 0 0 0 ( 8) ( 0) ( 0) ( 0)	(6) 1 0 0 0 (17) (0) (0) (0)	3 0 0 0 ( 23) ( 0) ( 0) ( 0)
Grade < a > b ( c )	1: Slight 2: Moderate 3: a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	Marked 4: Severe			

STUDY NO. : 0205 ANIMAL : RAT F344 REPORT TYPE : A1

: FEMALE

SEX

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

PAGE: 15

Organ	1	Froup Name Control  Fo. of Animals on Study 6  Frade 1 2 3 4  (%) (%) (%) (%)	500ppm 12 1 2 3 4 (%) (%) (%) (%)	1500ppm 6 1 2 3 4 (%) (%) (%) (%)	4500ppm 13 1 2 3 4 (%) (%) (%) (%)
[Hematapaie	rtic system]				
spleen	atrophy	<pre></pre>	<12> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	< 6> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<13> 0 0 2 0 ( 0) ( 0) ( 15) ( 0)
	deposit of hemosiderin	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 (0) (0)	1 0 0 0 (17) (0) (0) (0)	1 0 0 0 0 (8) (0) (0) (0)
	fibrosis	0 0 0 0 0 ( 0) ( 0)	1 0 0 0 0 (8) (0) (0) (0)	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 (0) (0)
	extramedullary hematopoiesis	0 0 2 0 ( 0) ( 33) ( 0)	2 0 0 0 (17) (0) (0) (0)	0 1 0 0 (0) (17) (0) (0)	1 4 1 0 ( 8) ( 31) ( 8) ( 0)
{Circulator	y system]				
heart	thrombus	( 0) ( 0) ( 0) ( 0)	0 1 0 0 ( 0) ( 8) ( 0) ( 0)	65 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	(13) 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 1 2 0 ( 0) ( 8) ( 15) ( 0)
	myocardial fibrosis	0 1 0 0 (0) (17) (0) (0)	2 1 0 0 (17) (8) (0) (0)	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 (0) (0)
Grade ( a > b ( c )	1: Slight 2: Moderate 3 a: Number of animals examined at the si b: Number of animals with lesion c: b / a * 100	: Marked 4 : Seuere te			

(HPT150)

BAIS3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

REPORT TYPE : A1
SEX : FEMALE

Organ	Findings	Group Name   Control No. of Animals on Study   6   Grade   1   2   3   4   (%)   (%)   (%)   (%)	12 12 1 2 3 4 (%) (%) (%) (%)	1500ppm 6 1 2 3 4 (%) (%) (%) (%)	4500ppm 13 13 (%) (%) (%) (%)
Digestive sys	stem]				
stomach	ulcer:forestomach	( 6> 1 0 0 0 ( 17) ( 0) ( 0) ( 0)	2 0 0 0 ( 17) ( 0) ( 0) ( 0)	3 0 0 0 (50) (0) (0) (0)	(13) 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	erosion:glandular stomach	0 0 0 0 0 0 (0)	1 0 0 0 0 ( 8) ( 0) ( 0) ( 0)	0 0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 0 ( 0) ( 0)
	ulcer:glandular stomach	1 0 0 0 0 (17) (17) (17) (17) (17)	1 0 0 0 0 (8) (0) (0) (0)	1 0 0 0 0 (17) (0) (0) (0)	0 0 0 0 0 (0) (0)
	mineralization:glandular stomach	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 ( 0) ( 0)	1 0 0 0 0 ( 8) ( 0) ( 0) ( 0)
arge intes	inflammation	(6> 1 0 0 0 (17) (0) (0) (0)	<12>	6> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
iver	herniation	<pre></pre>	<12> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	( 6) ( 0) ( 0) ( 0)	2 0 0 0 ( 15) ( 0) ( 0) ( 0)
	necrosis:facal	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 1 0 (0) (8) (0)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

STUDY NO. : 0205 ANIMAL : RAT F344 REPORT TYPE : A1

SEX : FEMALE

0rgan	Findings	Group Name Control  No. of Animals on Study 6  Grade 1 2 3 4  (%) (%) (%) (%)	500ppm 12 12 3 4 (%) (%) (%) (%)	1500ppm 6 1 2 3 4 (%) (%) (%) (%)	4500ppm 13 1 2 3 4 (%) (%) (%) (%)
[Digestive s	ystem]				
liver	fatty change:central	< 6> 0 1 0 0 ( 0) ( 17) ( 0) ( 0)	<12> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<pre></pre>	<13> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	degeneration:central	0 0 0 0 0 (0) (0)	0 0 1 0 (0) (8) (0)	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 0 (0) (0)
	granulation	1 1 0 0 (17) (17) (0) (0)	1 0 0 0 0 ( 8) ( 0) ( 0)	1 0 0 0 (17) (0) (0) (0)	2 0 0 0 (15) (0) (0) (0)
	basophilic cell focus	0 0 0 0 0 (0) (0)	1 0 0 0 0 ( 8) ( 0) ( 0) ( 0)	1 0 0 0 (17) (0) (0) (0)	0 0 0 0 0 0 ( 0) ( 0)
	bile duct hyperplasia	0 0 0 0 0 (0) (0)	3 0 0 0 (25) (0) (0) (0)	1 0 0 0 (17) (0) (0) (0)	1 0 0 0 0 ( 8) ( 0) ( 0) ( 0)
	biliary cyst	0 0 0 0 0 (0) (0)	0 0 0 0 0 0 (0) (0)	0 0 1 0 (0) (17) (0)	0 0 0 0 0 0 (0) (0)
pancreas	atrophy	< 6> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 1 0 ( 0) ( 0) ( 8) ( 0)	( 0) ( 0) ( 0) ( 0)	<13> 0 2 0 0 ( 0) ( 15) ( 0) ( 0)
[Urinary sys	etem]				
kidney	infarct	<pre></pre>	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	6> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 ( 8) ( 0) ( 0) ( 0)

(HPT150)

BAIS3

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

REPORT TYPE : A1 SEX : FEMALE

Organ	1	Group Name  do. of Animals on Study Grade 1 (%) (	Control 6 2 3 4 %) (%) (%)	12 500ppm 12 3 4 (%) (%) (%) (%)	1500ppm 6 1 2 3 4 (%) (%) (%)	4500ppm 13 1 2 3 4 (%) (%) (%) (%)
[Urinary sys	stem]					
kidney	deposit of hemosiderin		< 6> 2 0 0 3) ( 0) ( 0)	<12> 0 4 0 0 ( 0) ( 33) ( 0) ( 0)	6> 0 4 0 0 ( 0) ( 67) ( 0) ( 0)	(13) 0 4 0 0 (0) (31) (0) (0)
	chronic nephropathy		1 0 0 7) ( 0) ( 0)	2 0 0 0 (17) (0) (0) (0)	1 0 0 0 (17) (0) (0) (0)	0 2 1 0 ( 0) ( 15) ( 8) ( 0)
	tubular necrosis		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 3 0 0 (0) (25) (0) (0)	0 1 0 0 (0) (17) (0) (0)	0 1 1 0 ( 0) ( 8) ( 8) ( 0)
	papillary necrosis		0 0 0 0 0 0 0 0 0 0 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 3 0 ( 8) ( 15) ( 23) ( 0)
	mineralization:cortico-medullary junct		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	2 0 0 0 0 (17) (0) (0) (0)	3 1 0 0 (50) (17) (0) (0)	4 0 0 0 (31) (0) (0) (0)
	mineralization:papilla		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	4 0 0 0 0 (33) (0) (0) (0)	0 0 0 0 0 (0) (0)	2 0 0 0 (15) (0) (0) (0)
	mineralization:pelvis		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	2 0 0 0 0 (17) (0) (0) (0)	2 0 0 0 0 (33) (0) (0) (0)	3 0 0 0 (23) (0) (0) (0)
	mineralization:cortex		1 0 0 7) ( 0) ( 0)	0 0 0 0 0 0 (0)	0 0 0 0 0 0 ( 0) ( 0)	1 2 0 0 ( 8) ( 15) ( 0) ( 0)
Grade <a>&gt; b (c)</a>	1: Slight 2: Moderate 3 a: Number of animals examined at the si b: Number of animals with lesion c:b/a*100	: Marked 4 : Severe te				

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

REPORT TYPE : A1 SEX : FEMALE

0rgan	Group Name No. of Anim Grade	Control  als on Study 6  1 2 3 4  (%) (%) (%) (%)	500ppm 12 12 3 4 (%) (%) (%) (%)	1500ppm 6 1 2 3 4 (%) (%) (%) (%)	4500ppm 13 12 3 4 (%) (%) (%) (%)
[Urinary sys	tem]				
kidney	simple hyperplasia:transitional epithelium	6> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	2 0 0 0 ( 17) ( 0) ( 0) ( 0)	2 0 0 0 0 (33) (0) (0) (0)	5 0 0 0 0 (38) (0) (0) (0)
	nodular hyperplasia:transitional epithelium	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 ( 0) ( 0)	1 0 0 0 0 (8) (0) (0) (0)
	calculus	0 0 0 0 0 (0) (0)	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 ( 0) ( 0)	1 0 0 0 ( 8) ( 0) ( 0)
	mineralization:inner stripe,outer medulla	0 0 0 0 0 0 (0)	0 0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0)	0 1 0 0 ( 0) ( 0)
urin bladd	squamous cell metaplasia	< 6> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<12> 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<pre></pre>	1 0 0 0 ( 8) ( 0) ( 0) ( 0)
	nodular hyperplasia:transitional epithelium	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 ( 0) ( 0)	2 0 0 0 0 (15) (0) (0) (0)
	papillary hyperplasia:transitional 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)	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	2 0 0 0 0 (15) (0) (0) (0)
[Endocrine s	ystem]				
pituitary	cyst	<pre></pre>	1 0 0 0 ( 8) ( 0) ( 0) ( 0)	2 0 0 0 (33) (0) (0) (0)	3 0 0 0 (23) (0) (0) (0)
Grade <a>&gt; b (c)</a>	1: Slight 2: Moderate 3: Marked a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100	4 : Severe			
(HPT150)					BAIS3

STUDY NO. : 0205 ANIMAL : RAT F344
REPORT TYPE : A1 SEX : FEMALE

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

PAGE: 20

Organ	N.	Froup Name Control 6 6 6 7 1 2 3 4 7 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	500ppm 12 12 3 4 (%) (%) (%) (%)	1500ppm 6 1 2 3 4 (%) (%) (%) (%)	4500ppm 13 1 2 3 4 (%) (%) (%) (%)
[Endocrine s	ystem]				
pituitary	hyperplasia	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 ( 8) ( 0) ( 0) ( 0)	<pre></pre>	<13> 1 0 0 0 ( 8) ( 0) ( 0) ( 0)
thyroid	C-cell hyperplasia	< 6> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<12> 2 2 0 0 ( 17) ( 17) ( 0) ( 0)	< 6> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<13> 0 1 0 0 ( 0) ( 8) ( 0) ( 0)
adrena l	peliosis-like lesion	<pre></pre>	<12> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	(6) 1 0 0 0 (17) (0) (0) (0)	3 0 0 0 (23) (0) (0) (0)
	hyperplasia:medulla	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0)	0 1 0 0 (0) (17) (0) (0)	0 0 0 0 0 (0) (0)
	focal fatty change:cortex	0 0 0 0 0 ( 0) ( 0)	1 0 0 0 0 ( 8) ( 0) ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0)	1 0 0 0 0 ( 8) ( 0) ( 0) ( 0)
[Reproductiv	e system]				
uterus	cystic endometrial hyperplasia	3 1 0 0 (50) (17) (0) (0)	3 0 1 0 ( 25) ( 0) ( 8) ( 0)	(6) 1 0 0 0 (17) (0) (0) (0)	1 0 0 0 ( 8) ( 0) ( 0) ( 0)
Grade <a> b (c)</a>	1: Slight 2: Moderate 3: a: Number of animals examined at the sit b: Number of animals with lesion c: b / a * 100	Marked 4 : Severe e			
(IIPT150)					Е

STUDY NO. : 0205 ANIMAL : RAT F344 REPORT TYPE : A1

: FEMALE

SEX

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

PAGE: 21

Organ	Group Na No. of / Grade	me Control snimals on Study 6 \\ \frac{1}{(\%)} \frac{2}{(\%)} \frac{3}{(\%)} \frac{4}{(\%)} \\ \frac{(\%)}{(\%)} \frac{(\%)}{(\%)} \\ (\%	500ppm 12 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	4500ppm 13 1 2 3 4 (%) (%) (%) (%)
[Reproductive	e system]				
mammary gl	hyperplasia	<pre></pre>	\( \lambda 12 \rangle \) \( 1  0  0  0 \) \( 8 \rangle ( 0 ) ( 0 ) ( 0 ) \)	< 6> 0 0 0 0 0 0 0 0 0 0 0	<pre></pre>
	galactocolo	0 0 0 0 0 ( 0) ( 0)	0 1 0 0 (0) (8) (0) (0)	0 1 0 0 (0) (17) (0) (0)	1 0 0 0 0 (8) (0) (0) (0)
[Nervous syst	tem]				
brain	hemorrhage	( 6) 1 0 0 0 ( 17) ( 0) ( 0) ( 0)	1 0 0 0 ( 8) ( 0) ( 0) ( 0)	( 0) ( 0) ( 0) ( 0)	\( \lambda 13 \rangle \) \( 1  0  0  0 \) \( 8 \rangle ( 0 ) ( 0 ) ( 0 )
spinal cord	hemorrhage	< 6> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 ( 8) ( 0) ( 0) ( 0)	< 6> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 ( 8) ( 0) ( 0) ( 0)
[Special sens	se organs/appandage]				
еуе	hemorrhage	<pre></pre>	1 0 0 0 ( 8) ( 0) ( 0) ( 0)	< 6> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	\( \lambda \) \( 0 \) \( 0 \) \( 0 \) \( 0 \) \( 0 \) \( 0 \) \( 0 \) \( 0 \)
Grade <a>&gt; b (c)</a>	1: Slight 2: Moderate 3: Market a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	d 4 : Severe			
(HPT150)					ВА

STUDY NO. : 0205 ANIMAL : RAT F344 REPORT TYPE : A1

: FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

Group Name Control 500ppm 1500ppm 4500ppm No. of Animals on Study 6 12 13 3 Findings (%) (%) (%) (%) (%) (%) (%) (%) [Special sense organs/appandage] өуө < 6> <12> < 6> retinal atrophy 1 0 0 4 0 4 2 0 0 (50) (17) (0) (0) (33) (33) (0) (0) (67) (33) (0) (0) (54) (8) (0) (0) keratitis 0 0 0 1 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (8) (0) (0) (0) Harder gl 〈 6〉 < 6> <13> degeneration 2 0 0 0 1 1 0 0 0 0 0 0 0 0 0 0 (33) (0) (0) (0) (8)(8)(0)(0) ( 0) ( 0) ( 0) ( 0) (0)(0)(0)(0) lymphocytic infiltration 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 (17) (0) (0) (0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) nasolacr d < 6> <13> inflammation 0 0 0 0 2 1 0 0 0 1 0 0 1 2 0 0 (0)(0)(0)(0) (17) (8) (0) (0) (0)(17)(0)(0) (8) (15) (0) (0) [Musculoskeletal system] muscle < 6> < 6> mineralization 0 0 0 0 1 0 0 0 0 0 0 0 1 0 0 0 (0)(0)(0)(0) (8)(0)(0)(0) (0)(0)(0)(0) (8) (0) (0) (0) Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe <a>></a> a: Number of animals examined at the site b b: Number of animals with lesion (c) c:b/a \* 100

(HPT150)

STUDY NO. : 0205 ANIMAL : RAT F344 REPORT TYPE : A1

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

SEX : FEMALE

		roup Name o, of Animals on Study	6 6	antro l	L		12	500p 2	mag			1500p 6	<b>P</b> M		1	4500pp 3	m
0rgan	_ Findings	rade <u>1</u> (%)	2 (%)	3 (%)	<u>4</u> (%)	(%)	(%)	(%)	<u>4</u> (%)	1 (%)	2 (%)	3 (%)	<u>4</u> (%)	1 (%)	2 (%)	3 (%)	(%)
usculoske	əletal system]																
ne	asteasclerasis	1 ( 17)	< 6> 1 ( 17) (	2 33) (	0	0 ( 0)	(12 ( 8)	1	0 ( 0)	( 0) (	0 0)	6> 0 ( 0)	0 ( 0)	( 0) (	〈1 1 ( 8)	1	0
ade a > b c )	1: Slight 2: Moderate 3: a: Number of animals examined at the sit b: Number of animals with lesion c: b/a * 100	Marked 4 ; Severe															

#### APPENDIX K 3

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

RAT: MALE: SACRIFICED ANIMALS

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

REPORT TYPE : A1 SEX : MALE

0rgan		O Name Control of Animals on Study 37 (%) (%) (%) (%)	500ppm 41 1 2 3 4 (%) (%) (%) (%)	1500ppm 38 1 2 3 4 (%) (%) (%) (%)	4500ppm 31 1 2 3 4 (%) (%) (%) (%)
[Integumentar:	y system/appandage]				
skin/app	inflammation	37> 0 1 0 0 ( 0) ( 3) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	38> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	31> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	epidermal cyst	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 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
[Respiratory	system]				
nasal cavit	thrombus	<37> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	388> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)	31> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)
	mineralization	18 0 0 0 ( 49) ( 0) ( 0) ( 0)	17 0 0 0 (41) (0) (0) (0)	29 0 0 0 ( 76) ( 0) ( 0) ( 0)	16 1 0 0 (52) (3) (0) (0)
	eosinophilic change:olfactory epithelium	34 2 0 0 (92) (5) (0) (0)	33 3 0 0 (80) (7) (0) (0)	18 0 0 0 ( 47) ( 0) ( 0) ( 0)	10 0 0 0 (32) (0) (0) (0
	eosinophilic change:respiratory epithelium	26 0 0 0 ( 70) ( 0) ( 0) ( 0)	26 0 0 0 (63) (0) (0) (0)	14 0 0 0 ( 37) ( 0) ( 0) ( 0)	10 0 0 0 (32) ( 0) ( 0) ( 0
	inflammation:foreign body	8 2 1 0 ( 22) ( 5) ( 3) ( 0)	5 5 0 0 (12) (12) (0) (0)	7 4 0 0 (18) (11) (0) (0)	4 4 1 0 (13) (13) (3) (0

(HPT150)

BAIS3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

REPORT TYPE : A1
SEX : MALE

Group Name Control 500ppm 1500ppm 4500ppm No. of Animals on Study 37 41 31 Grade 3 (%) (%) (%) (%) (%) (%) Organ Findings [Respiratory system] nasal cavit <37> inflammation:respiratory epithelium 0 0 0 0 0 0 0 0 (5)(0)(0)(0) (7)(0)(0)(0) (5)(0)(0)(0) (3)(0)(0)(0) respiratory metaplasia:olfactory epithelium 1 0 0 0 2 0 0 0 (3)(0)(0)(0) (24) (0) (0) (0) (16) (0) (0) (0) (6)(0)(0)(0) respiratory metaplasia:gland (97) (0) (0) (0) (95) (0) (0) (0) (84) (0) (0) (0) (94) (0) (0) (0) nasopharynx ⟨37⟩ <41> ⟨31⟩ inflammation:foreign body 3 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 (8)(0)(0)(0) (0)(0)(0)(0) (3)(0)(0)(0) (0)(0)(0)(0) Larynx <37> <41> ⟨38⟩ 0 1 0 0 0 0 0 0 0 0 0 0 inflammation:foreign body (0)(3)(0)(0) ( 0) ( 0) ( 0) ( 0) (0)(0)(0)(0) (0)(0)(0)(0) lung <41> ⟨38⟩ inflammatory infiltration 0 0 0 0 0 0 0 1 0 0 0 0 1 0 0 (0)(0)(0)(0) (2)(0)(0)(0) (3)(0)(0)(0) (0)(3)(0)(0) accumulation of foamy cells 1 0 0 0 0 0 1 0 0 0 0 0 0 0 (3)(0)(0)(0) (0)(0)(0)(0) (3)(0)(0)(0) (0)(0)(0)(0) Grade 1 : Slight 2 : Moderate 4 : Severe <a>></a> a: Number of animals examined at the site b b: Number of animals with lesion (c) c:b/a\*100

(HPT150)

BAIS3

STUDY NO. : 0205 ANIMAL : RAT F344 REPORT TYPE : A1

: MALE

Findings\_

SEX

Organ\_\_\_\_

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

500ppm

(%)

(%)

Control

(%)

37

(%)

SACRIFICED ANIMALS (105W)

Group Name

No. of Animals on Study

[Respiratory system] ⟨37⟩ lung <41> <38> bronchopneumonia 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(3)(0) (0)(0)(0)(0) bronchiolar-alveolar cell hyperplasia 2 1 0 0 0 0 0 1 0 0 0 0 0 0 (5)(3)(0)(0) (2) (0) (0) (0) (0)(3)(0)(0) (0)(0)(0)(0) [Hematopoietic system] bone marrow ⟨37⟩ <41> <31> 0 0 0 0 0 0 3 0 0 0 3 0 0 angiectasis (8) (0) (0) (0) (15) (0) (0) (0) (8) (0) (0) (0) (19) (10) (0) (0) thrombus (0)(0)(0)(0) (2)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) granulation 0 1 0 1 1 0 0 3 0 0 0 (11) (0) (0) (0) (12) (2) (0) (0) (3)(3)(0)(0) (10) (0) (0) (0) increased hematopoiesis (13) (0) (0) (0) (5)(0)(0)(0) (0)(0)(0)(0) (3)(0)(0)(0) decreased hematopoiesis 0 0 0 0 0 0 0 1 0 0 (0)(0)(0)(0) (2)(0)(0)(0) (3)(0)(0)(0) (0)(3)(0)(0)

(HPT150)

Grade

<a>></a>

b

(c)

1: Slight

c : b / a \* 100

2 : Moderate

a: Number of animals examined at the site

b: Number of animals with lesion

3 : Marked

4 : Severe

PAGE: 3

4500ppm

(%) (%)

31

(%)

1500ppm

(%)

(%)

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

REPORT TYPE : A1
SEX : MALE

Group Name Control 500ppm 1500ppm 4500ppm No. of Animals on Study 41 31 3 Findings (%) (%) (%) (%) (%) (%) (%) [Hematopoietic system] bone marrow <37> <41> erythropoiesis:increased 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (6)(0)(0)(0) lymph node <37> <41> ⟨38⟩ <31> lymphadenitis 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) spleen ⟨37⟩ <41> <38> ⟨31⟩ deposit of hemosiderin 0 0 0 0 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (3)(0)(0)(0) (0)(0)(0)(0) inflammation 0 0 1 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(3)(0) (0)(0)(0)(0) fibrosis 2 0 0 0 1 2 0 0 (0)(8)(0)(0) (2) (0) (0) (0) (5)(0)(0)(0) (3)(6)(0)(0) extramedullary hematopoiesis 0 0 0 0 (0)(0)(0)(0) (2) (0) (0) (0) (0)(0)(3)(0) (6)(3)(0)(0) [Circulatory system] heart <41> ⟨31⟩ thrombus 0 1 0 0 1 0 0 0 0 0 0 0 0 0 0 0 (0)(3)(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> a : Number of animals examined at the site

b: Number of animals with lesion

c:b/a\*100

b

(c)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

REPORT TYPE : A1

: MALE SEX Control 1500-

			Control 37	500ppm 41	1500ppm 38	4500ppm 31
Organ	Findings	Grade <u>1 2</u> (%) (%)	3 4 (%)	1 2 3 4 (%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)	$\frac{1}{(\%)}$ $\frac{2}{(\%)}$ $\frac{3}{(\%)}$ $\frac{4}{(\%)}$
[Circulator	y system]					
heart	myocardial degeneration	0 0	37> 0 0 ( 0) ( 0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<38> 0 0 0 0 0 0 0 0 0 0 0	31> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)
	myocardial fibrosis	10 0 ( 27) ( 0)	0 0 (0)	14 0 0 0 (34) (0) (0) (0)	9 0 0 0 0 (24) (0) (0) (0)	4 2 0 0 (13) (6) (0) (0)
[Digestive	system]					
tongue	arteritis	3 0	37> 0 0 ( 0) ( 0)	0 1 0 0 ( 0) ( 2) ( 0) ( 0)	<pre></pre>	(31) 0 0 0 0 (0) (0) (0) (0)
stomach	ulcer:forestomach	0 0	0 0 (0) (0)	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<37> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)	<31> 0 0 0 0 0 0 0 0 0 0 0
	erosion:glandular stomach	1 0 ( 3) ( 0)	0 0 (0)	3 0 0 0 ( 7) ( 0) ( 0) ( 0)	2 0 0 0 0 (5) (0) (0) (0)	1 0 0 0 0 (3) (0) (0) (0)
Liver	herniation	0 0	0 0 ( 0) ( 0)	2 0 0 0 ( 5) ( 0) ( 0) ( 0)	38> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<31> 2 0 0 0 ( 6) ( 0) ( 0) ( 0)
Grade	1: Slight 2: Moderate	3 : Marked 4 : Severe	···			

< a >

b

a: Number of animals examined at the site

b: Number of animals with lesion

(c)

c:b/a\*100

(HPT150)

BAIS3

STUDY NO. : 0205 ANIMAL : RAT F344 REPORT TYPE : A1

: MALE

SEX

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

Organ	Group No. of No. of Grade	lame Control Animals on Study 37  1 2 3 4 (%) (%) (%) (%)	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	1500ppm 38 1 2 3 4 (%) (%) (%) (%)	4500ppm 31 1 2 3 4 (%) (%) (%) (%)
[Digestive	system]				
liver	necrosis:focal	<37> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 1 0 ( 0) ( 0) ( 2) ( 0)	(38) 0 0 0 0 (0) (0) (0) (0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	granulation	4 2 1 0 (11) (5) (3) (0)	1 6 1 0 ( 2) ( 15) ( 2) ( 0)	2 4 0 0 ( 5) ( 11) ( 0) ( 0)	2 4 0 0 ( 6) ( 13) ( 0) ( 0)
	clear cell focus	8 2 0 0 (22) (5) (0) (0)	4 1 1 1 (10) (2) (2) (2)	4 4 0 0 (11) (11) (0) (0)	3 0 0 0 (10) (0) (0) (0)
	acidophilic cell focus	2 0 0 0 0 ( 5) ( 0) ( 0)	0 0 0 0 0 (0) (0)	2 0 0 0 0 (5) (0) (0)	1 0 0 0 0 (3) ( 0) ( 0) ( 0)
	basophilic cell focus	6 2 0 0 (16) (5) (0) (0)	5 0 1 0 (12) (0) (2) (0)	4 1 0 0 (11) (3) (0) (0)	5 2 0 0 (16) (6) (0) (0)
	vacuolated cell focus	1 0 0 0 0 (3) ( 0) ( 0)	2 0 0 0 0 (5) (0) (0)	0 0 0 0 0 ( 0) ( 0)	1 0 0 0 0 (3) (0) (0)
	mixed cell focus	1 1 0 0 (3) (3) (0) (0)	1 0 1 0 ( 2) ( 0) ( 2) ( 0)	1 0 1 0 ( 3) ( 0) ( 3) ( 0)	1 1 0 0 (3) (3) (0) (0)
	spongiosis hepatis	2 1 0 0 ( 5) ( 3) ( 0) ( 0)	3 1 0 0 ( 7) ( 2) ( 0) ( 0)	16 2 0 0 (42) (5) (0) (0)	8 5 0 0 (26) (16) (0) (0)
Grade < a > b ( c )	1: Slight 2: Moderate 3: Marke a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	d 4 : Severe			

STUDY NO. : 0205 ANIMAL : RAT F344 HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

REPORT TYPE : A1 : MALE

Group Name Control 500ppm 1500ppm 4500ppm No. of Animals on Study 41 31 Grade 0rgan Findings (%) (%) (%) (%) (%) (%) (%) [Digestive system] Liver ⟨37⟩ <41> <31> bile duct hyperplasia 1 35 1 0 3 37 1 0 2 33 2 0 4 24 3 0 (3)(95)(3)(0) (7) (90) (2) (0) (5) (87) (5) (0) (13) (77) (10) (0) pancreas <37> <41> <38> <31> atrophy 4 1 0 4 0 0 6 3 0 0 5 3 0 0 (16) (11) (3) (0) (15) (10) (0) (0) (16) (8) (0) (0) (16) (10) (0) (0) hyperplasia 0 0 0 0 0 0 (0)(0)(0)(0) (0)(2)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) [Urinary system] kidney <37> <41> <38> <31> infarct 0 0 0 0 0 0 0 0 (0)(0)(0)(0) ( 0) ( 0) ( 0) ( 0) (0)(0)(0)(0) (0)(6)(0)(0) hyaline droplet (0)(0)(0)(0) ( 0) ( 0) ( 0) ( 0) (3)(0)(0)(0) (0)(0)(0)(0) deposit of hemosiderin 0 0 0 0 0 1 0 0 0 4 0 0 (0)(0)(0)(0) (2)(2)(0)(0) (0)(3)(0)(0) (0)(13)(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 b (c) c:b/a \* 100

(HPT150)

STUDY NO. : 0205 ANIMAL : RAT F344
REPORT TYPE : A1

SEX

: MALE

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

Organ		up Name Control of Animals on Study 37 de <u>1 2 3 4</u> (%) (%) (%) (%)	500ppm 41 1 2 3 4 (%) (%) (%) (%)	1500ppm 38 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
[Urinary sys	etem]				
kidney	squamous cell metaplasia	<37> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<41> 0 0 0 0 0 0 0 0 0 0 0 0	<38> 0 0 0 0 0 0 0 0	<31> 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
	chronic nephropathy	6 14 12 4 ( 16) ( 38) ( 32) ( 11)	5 17 14 3 (12) (41) (34) (7)	3 12 18 4 ( 8) ( 32) ( 47) ( 11)	10 7 8 3 ( 32) ( 23) ( 26) ( 10)
	hydronephrosis	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 ( 0) ( 0)	0 0 1 0 (0) (0) (0)
	pyelitis	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 ( 0) ( 0)	0 1 0 0 ( 0) ( 0)
	papillary necrosis	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 ( 0) ( 0)	1 0 2 0 (3) (0) (6) (0)
	mineralization:cortico-medullary junction	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0)	6 1 0 0 (19) (3) (0) (0)
	mineralization:papilla	9 0 0 0 (24) ( 0) ( 0) ( 0)	8 0 0 0 0 (20) (0) (0)	10 0 0 0 ( 26) ( 0) ( 0) ( 0)	12 2 1 0 (39) (6) (3) (0)
	mineralization:pelvis	6 2 0 0 (16) (5) (0) (0)	5 l 0 0 (12) (2) (0) (0)	6 0 0 0 (16) (0) (0) (0)	8 4 0 0 (26) (13) (0) (0)
Grade <a>&gt; b (c)</a>	1: Slight 2: Moderate 3: Market a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	arked 4 : Severe			

STUDY NO. : 0205 ANIMAL : RAT F344 REPORT TYPE : A1 : MALE

SEX

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

Organ	Group Name No. of Anim Grade	Control 37 1 2 3 4 (%) (%) (%)	500ppm 41 1 2 3 4 (%) (%) (%) (%)	1500ppm 38 1 2 3 4 (%) (%) (%) (%)	4500ppm 31 1 2 3 4 (%) (%) (%) (%)
[Urinary sys	stem]				
kidney	desquamation:pelvis	<37> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)	<41> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<38> 0 0 0 0 0 0 0 0 0 0 0	<pre></pre>
	simple hyperplasia:transitional epithelium	4 1 0 0 (11) (3) (0) (0)	7 1 0 0 (17) (2) (0) (0)	4 1 0 0 (11) (3) (0) (0)	11 4 1 0 (35) (13) (3) (0)
	nodular hyperplasia:transitional epithelium	0 0 0 0 0 (0) (0)	1 0 0 0 0 (2) (0) (0)	1 0 0 0 0 (3) (0) (0) (0)	8 7 1 0 (26) (23) (3) (0)
	calculus	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 (0) (0)	7 0 0 0 (23) (0) (0) (0)
ureter	dilatation	35> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	38> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	35> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)	\$\frac{\lambda27\rangle}{9}  4  0  0  (33)  (15)  (0)  (0)  (0)
	simple hyperplasia:transitional epithelium	1 0 0 0 ( 3) ( 0) ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0)	8 0 0 0 0 (30) (30) (0)
	nodular hyperplasia:transitional epithelium	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0)	0 1 0 0 ( 0) ( 4) ( 0) ( 0)
urin bladd	squamous cell metaplasia	(37) 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	(41) 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<38> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<pre></pre>
Grade ( a ) b ( c )	1: Slight 2: Moderate 3: Marked a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	4 : Severe			

STUDY NO. : 0205 ANIMAL : RAT F344 HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

REPORT TYPE : A1 SEX

: MALE

0rgan	Group No. of Grade Findings	Name Control 7 Animals on Study 37 (%) (%) (%) (%)	500ppm 41 1 2 3 4 (%) (%) (%) (%)	1500ppm 38 1 2 3 4 (%) (%) (%) (%)	4500ppm 31 1 2 3 4 (%) (%) (%) (%)
[Urinary sys	stem]				
urin bladd	squamous cell hyperplasia	<37> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<41> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<38> 0 0 0 0 0 0 0 0 0 0 0 0	<31> 4 6 1 0 ( 13) ( 19) ( 3) ( 0)
	inflammatory polyp	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 0 4 0 ( 3) ( 0) ( 13) ( 0)
	simple hyperplasia:transitional epithelium	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	6 0 0 0 0 (19) (0) (0)
	nodular hyperplasia:transitional epithelium	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	5 15 5 0 (16) (48) (16) (0)
	papillary hyperplasia:transitional epitheliu	0 0 0 0 0 0 ( 0) ( 0) ( 0)	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 0 (0) (0)	3 6 1 0 (10) (19) (3) (0)
	basal cell hyperplasia:transitional epitheli	( 0) ( 0) ( 0) ( 0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	8 12 4 0 (26) (39) (13) (0)
[Endocrine s	system]				
pituitary	angiectasis	(37) 1 0 0 0 ( 3) ( 0) ( 0) ( 0)	2 0 0 0 ( 5) ( 0) ( 0) ( 0)	<38> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	31> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)
Grade <a>&gt; b (c)</a>	1: Slight 2: Moderate 3: Mark a: Number of animals examined at the site b: Number of animals with lesion c:b/a*100	ted 4 : Severe			

STUDY NO. : 0205 ANIMAL : RAT F344 REPORT TYPE : A1

: MALE

SEX

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

0rgan	Group Na No. of A Grade Findings	me Control Inimals on Study 37  1 2 3 4  (%) (%) (%) (%)	500ppm 41 1 2 3 4 (%) (%) (%) (%)	1500ppm 38 1 2 3 4 (%) (%) (%) (%)	4500ppm 31 1 2 3 4 (%) (%) (%) (%)
(Endocrine s	/stem]				
pituitary	cyst	<37> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	(41) 1 0 0 0 ( 2) ( 0) ( 0) ( 0)	<38> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	31> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)
	hyperplasia	8 1 0 0 (22) (3) (0) (0)	7 0 0 0 (17) (0) (0) (0)	4 1 0 0 (11) (3) (0) (0)	2 0 0 0 0 (6) (6) (0) (0)
	hyperplasia:gland	0 0 0 0 0 (0) (0)	0 1 0 0 ( 0) ( 0)	0 1 0 0 (0) (3) (0) (0)	0 0 0 0 0 ( 0) ( 0)
	Rathke pouch	2 0 0 0 0 (5) (0) (0)	2 0 0 0 0 (5) (0) (0) (0)	2 0 0 0 ( 5) ( 0) ( 0) ( 0)	1 0 0 0 0 (3) (0) (0)
thyroid	ultimibranchial body remanet	<37> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	(41) 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	38> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)	31> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)
	C-cell hyperplasia	3 3 0 0 ( 8) ( 8) ( 0) ( 0)	7 2 0 0 (17) (5) (0) (0)	1 2 0 0 ( 3) ( 5) ( 0) ( 0)	3 2 0 0 (10) (6) (0) (0)
parathyroid	hyperplasia	<37> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<41> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	38> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)	<pre></pre>
Grade (a) b (c)	1: Slight 2: Moderate 3: Market a: Mumber of animals examined at the site b: Number of animals with lesion c: b / a * 100	d 4 : Severe			

STUDY NO. : 0205 ANIMAL : RAT F344 REPORT TYPE : A1

SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

Organ	N	roup Name Control (0. of Animals on Study 37 (%) (%) (%) (%) (%)	500ppm 41 1 2 3 4 (%) (%) (%) (%)	1500ppm 38 1 2 3 4 (%) (%) (%) (%)	4500ppm 31 1 2 3 4 (%) (%) (%) (%)
[Endocrine :	system]				
adrenal	cyst	37> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<38> 0 0 0 0 0 0 0 0 0 0 0	31> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	hyperplasia:medulla	1 0 0 0 0 (3) ( 0) ( 0) ( 0)	6 0 0 0 (15) (0) (0) (0)	2 0 0 0 0 (5) (0) (0)	3 0 0 0 (10) (0) (0) (0)
	focal fatty change:cortex	1 0 0 0 0 (3) ( 0) ( 0) ( 0)	1 0 0 0 0 ( 2) ( 0) ( 0) ( 0)	0 0 0 0 0 0 (0) (0)	2 0 0 0 0 (6) (6) (0) (0)
(Reproducti	ue system]				
testis	arteritis	<37> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)	4 1 0 0 ( 10) ( 2) ( 0) ( 0)	38> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)	31 0 0 0 (10) (0) (0) (0)
	interstitial cell hyperplasia	1 0 0 0 0 (3) ( 0) ( 0) ( 0)	1 0 0 0 0 (2) (0) (0) (0)	2 0 0 0 0 (5) ( 0) ( 0) ( 0)	1 0 0 0 0 (3) (0) (0) (0)
prostate	inflammation	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	(41) 1 0 0 0 ( 2) ( 0) ( 0) ( 0)	<38> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	31> 1 1 1 0 ( 3) ( 3) ( 3) ( 0)
Grade <a> b (c)</a>	1: Slight 2: Moderate 3: a: Number of animals examined at the sit b: Number of animals with lesion c: b/a*100	Marked 4 : Severe se			

STUDY NO. : 0205 ANIMAL : RAT F344 HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

REPORT TYPE : A1
SEX : MALE

PAGE: 13

Organ	Group No. of Grade Findings	ame Control Animals on Study 37  1 2 3 4 (%) (%) (%) (%) (%)	500ppm 41 1 2 3 4 (%) (%) (%) (%)	1500ppm 38 1 2 3 4 (%) (%) (%) (%)	4500ppm 31 1 2 3 4 (%) (%) (%) (%)
[Reproductive	e system]				
prostate	hyperplasia	37> 6 1 0 0 ( 16) ( 3) ( 0) ( 0)	8 0 0 0 ( 20) ( 0) ( 0) ( 0)	3 0 0 0 ( 8) ( 0) ( 0) ( 0)	3 0 0 0 (10) (0) (0) (0)
mammary gl	galactocele	<37> 2 0 0 0 ( 5) ( 0) ( 0) ( 0)	2 0 0 0 ( 5) ( 0) ( 0) ( 0)	<38> 2 0 0 0 ( 5) ( 0) ( 0) ( 0)	<31> 0 0 0 0 0 0 0 0 0
prep/cli gl	duct ectasia	37> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<41> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<38> 0 1 0 0 ( 0) ( 3) ( 0) ( 0)	<pre></pre>
[Special sens	se organs/appandage]				
өуө	cataract	37> 1 0 1 0 ( 3) ( 0) ( 3) ( 0)	\( \begin{array}{cccccccccccccccccccccccccccccccccccc	38> 0 3 0 0 ( 0) ( 8) ( 0) ( 0)	(31) 0 0 2 0 (0) (0) (6) (0)
	retinal atrophy	23 6 3 0 (62) (16) (8) (0)	23 5 5 1 ( 56) ( 12) ( 12) ( 2)	18 6 3 1 ( 47) ( 16) ( 8) ( 3)	17 6 3 0 (55) (19) (10) (0)
	keratitis	0 0 0 0 0 (0) (0)	1 1 0 0 (2) (2) (0) (0)	1 0 0 0 0 (3) (0) (0)	1 0 0 0 0 ( 0) ( 3) ( 0) ( 0)
Grade <a>&gt; b (c)</a>	1: Slight 2: Moderate 3: Marke a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	d 4: Severe			

(HPT150)

STUDY NO. : 0205 ANIMAL : RAT F344 REPORT TYPE : A1

: MALE

SEX

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

SHORTETOED MITTINES (

Group Name Control maq000 1500ppm 4500ppm No. of Animals on Study 41 38 31 3 0rgan Findings\_ (%) (%) (%) (%) (%) (%) (%) (%) (%) [Special sense organs/appandage] Harder gl <37> <41> <31> degeneration 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (3)(0)(0)(0) (6)(0)(0)(0) lymphocytic infiltration 1 0 0 0 1 0 0 0 (3)(0)(0)(0) (5)(0)(0)(0) (3)(0)(0)(0) (3)(0)(0)(0) nasolacr d <41> <31> inflammation 1 1 0 0 1 1 0 0 0 0 0 0 2 1 0 0 (3)(3)(0)(0) (2)(2)(0)(0) (0)(0)(0)(0) (6)(3)(0)(0) [Musculoskeletal system] bane <41> <38> ⟨31⟩ osteosclerosis 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 ( 0) ( 0) ( 0) ( 0) (0)(0)(0)(0) (3)(0)(0)(0) (0)(0)(0)(0)

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

b : Number of animals with lesion

(c) c:b/a\*100

(HPT150)

BAIS3

### APPENDIX K 4

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

RAT: FEMALE: SACRIFICED ANIMALS

STUDY NO. : 0205 ANIMAL : RAT F344 HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

REPORT TYPE : A1 : FEMALE

SEX

0rgan	Findings	Group Name Control No. of Animals on Study 44 Grade 1 2 3 4 (%) (%) (%) (%)	38 1 2 3 4 (%) (%) (%) (%)	1500ppm 44 1 2 3 4 (%) (%) (%) (%)	4500ppm 37 1 2 3 4 (%) (%) (%) (%)
[Integumentar	y system/appandage]				
skin/app	epidermal cyst	<44> 0 0 1 0 ( 0) ( 0) ( 2) ( 0)	<38> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<44> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<37> 0 1 0 0 ( 0) ( 3) ( 0) ( 0)
[Respiratory	system]				
nasal cavit	thrombus	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	38> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 ( 2) ( 0) ( 0) ( 0)	37> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	mineralization	10 0 0 0 (23) (0) (0) (0)	13 0 0 0 ( 34) ( 0) ( 0) ( 0)	9 0 0 0 0 (20) (0) (0)	20 0 0 0 (54) (0) (0) (0)
	goblet cell hyperplasia	1 0 0 0 ( 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)
	eosinophilic change:olfactory epithel	4 16 23 0 ( 9) ( 36) ( 52) ( 0)	2 22 13 1 ( 5) ( 58) ( 34) ( 3)	7 24 12 0 (16) (55) (27) (0)	6 24 5 0 (16) (65) (14) (0)
	eosinophilic change:respiratory epithe	38 0 0 0 0 (86) (0) (0) (0)	35 2 0 0 (92) (5) (0) (0)	36 1 0 0 (82) (2) (0) (0)	32 1 0 0 (86) (3) (0) (0)
	inflammation:foreign body	4 0 0 0 0 ( 9) ( 0) ( 0)	2 0 0 0 0 (5) (0) (0) (0)	5 1 0 0 (11) ( 2) ( 0) ( 0)	4 0 0 1 (11) (0) (0) (3)
Grade <a>&gt; b (c)</a>	1: Slight 2: Moderate 3 a: Number of animals examined at the s b: Number of animals with lesion c: b / a * 100	: Marked 4 : Severe te			

STUDY NO. : 0205 ANIMAL : RAT F344 REPORT TYPE : A1

SEX

: FEMALE

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

	Group Na No. of A	me Control nimals on Study 44	500ppm 38	1500ppm 44	4500ppm 37
Organ	Findings	1 2 3 4 (%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)
[Respiratory	system]				
nasal cavit	inflammation:respiratory epithelium	4 0 0 0 ( 9) ( 0) ( 0) ( 0)	38> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	(44) 1 0 0 0 ( 2) ( 0) ( 0) ( 0)	<pre></pre>
	respiratory metaplasia:olfactory epithelium	0 0 0 0 0 (0) (0)	1 0 0 0 ( 3) ( 0) ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0)	1 0 0 0 0 (3) (0) (0)
	respiratory metaplasia:gland	37 0 0 0 ( 84) ( 0) ( 0) ( 0)	35 2 0 0 (92) (5) (0) (0)	37 0 0 0 ( 84) ( 0) ( 0) ( 0)	33 0 0 0 (89) (0) (0) (0)
nasopharynx	inflammation:foreign body	<44> 0 0 0 0 0 0 0 0 0 0 0 0	<38> 0 0 0 0 0 0 0 0 0 0 0	<44> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<37> 0 1 0 0 ( 0) ( 3) ( 0) ( 0)
larynx	inflammation:foreign body	1 0 0 0 ( 2) ( 0) ( 0) ( 0)	38> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<37> 0 0 0 0 0 0 0 0 0
lung	inflammatory infiltration	\( \lambda 44 \rangle \) \( 1  0  0  0 \\ ( 2)  ( 0)  ( 0)  ( 0) \)	<38> 2 0 0 0 ( 5) ( 0) ( 0) ( 0)	<44> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<37> 0 0 0 0 0 0 0 0 0 0 0
	accumulation of foamy cells	1 0 0 0 0 (2) ( 0) ( 0) ( 0)	1 0 0 0 0 (3) ( 0) ( 0)	1 1 0 0 (2) (2) (0) (0)	1 0 0 0 0 (3) (0) (0)
Grade <a>&gt; b (c)</a>	1: Slight 2: Moderate 3: Marke a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	4 1: Severe			

STUDY NO. : 0205 ANIMAL : RAT F344 HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

REPORT TYPE : A1

: FEMALE

Organ	Findings	Group Name No. of Animals on Study Grade 1 2 (%) (%	Control 44 2 3 4 6) (%) (%)	38 1 2 3 4 (%) (%) (%) (%)	1500ppm 44 1 2 3 4 (%) (%) (%) (%)	4500ppm 37 1 2 3 4 (%) (%) (%) (%)
[Respiratory s	system]					
lung	bronchiolar-alveolar cell hyperplasia	2 (	<44> 0 0 0 0) ( 0) ( 0)	38> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	37> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	inflammation:foreign body		0 0 0	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 0 ( 0) ( 0)	0 1 0 0 ( 0) ( 0)
[Hematopoietio	c system]					
one marrow	angiectasis	1 (	<44> 0 0 0 0) ( 0) ( 0)	<38> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	37> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	granulation		0 0 0	6 1 0 0 (16) (3) (0) (0)	4 3 0 0 ( 9) ( 7) ( 0) ( 0)	11 0 0 0 (30) (0) (0) (0)
	increased hematopoiesis		0 0 0	0 0 0 0 0 0 (0) (0)	4 0 0 0 0 ( 9) ( 9) ( 0) ( 0)	3 0 0 0 0 (8) (0) (0) (0)
	decreased hematopoiesis	0 (	0 0 0	1 0 0 0 0 ( 3) ( 0) ( 0)	0 0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 0 (0) (0)
	erythropoiesis:increased	0 (	0 0 0	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 (0) (0) (0)	1 0 0 0 0 (3) (0) (0) (0)

STUDY NO. : 0205 ANIMAL : RAT F344

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

REPORT TYPE : A1

SEX : FEMALE

PAGE: 18

Organ	Findings	Group Name         Control           No. of Animals on Study         44           Grade         1 2 3 4           (%) (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	1500ppm 44 1 2 3 4 (%) (%) (%) (%)	4500ppm 37 1 2 3 4 (%) (%) (%) (%)
[Hematopoiet	ic system]				
bone marrow	reticulosis	<44> 0 2 0 0 ( 0) ( 5) ( 0) ( 0)	<38> 0 1 0 0 ( 0) ( 3) ( 0) ( 0)	<44> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<37> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
spleen	deposit of hemosiderin	<44> 4 1 0 0 ( 9) ( 2) ( 0) ( 0)	<38> 6 0 0 0 ( 16) ( 0) ( 0) ( 0)	6 1 0 0 (14) (2) (0) (0)	<37> 4 0 0 0 ( 11) ( 0) ( 0) ( 0)
	fibrosis	0 0 0 0 0 ( 0) ( 0)	0 1 0 0 (0) (0)	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 (0) (0) (0)
	extramedullary hematopoiesis	1 0 0 0 0 (2) (3) (6) (7)	1 0 0 0 0 ( 3) ( 0) ( 0) ( 0)	2 1 0 0 ( 5) ( 2) ( 0) ( 0)	2 1 0 0 (5) (3) (0) (0)
[Circulatory	system]				
heart	myocardial fibrosis	\( \langle 44 \rangle \) \( 1  0  0  0 \\ ( 2)  ( 0)  ( 0)  ( 0) \)	38> 4	5 0 0 0 (11) (0) (0) (0)	3 0 0 0 ( 8) ( 0) ( 0) ( 0)
[Digestive s	ystem]				
tongue	arteritis	2 0 0 0 ( 5) ( 0) ( 0) ( 0)	3 0 0 0 ( 8) ( 0) ( 0) ( 0)	3 1 0 0 ( 7) ( 2) ( 0) ( 0)	<37> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
Grade <a>&gt; b (c)</a>	1: Slight 2: Moderate a: Number of animals examined at the s b: Number of animals with lesion c: b / a * 100	3 : Marked 4 : Severe site			
(HPT150)				<del></del>	BAIS3

BAIS3

STUDY NO. : 0205
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 19

Organ		Group Name Control No. of Animals on Study 44 Grade 1 2 3 4 (%) (%) (%) (%)	500ppm 38 1 2 3 4 (%) (%) (%) (%)	1500ppm 44 1 2 3 4 (%) (%) (%) (%)	4500ppm 37 1 2 3 4 (%) (%) (%) (%)
[Digestive	system]				
stomach	ulcer:forestomach	<44> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<38> 0 0 0 0 0 0 0 0 0 0 0	3 0 0 0 ( 7) ( 0) ( 0) ( 0)	<37> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	erosion:glandular stomach	1 0 0 0 0 (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)
liver	herniation	3 0 0 0 ( 7) ( 0) ( 0) ( 0)	<38> 2 0 0 0 ( 5) ( 0) ( 0) ( 0)	<44> 4 0 0 0 ( 9) ( 0) ( 0) ( 0)	<37> 0 0 0 0 0 0 0 0 0 0 0 0
	necrosis:focal	1 0 0 0 0 (2) (0) (0)	1 0 0 0 0 (3) ( 0) ( 0) ( 0)	1 0 0 0 0 0 ( 2) ( 0) ( 0) ( 0)	2 0 0 0 0 (5) (0) (0) (0)
	granulation	20 11 1 0 ( 45) ( 25) ( 2) ( 0)	17 5 0 0 (45) (13) (0) (0)	20 6 1 0 (45) (14) (2) (0)	18 6 4 0 (49) (16) (11) (0)
	clear cell focus	3 1 0 0 ( 7) ( 2) ( 0) ( 0)	0 2 0 0 (0) (5) (0) (0)	3 0 0 0 ( 7) ( 0) ( 0) ( 0)	0 1 1 0 (0) (3) (3) (0)
	acidophilic cell focus	2 0 0 0 ( 5) ( 0) ( 0) ( 0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 ( 0) ( 0)
	basophilic cell focus	14 1 0 0 (32) (2) (0) (0)	16 2 0 0 (42) (5) (0) (0)	19 1 0 0 (43) (2) (0) (0)	15 2 0 0 (41) (5) (0) (0)
Grade <a>&gt; b (c)</a>	1: Slight 2: Moderate 3 a: Number of animals examined at the si b: Number of animals with lesion c: b/a * 100	: Marked 4 : Severe te			

(HPT150)

BAISS

STUDY NO. : 0205 ANIMAL : RAT F344

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

PAGE: 20

BAIS3

SACRIFICED ANIMALS (105W)

REPORT TYPE : A1 : FEMALE

(IIPT150)

Group Name Control 500ppm 1500ppm 4500ppm No. of Animals on Study 44 38 37 Grade 3 Organ\_ Findings\_ (%) (%) (%) (%) [Digestive system] liver <44> ⟨37⟩ vacuolated cell focus 0 0 0 0 0 0 0 (5)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) mixed cell focus 0 1 0 0 0 0 0 0 (0)(2)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) bile duct hyperplasia 5 (11) (5) (0) (0) (13) (0) (0) (0) (11) (2) (2) (0) (3)(0)(0)(0) pancreas <44> <38> **<44>** ⟨37⟩ atrophy 5 3 0 0 3 4 0 0 3 1 0 0 3 1 0 0 (11) (7) (0) (0) (8) (11) (0) (0) (7)(2)(0)(0) (8)(3)(0)(0) [Urinary system] kidney (44) infarct 0 0 1 0 0 0 0 0 0 0 0 5 2 0 0 (0)(2)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (14) (5) (0) (0) deposit of hemosiderin 0 2 0 0 1 17 0 21 0 0 (0)(5)(0)(0) (0)(11)(0)(0) (2) (39) (0) (0) (0)(57)(0)(0) Grade 1: Slight 2 : Moderate 3 : Marked 4 : Severe (a) a: Number of animals examined at the site b. b: Number of animals with lesion (c) c:b/a\*100

STUDY NO. : 0205 ANIMAL : RAT F344 REPORT TYPE : A1

: FEMALE

SEX

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

		oup Name Control of Animals on Study 44	500ppm 38	1500ppm 44	4500ppm 37
Organ	Gra Findings		1 2 3 4 (%) (%) (%) (%)	1 2 3 4 (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)
[Urinary sy	vstem]				
kidney	chronic nephropathy	<pre></pre>	<38> 25 7 1 0 ( 66) ( 18) ( 3) ( 0)	(44) 19 6 3 1 (43) (14) (7) (2)	37> 10 9 2 2 (27) (24) (5) (5)
	papillary necrosis	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	4 8 5 0 (11) (22) (14) (0)
	mineralization:cortico-medullary junction	20 0 0 0 0 (45) ( 0) ( 0) ( 0)	20 0 0 0 (53) (0) (0) (0)	20 2 0 0 ( 45) ( 5) ( 0) ( 0)	14 0 0 0 (38) (0) (0) (0)
	mineralization:papilla	2 0 0 0 0 (5) (6) (6)	2 0 0 0 0 (5) (0) (0) (0)	3 0 0 0 ( 7) ( 0) ( 0) ( 0)	10 1 0 0 (27) (3) (0) (0)
	mineralization:pelvis	11 0 0 0 ( 25) ( 0) ( 0) ( 0)	10 0 0 0 ( 26) ( 0) ( 0) ( 0)	15 1 0 0 (34) (2) (0) (0)	22 2 0 0 (59) (5) (0) (0)
	desquamation:pelvis	0 0 0 0 0 (0) (0)	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 (0) (0)	2 0 0 0 0 ( 5) ( 0) ( 0) ( 0)
	simple hyperplasia:transitional epitheli	3 0 0 0 (7)(0)(0)(0)	3 0 0 0 0 (8) (9) (9) (9)	10 0 0 0 (23) ( 0) ( 0) ( 0)	16 4 0 0 (43) (11) (0) (0)
	nodular hyperplasia:transitional epithel	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 0 (0) (0)	0 1 0 0 (0) (2) (0) (0)	7 4 0 0 (19) (11) (0) (0)
Grade (a) b (c)	1: Slight 2: Moderate 3: a : Number of animals examined at the site b : Number of animals with lesion c : b / a * 100	Marked 4 : Severe			

STUDY NO. : 0205 ANIMAL : RAT F344 REPORT TYPE : A1

SEX

: FEMALE

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

Organ		o Name Control of Animals on Study 44 of 1 2 3 4 (%) (%) (%) (%)	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	$4500$ ppm $37$ $\frac{1}{(\%)}$ $\frac{2}{(\%)}$ $\frac{3}{(\%)}$ $\frac{4}{(\%)}$
			(10) (10) (10)	(10) (10) (10)	(N) (N) (N)
[Urinary sys	tem]				
kidney	calculus	<44> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<38> 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	37> 2 0 0 0 ( 5) ( 0) ( 0) ( 0)
	mineralization:inner stripe,outer medulla	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	2 0 0 0 0 (5) (0) (0)	0 0 0 0 0 (0) (0)
ureter	dilatation	<29> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<30> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	38> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	(31) 4 2 0 0 (13) (6) (0) (0)
	simple hyperplasia:transitional epithelium	0 0 0 0 0 (0) (0)	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0)	2 0 0 0 0 (6) (6) (70) (70)
urin bladd	squamous cell metaplasia	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<38> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	3 0 0 0 (8) (0) (0) (0)
	squamous cell hyperplasia	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 ( 0) ( 0)	0 1 0 0 (0) (3) (0) (0)
	simple hyperplasia:transitional epithelium	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 0 ( 0) ( 0)	1 0 0 0 0 ( 2) ( 0) ( 0) ( 0)	1 0 0 0 0 (3) (0) (0)
Grade (a) b (c)	1: Slight 2: Moderate 3: Ma a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	rked 4: Severe			

STUDY NO. : 0205 ANIMAL : RAT F344 REPORT TYPE : A1 : FEMALE SEX

#### HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

0rgan	Group Name No. of Anima Grade Findings	Control als on Study 44  1 2 3 4  (%) (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	4500ppm 37 1 2 3 4 (%) (%) (%) (%)
[Urinary sys	tem]				
urin bladd	nodular hyperplasia:transitional epithelium	444> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)	<38> 0 0 0 0 0 0 0 0 0 0 0	<44> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<37> 1 2 0 0 ( 3) ( 5) ( 0) ( 0)
	papillary hyperplasia:transitional epithelium	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 ( 0) ( 0)	0 1 1 0 ( 0) ( 3) ( 3) ( 0)
	basal cell hyperplasia:transitional 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 0 (0)	0 0 0 0 0 (0) (0)	2 2 0 0 (5) (5) (0) (0)
[Endocrine s	eystem]				
pituitary	angiectasis	2 0 0 0 ( 5) ( 0) ( 0) ( 0)	38> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)	3 1 0 0 ( 7) ( 2) ( 0) ( 0)	3 0 0 0 ( 8) ( 0) ( 0) ( 0)
	cyst	6 0 0 0 0 (14) (0) (0) (0)	9 0 0 0 0 (24) (0) (0) (0)	8 0 0 0 0 (18) (0) (0) (0)	3 2 0 0 (8) (5) (0) (0)
	hyperplasia	1 0 0 0 0 (2) (0) (0) (0)	6 0 0 0 (16) ( 0) ( 0) ( 0)	8 0 0 0 0 (18) (0) (0) (0)	5 0 0 0 (14) (0) (0) (0)
	Rathke pouch	1 0 0 0 ( 2) ( 0) ( 0) ( 0)	0 0 0 0 0 (0) (0) (0)	1 0 0 0 0 (2) ( 0) ( 0) ( 0)	1 0 0 0 0 (3) ( 0) ( 0) ( 0)
Grade <a> b (c)</a>	1: Slight 2: Moderate 3: Marked a: Number of animals examined at the site b: Number of animals with Lesion c: b / a * 100	4 : Severe	<del></del>		

STUDY NO. : 0205 ANIMAL : RAT F344 REPORT TYPE : AI SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

Organ	N	iroup Name Control  do. of Animals on Study 44  irade 1 2 3 4  (%) (%) (%) (%)	500ppm 38 1 2 3 4 (%) (%) (%) (%)	1500ppm 44 1 2 3 4 (%) (%) (%) (%)	4500ppm 37 1 2 3 4 (%) (%) (%)
[Endocrine:	system]				
thyroid	ultimibranchial body remanet	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<38> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<pre></pre>	<37> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	C-cell hyperplasia	2 3 0 0 ( 5) ( 7) ( 0) ( 0)	5 0 0 0 (13) (0) (0) (0)	6 1 0 0 (14) (2) (0) (0)	3 2 0 0 ( 8) ( 5) ( 0) ( 0)
adrenal	peliosis-like lesion	9 0 0 0 ( 20) ( 0) ( 0) ( 0)	38> 14 1 0 0 (37) (3) (0) (0)	(44) 13 1 0 0 (30) (2) (0) (0)	(37) 16 1 1 0 (43) (3) (3) (0)
	hyperplasia:cortical cell	4 0 0 0 0 ( 9) ( 0) ( 0)	5 0 0 0 (13) (0) (0) (0)	6 0 0 0 0 (14) (0) (0) (0)	2 1 0 0 (5) (3) (0) (0)
	hyperplasia:medulla	0 0 0 0 0 (0) (0)	0 0 0 0 0 ( 0) ( 0)	2 1 0 0 ( 5) ( 2) ( 0) ( 0)	1 0 0 0 0 (3) (0) (0) (0)
	focal fatty change:cortex	6 0 0 0 0 (14) (0) (0) (0)	3 0 0 0 0	5 0 0 0 (11)(0)(0)(0)	6 0 0 0 0 (16) (0) (0)
[Reproducti	ue system]				
DUATY	granulation	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	38> 0 1 0 0 ( 0) ( 3) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<37> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
Grade ( a > b ( c )	1: Slight 2: Moderate 3: a: Number of animals examined at the sit b: Number of animals with lesion c:b/a*100	Marked 4 : Severe ce	`		

STUDY NO. : 0205 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE

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

		Group Name Control No. of Animals on Study 44	500ppm 38	1500ppm 44	4500ppm 37
0rgan	Findings	Grade 1 2 3 4 (%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)
[Reproductive	e system]				
uterus	cystic endometrial hyperplasia	\( \lambda 44 \rangle \) \( 10  4  2  0 \\ ( 23)  ( 9)  ( 5)  ( 0) \)	38> 13 1 2 0 (34) (3) (5) (0)	\( \lambda 44 \rangle \) \( \begin{array}{cccccccccccccccccccccccccccccccccccc	37> 12 5 0 0 ( 32) ( 14) ( 0) ( 0)
nammary gl	hyperplasia	\( \lambda 44 \rangle \) \( 1  0  1  0 \\ ( 2)  ( 0)  ( 2)  ( 0) \)	<37> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)	<44> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<37> 0 0 0 0 0 0 0 0 0 0 0 0
	galactocele	4 1 0 0 ( 9) ( 2) ( 0) ( 0)	0 0 0 0 0 0 (0) (0)	0 1 0 0 ( 0) ( 0)	0 1 0 0 ( 0) ( 0)
Special sens	se organs/appandage]				
<b>v</b> e	cataract	\( \lambda 44 \rangle \) \( 1  3  2  0 \\ ( 2)  ( 7)  ( 5)  ( 0) \)	<38> 0 0 2 0 ( 0) ( 0) ( 5) ( 0)	0 1 1 0 ( 0) ( 2) ( 2) ( 0)	37> 0 1 0 0 ( 0) ( 3) ( 0) ( 0)
	retinal atrophy	21 11 8 0 ( 48) ( 25) ( 18) ( 0)	21 7 4 0 (55) (18) (11) (0)	24 10 2 0 (55) (23) (5) (0)	24 10 1 0 (65) (27) (3) (0)
	keratitis	1 0 0 0 0 ( 2) ( 0) ( 0) ( 0)	0 0 0 0 0 (0) (0)	1 0 0 0 ( 2) ( 0) ( 0) ( 0)	0 1 0 0 ( 0) ( 0)
irade (a > b (c)	1: Slight 2: Moderate a: Number of animals examined at the b: Number of animals with lesion c: b / a * 100	3: Marked 4: Severe site			
( c ) (HPT150)	b : Number of animals with lesion				

STUDY NO. : 0205 ANIMAL : RAT F344

REPORT TYPE : A1 SEX : FEMALE HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

No.	of Animals on Study 44	38 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	4500ppm 37 1 2 3 4 (%) (%) (%) (%)
o organs/appandage]				
degeneration	\( \lambda 44\rangle \) \[ 1  0  0  0  (2)  (0)  (0)  (0)  (0)  (0) \]	<38> 0 0 0 0 0 0 0 0 0 0 0	<44> 2 0 0 0 ( 5) ( 0) ( 0) ( 0)	37> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
lymphocytic infiltration	3 0 0 0 ( 7) ( 0) ( 0) ( 0)	4 0 0 0 (11) (0) (0) (0)	5 0 0 0 (11) (0) (0) (0)	4 0 0 0 (11) (0) (0) (0)
inflammation	4 2 0 0 ( 9) ( 5) ( 0) ( 0)	<38> 0 1 2 0 ( 0) ( 3) ( 5) ( 0)	7 1 0 0 (16) (2) (0) (0)	<37> 4 0 0 0 ( 11) ( 0) ( 0) ( 0)
tal system]				
osteosclerosis	<44> 7 2 5 0 ( 16) ( 5) ( 11) ( 0)	38> 2 3 1 0 ( 5) ( 8) ( 3) ( 0)	2 0 3 0 ( 5) ( 0) ( 7) ( 0)	<37> 2 3 3 0 ( 5) ( 8) ( 8) ( 0)
1: Slight 2: Moderate 3: Ma a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	arked 4 ; Severe			
	Findings  organs/appandage]  degeneration  lymphocytic infiltration  inflammation  al system]  osteosclerosis  1: Slight 2: Moderate 3: Ma a: Number of animals examined at the site b: Number of animals with lesion	Findings Grade 1 2 3 4 (%) (%) (%) (%) (%) (%) (%) (%) (%) (%)	No. of Animals on Study	No. of Animals on Study

### APPENDIX K 5

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

MOSUE: MALE: DEAD AND MORIBUND ANIMALS

STUDY NO. : 0206 ANIMAL : MOUSE BDF1

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

REPORT TYPE : A1 SEX : MALE

0rgan	No	roup Name o, of Animals on Study rade 1 (%)	Control 15 2 3 4 (%) (%) (%)	667ppm 9 1 2 3 4 (%) (%) (%) (%)	2000ppm 9 1 2 3 4 (%) (%) (%) (%)	6000ppm 11 1 2 3 4 (%) (%) (%) (%)
[Respiratory	system]					
nasal cauit	mineralization	0 ( 0)	<15> 0 0 0 ( 0) ( 0) ( 0)	<pre></pre>	<pre></pre>	1 0 0 0 ( 9) ( 0) ( 0) ( 0)
	inflammation	0 ( 0)	0 1 0 ( 0) ( 7) ( 0)	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0)
	eosinophilic change:olfactory epithelium		0 0 0 0 ( 0) ( 0)	2 0 0 0 (22) (0) (0) (0)	1 0 0 0 0 (11) (0) (0) (0)	0 0 0 0 0 0 ( 0) ( 0)
	eosinophilic change:respiratory epithel		0 0 0 0 ( 0) ( 0)	2 1 0 0 (22) (11) (0) (0)	3 0 0 0 (33) (0) (0) (0)	1 0 0 0 0 ( 9) ( 9) ( 0) ( 0)
	respiratory metaplasia:olfactory epithe	lium 3 ( 20)	0 0 0 0 ( 0) ( 0)	2 1 0 0 (22) (11) (0) (0)	1 0 0 0 (11) (0) (0) (0)	4 2 0 0 (36) (18) (0) (0)
	respiratory metaplasia:gland	3 ( 20)	1 0 0 ( 7) ( 0) ( 0)	1 1 0 0 (11) (11) (0) (0)	3 0 0 0 0 (33) (0) (0) (0)	6 2 0 0 (55) (18) (0) (0)
	atrophy:olfactory epithelium	0 ( 0)	0 0 0 0 ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0)	3 1 0 0 (33) (11) (0) (0)	7 1 0 0 (64) (9) (0) (0)
	necrosis:olfactory epithelium	( 0)	1 0 0 (7) (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 0 0 ( 0) ( 0)
Grade (a) b (c)	1: Slight 2: Moderate 3: a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	Marked 4: Severe	)			

STUDY NO. : 0206 ANIMAL : MOUSE BDF1 HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0-105W)

REPORT TYPE : A1 SEX

: MALE

	Group Nam				6000ppm	
rgan	Findings	15 1 2 3 4 (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)	11 (%) (%) (%) (%) (%)	
Respiratory	system]			•		
nasopharynx	eosinophilic change:respiratory epithelium	<15> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	(9) 1 0 0 0 (11) (0) (0) (0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 ( 9) ( 0) ( 0) ( 0)	
ung	congestion	<15> 0 1 0 0 ( 0) ( 7) ( 0) ( 0)	<pre></pre>	<pre></pre>	<11> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	
	inflammatory infiltration	1 0 0 0 0 (7) (0) (0)	1 0 0 0 0 (11) (0) (0)	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 2 0 0 ( 0) ( 18) ( 0) ( 0)	
[Hematopoieti	c system]					
one marrow	increased hematopoiesis	<15> 0 0 0 0 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 0 0 0 ( 9) ( 0) ( 0) ( 0)	
	megakaryocyte:increased	0 0 0 0 0 0 ( 0) ( 0)	( 0) ( 0) ( 0) ( 0)	0 0 0 0 0 0 (0)	0 1 0 0 ( 0) ( 0)	
	granulopoiesis:increased	1 0 0 0 0 (7) (0) (0)	0 0 0 0 0 (0) (0)	0 1 0 0 (0) (11) (0) (0)	0 0 0 0 0 (0) (0)	
Grade (a) b (c)	1: Slight 2: Moderate 3: Marked a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	4 : Severe	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	·		

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL : MOUSE BDF1

REPORT TYPE : A1
SEX : MALE

DEAD AND MORIBUND ANIMALS (0-105W)

PAGE: 3 Group Name Control 667ppm 2000ppm 6000ppm No. of Animals on Study 15 9 9 11 Grade (%) Organ Findings (%) (%) (%) (%) (%) (%) (%) [Hematopoietic system] spleen <15> ⟨ 9> < 9> <11> deposit of melanin 1 0 0 0 0 0 (0)(7)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (9)(0)(0)(0) extramedullary hematopoiesis 1 3 0 0 1 3 0 0 1 1 0 0 0 2 (7) (20) (0) (0) (11) (11) (0) (0) (0)(22)(0)(0) (9)(27)(0)(0) [Circulatory system] heart <15> < 9> <11> 0 0 0 0 1 0 0 thrombus 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(9)(0)(0) mineralization 0 0 0 1 0 0 0 0 0 0 (0)(0)(0)(0) (0)(11)(0)(0) (11) (0) (0) (0) (0)(0)(0)(0) 0 1 0 0 arteritis 0 1 0 0 0 1 0 0 0 0 0 0 (0)(7)(0)(0) (0)(11)(0)(0) (0)(11)(0)(0) (0)(0)(0)(0) [Digestive system] tooth <15> < 9> < 9> <11> 0 0 0 0 0 1 0 0 cyst 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(11)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) 1 : Slight Grade 2 : Moderate 3 : Marked 4 : Severe (a) a: Number of animals examined at the site b b: Number of animals with lesion (c) c : b / a \* 100

STUDY NO. : 0206 ANIMAL : MOUSE BDF1 HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0-105W)

REPORT TYPE : A1

SEX : MALE

0rgan	Group 1 No. of Grade	Name Control Animals on Study 15  1 2 3 4 (%) (%) (%) (%)	9 667ppm 9 1 2 3 4 (%) (%) (%)	2000ppm 9 1 2 3 4 (%) (%) (%) (%)	6000ppm 11 1 2 3 4 (%) (%) (%) (%)
[Digestive sy	vstem]				
tooth	dysplasia	5 1 0 1 ( 33) ( 7) ( 0) ( 7)	2 1 1 0 ( 22) ( 11) ( 11) ( 0)	4 0 0 0 (44) (0) (0) (0)	4 2 0 0 ( 36) ( 18) ( 0) ( 0)
tongue	mineralization	<15> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	( 0) ( 0) ( 0) ( 0) ( 0) ( 0) ( 0) ( 0)	( 0) ( 0) ( 0) ( 0)	1 0 0 0 ( 9) ( 0) ( 0) ( 0)
	arteritis	0 2 0 0 (0) (13) (0) (0)	0 0 1 0 (0) (11) (0)	0 1 0 0 (0) (11) (0) (0)	0 0 0 0 0 (0) (0)
salivary gl	arteritis	<15> 0 1 0 0 ( 0) ( 7) ( 0) ( 0)	( 0) ( 0) ( 0) ( 0)	<pre></pre>	<11> 0 0 0 0 0 0 0 0 0 0 0 0
stomach	mineralization	2 0 0 0 ( 13) ( 0) ( 0) ( 0)	( 0) ( 0) ( 0) ( 0)	1 0 0 0 (11) (0) (0) (0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	ulcer:forestomach	1 0 0 0 0 (7) ( 0) ( 0) ( 0)	0 0 0 0 0 (0) (0)	1 0 0 0 (11) (0) (0) (0)	0 0 0 0 0 ( 0) ( 0)
	hyperplasia:forestomach	0 0 0 0 0 (0) (0)	1 0 0 0 0 (11) (0) (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 ( 0) ( 0)
Grade (a> b (c)	1: Slight 2: Moderate 3: Marka a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	ed 4: Severe			

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : MALE DEAD AND MORIBUND ANIMALS (0-105W)

Group Name Control 667ppm 2000ppm 6000ppm No. of Animals on Study 9 15 11 Grade Findings (%) (%) (%) (%) (%) (%) (%) 0rgan\_ [Digestive system] stomach <15> 〈 9> 〈 9〉 <11> erosion:glandular stomach 0 0 0 0 0 0 (0)(0)(0)(0)(11) (0) (0) (0) (0)(0)(0)(0) (0)(0)(0)(0) Liver <15> < 9> < 9> <11> 0 0 0 0 0 0 angiectasis 0 1 1 0 0 0 0 ( 0) ( 0) ( 0) ( 0) (0)(0)(0)(0) (0)(11)(11)(0) (0)(0)(0)(0) necrosis:central (0)(13)(0)(0) (0)(11)(0)(0) (0)(0)(0)(0) (0)(0)(9)(0) necrosis:focal (7)(0)(0)(0) (11) (11) (0) (0) (0)(0)(0)(0) (0)(0)(0)(0) degeneration:central (0)(0)(0)(0) (0)(0)(0)(0) (0)(11)(0)(0) (0)(0)(0)(0) granulation (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (9)(0)(0)(0) mixed cell focus (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (9)(0)(0)(0) pancreas <15> < 9> <11> 0 0 0 0 necrosis:focal 0 0 0 0 0 0 0 0 1 0 0 (0)(0)(0)(0) (0)(0)(0)(0) ( 0) ( 0) ( 0) ( 0) (0)(9)(0)(0) 3 : Marked Grade 1 : Slight 2 : Moderate 4 : Severe (a) a : Number of animals examined at the site b b: Number of animals with lesion (c) c:b/a\*100

(IIPT150)

BAIS3

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

ANIMAL : MOUSE BDF1 REPORT TYPE : A1 : MALE

Organ	ı	roup Name Control  o. of Animals on Study 15  rade 1 2 3 4  (%) (%) (%) (%)	667ppm 9 1 2 3 4 (%) (%) (%) (%)	2000ppm 9 1 2 3 4 (%) (%) (%) (%)	6000ppm 11 1 (%) (%) (%) (%)
or sur	. nango	(8) (8) (8)	(8) (8) (8)	(6) (6) (6)	(h) (h) (h)
[Urinary s	ystem]				
kidney	necrosis	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 1 0 ( 0) ( 0) ( 11) ( 0)	( 0) ( 0) ( 0) ( 0)	(11) 0 0 0 0 0 0 0 0 0 0 0 0
	hyalino droplet	1 0 0 0 ( 7) ( 0) ( 0) ( 0)	1 0 0 0 (11) (0) (0) (0)	1 0 0 0 (11) (0) (0) (0)	1 0 0 0 0 (9) (9) (0) (0)
	basophilic change	1 0 0 0 ( 7) ( 0) ( 0) ( 0)	1 0 0 0 (11) (0) (0) (0)	2 0 0 0 0 (22) (0) (0) (0)	1 0 0 0 ( 9) ( 9) ( 0) ( 0)
	hydronephrosis	0 0 0 0 0 (0) (0)	0 0 0 1 (0) (0) (11)	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0) (0)
	pyelonephritis	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 0 (0) (9) (0)
	mineralization:papilla	0 0 0 0 0 (0) (0)	1 0 0 0 (11) (0) (0) (0)	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0) (0)
	mineralization:pelvis	1 0 0 0 0 (7) ( 0) ( 0) ( 0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 ( 0) ( 0)	1 0 0 0 0 (9) (9) (0) (0)
	mineralization:cortex	8 3 0 0 (53) (20) (0) (0)	5 2 0 0 (56) (22) (0) (0)	5 3 0 0 (56) (33) (0) (0)	5 2 0 0 (45) (18) (0) (0)
Grade <a> b (c)</a>	1: Slight 2: Moderate 3 a: Number of animals examined at the sib: Number of animals with lesion c: b / a * 100	: Marked 4 : Severe te			

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

ANIMAL : MOUSE BDF1
REPORT TYPE : A1 SEX

: MALE

Organ	N	Froup Name fo. of Animals on Study Frade $\frac{1}{(\%)}$	Control 15 3 4 (%) (%)	667ppm 9 1 2 3 4 (%) (%) (%) (%)	2000ppm 9 1 2 3 4 (%) (%) (%) (%)	6000ppm 111 1 2 3 4 (%) (%) (%) (%)
[Urinary syst	cem]					
kidney	desquamation:pelvis	0 0	(15) 0 0 0 ( 0) ( 0)	<pre></pre>	<pre></pre>	<pre></pre>
	mineralization:inner stripe,outer medul	la 1 0 ( 7) ( 0)	0 0 0	1 0 0 0 (11) (0) (0) (0)	4 0 0 0 (44) (0) (0) (0)	3 0 0 0 (27) (0) (0) (0)
urin bladd	simple hyperplasia:transitional epithel	.ium 1 0	0 0 0 ( 0) ( 0)	<pre></pre>	( 0) ( 0) ( 0) ( 0) 0 0 0 0 0 0 0	(11) 0 0 0 0 (0) (0) (0) (0)
[Endocrine sy	rstem]					
pituitary	Rathke pouch	1 0	0 0 (0) (0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
adrenal	necrasis	0 0	0 0 (0) (0)	0 1 0 0 ( 0) ( 11) ( 0) ( 0)	<pre></pre>	<11> 0 0 0 0 0 0 0 0 0 0 0 0
[Reproductive	system]					
testis	atrophy	0 0	0 0 (0) (0)	1 0 0 0 (11) (0) (0) (0)	( 0) ( 0) ( 0) ( 0) ( 0) ( 0) ( 0) ( 0)	(11) 1 0 0 0 ( 9) ( 0) ( 0) ( 0)
Grade < a > b ( c )	1: Slight 2: Moderate 3: a: Number of animals examined at the sit b: Number of animals with lesion c: b/a*100	Marked 4: Severe e				

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : MALE HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

Organ	Group A No. of Grade Findings	Name Control Animals on Study 15  1 2 3 4 (%) (%) (%) (%)	667ppm 9 1 2 3 4 (%) (%) (%) (%)	2000ppm 9 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
[Reproductive	system]				
testis	necrasis	<15> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<pre></pre>	<pre></pre>	<11> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
	mineralization	9 0 0 0 0 (60) (60) (60)	4 1 0 0 (44) (11) (0) (0)	7 0 0 0 (78) (0) (0) (0)	0 0 0 0 0 ( 0) ( 0)
epididymis	spermatogenic granuloma	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	(9) 1 0 0 0 (11) (0) (0) (0)	<pre></pre>	(11) 0 0 0 0 (0) (0) (0) (0)
semin ves	hemorrhage	0 1 0 0 ( 0) ( 7) ( 0) ( 0)	<pre></pre>	<pre></pre>	<11> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
prostate	inflammation	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<pre></pre>	<pre></pre>	<11> 0 1 0 0 ( 0) ( 9) ( 0) ( 0)
prep/cli gl	duct cell	<15> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<pre></pre>	<pre></pre>	<11> 0 1 0 0 ( 0) ( 9) ( 0) ( 0)
	inflammation	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 1 0 0 ( 9) ( 9) ( 0) ( 0)
Grade <a> b (c)</a>	1: Slight 2: Moderate 3: Marka a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	ed 4 : Severe			

ANIMAL : MOUSE BDF1 REPORT TYPE : A1

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

SEX : MALE

Organ		Group Name Control No. of Animals on Study 15 Grade 1 2 3 4 (%) (%) (%) (%)	667ppm 9 1 2 3 4 (%) (%) (%) (%)	2000ppm 9 1 2 3 4 (%) (%) (%) (%)	6000ppm 11 1 2 3 4 (%) (%) (%) (%)
[Nervous syst	tem]				
brain	mineralization	5 4 0 0 ( 33) ( 27) ( 0) ( 0)	(9) 1 6 0 0 (11) (67) (0) (0)	5 1 0 0 (56) (11) (0) (0)	3 5 0 0 (27) (45) (0) (0)
[Special sens	se organs/appandage]				
nasolacr d	inflammation	1 0 0 0 ( 7) ( 0) ( 0) ( 0)	( 0) ( 0) ( 0) ( 0)	( 9) 0 0 ( 11) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
Grade <a>&gt; b (c)</a>	1: Slight 2: Moderate 3 a: Number of animals examined at the si b: Number of animals with lesion c: b / a * 100	: Marked 4 : Severe te			
(IIPT150)					BAIS

### APPENDIX K 6

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

MOSUE: FEMALE: DEAD AND MORIBUND ANIMALS

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : FEMALE HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0-105W)

Organ		up Name of Animals on Study 1 de (%) (%)	Control 9 3 4 (%) (%)	667ppm 28 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	6000ppm 17 17 1 2 3 4 (%) (%) (%) (%)
[Respiratory	eveteml					
nasal cavit	thrombus	0 0 ( 0) ( 0)	0 0	<28> 0 0 1 0 0 0 ( 0) ( 4) ( 0)	<25> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<17> 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)	1 0 0 0 0 (4) (0) (0) (0)	0 0 0 0 0 ( 0) ( 0) ( 0)
	catarrh	0 1 (0) (5)	0 0	0 2 0 0 ( 0) ( 7) ( 0) ( 0)	0 2 0 0 (0) (8) (0) (0)	0 0 0 0 0 ( 0) ( 0)
	basal cell hyperplasia	0 0 (0) (0)	0 0 (0) (0)	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0)	1 0 0 0 (6) (6) (70) (70)
	eosinophilic change:olfactory epithelium	5 0 ( 26) ( 0)	0 0 (0) (0)	6 0 0 0 0 (21) (0) (0)	1 1 0 0 (4) (4) (6) (6)	0 0 0 0 0 ( 0) ( 0) ( 0)
	eosinophilic change:respiratory epitheliu	m 11 1 (58) (5)	1 0 ( 5) ( 0)	15 3 1 0 (54) (11) (4) (0)	9 2 2 0 (36) (8) (8) (0)	4 1 0 0 (24) (6) (0) (0)
	inflammation:foreign body	0 0 (0)	0 0	1 0 0 0 0 (4) (0) (0) (0)	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 (0) (0) (0)
	inflammation:respiratory 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)	0 0 0 0 0 ( 0) ( 0)	1 0 0 0 0 (4) (0) (0) (0)	0 0 0 0 0 ( 0) ( 0) ( 0)
Grade <a>&gt; b (c)</a>	1: Slight 2: Moderate 3: Material a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	arked 4 : Severe				

ANIMAL : MOUSE BDF1

REPORT TYPE : A1

SEX : FEMALE

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

Organ	Group Name No. of Anima Grade	Control Is on Study 19  1 2 3 4 (%) (%) (%) (%)	667ppm 28 1 2 3 4 (%) (%) (%) (%)	2000ppm 25 1 2 3 4 (%) (%) (%) (%)	6000ppm 17 1 2 3 4 (%) (%) (%) (%)
[Respiratory s	system]				
nasal cavit	respiratory metaplasia:olfactory epithelium	3 0 0 0 (16)(0)(0)(0)	28> 1 0 0 0 ( 4) ( 0) ( 0) ( 0)	25> 2 0 0 0 ( 8) ( 0) ( 0) ( 0)	2 0 0 0 ( 12) ( 0) ( 0) ( 0)
	respiratory metaplasia:gland	5 0 0 0 ( 26) ( 0) ( 0) ( 0)	1 0 0 0 0 (4) (0) (0) (0)	6 0 0 0 (24) (0) (0) (0)	1 0 0 0 ( 6) ( 0) ( 0) ( 0)
	atrophy:olfactory epithelium	0 0 0 0 0 ( 0)	0 0 0 0 0 (0) (0)	9 2 0 0 (36) (8) (0) (0)	8 3 1 0 (47) (18) (6) (0)
nasopharynx	eosinophilic change:respiratory epithelium	19> 1 0 0 0 (5) (0) (0) (0)	28> 2 1 0 0 ( 7) ( 4) ( 0) ( 0)	<25> 0 1 0 0 ( 0) ( 4) ( 0) ( 0)	2 1 0 0 (12) (6) (0) (0)
lung	hemorr'hage	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	(28) 0 1 0 0 ( 0) ( 4) ( 0) ( 0)	<25> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<17> 0 0 0 0 0 0 0 0 0 0 0 0
	inflammatory infiltration	1 0 0 0 ( 5) ( 0) ( 0) ( 0)	3 0 0 0 0 (11) (0) (0) (0)	1 0 0 0 0 (4) (0) (0) (0)	1 0 0 0 0 (6) (6) (0) (0)
[Hematopoieti	c system]				
bone marrow	congestion	(19) 0 0 0 0 (0) (0) (0) (0)	<28> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<25> 0 2 0 0 ( 0) ( 8) ( 0) ( 0)	<17> 0 0 0 0 0 0 0 0 0 0 0 0
Grade <a> b (c)</a>	1: Slight 2: Moderate 3: Marked a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100	4 : Severe			

ANIMAL : MOUSE BDF1

REPORT TYPE : A1

SEX : FEMALE

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

Organ	No.	roup Name Control of Animals on Study 19 rade 1 2 3 4 (%) (%) (%) (%)	667ppm 28 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	6000ppm 17 1 2 3 4 (%) (%) (%) (%)
[Hematopoiet	ic system]				
oone marrow	increased hematopoiesis	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	(28) 1 0 0 0 ( 4) ( 0) ( 0) ( 0)	<25> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<17> 1 0 0 0 ( 6) ( 0) ( 0) ( 0)
	granulopoiesis: increased	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	3 0 0 0 (11) (0) (0) (0)	1 0 0 0 0 (4) ( 0) ( 0)	1 0 0 0 0 (6) (6) (0) (0)
lymph node	lymphadenitis	<19> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<28> 0 1 0 0 ( 0) ( 4) ( 0) ( 0)	<25> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
spleen	deposit of hemosiderin	1 0 0 0 ( 5) ( 0) ( 0) ( 0)	<28> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<25> 0 0 0 0 0 0 0 0 0 0 0	<17> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
	extramedullary hematopoiesis	1 4 0 0 ( 5) ( 21) ( 0) ( 0)	8 4 0 0 (29) (14) (0) (0)	4 5 0 0 (16) (20) (0) (0)	4 2 0 0 ( 24) ( 12) ( 0) ( 0)
	engargement of erythrocyte	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)
	follicular hyperplasia	0 1 0 0 (0) (0)	0 0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 0 (0) (0)
rade a > b c )	1: Slight 2: Moderate 3: a: Number of animals examined at the site b: Number of animals with lesion c: b/a*100	Marked 4: Severe			

Organ

heart

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL : MOUSE BDF1

REPORT TYPE : A1

Findings\_

mineralization

arteritis

: FEMALE

[Circulatory system]

DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 13 Group Name Control 667ppm 2000ppm 6000ppm No. of Animals on Study 19 28 25 17 Grade (%) (%) (%) (%) (%) (%) (%) <19> (17) 0 0 0 0 0 2 0 0 0 0 0 0 1 1 0 0 (0)(0)(0)(0) (0)(7)(0)(0) (0)(0)(0)(0) (6)(6)(0)(0) 0 0 0 0 1 0 0 0 0 1 0 0 ( 0) ( 0) ( 0) ( 0) (4)(0)(0)(0) (0)(0)(0)(0) (0)(6)(0)(0)

(0)(0)(0)(0)

(0)(4)(0)(0)

[Digestive	system]		

tooth		<19>	<28>	<25>	<17>
	inflammation	0 0 0 0	0 0 0 0	0 1 0 0	0 0 0 0
		( 0) ( 0) ( 0) ( 0)	( 0) ( 0) ( 0) ( 0)	( 0) ( 4) ( 0) ( 0)	(0)(0)(0)(0)
	dysplasia	1 0 0 0 ( 5) ( 0) ( 0) ( 0)	2 1 0 0 (7) (4) (0) (0)	3 1 1 0 (12) (4) (4) (0)	1 0 1 0 (6)(0)(6)(0)
	inflammation:foreign body	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 (0) (0) (0)	0 0 0 0 (0) (0) (0)	0 1 0 0 (0) (6) (0) (0)
tongue	arteritis	<19> 0 1 0 0	<28> 0 0 0 0	<25> 0 1 0 0	<17> 0 1 0 0

(0)(5)(0)(0)

Grade

1: Slight

2 : Moderate

3 : Marked

4 : Severe

<a>></a>

a: Number of animals examined at the site

b b: Number of animals with Lesion

c : b / a \* 100

(HPT150)

(c)

BAIS3

(0)(6)(0)(0)

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

DEAD AND MORIBUND ANIMALS (0-105W)

Group Name Control 667ppm 2000ppm 6000ppm No. of Animals on Study 19 28 25 17 Grade (%) (%) Findings\_ (%) (%) (%) (%) (%) (%) [Digestive system] stomach <19> ⟨28⟩ (17) mineralization 0 0 0 (0)(0)(0)(0) (14) (0) (0) (0) (0)(0)(0)(0) (6)(0)(0)(0) hyperplasia:glandular stomach 0 0 (5)(0)(0)(0) (4)(0)(0)(0) (12) (0) (0) (0) (0)(0)(0)(0) large intes <19> <17> necrosis 0 0 0 1 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(4)(0)(0) (0)(0)(0)(0) ( 0) ( 0) ( 0) ( 0) liver <19> ⟨28⟩ <25> (17) angiectasis 0 0 0 0 0 (0)(5)(0)(0) (4)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) necrosis:central 0 1 0 0 (0)(0)(5)(0) (0)(0)(0)(0) (0)(4)(0)(0) (0)(0)(0)(0) necrosis:focal 0 1 (0)(5)(0)(0) (4)(11)(0)(0) (4)(12)(4)(0) (12) (0) (0) (0) fatty change (0)(5)(0)(0) ( 0) ( 0) ( 0) ( 0) (0)(0)(0)(0) (0)(0)(0)(0) Grade 1: Slight 2 : Moderate 3 : Marked 4 : Severe <a>></a> a: Number of animals examined at the site b b: Number of animals with lesion (c) c:b/a\*100

(IIPT150)

BAIS3

STUDY NO. : 0206 ANIMAL : MOUSE BDF1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

REPORT TYPE : A1
SEX : FEMALE

Group Name Control 667ppm 2000ppm 6000ppm No. of Animals on Study 19 28 17 Findings\_ (%) (%) (%) (%) (%) (%) (%) (%) [Digestive system] Liver <19> ⟨28⟩ (17) inflammatory infiltration 0 0 0 0 1 0 0 0 1 0 0 0 0 0 (0)(0)(0)(0) (0)(4)(0)(0) (0)(4)(0)(0) (0)(0)(0)(0) granulation 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(4)(0)(0) (0)(4)(0)(0) (0)(0)(0)(0) clear cell focus 1 0 0 0 (5)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) acidophilic cell focus (0)(0)(0)(0) (4)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) basophilic cell focus 0 0 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (12) (4) (0) (0) (0)(0)(0)(0) [Urinary system] kidney <19> ⟨28⟩ <25> <17> hyaline droplet 4 2 0 0 5 3 0 0 0 0 0 (21) (11) (0) (0) (18) (11) (0) (0) (36) (0) (0) (0) (47) (0) (0) (0) basophilic change 0 0 1 1 0 0 ( 0) ( 0) ( 0) ( 0) (0)(0)(0)(0) ( 0) ( 4) ( 0) ( 0) (6)(6)(0)(0) Grade 1: Slight 2 : Moderate 3 : Marked 4 : Severe

<a>></a>

b (c) a: Number of animals examined at the siteb: Number of animals with lesion

c:b/a\*100

STUDY NO. : 0206 ANIMAL : MOUSE BDF1

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

REPORT TYPE : A1

: FEMALE SEX

Organ	i	Group Name Control No. of Animals on Study 19 Grade 1 2 3 4 (%) (%) (%) (%)	28 1 2 3 4 (%) (%) (%) (%)	2000ppm 25 1 2 3 4 (%) (%) (%) (%)	6000ppm 17 1 2 3 4 (%) (%) (%) (%)
[Urinary s	system]				
kidney	deposit of amyloid	0 0 1 0 ( 0) ( 0) ( 5) ( 0)	<28> 0 0 0 0 0 0 0 0 0 0 0	<25> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<17> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	inflammatory infiltration	0 0 0 0 0 (0) (0)	0 1 0 0 (0) (4) (0) (0)	1 0 0 0 ( 4) ( 0) ( 0) ( 0)	0 0 0 0 0 (0) (0)
	inflammatory polyp	0 0 0 0 0 (0) (0)	0 1 0 0 (0) (4) (0) (0)	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0)
	hydronephrasis	0 0 1 0 ( 0) ( 5) ( 0)	1 3 0 0 (4) (11) (0) (0)	0 1 0 0 (0) (4) (0) (0)	0 0 0 0 0 ( 0) ( 0)
	tubular necrosis	0 0 0 0 0 (0) (0)	0 1 1 0 ( 0) ( 4) ( 4) ( 0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 ( 0) ( 0)
	mineralization:papilla	2 0 0 0 (11) (0) (0) (0)	4 0 0 0 0 (14) (0) (0) (0)	2 0 0 0 0 ( 8) ( 0) ( 0) ( 0)	1 0 0 0 0 (6) (6) (0) (0)
	mineralization:cortex	1 0 0 0 ( 5) ( 0) ( 0) ( 0)	2 0 0 0 0 (7) (0) (0) (0)	3 0 0 0 (12) ( 0) ( 0) ( 0)	1 0 0 0 0 (6) (6) (70) (70)
	desquamation:pelvis	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0) (0)	4 0 0 0 (24) (0) (0) (0)
Grade < a > b ( c ) (HPT150)	1: Slight 2: Moderate 3 a: Number of animals examined at the si b: Number of animals with lesion c: b/a*100	: Marked 4 : Severe te			

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL : MOUSE BDF1

REPORT TYPE : A1

: FEMALE

DEAD AND MORIBUND ANIMALS (0-105W)

Group Name Control 667ppm 2000ppm 6000ppm No. of Animals on Study 19 28 17 Grade Findings (%) (%) (%) [Urinary system] kidnev (17) mineralization: inner stripe, outer medulla 0 0 0 0 2 0 0 0 0 0 (0)(0)(0)(0) (7)(0)(0)(0) (12) (0) (0) (0) (24) (0) (0) (0) [Endocrine system] pituitary <19> <27> cyst 1 0 0 0 0 0 0 0 2 0 0 0 1 0 0 0 (5)(0)(0)(0) (0)(0)(0)(0) (6)(0)(0)(0) (8) (0) (0) (0) hyperplasia 0 0 0 0 (11) (0) (0) (0) (0)(0)(0)(0) (4)(0)(0)(0) (0)(0)(0)(0) adrenal <19> <28> (25) hyperplasia:cortical cell 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 ( 0) ( 0) ( 0) ( 0) (4)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) [Reproductive system] ovary <19> 0 0 0 0 cyst 1 0 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (4)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) Grade 1 : Slight 2 : Moderate 4 : Severe (a) a: Number of animals examined at the site b b: Number of animals with lesion (c) c : b / a \* 100(HPT150)

BAIS3

STUDY NO. : 0206 ANIMAL : MOUSE BDF1 HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0-105W)

REPORT TYPE : A1

SEX : FEMALE

No.	of Animals on Study 19	28 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	6000ppm 17 12 3 4 (%) (%) (%) (%)
system]				
lymphocytic infiltration	<19> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<28> 0 0 0 0 0 0 0 0 0 0 0	<25> 0 1 0 0 ( 0) ( 4) ( 0) ( 0)	<17> 0 0 0 0 0 0 0 0 0 0 0 0
cystic endometrial hyperplasia	<19> 4 3 0 0 ( 21) ( 16) ( 0) ( 0)	5 3 0 0 (18) (11) (0) (0)	3 3 0 0 (12) (12) (0) (0)	2 0 0 0 ( 12) ( 0) ( 0) ( 0)
eem]				
mineralization	(19) 1	<28> 9 5 0 0 ( 32) ( 18) ( 0) ( 0)	(25) 4 5 0 0 (16) (20) (0) (0)	3 3 0 0 (18) (18) (0) (0)
necrosis	(19) 0 0 0 0 (0) (0) (0) (0)	<28> 0 0 0 0 0 0 0 0 0 0 0	<25> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<17> 0 1 0 0 ( 0) ( 6) ( 0) ( 0)
se organs/appandage]				
degeneration	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 1 0 0 ( 0) ( 4) ( 0) ( 0)	<25> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
			444	
	Findings  system]  lymphocytic infiltration  cystic endometrial hyperplasia  cem]  mineralization  necrosis  se organs/appandage]  degeneration  1: Slight 2: Moderate 3: i a: Number of animals examined at the site b: Number of animals with lesion	No. of Animals on Study   18   1   2   3   4     (%) (%) (%) (%) (%) (%) (%) (%) (%) (%)	No. of Animals on Study   19   28   3   4   1   2   3   4   (%) (%) (%) (%) (%) (%) (%) (%) (%) (%)	No. of Animals on Study

SEX

ANIMAL : MOUSE BDF1 REPORT TYPE : A1 : FEMALE

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

Organ	No	oup Name Control . of Animals on Study 19 ade 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	2000ppm 25 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$
[Special sens	e organs/appandage]				
Harder gl	inflammation	<19> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<28> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<25> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 ( 6) ( 0) ( 0) ( 0)
nasolacr d	inflammation	<19> 0 0 0 0 0 0 0 0 0 0 0	28> 1 0 0 0 ( 4) ( 0) ( 0) ( 0)	<25> 0 1 0 0 ( 0) ( 4) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
(Musculoskele	otal system]				
nuscle	mineralization	<19> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<28> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<25> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	(17) 1 0 0 0 (6) (0) (0) (0)
[Body cavitie	(se				
dipose	granulation	<19> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<pre></pre>	(25) 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<17> 0 0 0 0 0 0 0 0 0 0 0 0
irade (a > b (c)	1: Slight 2: Moderate 3: a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	Marked 4 : Severe		A-77	

### APPENDIX K 7

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

MOSUE: MALE: SACRIFICED ANIMALS

STUDY NO. : 0206 ANIMAL. : MOUSE BDF1 HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

REPORT TYPE : AI

SEX : MALE

Organ	1	Group Name  Jo. of Animals on Study  Grade 1 (%)	Control 35 2 3 4 (%) (%) (%)	667ppm 41 1 2 3 4 (%) (%) (%) (%)	2000ppm 41 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
[Respiratory	system]					
nasal cavit	mineralization	0 ( 0)	<35> 0 0 0 ( 0) ( 0) ( 0)	<pre></pre>	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	39> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)
	catarrh	0 ( 0)	0 0 0 0 ( 0) ( 0)	0 0 0 0 0 0 ( 0) ( 0)	0 1 0 0 ( 0) ( 0)	0 1 0 0 ( 0) ( 0)
	epidermal cyst	0 ( 0)	0 0 0 0 (0) (0)	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (3) ( 0) ( 0) ( 0)
	eosinophilic change:olfactory epitheli		0 0 0 0 (0) (0)	9 0 0 0 0 (22) (0) (0) (0)	5 0 0 0 (12) (0) (0) (0)	5 0 0 0 (13) (0) (0) (0)
	eosinophilic change:respiratory epithe		8 0 0 (23) ( 0) ( 0)	13 2 1 0 (32) (5) (2) (0)	13 1 0 0 (32) (2) (0) (0)	4 0 0 0 0 (10) (10) (10)
	inflammation:foreign body	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 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 0 (0) (0)
	respiratory metaplasia:olfactory epith		6 0 0 (17) (0) (0)	13 4 0 0 ( 32) ( 10) ( 0) ( 0)	11 4 0 0 ( 27) ( 10) ( 0) ( 0)	16 5 0 0 ( 41) ( 13) ( 0) ( 0)
	respiratory metaplasia:gland	13 ( 37)	6 0 0 (17) ( 0) ( 0)	13 4 0 0 (32) (10) (0) (0)	17 3 0 0 (41) (7) (0) (0)	28 4 0 0 (72) (10) (0) (0)
Grade <a> b (c)</a>	1: Slight 2: Moderate 3 a: Number of animals examined at the si b: Number of animals with lesion c: b / a * 100	Marked 4: Severe te				

STUDY NO. : 0206 ANIMAL : MOUSE BDF1

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

REPORT TYPE : A1
SEX : MALE

0rgan	Group Nar No. of Ar Grade Findings	ne Control nimals on Study 35  1 2 3 4 (%) (%) (%) (%)	667ppm 41 1 2 3 4 (%) (%) (%) (%)	2000ppm 41 1 2 3 4 (%) (%) (%) (%)	6000ppm 39 1 2 3 4 (%) (%) (%) (%)
[Respiratory	system]				
nasal cavit	desquamation:olfactory epithelium	<35> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<pre></pre>	<41> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)	39> 3 0 0 0 (8) (0) (0) (0)
	atrophy:olfactory epithelium	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0) (0)	29 5 0 0 (71) (12) (0) (0)	16 21 0 0 (41) (54) (0) (0)
	necrosis:olfactory epithelium	0 0 0 0 0 (0) (0)	1 0 0 0 0 (2) (0) (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0) (0)
nasopharynx	eosinophilic change:respiratory epithelium	<35> 5 0 0 0 ( 14) ( 0) ( 0) ( 0)	<41> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<41> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)	<39> 0 0 0 0 0 0 0 0 0 0 0
lung	inflammatory infiltration	<35> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<41> 0 0 0 0 0 0 0 0 0 0 0 0	<41> 0 0 0 0 0 0 0 0 0 0 0 0	39> 1 0 0 0 ( 3) ( 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)	1 0 0 0 0 (3) (0) (0)
	bronchiolar-alveolar cell hyperplasia	0 0 0 0 0 ( 0) ( 0)	3 0 0 0 0 (7) (0) (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
Grade <a>&gt;</a> b <a></a>	1: Slight 2: Moderate 3: Marked a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	4 : Severe		<del></del>	
(HPT150)					BAISS

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

ANIMAL : MOUSE BDF1 REPORT TYPE : A1

PAGE: 3 SEX : MALE

0rgan		up Name Cantrol of Animals on Study 35 de 1 2 3 4 (%) (%) (%) (%)	667ppm 41 1 2 3 4 (%) (%) (%) (%)	2000ppm 41 1 2 3 4 (%) (%) (%) (%)	6000ppm 39 1 2 3 4 (%) (%) (%) (%)
[Nematopoieti	c system]				
bone marrow	granulation	(35> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<pre></pre>
	increased hematopoiesis	1 0 0 0 ( 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)
	granulopoiesis:increased	0 0 0 0 0 (0) (0)	1 0 0 0 0 (2) ( 0) ( 0) ( 0)	0 3 0 0 (0) (7) (0) (0)	2 0 0 0 0 (5) (0) (0)
lymph node	xanthogranuloma	<35> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<pre></pre>	<41> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<39> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
spleen	deposit of melanin	<pre></pre>	0 1 0 0 ( 0) ( 3) ( 0) ( 0)	0 1 0 0 ( 0) ( 2) ( 0) ( 0)	39> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)
	extramedullary hematopoiesis	1 1 0 0 (3) (3) (0) (0)	1 2 0 0 (3) (5) (0) (0)	1 1 0 0 (2) (2) (0) (0)	0 0 0 0 0 ( 0) ( 0)
	follicular hyperplasia	1 1 0 0 ( 3) ( 3) ( 0) ( 0)	0 3 0 0 (0) (8) (0) (0)	0 3 0 0 (0) (7) (0) (0)	0 2 0 0 (0) (5) (0) (0)
Grade < a > b ( c )	1: Slight 2: Moderate 3: 1 a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	Marked 4: Severe			

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : MALE

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

0rgan		up Name Control of Animals on Study 35 de 1 2 3 4 (%) (%) (%) (%)	667ppm 41 1 2 3 4 (%) (%) (%) (%)	2000ppm 41 1 2 3 4 (%) (%) (%) (%)	6000ppm 39 1 2 3 4 (%) (%) (%) (%)
[Circulator:	y system]				
heart	arteritis	<35> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	39> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)
(Digestive :	system]				
tooth	aplasia	<pre></pre>	1 0 0 0 ( 2) ( 0) ( 0) ( 0)	(41) 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<pre></pre>
	cyst	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 ( 0) ( 0) ( 0)	0 1 0 0 (0) (0)
	dysplasia	21 2 1 0 (60) (6) (3) (0)	25 1 2 0 (61) (2) (5) (0)	32 3 0 0 (78) (7) (0) (0)	25 0 2 0 (64) (0) (5) (0)
tongue	arteritis	<35> 0 0 0 0 0 0 0 0 0 0 0	441> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)	<pre></pre>	<pre></pre>
stomach	mineralization	35> 3 0 0 0 ( 9) ( 0) ( 0) ( 0)	41> 4 0 0 0 ( 10) ( 0) ( 0) ( 0)	2 0 0 0 ( 5) ( 0) ( 0) ( 0)	39> 3 0 0 0 ( 8) ( 0) ( 0) ( 0)
Grade <a> b (c)</a>	1: Slight 2: Moderate 3: 1 a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	farked 4 : Severe			

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL : MOUSE BDF1
REPORT TYPE : A1

REPORT TYPE : A1
SEX : MALE

SACRIFICED ANIMALS (105W)

Organ	Findings	Group Name Control No. of Animals on Study 35 Grade 1 2 3 4 (%) (%) (%) (%)	667ppm 41 1 2 3 4 (%) (%) (%) (%)	2000ppm 41 1 2 3 4 (%) (%) (%) (%)	6000ppm 39 1 2 3 4 (%) (%) (%) (%)
[Digestive	system]				
stomach	ulcer:farestomach	35> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	(41) 1 0 0 0 (2) (0) (0) (0)	39> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	hyperplasia:glandular stomach	6 0 0 0 (17) (0) (0) (0)	5 0 0 0 (12) (0) (0) (0)	5 0 0 0 (12) ( 0) ( 0) ( 0)	4 0 0 0 (10) (0) (0) (0)
liver	necrasis:facal	<pre></pre>	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	(41) 1 0 0 0 (2) (0) (0) (0)	<39> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	granulation	12 6 0 0 ( 34) ( 17) ( 0) ( 0)	13 9 0 0 (33) (23) (0) (0)	8 8 0 0 (20) (20) (0) (0)	8 5 0 0 (21) (13) (0) (0)
	clear cell focus	0 1 0 0 (0) (0)	2 4 0 0 ( 5) ( 10) ( 0) ( 0)	1 0 1 0 (2) ( 0)	0 0 0 0 0 (0) (0)
	acidophilic cell focus	0 0 0 0 0 (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 1 0 0 ( 0) ( 0)
	basophilic cell focus	0 0 0 0 0 ( 0) ( 0)	3 2 1 0 (8) (5) (3) (0)	1 0 0 0 0 (2) ( 0) ( 0) ( 0)	2 0 0 0 0 (5) (0) (0) (0)
	vacuolated cell focus	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 0 ( 0) ( 0)	1 0 0 0 0 (3) ( 0) ( 0) ( 0)
Grade < a > b ( c )	1: Slight 2: Moderate a: Number of animals examined at th b: Number of animals with lesion c: b/a * 100	3 : Marked 4 : Severe ne site			

ANIMAL : MOUSE BDF1 REPORT TYPE : A1 : MALE SEX

#### HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

0rgan		O Name Control of Animals on Study 35 (%) (%) (%) (%)	667ppm 41 1 2 3 4 (%) (%) (%) (%)	2000ppm 41 1 2 3 4 (%) (%) (%) (%)	6000ppm 39 1 2 3 4 (%) (%) (%) (%)
[Digestive s	system]				
liver	mixed cell focus	<35> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	(40) 0 1 0 0 ( 0) ( 3) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	39> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)
	spongiosis hepatis	1 0 0 0 0 (3) ( 0) ( 0)	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
	biliary cyst	0 0 0 0 0 (0) (0)	1 0 0 0 0 (3) (0) (0)	0 0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 (0) (0)
pancreas	atrophy	<35> 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)
[Urinary sys	stem]				
kidney	infarct	<35> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<39> 4 1 0 0 (10) (3) (0) (0)
	cyst	0 0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 0 (0) (0)	1 0 0 0 0 (2) ( 0) ( 0) ( 0)	0 0 0 0 0 (0) (0)
Grade <a>&gt; b (c)</a>	1: Slight 2: Moderate 3: Ma a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	rked 4 : Severe			

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : MALE HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

Organ	Group Na No. of A Grade Findings	me Control nimals on Study 35  1 2 3 4 (%) (%) (%) (%)	667ppm 41 1 2 3 4 (%) (%) (%) (%)	2000ppm 41 1 2 3 4 (%) (%) (%) (%)	6000ppm 39 1 2 3 4 (%) (%) (%) (%)
[Urinary sy	vstem]				
kidney	basophilic change	<35> 17	(41) 19 10 0 0 (46) (24) (0) (0)	<pre></pre>	39> 21 5 0 0 (54) (13) (0) (0)
	inflammatory polyp	0 0 0 0 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)
	vacuolization of proximal tubule	3 0 0 0 0 ( 9) ( 0) ( 0)	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 ( 0) ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0)
	hydranephrasis	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 1 (0) (0) (2)	0 0 0 0 0 ( 0) ( 0)
	pyelanephritis	0 1 0 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:cortico-medullary junction	0 0 0 0 0 (0) (0)	1 0 0 0 0 (2) (0) (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 ( 0) ( 0)
	mineralization:papilla	1 0 0 0 0 (3) ( 0) ( 0)	2 0 0 0 ( 5) ( 0) ( 0) ( 0)	2 0 0 0 ( 5) ( 0) ( 0) ( 0)	1 0 0 0 0 (3) (0) (0) (0)
	mineralization:pelvis	6 0 0 0 (17) (0) (0) (0)	3 0 0 0 ( 7) ( 0) ( 0) ( 0)	5 0 0 0 (12) ( 0) ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0)
Grade <a>&gt; b (c)</a>	1: Slight 2: Moderate 3: Marked a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	1 4: Severe			·

ANIMAL : MOUSE BDF1

REPORT TYPE : A1
SEX : MALE

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

ITANES (100M)

)rgan		o Name Control of Animals on Study 35 (%) (%) (%) (%)	667ppm 41 1 2 3 4 (%) (%) (%) (%)	2000ppm 41 1 2 3 4 (%) (%) (%) (%)	6000ppm 39 1 2 3 4 (%) (%) (%) (%)
[Urinary sys	stem]				
cidney	mineralization:cortex	\( \lambda 35 \) \[ 14  19  0  0 \\ (40)  (54)  (0)  (0) \]	\( \lambda 41 \rangle \) 17	241> 12 28 0 0 ( 29) ( 68) ( 0) ( 0)	<pre></pre>
	desquamation:pelvis	0 0 0 0 0 0 ( 0)	0 0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 0 (0) (0)	6 1 0 0 (15) (3) (0) (0)
	mineralization:inner stripe,outer medulla	8 0 0 0 (23) (0) (0) (0)	7 0 0 0 (17) (0) (0) (0)	10 0 0 0 (24) (0) (0) (0)	11 0 0 0 ( 28) ( 0) ( 0) ( 0)
Endocrine s	system]				
ituitary	cyst	34> 2 0 0 0 ( 6) ( 0) ( 0) ( 0)	2 0 0 0 ( 5) ( 0) ( 0) ( 0)	0 1 0 0 ( 0) ( 2) ( 0) ( 0)	39> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)
	Rathke pouch	2 0 0 0 0	2 0 0 0 0 (5) ( 0) ( 0) ( 0)	4 0 0 0 0 (10) (10) (10)	1 0 0 0 0 (3) (0) (0)
adrena l	hyperplasia:cortical cell	<pre></pre>	41> 1 0 0 0 ( 2) ( 0) ( 0) ( 0)	3 1 0 0 ( 7) ( 2) ( 0) ( 0)	39> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
rade a > b	1: Slight 2: Moderate 3: Man a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	rked 4 : Severe			

(HPT150)

ANIMAL : MOUSE BDF1

REPORT TYPE : A1
SEX : MALE

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

PAGE: 9

Group Name Control 667ppm 2000ppm 6000ppm No. of Animals on Study 35 41 41 39 Grade 0rgan Findings\_ (%) (%) (%) [Reproductive system] testis ⟨35⟩ (41) <41> atrophy 0 0 0 0 0 0 0 0 5 0 (3)(0)(0)(0) (5)(0)(0)(0) (10) (0) (0) (0) (13) (0) (0) (0) mineralization 32 0 0 0 3 0 0 (91) (0) (0) (0) (83) (7) (0) (0) (93) (2) (0) (0) (23) (0) (0) (0) epididymis <41> <41> 0 0 0 0 0 0 1 1 0 0 spermatogenic granuloma 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (2)(2)(0)(0) (0)(0)(0)(0) prep/cli gl <41> **<41>** duct cell 6 0 0 0 14 0 0 0 10 0 0 (6) (17) (0) (0) (0)(34)(0)(0) (0)(24)(0)(0) (3) (18) (0) (0) inflammation 0 0 0 0 0 0 0 0 0 1 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(2)(0)(0) (0)(0)(0)(0) [Nervous system] brain <35> (41) <41> mineralization 9 14 0 0 8 21 0 0 9 17 0 0 (26) (40) (0) (0) (20) (51) (0) (0) (22) (41) (0) (0) (18) (59) (0) (0) Grade 1: Slight 2 : Moderate 3 : Marked 4 : Severe < a > a: Number of animals examined at the site b b: Number of animals with lesion (c) c:b/a\*100

(HPT150)

ANIMAL : MOUSE BDF1

REPORT TYPE : A1
SEX : MALE

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

		up Name of Animals on Study 3			2000ppm 41	6000ppm 39	
rgan	Grad Findings	de <u>1 2</u> (%) (%)	3 4 (%) (%)	1 2 3 4 (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)	
Special sense	organs/appandage]						
arder gl	hyperplasia	1 0	35> 0 0 (0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<39> 0 0 0 0 0 0 0 0 0 0 0	<pre></pre>	
asolacr d	inflammation	0 0 ( 0) ( 0)		(41) 1 0 0 0 ( 2) ( 0) ( 0) ( 0)	(41) 1 0 0 0 (2) (0) (0) (0)	<pre></pre>	
Body cavities	5]						
dipose	granulation	0 1	35> 0 0 ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<pre></pre>	
a > b	1: Slight 2: Moderate 3: Ma a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	arked 4: Severe					
c ) HPT150)	c:b/a*100						

### APPENDIX K 8

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

MOSUE: FEMALE: SACRIFICED ANIMALS

STUDY NO. : 0206 ANIMAL : MOUSE BDF1

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

REPORT TYPE : A1
SEX : FEMALE

0rgan	1	Froup Name  No. of Animals on Study  Frade $\frac{1}{(\%)}$	Control 31 2 3 (%) (%)	4 (%) 1 (%)	22 2 3 (%) (%)	200m 	1 (%)	200 25 2 3 (%) (%	Оррт 4 ) (%)	1 (%)	6000ppm 32 2 3 4 (%) (%) (%
[Respiratory :	system]										
nasal cavit	catarrh	0 ( 0)	<31> 0 0 ( 0) ( 0) (	0 1 0) ( 5)	<22> 2 0 ( 9) ( 0)	0 ( 0)	0 ( 0) (	<25> 1 0 4) ( 0	0 ( 0)	0 ( 0) (	<32> 5 0 0 16) ( 0) ( 0
٠	eosinophilic change:olfactory epitheli	um 11 (35)	0 0 (	0 3 0) (14)	0 0	0 ( 0)	1 ( 4) (	0 0	0 ) ( 0)	6 (19) (	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
	eosinophilic change:respiratory epithe		7 0 (23) (0) (	1 11 3) (50)	2 0 ( 9) ( 0)	0 ( 0)	13 ( 52) (	2 0	0) (0)	21 (66) (	2 0 0
	inflammation:respiratory epithelium	2 ( 6)	0 0 (0) (	0 0) ( 0)	0 0 (0)	0 ( 0)	0 (0) (	0 0		0 ( 0) (	0 0 0
	respiratory metaplasia:olfactory epith		0 0 ( 0) (	0 2 0) ( 9)	0 0 (0)	0 ( 0)	6 ( 24) (	0 (	0	8 ( 25) (	0 0 0
	respiratory metaplasia:gland	10 ( 32)	0 0 (	0 2 0) ( 9)	0 0 (0)	0 ( 0)	6 ( 24) (	1 (		6 ( 19) (	0 0 0
	desquamation:olfactory epithelium	0 ( 0)	0 0 (	0 1 0) ( 5)	0 0 (0)	0 ( 0)	( 0) (	0 (	0) (0)	3 ( 9) (	0 0 0
	granulopoiesis:increased	0 ( 0)	1 0 ( 3) ( 0) (	0 0 0	( 0) ( 0)	0 ( 0)	( 0) (	0 (	0)) ( 0)	( 0) (	0 0 0
Grade ( a > b ( c )	1: Slight 2: Moderate 3 a: Number of animals examined at the si b: Number of animals with lesion c: b/a * 100	: Marked 4 : Sever te	ө								

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

ANIMAL : MOUSE BDF1 REPORT TYPE : A1

SEX : FEMALE

Organ	Group N No. of Grade Findings	ame Control Animals on Study 31  1 2 3 4  (%) (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	2000ppm 25 1 2 3 4 (%) (%) (%) (%)	6000ppm 32 1 2 3 4 (%) (%) (%) (%)
[Respiratory	system]				
nasal cavit	atrophy:olfactory epithelium	<pre></pre>	<22> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<25> 16 3 0 0 (64) (12) (0) (0)	<32> 15 16 0 0 ( 47) ( 50) ( 0) ( 0)
	necrosis:alfactory 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 0	1 0 0 0 0 (4) (0) (0) (0)	1 0 0 0 0 (3) ( 3) ( 0) ( 0) ( 0)
nasopharynx	eosinophilic change:respiratory epithelium	1 0 1 0 ( 3) ( 0) ( 3) ( 0)	1 0 0 0 ( 5) ( 0) ( 0) ( 0)	25> 2 0 0 0 ( 8) ( 0) ( 0) ( 0)	32> 2 1 0 0 ( 6) ( 3) ( 0) ( 0)
lung	lymphacytic infiltration	<31> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<22> 1 0 0 0 ( 5) ( 0) ( 0) ( 0)	<25> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<32> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	bronchiolar-alueolar cell hyperplasia	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	1 0 0 0 ( 5) ( 0) ( 0) ( 0)	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 (0) (0)
[Hematopoieti	c system]				
bone marrow	increased hematopolesis	<31> 0 0 0 0 0 0 0 0 0 0 0 0	222> 1 0 0 0 ( 5) ( 0) ( 0) ( 0)	<25> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	32> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
<a>&gt; b</a>	1: Slight 2: Moderate 3: Marke a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	d 4 : Severe			,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,

STUDY NO. : 0206 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : FEMALE

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

PAGE: 13

Organ		Tup Name Control of Animals on Study 31 side 1 2 3 4 (%) (%) (%) (%)	667ppm 22 1 2 3 4 (%) (%) (%) (%)	2000ppm 25 1 2 3 4 (%) (%) (%) (%)	6000ppm 32 1 2 3 4 (%) (%) (%) (%)
[Hematopoiet	ic system]				
oone marrow	myelofibrasis	( 0) ( 0) ( 0) ( 0) 0 0 0 0 0 0 0	(22) 1 0 0 0 ( 5) ( 0) ( 0) ( 0)	<25> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	32> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	granulopoiesis:increased	0 1 0 0 ( 0) ( 0)	0 0 0 0 0	0 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	deposit of melanin	<31> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<25> 0 0 0 0 0 0 0 0 0 0 0 0	2 0 0 0 ( 6) ( 0) ( 0) ( 0)
	extramedullary hematopoiesis	3 0 0 0 (10) (0) (0) (0)	2 0 0 0 0 ( 9) ( 0) ( 0)	1 1 0 0 ( 4) ( 4) ( 0) ( 0)	5 2 0 0 (16) (6) (0) (0)
	follicular hyperplasia	0 0 0 0 0 (0)	0 1 0 0 ( 0) ( 5) ( 0) ( 0)	0 5 0 0 (0) (20) (0) (0)	0 1 0 0 ( 0) ( 0)
(Circulatory	system]				
heart	arteritis	<31> 0 0 0 0 0 0 0 0 0 0 0 0	<22> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<25> 1 0 0 0 ( 4) ( 0) ( 0) ( 0)	<32> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
Grade <a> b (c)</a>	1: Slight 2: Moderate 3: a: Number of animals examined at the site b: Number of animals with lesion c: b/a*100	farked 4 : Severe			

(HPT150)

BAIS3

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

ANIMAL : MOUSE BDF1

REPORT TYPE : A1
SEX : FEMALE

Organ	Group Name No. of Anim Grade	Control mals on Study 31  1 2 3 4  (%) (%) (%) (%)	667ppm 22 1 2 3 4 (%) (%) (%) (%)	2000ppm 25 1 2 3 4 (%) (%) (%) (%)	6000ppm 32 1 2 3 4 (%) (%) (%) (%)
(Digestive sy	ystem]				
tooth	cyst	( 0) ( 0) ( 0) ( 0) ( 0) ( 0) ( 0) ( 0)	<22> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	(25) 0 0 1 0 ( 0) ( 0) ( 4) ( 0)	32> 0 0 1 0 ( 0) ( 0) ( 3) ( 0)
	dysplasia	7 0 0 0 (23) (0) (0) (0)	6 0 1 0 (27) (0) (5) (0)	5 0 1 0 (20) (0) (4) (0)	4 4 1 0 (13) (13) (3) (0)
	inflammation:foreign body	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 1 0 0 ( 0) ( 0)
tongue	arteritis	(31) 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<222> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<25> 0 1 0 0 ( 0) ( 4) ( 0) ( 0)	32> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)
salivary gl	lymphocytic infiltration	4 0 0 0 ( 13) ( 0) ( 0) ( 0)	4 0 0 0 (18) (0) (0) (0)	25> 2 0 0 0 ( 8) ( 0) ( 0) ( 0)	32> 3 0 0 0 ( 9) ( 0) ( 0) ( 0)
stomach	mineralization	31> 9 0 0 0 (29) (0) (0) (0)	3 0 0 0 (14) (0) (0) (0)	<25> 6 0 0 0 ( 24) ( 0) ( 0) ( 0)	32> 6 0 0 0 (19) ( 0) ( 0) ( 0)
	erosion:glandular stomach	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 ( 3) ( 0) ( 0) ( 0)
Grade (a > b (c)	1: Slight 2: Moderate 3: Marked a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100	4 : Severe			

ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : FEMALE

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

0rgan	Group N No. of Grade Findings	Animals on Study 31  1 2 3 4 (%) (%) (%) (%)	667ppm 22 1 2 3 4 (%) (%) (%) (%)	2000ppm 25 1 2 3 4 (%) (%) (%) (%)	6000ppm 32 1 2 3 4 (%) (%) (%) (%)
(Digestive	system]				
stomach	hyperplasia:glandular stomach	31> 8 1 0 0 (26) (3) (0) (0)	4 1 0 0 (18) (5) (0) (0)	(25) 4 0 0 0 (16) (0) (0) (0)	<32> 4 0 0 0 ( 13) ( 0) ( 0) ( 0)
liver	angiectasis	<pre></pre>	(22>) 1 2 0 0 ( 5) ( 9) ( 0) ( 0)	<25> 3 1 0 0 (12) (4) (0) (0)	32> 2 0 0 0 ( 6) ( 0) ( 0) ( 0)
	necrosis:facal	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 (0) (0)	1 1 0 0 ( 4) ( 4) ( 0) ( 0)	1 1 0 0 (3) (3) (0) (0)
	granulation	7 15 3 0 (23) (48) (10) (0)	3 9 1 0 (14) (41) (5) (0)	11 7 1 0 (44) (28) (4) (0)	7 10 0 0 (22) (31) (0) (0)
	clear cell focus	1 0 0 0 0 (3) ( 0) ( 0)	1 0 0 0 0 (5) ( 0) ( 0) ( 0)	0 3 0 0 (0) (12) (0) (0)	1 1 0 0 ( 3) ( 3) ( 0) ( 0)
	basophilic cell focus	1 0 0 0 0 (3) ( 3) ( 0) ( 0)	1 0 0 0 0 (5) ( 0) ( 0) ( 0)	5 3 0 0 (20) (12) (0) (0)	4 1 1 0 (13) (3) (3) (0)
[Urinary sy	stem]				
kidney	hyaline droplet	<31> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	222> 2 0 0 0 ( 9) ( 0) ( 0) ( 0)	<25> 1 0 0 0 ( 4) ( 0) ( 0) ( 0)	<32> 2 0 0 0 ( 6) ( 0) ( 0) ( 0)
Grade < a > b ( c )	1: Slight 2: Moderate 3: Marke a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	ed 4: Severe			

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

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : FEMALE

Organ		up Name Control of Animals on Study 31 de 1 2 3 4 (%) (%) (%) (%)	667ppm 22 1 2 3 4 (%) (%) (%) (%)	2000ppm 25 1 2 3 4 (%) (%) (%) (%)	6000ppm 32 1 2 3 4 (%) (%) (%) (%)
[Urinary sy	vstem]				
kidney	basophilic change	31> 5 0 0 0 ( 16) ( 0) ( 0) ( 0)	(22> 1 0 0 0 ( 5) ( 0) ( 0) ( 0)	<25> 4 0 0 0 ( 16) ( 0) ( 0) ( 0)	<pre></pre>
	lymphocytic infiltration	0 0 0 0 0 0 (0) (0)	2 0 0 0 0 ( 9) ( 0) ( 0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 ( 0) ( 0)
	hydronephrosis	0 1 0 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:cortico-medullary junction	0 0 0 0 0 ( 0) ( 0) ( 0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	4 0 0 0 (13) ( 0) ( 0) ( 0)
	mineralization:papilla	6 0 0 0 (19) (0) (0) (0)	3 0 0 0 (14) ( 0) ( 0) ( 0)	8 0 0 0 0 (32) ( 0) ( 0) ( 0)	4 0 0 0 (13) (0) (0) (0)
	mineralization:pelvis	0 0 0 0 0 ( 0) ( 0)	0 0 0 0 0 (0) (0)	( 0) ( 0) ( 0) ( 0)	1 0 0 0 0 (3) ( 0) ( 0) ( 0)
	mineralization:cortex	5 0 0 0 (16) (0) (0) (0)	3 0 0 0 (14) ( 0) ( 0) ( 0)	8 0 0 0 0 (32) (0) (0) (0)	9 0 0 0 0 (28) (0) (0) (0)
	desquamation:pelvis	4 0 0 0 0 (13) (13) (10) (10)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	11 0 0 0 (34) (0) (0) (0)
Grade <a> b (c)</a>	1: Slight 2: Moderate 3: M a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	arked 4: Severe			

ANIMAL : MOUSE BDF1

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

REPORT TYPE : A1

SEX : FEMALE

	Group No. o	Name Control f Animals on Study 31	667ppm 22	2000ppm 25	6000ppm 32	
)rgan	Findings	<u>1 2 3 4</u> (%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)	
[Urinary sys	stem]					
kidney	mineralization:inner stripe,outer medulla	31> 3 0 0 0 (10) (0) (0) (0)	3 0 0 0 (14) (0) (0) (0)	<25> 9 0 0 0 (36) (0) (0) (0)	<pre></pre>	
(Endocrine s	system]					
pituitary	cyst	<31> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	(22) 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<25> 2 0 0 0 ( 8) ( 0) ( 0) ( 0)	<pre></pre>	
	hyperplasia	4 0 0 0 (13) (0) (0) (0)	2 0 0 0 0 ( 9) ( 0) ( 0) ( 0)	0 0 0 0 0 (0) (0) (0)	5 0 0 0 (16) ( 0) ( 0) ( 0)	
	Rathke pouch	0 0 0 0 0 (0) (0)	0 0 0 0 0 ( 0) ( 0)	1 0 0 0 0 (4) (0) (0) (0)	1 0 0 0 0 (3) (0) (0)	
adrena l	fatty change	31> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)	<222> 0 1 0 0 ( 0) ( 5) ( 0) ( 0)	<25> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<pre></pre>	
	hyperplasia:cortical cell	1 0 0 0 ( 3) ( 0) ( 0) ( 0)	0 0 0 0 0 0 (0) (0) (0)	0 1 0 0 ( 0) ( 4) ( 0) ( 0)	0 0 0 0 0 (0) (0)	
Grade (a) b (c)	1: Slight 2: Moderate 3: Mar a: Number of animals examined at the site b: Number of animals with lesion c: b/a*100	ked 4: Severe				

(HPT150)

BAIS3

ANIMAL : MOUSE BDF1 REPORT TYPE : A1

SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

)rgan		p Name Control of Animals on Study 31 de <u>1 2 3 4 (%) (%) (%) (%) (%) (%) (%) (%) (%) (%)</u>	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	2000ppm 25 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
Endacrine	system]				
drenal	hyperplasia:medulla	<31> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	(22) 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	(25) 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	32> 1 0 0 0 ( 3) ( 0) ( 0) ( 0)
Reproducti	ve system]				
Vary	thrombus	<31> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	<25> 0 0 0 0 ( 0) ( 0) ( 0) ( 0)	32> 0 1 0 0 ( 0) ( 3) ( 0) ( 0)
	cyst	1 1 0 0 (3) (3) (0) (0)	1 0 0 0 ( 5) ( 0) ( 0) ( 0)	1 0 0 0 0 (4) ( 0) ( 0) ( 0)	1 0 0 0 0 (3) ( 0) ( 0) ( 0)
terus	cystic endometrial hyperplasia	31> 9 16 1 0 ( 29) ( 52) ( 3) ( 0)	<22> 6 10 0 0 ( 27) ( 45) ( 0) ( 0)	<25> 6 12 1 0 ( 24) ( 48) ( 4) ( 0)	<32> 10 5 1 0 ( 31) ( 16) ( 3) ( 0)
Nervous s	vstem]				
rain	mineralization	\( \lambda 31 \rangle \) 12 8 0 0 ( 39) ( 26) ( 0) ( 0)	4 9 0 0 (18) (41) (0) (0)	<25> 7 9 0 0 ( 28) ( 36) ( 0) ( 0)	<32> 2 7 0 0 ( 6) ( 22) ( 0) ( 0)
rade a > b c )	1: Slight 2: Moderate 3: Ma a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	arked 4: Severe			

ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

Organ	N	roup Name  o. of Animals on Study  rade 1 (%)	31 2	ntrol 3 4 %) (%)	1 2		1 (%)	2000ppm 25 2 3 4 (%) (%) (%)	1 2 (%) (%	
[Special sens	se organs/appandage]									
өуө	cataract	0 ( 0)	<31> 0 ( 0) (	0 0 0) ( 0)	0 1 ( 0) ( 5		( 0) (	<25> 0 0 0 0) ( 0) ( 0)	0 0	<32> 0 0 0 0 (0) (0)
Marder gl	degeneration	0 ( 0)		0 0 0) ( 0)	0 0	<22> 0 0 ) ( 0) ( 0)	1 ( 4) (	<25> 0 0 0 0) ( 0) ( 0)	0 0	<32> 0 0 0 0 0 (0) (0)
Grade ( a > b ( c )	1: Slight 2: Moderate 3: a: Number of animals examined at the sit b: Number of animals with lesion c: b/a * 100	Marked 4: Severe e								

# APPENDIX L 1

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

RAT: MALE

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

STUDY NO. ANIMAL

: 0205 : RAT F344

REPORT TYPE : A1
SEX : MALE

SEX	: MALE					PAGE:
Time-related Weeks	Items	Groupe Name	Control	500ppm	1500ppm	4500ppm
0-52	NO. OF EXAMINED ANIMALS		0	1	1	1
	NO. OF ANIMALS WITH TUMORS		0	. 1	1	0
	NO. OF ANIMALS WITH SINGLE TUMORS		0	1	1	0
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	0	0	0
	NO. OF BENIGN TUMORS		0	0	0	0
	NO. OF MALIGNANT TUMORS		0	1	1	0
	NO. OF TOTAL TUMORS		0	1	1	0
53-78	NO. OF EXAMINED ANIMALS		2	2	1	5
	NO. OF ANIMALS WITH TUMORS		2	2	1	5
	NO. OF ANIMALS WITH SINGLE TUMORS		1	1	0	1
	NO. OF ANIMALS WITH MULTIPLE TUMORS		1	1	1	4
	NO. OF BENIGN TUMORS		2	1	1	4
	NO. OF MALIGNANT TUMORS		1	2	1	5
	NO. OF TOTAL TUMORS		3	3	2	9
79-105	NO. OF EXAMINED ANIMALS		11	6	10	13
	NO. OF ANIMALS WITH TUMORS		11	6	10	13
	NO. OF ANIMALS WITH SINGLE TUMORS		2	0	1	2
	NO. OF ANIMALS WITH MULTIPLE TUMORS		9	6	9	11
	NO. OF BENIGN TUMORS		22	11	15	18
	NO. OF MALIGNANT TUMORS		7	5	7	14
	NO. OF TOTAL TUMORS		29	16	22	32
AT SACRIFICED	NO. OF EXAMINED ANIMALS		37	41	38	31
	NO. OF ANIMALS WITH TUMORS		37	41	37	31
	NO. OF ANIMALS WITH SINGLE TUMORS		10	14	12	4
	NO. OF ANIMALS WITH MULTIPLE TUMORS		27	27	25	27
	NO. OF BENIGN TUMORS		70	66	80	63
	NO. OF MALIGNANT TUMORS		8	16	15	28
· · · · · · · · · · · · · · · · · · ·	NO. OF TOTAL TUMORS		78	82	95	91

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

STUDY NO. : 0205

ANIMAL : RAT REPORT TYPE : A1 : RAT F344

SEX

	: MALE					PAGE:	2
		 				111012.	4
4010101	T4	^	3.7	ο .			

Time-related Weeks	Items	Groupe Name	Control	500ррт	1500ppm	4500ppm
TOTAL	NO. OF EXAMINED ANIMALS		50	50	50	50
	NO. OF ANIMALS WITH TUMORS		50	50	49	49
	NO. OF ANIMALS WITH SINGLE TUMORS		13	16	14	7
	NO. OF ANIMALS WITH MULTIPLE TUMORS		37	34	35	42
	NO. OF BENIGN TUMORS		94	78	82	85
	NO. OF MALIGNANT TUMORS		16	24	22	47
	NO. OF TOTAL TUMORS		110	102	104	132

# APPENDIX L 2

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

RAT: FEMALE

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

STUDY NO. : 0205 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE

Y : FEMALE PAGE: 3

	PEWALE					PAGE: 3
Time-related Weeks	Items	Groupe Name	Control	500ppm	1500ppm	4500ppm
0-52	NO. OF EXAMINED ANIMALS		0	0	0	3
	NO. OF ANIMALS WITH TUMORS		0	0	0	0
	NO. OF ANIMALS WITH SINGLE TUMORS		0	0	0 .	0
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	0	0	0
	NO. OF BENIGN TUMORS		0	0	0	0
	NO. OF MALIGNANT TUMORS		0	0	0	0
	NO. OF TOTAL TUMORS		0	0	0	0
53-78	NO. OF EXAMINED ANIMALS		2	3	2	1
	NO. OF ANIMALS WITH TUMORS		2	3	2	1
	NO. OF ANIMALS WITH SINGLE TUMORS		1	3	2	1
	NO. OF ANIMALS WITH MULTIPLE TUMORS		1	0	0	0
	NO. OF BENIGN TUMORS		2	0	0	0
	NO. OF MALIGNANT TUMORS		1	3	2	1
	NO. OF TOTAL TUMORS		3	3	2	1
79-104	NO. OF EXAMINED ANIMALS		4	9	4	
	NO. OF ANIMALS WITH TUMORS		4	8	4	9
	NO. OF ANIMALS WITH SINGLE TUMORS		0	2	3	58
	NO. OF ANIMALS WITH MULTIPLE TUMORS		4	6	1	3
	NO. OF BENIGN TUMORS		4	9	2	5
	NO. OF MALIGNANT TUMORS		4	6	4	6
	NO. OF TOTAL TUMORS		8	15	6	11
AT SACRIFICED	NO. OF EXAMINED ANIMALS		44	38	44	37
	NO. OF ANIMALS WITH TUMORS		36	30	34	25
	NO. OF ANIMALS WITH SINGLE TUMORS		22	16	18	12
	NO. OF ANIMALS WITH MULTIPLE TUMORS		14	14	16	13
	NO. OF BENIGN TUMORS		41	34	42	33
	NO. OF MALIGNANT TUMORS		14	14	12	8
	NO. OF TOTAL TUMORS		55	48	54	41

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

STUDY NO. : 0205

ANIMAL ANIMAL : RAT F344 REPORT TYPE : A1

SEX	: FEMALE					PAGE:	4
Time-related	Items	Groupe Name	Control	500ppm	1500ppm	4500ppm	_

Time-related Weeks	Items	Groupe Name	Control	500ppm	1500ppm	4500ppm
TOTAL	NO. OF EXAMINED ANIMALS		50	50	50	50
	NO. OF ANIMALS WITH TUMORS		50	50	49	49
	NO. OF ANIMALS WITH SINGLE TUMORS		13	16	14	7
	NO. OF ANIMALS WITH MULTIPLE TUMORS		37	34	35	42
	NO. OF BENIGN TUMORS		94	78	82	85
	NO. OF MALIGNANT TUMORS		16	24	22	47
	NO. OF TOTAL TUMORS	- National Control of the Control of	110	102	104	132

# APPENDIX L 3

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

MOUSE: MALE

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

STUDY NO. : 0206

ANIMAL : MOUSE BDF1

REPORT TYPE : A1

	ALE					PAGE:
	Items	Groupe Name	Control	667ppm	2000ppm	6000ppm
Weeks						
0-52	NO. OF EXAMINED ANIMALS		1	0	1	0
	NO. OF ANIMALS WITH TUMORS			_		
	NO. OF ANIMALS WITH TUMORS  NO. OF ANIMALS WITH SINGLE TUMORS		0	0	0	0
	NO. OF ANIMALS WITH SINGLE TUMORS  NO. OF ANIMALS WITH MULTIPLE TUMORS		0	0	0	0
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	0	0	0
	NO. OF BENIGN TUMORS		0	0	0	0
	NO. OF MALIGNANT TUMORS		0	0	0	0
	NO. OF TOTAL TUMORS		0	0	0	0
53-78	NO. OF EXAMINED ANIMALS		3	2	2	4
	NO. OF ANIMALS WITH TUMORS		2	1	2	2
	NO. OF ANIMALS WITH SINGLE TUMORS		$\overset{-}{2}$	1	2	1
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	0	0	1
	NO. OF BENIGN TUMORS		1	0	0	0
	NO. OF MALIGNANT TUMORS		1	1	2	0
	NO. OF TOTAL TUMORS		2	1	2	3 3
79-105	NO. OF EXAMINED ANIMALS		11	7	6	7
	NO. OF ANIMALS WITH TUMORS		9	5	6	0
	NO. OF ANIMALS WITH SINGLE TUMORS		5	2	2	8 5
	NO. OF ANIMALS WITH MULTIPLE TUMORS		4	3	4	1
	NO. OF BENIGN TUMORS		2	0		
	NO. OF MALIGNANT TUMORS		14	2 7	2	0
	NO. OF TOTAL TUMORS		16	9	8 10	8 8
AT SACRIFICED	NO. OF EXAMINED ANIMALS		35	41	41	39
	NO. OF ANIMALS WITH TUMORS		18	32	oc.	10
	NO. OF ANIMALS WITH SINGLE TUMORS		12	32 22	26	18
	NO. OF ANIMALS WITH MULTIPLE TUMORS		6	10	21 5	12 6
	NO OF DEMONSTRACES				-	J
	NO. OF BENIGN TUMORS NO. OF MALIGNANT TUMORS		10	20	14	11
			14	24	23	14
	NO. OF TOTAL TUMORS		24	44	37	25

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

STUDY NO. : 0206

ANIMAL : MOUSE REPORT TYPE : A1 SEX : MALE : MOUSE BDF1

Time-related Weeks	Items	Groupe Name	Control	667ppm	2000ppm	6000ppm
TOTAL	NO. OF EXAMINED ANIMALS		50	50	50	50
	NO. OF ANIMALS WITH TUMORS		29	38	34	26
	NO. OF ANIMALS WITH SINGLE TUMORS		19	25	25	18
	NO. OF ANIMALS WITH MULTIPLE TUMORS		. 10	13	9	8
	NO. OF BENIGN TUMORS		13	22	16	11
	NO. OF MALIGNANT TUMORS		29	32	33	25
	NO. OF TOTAL TUMORS		42	54	49	36

### APPENDIX L4

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

MOUSE: FEMALE

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

STUDY NO. : 0206 ANIMAL : MOUS : MOUSE BDF1

REPORT TYPE : A1

	EMALE					PAGE:
Weeks	Items	Groupe Name	Control	667ppm	2000ppm	6000ppm
		<del>,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,</del>	·····			
0-52	NO. OF EXAMINED ANIMALS		2	0	1	1
	NO OD ANIMALO WINDY DVD AODO					
	NO. OF ANIMALS WITH TUMORS		1	0	0	0
	NO. OF ANIMALS WITH SINGLE TUMORS		1	0	0	0
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	0	0	0
	NO. OF BENIGN TUMORS		0	0	0	0
	NO. OF MALIGNANT TUMORS		1	0	0	0
	NO. OF TOTAL TUMORS		1	0	0	0
53-78	NO. OF EXAMINED ANIMALS		1	5	5	2
	NO. OF ANIMALS WITH TUMORS		1	2	5	2
	NO. OF ANIMALS WITH SINGLE TUMORS		1	2	4	2
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	0	1	0
	NO. OF BENIGN TUMORS		0	0	0	0
	NO. OF MALIGNANT TUMORS		1	2	6	$\frac{\circ}{2}$
	NO. OF TOTAL TUMORS		1	2	6	2
79-104	NO. OF EXAMINED ANIMALS		16	23	19	14
	NO. OF ANIMALS WITH TUMORS		16	21	17	14
	NO. OF ANIMALS WITH SINGLE TUMORS		11	16	12	11
	NO. OF ANIMALS WITH MULTIPLE TUMORS		5	5	5	3
	NO. OF BENIGN TUMORS		1	3	2	4
	NO. OF MALIGNANT TUMORS		20	27	20	14
	NO. OF TOTAL TUMORS		21	30	22	18
AT SACRIFICED	NO. OF EXAMINED ANIMALS		31	22	25	32
	NO. OF ANIMALS WITH TUMORS		24	16	21	97
	NO. OF ANIMALS WITH SINGLE TUMORS		17	7	9	27 16
	NO. OF ANIMALS WITH MULTIPLE TUMORS		7	9	12	11
	NO. OF BENIGN TUMORS		16	15	24	17
	NO. OF MALIGNANT TUMORS		18	15	15	17 23
	NO. OF TOTAL TUMORS		34	30	39	23 40

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

STUDY NO. : 0206 ANIMAL : MOUSE BDF1

REPORT TYPE : A1

SEX : FEMALE

PAGE · A

Time-related Weeks	Items	Groupe Name	Control	667ppm	2000ppm	6000ppm
TOTAL	NO. OF EXAMINED ANIMALS		50	50	50	49
	NO. OF ANIMALS WITH TUMORS		42	39	43	43
	NO. OF ANIMALS WITH SINGLE TUMORS		30	25	25	29
	NO. OF ANIMALS WITH MULTIPLE TUMORS		12	14	18	14
	NO. OF BENIGN TUMORS		17	18	26	21
	NO. OF MALIGNANT TUMORS		40	44	41	39
	NO. OF TOTAL TUMORS		57	62	67	60

### APPENDIX M 1

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

RAT : MALE :

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

REPORT TYPE : A1 : MALE

0rgan	Findings	Group Name No. of animals on Study	Control 50	500ppm 50	1500ppm 50	4500ppm 50
[Integumentary	v system/appandage]					
skin/app	squamous cell papilloma	2	<50> 2 ( 4%)	<50> 0 ( 0%)	<50> 1 ( 2%)	<50> 0 ( 0%)
	keratoacanthoma	1	( 2%)	2 ( 4%)	0 ( 0%)	1 ( 2%)
	sebaceous adenoma	(	) ( 0%)	1 ( 2%)	0 ( 0%)	0 ( 0%)
	squamous cell carcinoma	1	( 2%)	0 ( 0%)	0 ( 0%)	0 ( 0%)
subcutis	fibroma	Ę	<50> 5 ( 10%)	<50> 5 ( 10%)	<50> 2 ( 4%)	<50> 2 ( 4%)
	lipoma	1	( 2%)	0 ( 0%)	1 ( 2%)	0 ( 0%)
	fibrosarcoma	1	1 ( 2%)	1 ( 2%)	1 ( 2%)	1 ( 2%)
[Respiratory s	system]					
nasal cavit	chandrama	(	<50> ) ( 0%)	<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 1 ( 2%)
nasopharynx	squamous cell carcinoma	(	<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 1 (2%)
lung	bronchiolar-alveolar adenoma		<50> 1 ( 2%)	<50> 2 ( 4%)	<50> 2 ( 4%)	<50> 2 ( 4%)
[Hematopoietic	o system]					
lymph node	malignant lymphoma	(	<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 1 ( 2%)	<50> 0 ( 0%)
(a)	a: Number of animals examined at the site b: Number of animals with neoplasm c:b/a*1	00	· · · · · · · · · · · · · · · · · · ·			

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

REPORT TYPE : A1 SEX : MALE

)rgan	Findings	Group Name No. of animals on Study		Control 50		500ppm 50		1500ppm 50		4500ppm 50
[Nematopoietic	system]									
spleen	histiocytic sarcoma			<50> ( 0%)	1	<50> ( 2%)	0	<50> ( 0%)	0	<50> ( 0%)
	mononuclear cell leukemia	,	7	( 14%)	12	( 24%)	10	( 20%)	9	( 18%)
	hemangiosarcoma		1	( 2%)	0	( 0%)	0	( 0%)	0	( 0%)
[Digestive sys	tem]									
oral cauity	squamous cell carcinoma			<50> ( 0%)	0	<50> ( 0%)	0	<50> ( 0%)	1	<50> ( 2%)
tangue	squamous cell papilloma			<50> ( 0%)	0	<50> ( 0%)	2	<50> ( 4%)	0	<50> ( 0%)
salivary gl	schwannoma:malignant			<50> ( 0%)	0	<50> ( 0%)	0	<50> ( 0%)	1	<50> ( 2%)
stomach	squamous cell carcinoma			<49> ( 0%)	1	<50> ( 2%)	0	<49> ( 0%)	0	<50> ( 0%)
liver	hepatocellular adenoma		1	<50> ( 2%)	0	<50> ( 0%)	0	<50> ( 0%)	0	<50> ( 0%)
	histiocytic sarcoma		0	( 0%)	0	( 0%)	1	( 2%)	0	( 0%)
pancreas	acinar cell adenoma			<50> ( 2%)	0	<50> ( 0%)	0	<50> ( 0%)	0	<50> ( 0%)
	sarcoma:NOS		0	( 0%)	0	( 0%)	0	( 0%)	1	( 2%)
[Urinary syste	em]									
kidney	renal cell adenoma			<50> ( 2%)	0	<50> ( 0%)	0	<50> ( 0%)	0	<50> ( 0%)

<sup>(</sup>HPT085)

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

REPORT TYPE : A1
SEX : MALE

rgan	Findings	Group Name No. of animals on Study		Control 50		500ppm 50		1500ppm 50		4500ppm 50
rinary syste	m]									
dney	sarcoma:NOS	(		(50> ( 0 <b>%)</b>	1	<50> ( 2%)	1	<50> ( 2%)	0	<50> ( 0%)
	nephroblastoma	;	1 (	( 2%)	0	( 0%)	0	( 0%)	1	( 2%)
in bladd	squamous cell papilloma			<50> ( 0%)	0	<50> ( 0%)	0	<50> ( 0%)	1	<50> ( 2%)
	transitional cell papilloma	1	0 1	( 0%)	0	( 0%)	0	( 0%)	10	( 20%)
	squamous cell carcinoma		0	( 0%)	0	( 0%)	0	( 0%)	1	( 2%)
	transitional cell carcinoma	•	0	( 0%)	0	( 0%)	0	( 0%)	24	( 48%)
Endocrine sys	tem]									
ituitary	adenoma	1.		<50> ( 28%)	12	<50> ( 24%)	10	<50> ( 20%)	8	<50> ( 16%)
nyroid	C-cell adenoma			<50> ( 6%)	3	<50> ( 6%)	7	<50> ( 14%)	3	<50> ( 6%)
	C-cell carcinoma		0	( 0%)	3	(6%)	1	( 2%)	0	( 0%)
	follicular adenocarcinoma		1	( 2%)	0	( 0%)	1	( 2%)	2	( 4%)
panc islet	islet cell adenoma			<50> ( 14%)	0	<50> ( 0%)	1	<50> ( 2%)	1	<50> ( 2%)
adrenal	pheachromocytoma			<50> ( 10%)	4	<50> ( 8%)	c	<50> ( 16%)	7	<50> ( 14%)

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

ANIMAL : RAT F344 REPORT TYPE : A1 SEX

: MALE

0rgan	Findings	Group Name No. of animals on Study		Control 50		500ppm 50			1500ppm 50	33774	4500ppm 50
(Endocrine sy	rstem]										
adrenal	cortical adenoma			(50> ( 0%)	1	<50> ( 2%)			<50> ( 0%)	0	<50> ( 0%)
	pheochromocytoma: malignant		0	( 0%)	1	( 2%)		0	( 0%)		( 0%)
(Reproductive	system]										
testis	interstitial cell tumor	4		(50> ( 88%)	44	<50> ( 88%)	Ĺ		<50> ( 90%)	48	<50> ( 96%)
mammary gį	adenoma			(50> ( 0%)	2	<50> ( 4%)			<50> ( 0%)	0	<50> ( 0%)
	fibroadenoma		1	( 2%)	0	( 0%)		1	( 2%)	0	( 0%)
	adenocarcinoma		0	( 0%)	1	( 2%)		0	( 0%)	0	( 0%)
prep/cli gl	adenoma			(50> ( 12 <b>%</b> )	1	<50> ( 2%)		0	<50> ( 0%)	1	<50> ( 2%)
(Nervous syst	em]										
brain	meningiama:benign			(50> ( 0%)	0	<50> ( 0%)		1	<50> ( 2%)	0	<50> ( 0%)
	malignant reticulosis		0	( 0%)	0	( 0%)		0	( 0%)	1	( 2%)
	glioma		0	( 0%)	0	( 0%)		1	( 2%)	0	( 0%)
[Special sens	se organs/appandage]										
Zymbal gl	sebaceous adenoma			<50> ( 0%)	1	<50> ( 2%)		0	<50> ( 0%)	C	<50> (_0%)
(a) b (c)	a: Number of animals examined at the site b: Number of animals with neoplasm c:b/a	* 100								<del></del>	

HISTOLOGICAL FINDINGS: NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0-105W)

REPORT TYPE : A1
SEX : MALE

Group Name Control 500ppm 1500ppm 4500ppm 0rgan Findings\_ No. of animals on Study 50 50 50 50 [Special sense organs/appandage] Zymbal gl <50> <50> <50> <50> squamous cell carcinoma 1 (2%) 0 (0%) 1 (2%) 0 (0%) [Musculoskeletal system] muscle <50> <50> <50> <50> fibroma 0 (0%) 0 (0%) 1 (2%) 0 (0%) bone ⟨50⟩ <50> <50> ⟨50⟩ osteosarcoma 0 (0%) 2 (4%) 0 (0%) 0 (0%) vertebra ⟨50⟩ <50> ⟨50⟩ <50> sarcoma:NOS 0 (0%) 0 (0%) 1 (2%) 0 (0%) [Body cauities] pleura (50) ⟨50⟩ (50) <50> mesothelioma 1 (2%) 0 (0%) 1 (2%) 0 (0%) peritoneum ⟨50⟩ ⟨50⟩ <50> ⟨50⟩ mesothelioma 1 (2%) 1 (2%) 2 (4%) 4 (8%) retroperit ⟨50⟩ <50> <50> <50> paraganglioma:benign 1 (2%) 0 (0%) 0 (0%) 0 (0%) malignant fibrous histiocytoma 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

## APPENDIX M 2

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

RAT: FEMALE:

ANIMAL : RAT F344

REPORT TYPE : A1 SEX : FEMALE HISTOLOGICAL FINDINGS: NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0-105W)

0rgan	Findings	Group Name No. of animals on Study		Control 50		500ppm 50		1500ppm 50		4500ppm 50
[Integumentary	system/appandage]									
skin/app	squamous cell papilloma			<50> ( 0%)	1	<50> ( 2%)	0	<50> ( 0%)	0	<50> ( 0%)
subcutis	fibroma			<50> ( 0%)	1	<50> ( 2%)	0	<50> ( 0%)	1	<50> ( 2%)
	fibrosarcoma		1	( 2%)	0	( 0%)	0	( 0%)	0	( 0%)
[Respiratory s	ystem]									
.ung	bronchiolar-alveolar adenoma			<50> ( 0%)	1	<50> ( 2%)	0	<50> ( 0%)	0	<50> ( 0%)
Hematopoietic	system]									
one marrow	malignant histiocytosis			<50> ( 0%)	0	<50> ( 0%)	0	<50> ( 0%)	1	<50> ( 2%)
ymph nade	malisnant lymphoma			<50> ( 0%)	0	<49> ( 0%)	0	<50> ( 0%)	1	<50> ( 2%)
pleen	mononuclear cell leukemia			<50> ( 14%)	16	<50> ( 32%)	12	<50> ( 24%)	8	<50> ( 16%)
Circulatory s	ystem]									
neart	schwannoma:malignant			<50> ( 0%)	1	<50> ( 2%)	0	<50> ( 0%)	0	<50> ( 0%)
Digestive sys	tem]									
oral cavity	squamous cell carcinoma			<50> ( 0%)	0	<50> ( 0%)	0	<50> ( 0%)	1	<50> ( 2%)
<a>&gt;</a>	a: Number of animals examined at the site							<del></del>		

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

REPORT TYPE : A1

SEX : FEMALE

Organ	Findings	Group Name No. of animals on Study		Control 50		500ppm 50		1500ppm 50		4500ppm 50
[Digestive syst	rem]									
tongue	squamous cell carcinoma			<50> ( 0%)	1	<50> ( 2¾)	0	<50> ( 0%)	0	<50> ( 0%)
liver	hepatocellular adenoma			<50> ( 0%)	0	<50> ( 0%)	0	<50> ( 0%)	2	<50> ( 4%)
	histiocytic sarcoma		1	( 2%)	0	( 0%)	0	( 0%)	0	( 0%)
[Urinary system	a]									
kidney	sarcoma:NOS			<50> ( 0%)	0	<50> ( 0%)	0	<50> ( 0%)	1	<50> ( 2%)
[Endocrine syst	rem]									
pituitary	adenoma	2	23	<50> ( 46%)	18	<50> ( 36%)	19	<50> ( 38%)	16	<50> ( 32%)
	adenocarcinoma		2	( 4%)	1	( 2%)	1	( 2%)	0	( 0%)
thyroid	C-cell adenoma		6	<50> ( 12%)	4	<50> ( 8%)	2	<50> ( 4%)	2	<50> ( 4%)
	follicular adenoma		0	( 0%)	1	( 2%)	1	( 2%)	0	( 0%)
	C-cell carcinoma		4	( 8%)	1	( 2%)	2	( 4%)	1	( 2%)
	follicular adenocarcinoma		0	( 0%)	0	( 0%)	1	( 2%)	0	( 0%)
panc islet	islet cell adenoma		1	<50> ( 2%)	0	<50> ( 0%)	1	<50> ( 2%)	1	<50> ( 2%)
(a) b (c)	a: Number of animals examined at the site b: Number of animals with neoplasm c: A	o/a*100								<del></del>

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

REPORT TYPE : A1 SEX : FEMALE

Organ		roup Name o. of animals on Study	Control 50	500ppm 50	1500ppm 50	4500ppm 50
[Endocrine sy	stem]					
adrenal	pheachromocytoma		<50> 0 ( 0%)	<50> 3 ( 6%)	<50> 2 ( 4%)	<50> 1 (2%)
	comtical adenoma		0 ( 0%)	0 ( 0%)	2 ( 4%)	0 ( 0%)
	pheochromocytoma:malignant		1 (2%)	0 ( 0%)	0 ( 0%)	0 ( 0%)
[Reproductive	system]					
DUary	granulosa-theca cell tumor:malignant		<50> 0 ( 0%)	<50> 1 ( 2%)	<50> 0 ( 0%)	<50> 0 ( 0%)
rterus	hemangioma		<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 1 (2%)
	endometrial stromal polyp		5 (10%)	2 ( 4%)	8 (16%)	8 (16%)
	adenocarcinoma		0 ( 0%)	1 ( 2%)	0 ( 0%)	0 ( 0%)
	endometrial stromal sarcoma		0 ( 0%)	0 ( 0%)	1 ( 2%)	1 ( 2%)
Jagina	squamous cell carcinoma		<50> 1 ( 2%)	<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 0 ( 0%)
nammary gl	adenoma		<50> 0 ( 0%)	<49> 1 ( 2%)	<50> 1 ( 2%)	<50> 0 ( 0%)
	fibroadenoma		8 (16%)	7 (14%)	6 (12%)	6 (12%)
	adenocarcinoma		2 ( 4%)	1 ( 2%)	0 ( 0%)	0 ( 0%)
<a>&gt; (a)</a>	a: Number of animals examined at the site b: Number of animals with neoplasm c: b/a * 100					

SEX

ANIMAL : RAT F344 REPORT TYPE : A1

: FEMALE

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

0rgan	Findings	Group Name No. of animals on Study	Control 50	500ppm 50	1500ppm 50	4500ppm 50
[Reproductive	system]					
prep/cli gl	adenoma		<50> 3 ( 6%)	<50> 2 ( 4%)	<50> 2 ( 4%)	<50> 0 ( 0%)
(Nervous syste	em]					
brain	meningioma:benign		<50> 0 ( 0%)	<50> 1 ( 2%)	<50> 0 ( 0%)	<50> 0 ( 0%)
[Musculoskele	tal system]					
bane	osteosarcoma		<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 1 ( 2%)	<50> 0 ( 0%)
(Body cavities	sl					
retroperit	hemangiosarcoma		<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 1 ( 2%)
adipose	lipoma		<50> 1 ( 2%)	<50> 1 ( 2%)	<50> 0 ( 0%)	<50> 0 ( 0%)
(a) b (c)	a: Number of animals examined at the site b: Number of animals with neoplasm c:b/a*	100				44
(IIPT085)						BAI

### APPENDIX M 3

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

MOUSE: MALE

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : MALE

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

0rgan	Findings	Group Name No. of animals on Study		Control 50		667ppm 50		2000ppm 50		6000ppm 50
[Integumentary	system/appandage]									
subcutis	leiomyosarcoma			<50> ( 0%)	0	<50> ( 0%)	1	<50> ( 2%)	0	<50> ( 0%)
[Respiratory s			Ť	( 0,0)	v	( 0,0)	•	( 20)	v	( 0,0)
lung	bronchiolar-alveolar adenoma		3	<50> ( 6%)	8	<50> ( 16%)	5	<50> ( 10%)	3	<50> ( 6%)
	bronchiolar-alveolar carcinoma		2	( 4%)	4	( 8%)	5	( 10%)	1	( 2%)
[Hematopoietic	system]									
bone marrow	hemangioma		1	<50> ( 2%)	1	<50> ( 2%)	0	<50> ( 0%)	1	<50> ( 2%)
	mastoytoma:malisnant		0	( 0%)	1	( 2%)	0	( 0%)	0	( 0%)
	hemangiosarcoma		1	( 2%)	0	( 0%)	0	( 0%)	0	( 0%)
lymph nade	mastcytoma:benign		0	<50> ( 0%)	0	<50> ( 0%)	0	<50> ( 0%)	1	<50> ( 2%)
	malignant lymphoma		4	( 8%)	7	( 14%)	6	( 12%)	7	( 14%)
spleen	malignant lymphoma		2	<50> ( 4%)	0	<49> ( 0%)	2	<50> ( 4%)	3	<50> ( 6%)
	hemangiosarcoma		3	( 6%)	3	( 6%)	5	( 10%)	3	( 6%)
[Circulatory s	system]									
heart	hemangiosarcoma		0	<50> ( 0%)	0	<50> ( 0%)	1	<50> ( 2%)	0	<50> ( 0%)

ANIMAL : MOUSE 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 50	667ppm 50	2000ppm 50	6000ppm 50
Digestive s	ystem]					
salivary gl	histiocytic sarcoma		<50> 1 ( 2%)	<50> 1 ( 2%)	<50> 1 ( 2%)	<50> 0 ( 0%)
stomach	neuroendocrine cell tumor:malignant		<50> 0 ( 0%)	<50> 1 ( 2%)	<50> 0 ( 0%)	<50> 0 ( 0%)
	mastcytoma:malignant		0 ( 0%)	1 ( 2%)	0 ( 0%)	0 (0%)
liver	hemangioma		<50> 0 ( 0%)	<49> 1 ( 2%)	<50> 1 ( 2%)	<50> 0 ( 0%)
	hepatocellular adenoma		8 (16%)	6 (12%)	7 (14%)	3 (6%)
	histiocytic sarcoma		2 ( 4%)	2 ( 4%)	0 ( 0%)	1 ( 2%)
	hemangiosarcoma		4 (8%)	2 ( 4%)	2 ( 4%)	1 ( 2%)
	hepatocellular carcinoma		8 (16%)	8 (16%)	5 (10%)	4 ( 8%)
[Urinary sys	tem]					
kidney	hemangioma		<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 0 ( 0%)	<50> 1 ( 2%)
	adenocarcinoma		0 ( 0%)	0 ( 0%)	1 ( 2%)	1 ( 2%)
	transitional cell carcinoma		0 ( 0%)	0 ( 0%)	0 ( 0%)	1 ( 2%)
urin bladd	histiocytic sarcoma		<50> 0 ( 0%)	<50> 2 ( 4%)	<50> 1 ( 2%)	<50> 0 ( 0%)
< a >	a : Number of animals examined at the site					

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BAIS3

STUDY NO. : 0206 ANIMAL : MOUSE HISTOLOGICAL FINDINGS: NEOPLASTIC LESIONS (SUMMARY)

: MOUSE BDF1 ALL ANIMALS (0-105W)

REPORT TYPE : A1

SEX : MALE

Group Name	Control	667ppm	2000ppm	6000ppm
No. of animals on Study	50	50	50	50
	<49>	<50>	<50>	<49>
	0 ( 0%)	1 ( 2%)	0 ( 0%)	1 ( 2%)
	<50>	<50>	<50>	<50>
	0 ( 0%)	0 ( 0%)	0 ( 0%)	1 ( 2%)
	<50>	<50>	<50>	<50>
	1 ( 2%)	0 ( 0%)	0 ( 0%)	0 ( 0%)
	1 (2%)	0 ( 0%)	2 ( 4%)	0 ( 0%)
	<50>	<50>	<50>	<50>
	0 ( 0%)	0 ( 0%)	1 ( 2%)	0 ( 0%)
	<50>	<50>	<50>	<50>
	1 ( 2%)	0 ( 0%)	0 ( 0%)	1 ( 2%)
	<50>	<50>	<48>	<50>
	0 ( 0%)	5 ( 10%)	2 ( 4%)	0 ( 0%)
	<50>	<50>	<50>	<50>
	0 ( 0%)	0 ( 0%)	0 ( 0%)	2 ( 4%)
	<50>	<50>	<50>	<50>
	0 ( 0%)	0 ( 0%)	1 ( 2%)	0 ( 0%)
9	site c:b/a*100	0 ( 0%) site	0 ( 0%) 0 ( 0%) site	0 (0%) 0 (0%) 1 (2%)

## APPENDIX M 4

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

MOUSE: FEMALE

ANIMAL

SEX

: MOUSE BDF1

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

REPORT TYPE : A1

: FEMALE

Group Name Control 667ppm 2000ppm 6000ppm Organ\_ Findings\_ No. of animals on Study 50 50 49 50 [Integumentary system/appandage] skin/app ⟨50⟩ <50> <50> <49> squamous cell papilloma 0 (0%) 1 (2%) 0 (0%) 0 (0%) subcutis <50> <50> <50> **<49>** mastcytoma:benign 0 (0%) 1 (2%) 0 (0%) 0 (0%) histiocytic sarcoma 1 (2%) 0 (0%) 1 (2%) 0 (0%) sarcoma:NOS 0 (0%) 0 (0%) 1 (2%) 0 (0%) [Respiratory system] lung ⟨50⟩ ⟨50⟩ **<50>** <49> bronchiolar-alveolar adenoma 3 (6%) 1 (2%) 1 (2%) 1 (2%) bronchiolar-alveolar carcinoma 4 (8%) 2 (4%) 1 (2%) 2 (4%) [Hematopoietic system] tymph nade **<50>** <50> <49> mastcytoma:benign 0 (0%) 1 (2%) 0 (0%) 0 (0%) malignant lymphoma 14 (28%) 15 (30%) 11 (22%) 7 (14%) thymus <49> <49> **<48>** <49> malignant lymphoma 1 (2%) 0 (0%) 0 (0%) 0 (0%) spleen <50> ⟨50⟩ ⟨50⟩ **<49>** malignant lymphoma 6 (12%) 4 (8%) 3 (6%) 4 (8%) 1 (2%) hemangiosarcoma 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

HISTOLOGICAL FINDINGS: NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0-105W)

ANIMAL : MOUSE BDF1
REPORT TYPE : A1

SEX : FEMALE

)rgan	Findings	Group Name Co No. of animals on Study 50	ontrol ) 	667ppm 50	2000ppm 50	6000ppm 49
[Digestive sys	tem]					
sali∪ary gl	histiocytic sarcoma	<50 0 (		<50> ( 0%) 0	<50> ( 0%) 1	<49> ( 2%)
tomach	squamous celi papilloma	<50 0 (		<50> ( 0%) 0	<50> ( 0%) 1	<49> ( 2%)
arge intes	leiomyoma	<50 0 (		<50> ( 0%) 1	<50> ( 2%) 0	<49> ( 0%)
Liver	hemangioma	<50 0 (		<50> ( 2%) 3	<50> (6%) 1	<49> ( 2%)
	hepatocellular adenoma	2 (	4%) 3	( 6%) 12	( 24%) 10	( 20%)
	histiocytic sarcoma	2 (	4%) 1	( 2%) 1	( 2%) 1	( 2%)
	hemangiosarcoma	2 (	4%) 0	( 0%) 1	( 2%) 4	( 8%)
	hepatocellular carcinoma	1 (	2%) 5	( 10%) 7	( 14%) 5	( 10%)
(Urinary syste	om]					
<idney< td=""><td>adenocarcinoma</td><td>&lt;56 0 (</td><td></td><td>&lt;50&gt; ( 0%) 1</td><td>&lt;50&gt; ( 2%) 0</td><td>&lt;49&gt; ( 0%)</td></idney<>	adenocarcinoma	<56 0 (		<50> ( 0%) 1	<50> ( 2%) 0	<49> ( 0%)
[Endocrine sys	etem]					
oituitary	adenoma	<56 5 ( )		<49> (12%) 5	<50> ( 10%) 4	<49> ( 8%)
[Reproductive	system]					
DUary	cystadenoma	<5i 3 (		<50> ( 2%) 1	<50> ( 2%) 0	<49> ( 0%)

ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : FEMALE

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

Organ	Findings	Group Name No. of animals on Study		Control 50		667ppm 50	***	2000ppm 50		6000ppm 49
[Reproductive	system]									
uterus	schwannoma			<50> ( 0%)	0	<50> ( 0%)	0	<50> ( 0%)	1	<49> ( 2%)
	hemangioma		0	( 0%)	0	( 0%)	0	( 0%)	1	( 2%)
	endometrial stromal polyp		1	( 2%)	0	( 0%)	2	( 4%)	1	( 2%)
	histiocytic sarcoma		8	( 16%)	13	( 26%)	12	( 24%)	15	( 31%)
vagina	squamous cell papilloma			<50> ( 2%)	0	<50> ( 0%)	0	<50> ( 0%)	0	<49> ( 0%)
mammary gl	adenocarcinoma			<50> ( 0%)	2	<50> ( 4%)	0	<50> ( 0%)	0	<49> ( 0%)
(Nervous syste	em]									
spinal cord	histiocytic sarcoma			<50> ( 0%)	0	<50> ( 0%)	1	<50> ( 2%)	0	<49> ( 0%)
periph neru	histiocytic sarcoma			<50> ( 0%)	1	<50> ( 2%)	0	<50> ( 0%)	0	<49> ( 0%)
[Special sense	e organs/appandage]									
Harder gl	adenoma		1	<50> ( 2%)	4	<50> ( 8%)	1	<50> ( 2%)	1	<49> ( 2%)
[Body cavities	sì									
retroperit	histiocytic sarcoma			<50> ( 0%)	0	<50> ( 0%)	1	<50> ( 2%)	0	<49> ( 0%)
(a) b (c)	a: Number of animals examined at the site b: Number of animals with neoplasm	c:b/a*100			·				************	· · · · · · · · · · · · · · · · · · ·

### APPENDIX N 1

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

RAT: MALE

STUDY No. : 0205 ANIMAL : RAT F344

SEX : MALE

Group Name	Control	500ppm	1500ppm	4500ppm
	SITE : skin/appendage TUMOR : squamous cell papill	oma.sowamows cali carcinoma		
Tumor rate	Tonon - Baddinas ober papier			
Overall rates(a)	3/50( 6.0)	0/50( 0.0)	1/50( 2.0)	0/50( 0.0)
Adjusted rates(b)	8.11	0.0	2.44	0.0
Terminal rates(c) Statistical analysis Peto test	3/37( 8.1)	0/41( 0.0)	0/38( 0.0)	0/31( 0.0)
Standard method(d)	P =			
Prevalence method(d)	P = 0.9329			
Combined analysis(d)	P =			
Cochran-Armitage test(e)	P = 0.1480	D 0 1005	D 0 0005	D 0.1005
Fisher Exact test(e)		P = 0.1325	P = 0.3235	P = 0.1325
	SITE : subcutis			
	TUMOR : fibroma			
Tumor rate	E/E0/ 10 0)	5/50( 10.0)	2/50( 4.0)	2/50( 4.0)
Overall rates(a) Adjusted rates(b)	5/50( 10.0) 9.09	7.32	2/30( 4.0) 5.26	6.45
Terminal rates(c)	3/37( 8.1)	3/41( 7.3)	2/38( 5.3)	2/31( 6.5)
Statistical analysis	0,0.( 0.1)	0,41( 7,0)	2,000 0.0,	2,02( 0.0)
Peto test				
Standard method(d)	P = 0.9106			
Prevalence method(d)	P = 0.7364		•	
Combined analysis(d)	P = 0.8837			
Cochran-Armitage test(e)	P = 0.1902	D 0.0710	D A 0405	$\mathbf{p} = 0 \cdot \mathbf{page}$
Fisher Exact test(e)		P = 0.3710	P = 0.2425	P = 0.2425
	SITE : subcutis			
	TUMOR : fibroma,fibrosarcoma	ı		
Tumor rate	0(50( 10 0)	0/50/ 19 0)	2/50/	2/50/ 4.0)
Overall rates(a) Adjusted rates(b)	6/50(12.0) 11.36	6/50( 12.0) 7.32	3/50( 6.0) 7.89	2/50( 4.0) 6.45
Adjusted rates(b) Terminal rates(c)	4/37( 10.8)	3/41( 7.3)	3/38( 7.9)	2/31( 6.5)
Statistical analysis	1,01 ( 10.0)	0/11( 110/	0,00( 1.0)	2,01( 0.0)
Peto test				
Standard method(d)	P = 0.9380			
Prevalence method(d)	P = 0.8019			
Combined analysis(d)	P = 0.9332			
Cochran-Armitage test(e)	P = 0.1061		D 4 0500	D 0.4000
Fisher Exact test(e)		P = 0.3807	P = 0.2728	P = 0.1606

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STUDY No. : 0205 ANIMAL : RAT F344
SEX : MALE

Group Name	Control	500ppm	1500ppm	4500ppm
	SITE : spleen			
Cumor rate	TUMOR : mononuclear cell leukemia			
Overall rates(a)	7/50( 14.0)	12/50( 24.0)	10/50( 20.0)	9/50(18.0)
Adjusted rates(b)	10.81	24.39	19.05	16.13
Terminal rates(c) Statistical analysis Peto test	4/37( 10.8)	10/41( 24.4)	7/38( 18.4)	5/31( 16.1)
Standard method(d)	P = 0.1956			
Prevalence method(d)	P = 0.5566			
Combined analysis(d)	P = 0.3523			
Cochran-Armitage test(e)	P = 0.9794			
Fisher Exact test(e)		P = 0.2119	P = 0.3417	P = 0.4234
	SITE : urinary bladder	· · · · · · · · · · · · · · · · · · ·		
	TUMOR : transitional cell papilloma			
Tumor rate	Tonon - El dilos Eronac occe papi ecolia			
Overall rates(a)	0/50( 0.0)	0/50( 0.0)	0/50( 0.0)	10/50( 20.0)
Adjusted rates(b)	0.0	0.0	0.0	25.81
Terminal rates(c)	0/37( 0.0)	0/41( 0.0)	0/38( 0.0)	8/31( 25.8)
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 = 0.5000	P = 0.5000	P = 0.0016**
	SITE : urinary bladder			
Tumor rate	TUMOR : transitional cell carcinoma			
Overall rates(a)	0/50( 0.0)	0/50( 0.0)	0/50( 0.0)	24/50( 48.0)
Adjusted rates(b)	0.0	0.0	0.0	51.52
Terminal rates(c)	0/37( 0.0)	0/41( 0.0)	0/38( 0.0)	15/31( 48.4)
Statistical analysis				
Peto test				
Standard method(d)	P < 0.0001**?			
Prevalence method(d) Combined analysis(d)	P < 0.0001**? P < 0.0001**?			
Cochran—Armitage test(e)	P < 0.0001**! P < 0.0001**		•	
Condition to	1 / 0.0001	P = 0.5000		

(HPT360A)

STUDY No. : 0205 NEOPLASTIC LESIONS-INCID ANIMAL : RAT F344 SEX : MALE

Group Name	Control	500ppm	1500ppm	4500ppm	
	SITE : urinary bladder				
`umor rate	TUMOR : transitional cell pap	illoma, transitional cell carcinoma			
Overall rates(a)	0/50( 0.0)	0/50( 0.0)	0/50( 0.0)	31/50(62.0)	
Adjusted rates(b)	0.0	0.0	0.0	66.67	
Terminal rates(c)	0/37( 0.0)	0/41( 0.0)	0/38( 0.0)	20/31(64.5)	
Statistical analysis					
Peto test					
Standard method(d)	P < 0.0001**?				
Prevalence method(d) Combined analysis(d)	P < 0.0001**? P < 0.0001**?		•		
Cochran-Armitage test(e)	P < 0.0001**; P < 0.0001**				
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P < 0.0001**	
Fumor rate Overall rates(a) Adjusted rates(b) Terminal rates(c) Statistical analysis Peto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e)	TUMOR : transitional cell par 0/50( 0.0) 0.0 0/37( 0.0) P < 0.0001**? P < 0.0001**? P < 0.0001**? P < 0.0001**	0/50( 0.0) 0.0 0.0 0/41( 0.0) P = 0.5000	mous cell papilloma, squamous cell carci 0/50( 0.0) 0.0 0/38( 0.0) P = 0.5000	noma 31/50( 62.0) 66.67 20/31( 64.5)  P < 0.0001**	
	SITE : pituitary gland TUMOR : adenoma				
Cumor rate	14/50( 20 0)	19/50/ 94 0	10/50/ 20 0)	0/50/ 10 0	
Overall rates(a) Adjusted rates(b)	14/50( 28.0) 23.81	12/50( 24.0) 24.39	10/50( 20.0) 15.79	8/50( 16.0) 25.81	
Terminal rates(c)	8/37( 21.6)	10/41( 24.4)	6/38( 15.8)	8/31 (25.8)	
Statistical analysis	-, o. ( maro)	20, 12( 2.1.1,	3,33( 13,3)	5,52 ( 10.5)	
Peto test Standard method(d)	P = 0.9555				
Prevalence method(d)	P = 0.9555 P = 0.5913				
	P = 0.8513	-			
Combined analysis(d) Cochran—Armitage test(e)	P = 0.8513 P = 0.1562	•			

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ANIMAL : RAT F344

STUDY No. : 0205 SEX : MALE

Group Name	Control	500ppm	1500ppm	4500ppm
	SITE : pituitary gland TUMOR : adenoma,adenocarcinoma			
umor rate	Tomon • adel iulia, adel iucal chi iulia			
Overall rates(a)	14/50(28.0)	12/50( 24.0)	10/50( 20.0)	8/50(16.0)
Adjusted rates(b)	23.81	24.39	15.79	25.81
Terminal rates(c) tatistical analysis Peto test	8/37( 21.6)	10/41( 24.4)	6/38( 15.8)	8/31(25.8)
Standard method(d)	P = 0.9555			
Prevalence method(d)	P = 0.5913			
Combined analysis(d)	P = 0.8513			
Cochran-Armitage test(e)	P = 0.1562			
Fisher Exact test(e)		P = 0.4489	P = 0.3071	P = 0.1781
	SITE : thyroid			
	TUMOR : C-cell adenoma			
'umor rate				
Overall rates(a)	3/50( 6.0)	3/50( 6.0)	7/50( 14.0)	3/50( 6.0)
Adjusted rates(b)	6.98	7,32	16.67	9.68
Terminal rates(c) Hatistical analysis	1/37( 2.7)	3/41( 7.3)	5/38( 13.2)	3/31( 9.7)
Peto test				
Standard method(d)	P =			
Prevalence method(d)	P = 0.4912			
Combined analysis(d)	P =			
Cochran-Armitage test(e)	P = 0.9405	D 0000	D 0.1018	D 0.000
Fisher Exact test(e)		P = 0.3392	P = 0.1917	P = 0.3392
	SITE : thyroid		1951/1940 - 45-1-4-1-4-1-4-1-4-1-4-1-4-1-4-1-4-1-4-1	
	TUMOR : C-cell carcinoma			
umor rate		- ( ()		
Overall rates(a)	0/50( 0.0)	3/50( 6.0)	1/50( 2.0)	0/50( 0.0)
Adjusted rates(b) Terminal rates(c)	0.0 0/37( 0.0)	6.98 1/41( 2.4)	2.63	0.0
tatistical analysis	0/3/( 0.0)	1/41( 2.4)	1/38( 2.6)	0/31( 0.0)
Peto test				
Standard method(d)	P =			
Prevalence method(d)	P = 0.8033			
Combined analysis(d)	P =		•	
Cochran—Armitage test(e) Fisher Exact test(e)	P = 0.3112	P = 0.1325	P = 0.4950	P = 0.5000
LIZHOL EXACT FAST(8)		r = 0.1020	r = 0.4900	r = 0.0000

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STUDY No. : 0205 ANIMAL : RAT F344

SEX : MALE

Group Name	Control	500ppm	1500ppm	4500ppm	
	SITE : thyroid TUMOR : C-cell adenoma,C-cell ca	ercinoma			
Tumor rate	10000 1 0 doce data landy o doce de	a on and			
Overall rates(a)	3/50( 6.0)	6/50(12.0)	8/50(16.0)	3/50( 6.0)	
Adjusted rates(b)	6.98	13.95	19.05	9.68	
Terminal rates(c) Statistical analysis	1/37( 2.7)	4/41( 9.8)	6/38( 15.8)	3/31( 9.7)	
Peto test					
Standard method(d)	P =				
Prevalence method(d)	P = 0.6601				
Combined analysis(d)	P =				
Cochran-Armitage test(e)	P = 0.5891				
Fisher Exact test(e)		P = 0.2728	P = 0.1322	P = 0.3392	
	SITE : pancreas islet TUMOR : islet cell adenoma				
Tumor rate	T(T0( 14 0)	0/50/ 0.0	1/50( 0.0)	4 (50 ( . 0.0)	
Overall rates(a) Adjusted rates(b)	7/50( 14.0) 15.38	0/50( 0.0) 0.0	1/50( 2.0) 2.50	1/50( 2.0) 3.23	
Terminal rates(c)	5/37( 13.5)	0/41( 0.0)	0/38( 0.0)	1/31( 3.2)	
Statistical analysis	0,01 ( 10.0)	0,11( 0.0)	0,00( 0.0)	1,01( 0.2)	
Peto test					
Standard method(d)	P =				
Prevalence method(d)	P = 0.9564				
Combined analysis(d) Cochran—Armitage test(e)	P = P = 0.0919				
Fisher Exact test(e)	r = 0.0919	P = 0.0101*	P = 0.0430*	P = 0.0430*	
	SITE : adrenal gland				
_	TUMOR : pheochromocytoma				
Tumor rate	F/F0/ 10 0)	4/50( 0.0)	0/50/ 10 0)	7/70/ 14 0	
Overall rates(a) Adjusted rates(b)	5/50( 10.0) 10.81	4/50( 8.0) 8.33	8/50( 16.0) 21.05	7/50( 14.0) 19.35	
Terminal rates(c)	4/37( 10.8)	3/41( 7.3)	8/38( 21.1)	6/31( 19.4)	
Statistical analysis	-, -, -, -, -, -, -, -, -, -, -, -, -, -	0, 11(,	0,000 2212,	0,01(10,1)	
Peto test					
Standard method(d)	P =				
Prevalence method(d)	P = 0.1375				
Combined analysis(d)	P =				
Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.4178	P = 0.4883	P = 0.3141	P = 0.4062	
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STUDY No. : 0205 ANIMAL : RAT F344

SEX : MALE

Group Name	Control	500ppm	1500ppm	4500ppm	
	SITE : adrenal gland			,	
Cumor rate	TUMOR : pheachromocytoma, pheachromo	cytoma:mallgnant			
Overall rates(a)	5/50( 10.0)	5/50( 10.0)	8/50(16.0)	7/50( 14.0)	
Adjusted rates(b)	10.81	10.42	21.05	19.35	
Terminal rates(c)	4/37( 10.8)	3/41( 7.3)	8/38( 21.1)	6/31( 19.4)	
Statistical analysis	4, -, (, -,	5, 12( 115,	5, 55 ( 55,57)	0,01(10,1)	
Peto test					
Standard method(d)	P =				
Prevalence method(d)	P = 0.1874				
Combined analysis(d)	P =				
Cochran-Armitage test(e)	P = 0.5103				
Fisher Exact test(e)		P = 0.3710	P = 0.3141	P = 0.4062	
lumor rate	SITE : testis TUMOR : interstitial cell tumor				
Overall rates(a)	44/50( 88.0)	44/50( 88.0)	45/50( 90.0)	48/50(96.0)	
Adjusted rates(b)	97.67	95.35	97.37	100.00	
Terminal rates(c)	36/37(97.3)	39/41(95.1)	37/38( 97.4)	31/31(100.0)	
Statistical analysis			, ,	. , ,	
Peto test					
Standard method(d)	P =				
Prevalence method(d)	P = 0.0017**				
Combined analysis(d)	P =				
Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.1161	P = 0.4419	D = 0.4790	D = 0.4070	
Ligher Exact feat(e)		r = 0.4419	P = 0.4726	P = 0.4379	
	SITE : preputial/clitoral gland TUMOR : adenoma				
Tumor rate	was remain				
Overall rates(a)	6/50(12.0)	1/50( 2.0)	0/50( 0.0)	1/50( 2.0)	
Adjusted rates(b)	14.63	2.44	0.0	3.23	
Terminal rates(c)	4/37( 10.8)	1/41( 2.4)	0/38( 0.0)	1/31( 3.2)	
Statistical analysis					
Peto test	D				
Standard method(d)	P = 0.0500				
Prevalence method(d) Combined analysis(d)	P = 0.9590 P =				
Cochran-Armitage test(e)	P = 0.0982		•		
Fisher Exact test(e)	1 - 0.0002	P = 0.0724	P = 0.0190*	P = 0.0724	
TOTAL BAGGE COGE(O)		raiv.v	1 - 0.01004	1 - 0.0164	

#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

ANIMAL : RAT F344

SEX : MALE

Group Name Control maa003 1500ppm 4500ppm SITE : peritoneum TUMOR : mesothelioma Tumor rate Overall rates(a) 1/50( 2.0) 1/50( 2.0) 2/50( 4.0) 4/50( 8.0) Adjusted rates(b) 2.70 2.44 10.00 0.0 Terminal rates(c) 1/37( 2.7) 1/41( 2.4) 0/38( 0.0) 3/31(9.7) Statistical analysis Peto test Standard method(d) P = 0.4590Prevalence method(d) P = 0.0229\*Combined analysis(d) P = 0.0430\*Cochran-Armitage test(e) P = 0.0789Fisher Exact test(e) P = 0.2475P = 0.4926P = 0.1998

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PAGE :

Standard method : Death analysis

Prevalence method: Incidental tumor test

Combined analysis: Death analysis + Incidental tumor test

Significant difference;  $*: P \le 0.05$   $**: P \le 0.01$ 

<sup>(</sup>a): Number of tumor-bearing animals/number of animals examined at the site.

<sup>(</sup>b): Kaplan-Meire estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.

<sup>(</sup>c): Observed tumor incidence at terminal kill.

<sup>(</sup>d): Beneath the control incidence are the P-values associated with the trend test.

<sup>(</sup>e): The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.

<sup>?:</sup> The conditional probabities of the largest and smallest possible out comes can not estimated or this P-value is beyond the estimated P-value.

<sup>----:</sup> There is no data which should be statistical analysis.

### APPENDIX N 2

## NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

RAT: FEMALE

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STUDY No. : 0205 ANIMAL : RAT F344
SEX : FEMALE

SEX

Group Name	Control	500ppm	1500pm	4500ppm	
	SITE : spleen				
P	TUMOR : mononuclear cell leukem	ia			
Tumor rate Overall rates(a)	7/50( 14.0)	16/50( 32.0)	12/50( 24.0)	8/50( 16.0)	
Adjusted rates(b)	11.36	23.68	12,50( 24.0)	18.92	
Terminal rates(c)	5/44( 11.4)	9/38( 23.7)	8/44( 18.2)	7/37( 18.9)	
Statistical analysis	5, 11( 111 2)	0,00( 2011)	0,11(10,1)	1,01(1010)	
Peto test					
Standard method(d)	P = 0.8946				
Prevalence method(d)	P = 0.3421				
Combined analysis(d)	P = 0.6636				
Cochran-Armitage test(e)	P = 0.4374				
Fisher Exact test(e)		P = 0.0704	P = 0.2119	P = 0.4854	
	SITE : pituitary gland TUMOR : adenoma				
Tumor rate	Tonon • adol idina				
Overall rates(a)	23/50(46.0)	18/50(36.0)	19/50(38.0)	16/50( 32.0)	
Adjusted rates(b)	45.45	41.03	40.91	39.47	
Terminal rates(c)	20/44( 45.5)	15/38(39.5)	18/44( 40.9)	14/37( 37.8)	
Statistical analysis		, , , ,	,	,,	
Peto test					
Standard method(d)	P = 0.5949				
Prevalence method(d)	P = 0.7418				
Combined analysis(d)	P = 0.7645				
Cochran-Armitage test(e)	P = 0.2426				
Fisher Exact test(e)		P = 0.3187	P = 0.3695	P = 0.2231	
	SITE : pituitary gland				
_	TUMOR : adenoma, adenocarcinoma				
Tumor rate	05/50/ 50 0)	10/50/ 05 5	00/50/	and the district of the second	
Overall rates(a)	25/50(50.0)	19/50( 38.0)	20/50(40.0)	16/50( 32.0)	
Adjusted rates(b)	50.00	43.59	43.18	39.47	
Terminal rates(c)	22/44(50.0)	16/38(42.1)	19/44( 43.2)	14/37( 37.8)	
Statistical analysis					
Peto test Standard method(d)	P = 0.5949				
Prevalence method(d)	P = 0.8458				
Combined analysis(d)	P = 0.8581				
Cochran-Armitage test(e)	P = 0.1261				
	. 31101	P = 0.2836	P = 0.3304	D = 0.1E00	
Fisher Exact test(e)		r = 0.2000	r ~ v.33v4	P = 0.1586	

STUDY No. : 0205 ANIMAL : RAT F344 SEX : FEMALE

Group Name	Control	500ppm	1500ppm	4500ppm
	SITE : thyroid			
iumor rate	TUMOR : C-cell adenoma			
Overall rates(a)	6/50(12.0)	4/50( 8.0)	2/50( 4.0)	2/50( 4.0)
Adjusted rates(b)	13.64	8.89	4.55	5.41
Terminal rates(c)	6/44( 13.6)	3/38( 7.9)	2/44( 4.5)	2/37( 5.4)
Statistical analysis				, ,
Peto test				
Standard method(d)	P =			
Prevalence method(d)	P = 0.9038			
Combined analysis(d)	P =			
Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.1648	D - 0 2044	D 0 1000	D 0 1000
risier Exact test(e)		P = 0.3944	P = 0.1606	P = 0.1606
	SITE : thyroid			
	TUMOR : C-cell carcinoma			
îumor rate	2 3 3 5 5 5 5 5 T T T T T T T T T T T T T			
0∪erall rates(a)	4/50( 8.0)	1/50( 2.0)	2/50( 4.0)	1/50( 2.0)
Adjusted rates(b)	8,70	2.63	4.55	2.22
Terminal rates(c)	3/44( 6.8)	1/38( 2.6)	2/44( 4.5)	0/37( 0.0)
Statistical analysis				
Peto test	D			
Standard method(d) Prevalence method(d)	P = P = 0.8312			
Combined analysis(d)	P =			
Cochran-Armitage test(e)	P = 0.3013			
Fisher Exact test(e)	. 0.0010	P = 0.1998	P = 0.3574	P = 0.1998
	SITE : thyroid			
	TUMOR : C-cell adenoma, C-cell	carcinoma		•
ľumor rate				
Overall rates(a)	10/50( 20.0)	5/50( 10.0)	4/50( 8.0)	3/50( 6.0)
Adjusted rates(b)	21.74	11.11	9.09	6.67
Terminal rates(c)	9/44( 20.5)	4/38( 10.5)	4/44( 9.1)	2/37( 5.4)
Statistical analysis				
Peto test Standard method(d)	P =			
Prevalence method(d)	P = 0.9597			
Combined analysis(d)	P =			
	P = 0.0750			
Cochran-Armitage test(e)				

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STUDY No. : 0205 ANIMAL : RAT F344

SEX : FEMALE

Group Name	Control	500ppm	1500ppm	4500ppm
	SITE : adrenal gland			
iumor rate	TUMOR : pheachromacytama			
Overall rates(a)	0/50( 0.0)	3/50( 6.0)	2/50( 4.0)	1/50( 2.0)
Adjusted rates(b)	0.0	7.89	4.55	2.70
Terminal rates(c)	0/44( 0.0)	3/38( 7.9)	2/44( 4.5)	1/37( 2.7)
Statistical analysis Peto test				
Standard method(d)	P =			
Prevalence method(d)	P = 0.4964			
Combined analysis(d)	P =			
Cochran-Armitage test(e)	P = 0.8586			
Fisher Exact test(e)		P = 0.1325	P = 0.2574	P = 0.4950
	SITE : adrenal gland TUMOR : pheochromocytoma,pheochr	omocytoma:malignant		
lumor rate Overall rates(a)	1/50( 2.0)	2/50/ (5.0)	0/50/ 4.0)	1/50/ 0.0
Adjusted rates(b)	2.27	3/50( 6.0) 7.89	2/50( 4.0) 4.55	1/50( 2.0) 2.70
Terminal rates(c)	1/44( 2.3)	3/38( 7.9)	2/44( 4.5)	1/37( 2.7)
National Action	, , ,		.,,	2,2.( 27.,
Statistical analysis				
Peto test	_			
Peto test Standard method(d)	P =			
Peto test Standard method(d) Prevalence method(d)	P = 0.6337			
Peto test Standard method(d)	•			
Peto test Standard method(d) Prevalence method(d) Combined analysis(d)	P = 0.6337 P =	P = 0.3235	P = 0.4926	P = 0.2475
Peto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e)	P = 0.6337 P = P = 0.6006 SITE : uterus		P = 0.4926	P = 0.2475
Peto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.6337 P = P = 0.6006		P = 0.4926	P = 0.2475
Peto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.6337 P = P = 0.6006  SITE : uterus TUMOR : endometrial stromal poly	<i>γ</i> ρ		
Peto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e)  Tumor rate Overall rates(a)	P = 0.6337 P =	/p 2/50( 4.0)	8/50( 16.0)	8/50( 16.0)
Peto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.6337 P = P = 0.6006  SITE : uterus TUMOR : endometrial stromal poly	<i>γ</i> ρ		8/50( 16.0) 18.92
Peto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e)  Fumor rate Overall rates(a) Adjusted rates(b) Terminal rates(c) Statistical analysis	P = 0.6337 P =	2/50( 4.0) 2.63	8/50( 16.0) 17.02	8/50( 16.0)
Peto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e)  Fumor rate Overall rates(a) Adjusted rates(b) Terminal rates(c) Statistical analysis Peto test	P = 0.6337 P = P = 0.6006 SITE : uterus TUMOR : endometrial stromal poly 5/50( 10.0) 11.36 5/44( 11.4)	2/50( 4.0) 2.63	8/50( 16.0) 17.02	8/50( 16.0) 18.92
Peto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e)  Tumor rate Overall rates(a) Adjusted rates(b) Terminal rates(c) Statistical analysis Peto test Standard method(d)	P = 0.6337 P = P = 0.6006 SITE : uterus TUMOR : endometrial stromal poly 5/50( 10.0) 11.36 5/44( 11.4) P = 0.2219	2/50( 4.0) 2.63	8/50( 16.0) 17.02	8/50( 16.0) 18.92
Peto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e)  Tumor rate Overall rates(a) Adjusted rates(b) Terminal rates(c) Statistical analysis Peto test Standard method(d) Prevalence method(d)	P = 0.6337 P =	2/50( 4.0) 2.63	8/50( 16.0) 17.02	8/50( 16.0) 18.92
Peto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e)  Tumor rate Overall rates(a) Adjusted rates(b) Terminal rates(c) Statistical analysis Peto test Standard method(d)	P = 0.6337 P = P = 0.6006 SITE : uterus TUMOR : endometrial stromal poly 5/50( 10.0) 11.36 5/44( 11.4) P = 0.2219	2/50( 4.0) 2.63	8/50( 16.0) 17.02	8/50( 16.0) 18.92

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BAIS3

ANIMAL : RAT F344
SEX : FEMALE

Group Name	Control	500ppm	1500ppm	4500ppm	
	SITE : uterus				
P	TUMOR : endometrial stromal polyp	endometrial stromal sarcoma			
Tumor rate Overall rates(a)	5/50( 10.0)	2/50( 4.0)	9/50( 18.0)	0/50/ 19 0)	
Adjusted rates(b)	11.36	2,63	19.15	9/50( 18.0) 18.92	
Terminal rates(c)	5/44( 11.4)	1/38( 2.6)	8/44( 18.2)	7/37( 18.9)	
tatistical analysis	, , , ,	-, ,	-,,,	1,01 ( 2010)	
Peto test					
Standard method(d)	P = 0.0721				
Prevalence method(d)	P = 0.0577				
Combined analysis(d) Cochran-Armitage test(e)	P = 0.0211* P = 0.0783				
Fisher Exact test(e)	r = 0.0765	P = 0.2425	P = 0.2379	P = 0.2379	
TISHO ENGLE LOSE(O)		1 - 0,2420	1 - 0.2019	1 - 0.2318	
	CITE •				
	SITE : mammary gland TUMOR : fibroadenoma				
umor rate	TOTION . THE DAGGRAPHA				
Overall rates(a)	8/50( 16.0)	7/49( 14.3)	6/50( 12.0)	6/50( 12.0)	
Adjusted rates(b)	16.33	16,28	13.64	13.64	
Terminal rates(c)	6/44( 13.6)	4/37( 10.8)	6/44( 13.6)	4/37( 10.8)	
tatistical analysis					
Peto test					
Standard method(d)	P = P = 0.6530				
Prevalence method(d) Combined analysis(d)	P = 0.0030 P =				
Cochran-Armitage test(e)	P = 0.5919				
Fisher Exact test(e)	. 0.0013	P = 0.4706	P = 0.4157	P = 0.4157	
Trans. Blast Eost (c)					
	SITE : mammary gland				
	TUMOR : adenoma, fibroadenoma				
umor rate	·				
Overall rates(a)	8/50(16.0)	8/49( 16.3)	7/50( 14.0)	6/50( 12.0)	
Adjusted rates(b)	16.33	18.60	15,91	13.64	
Perminal rates(c)	6/44( 13.6)	5/37(13.5)	7/44( 15.9)	4/37( 10.8)	
tatistical analysis					
Peto test Standard method(d)	P =				
Prevalence method(d)	P = 0.6993				
Combined analysis(d)	P =				
Cochran-Armitage test(e)	P = 0.5058				
Fisher Exact test(e)		P = 0.4089	P = 0.4854	P = 0.4157	
Dmoos 1)					
T360A)					R

(HPT360A)

STUDY No. : 0205

BAIS3

Group Name Control 500ppm 1500ppm 4500ppm SITE : mammary gland TUMOR : adenoma, fibroadenoma, adenocarcinoma Tumor rate Overall rates(a) 10/50(20.0) 9/49(18.4) 7/50(14.0) 6/50(12.0) Adjusted rates(b) 20.41 20.93 15.91 13.64 Terminal rates(c) 7/44(15.9) 6/37(16.2) 7/44(15.9) 4/37(10.8) Statistical analysis Peto test Standard method(d) P = -----Prevalence method(d) P = 0.8400Combined analysis(d) P = -----Cochran-Armitage test(e) P = 0.2611Fisher Exact test(e) P = 0.4676P = 0.3417P = 0.2557SITE : preputial/clitoral gland TUMOR : adenoma Tumor rate Overall rates(a) 3/50(6.0) 2/50( 4.0) 2/50( 4.0) 0/50( 0.0) Adjusted rates(b) 6.67 5.26 4,55 0.0

2/44( 4.5)

P = 0.4909

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Terminal rates(c)

Statistical analysis Peto test

Standard method(d) Prevalence method(d)

Combined analysis(d)

Fisher Exact test(e)

Cochran-Armitage test(e)

STUDY No. : 0205

ANIMAL SEX : RAT F344

: FEMALE

BAIS3

0/37( 0.0)

P = 0.1325

PAGE: 12

2/44( 4.5)

P = ----

P = 0.9504

P = -----

P = 0.1040

Standard method : Death analysis

Prevalence method: Incidental tumor test

Combined analysis: Death analysis + Incidental tumor test

2/38(5.3)

P = 0.4909

Significant difference;  $*: P \le 0.05$   $**: P \le 0.01$ 

<sup>(</sup>a): Number of tumor-bearing animals/number of animals examined at the site.

<sup>(</sup>b): Kaplan-Meire estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.

<sup>(</sup>c): Observed tumor incidence at terminal kill.

<sup>(</sup>d): Beneath the control incidence are the P-values associated with the trend test.

<sup>(</sup>e): The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.

<sup>?:</sup> The conditional probabities of the largest and smallest possible out comes can not estimated or this P-value is beyond the estimated P-value.

<sup>----:</sup> There is no data which should be statistical analysis.

# APPENDIX N 3

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

MOSUE: MALE

STUDY No. : 0206
ANIMAL : MOUSE BDF1

SEX : MALE

Group Name Control 667ppm 2000ppm 6000ppm

Group Name	Control	667ppm	2000ppm	6000ppn	
	SITE : lung TUMOR : bronchiplar-alveplar	ackanoma			
Tumor rate	TONOR • DI DI CITTO CAL PACOBOCAL	addi ibilia			
Overall rates(a)	3/50( 6.0)	8/50( 16.0)	5/50(10.0)	3/50( 6.0)	
Adjusted rates(b)	6.12	19.51 8/41( 19.5)	11.36 4/41( 9.8)	7.69 3/39( 7.7)	
Terminal rates(c) Statistical analysis	2/35( 5.7)	6/41(19.5)	4/41( 5.0)	3/39( 1.1)	
Peto test					
Standard method(d)	P =				
Prevalence method(d) Combined analysis(d)	P = 0.7957 P =				
Cochran-Armitage test(e)	P = 0.4170				
Fisher Exact test(e)		P = 0.1322	P = 0.3790	P = 0.3392	
Tumor rate Overall rates(a)	SITE : lung TUMOR : bronchiolar—alveolar 2/50( 4.0)	4/50( 8.0)	5/50( 10.0)	1/50( 2.0)	
Adjusted rates(b)	2.86	9.76	9.09	2.56	
Terminal rates(c) Statistical analysis Peto test	1/35( 2.9)	4/41( 9.8)	3/41( 7.3)	1/39( 2.6)	
Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.7164 P = 0.7705 P = 0.8412 P = 0.3482	P = 0.3574	P = 0.2425	P = 0.4926	
-	SITE : lung	s adamana kranahislar alugalar garainana			
Tumor rate	TUMOR • Drunchtutar =atoeutar	r adenoma,bronchiolar-alveolar carcinoma			
Overall rates(a)	4/50( 8.0)	12/50( 24.0)	9/50( 18.0)	4/50( 8.0)	
Adjusted rates(b)	6.25	29.27	18.18	10.26	
Terminal rates(c) Statistical analysis	2/35( 5.7)	12/41( 29.3)	7/41( 17.1)	4/39( 10.3)	
Peto test					
Standard method(d)	P = 0.7164		•		
Prevalence method(d)	P = 0.8437				
Combined analysis(d)	P = 0.8821		•		
Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.2682	P = 0.0539	P = 0.1562	P = 0.3579	

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BAIS3

ANIMAL : MOUSE BDF1
SEX : MALE
PAGE: 2

Group Name	Control	667ppm	2000ppm	6000ppm	
			,		<del></del>
	SITE : Lymph node TUMOR : malignant Lymphoma				
umor rate	TOTOK . Matignant tymphoma				
Overall rates(a)	4/50( 8.0)	7/50( 14.0)	6/50(12.0)	7/50( 14.0)	
Adjusted rates(b)	5.71	13.64	12.20	10.26	
Germinal rates(c) tatistical analysis Peto test	2/35( 5.7)	5/41( 12.2)	5/41( 12.2)	4/39( 10.3)	
Standard method(d)	P = 0.1953				
Prevalence method(d)	P = 0.4534				
Combined analysis(d) Cochran—Armitage test(e)	P = 0.2831 P = 0.5331				
Fisher Exact test(e)	F - 0.0001	P = 0.2958	P = 0.3944	P = 0.2958	
	SITE : spleen				
umor rate	TUMOR : malignant lymphoma				
Overall rates(a)	2/50( 4.0)	0/49( 0.0)	2/50( 4.0)	3/50( 6.0)	
Adjusted rates(b)	5.41	0.0	2.44	7.69	
Terminal rates(c)	1/35( 2.9)	0/40( 0.0)	1/41( 2.4)	3/39( 7.7)	
tatistical analysis					
Peto test Standard method(d)	P = 0.3798				
Prevalence method(d)	P = 0.1222				
Combined analysis(d)	P = 0.1458				
Cochran-Armitage test(e)	P = 0.2630				
Fisher Exact test(e)		P = 0.2626	P = 0.3088	P = 0.4909	
	SITE : spleen				
	TUMOR : hemangiosarcoma				
umor rate	. (	2/22/ 2.43	T (TO ( 10 0)	- Mark (	
Overall rates(a)	3/50( 6.0)	3/49( 6.1)	5/50( 10.0)	3/50( 6.0)	
Adjusted rates(b) Terminal rates(c)	6.82 0/35( 0.0)	7.50 3/40( 7.5)	12.20 5/41( 12.2)	6.38 1/39( 2.6)	
tatistical analysis	0/30( 0.0)	5/40( 7.8)	0/41( 12.2)	1/35( 2.0)	
Peto test Standard method(d)	P =				
Prevalence method(d)	P = 0.5091				
Combined analysis(d)	P =		-		
Cochran-Armitage test(e)	P = 0.9584				
Fisher Exact test(e)		P = 0.3483	P = 0.3790	P = 0.3392	

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STUDY No. : 0206

PAGE: 3

STUDY No. : 0206 ANIMAL : MOUSE BDF1

SEX : MALE

Group Name	Control	667ppm	2000ppm	6000pm
	SITE : liver TUMOR : hepatocellular adenoma			
mor rate	TONOK · Hepatocettotal adeliona			
verall rates(a)	8/50( 16.0)	6/49( 12.2)	7/50( 14.0)	3/50(6.0)
djusted rates(b)	20.00	15.00	16.67	7.69
erminal rates(c) atistical analysis eto test	7/35( 20.0)	6/40( 15.0)	6/41( 14.6)	3/39( 7.7)
Standard method(d)	P =			
Prevalence method(d)	P = 0.9468			
Combined analysis(d)	P =			
Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.1307	P = 0.4299	P = 0.4854	P = 0.1322
			. 0.1001	1 0.1000
	SITE : Liver TUMOR : hemangiosarcoma			
mor rate	Tomal Cross			
Nerall rates(a)	4/50( 8.0)	2/49( 4.1)	2/50( 4.0)	1/50( 2.0)
Ndjusted rates(b) Ferminal rates(c)	0.0 0/35( 0.0)	2.50 1/40( 2.5)	2.44	0.0
tatistical analysis Peto test	0/30( 0.0)	1/40( 2.5)	1/41( 2.4)	0/39( 0.0)
Standard method(d)	P = 0.8651			
Prevalence method(d)	P = 0.6367			
Combined analysis(d)	P = 0.8940			
Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.2281	P = 0.3668	P = 0.3574	P = 0.1998
70101 12/401 1031(0)			1 - 0.0074	1 - 0.1000
	SITE : liver			
	TUMOR : hepatocellular carcinoma			
umor rate Overall rates(a)	8/50( 16.0)	8/49( 16.3)	5/50( 10.0)	4/50( 8.0)
Mdjusted rates(b)	22.86	15.22	6.67	4/50( 8.0) 7.69
Terminal rates(c)	8/35( 22.9)	6/40( 15.0)	2/41( 4.9)	3/39( 7.7)
atistical analysis				
Peto test	D 0000			
Standard method(d) Prevalence method(d)	P = 0.3303 P = 0.9661			
Combined analysis(d)	P = 0.9280	*		
ochran-Armitage test(e)	P = 0.1681			
isher Exact test(e)		P = 0.4089	P = 0.3141	P = 0.2169

### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

ANIMAL : MOUSE BDF1
SEX : MALE PAGE: 4

Group Name	Control	667ppm	2000ppm	6000ppm	
	SITE : liver			•	·
	TUMOR : hemangioma, hemangio	sarcoma			
umor rate		-11	. ( ()		
Overall rates(a)	4/50( 8.0)	3/49( 6.1)	3/50( 6.0)	1/50( 2.0)	
Mdjusted rates(b)	0.0	5.00	4.88	0.0	
Terminal rates(c)	0/35( 0.0)	2/40( 5.0)	2/41( 4.9)	0/39( 0.0)	
tatistical analysis					
Peto test					
Standard method(d)	P = 0.8651				
Prevalence method(d)	P = 0.7557				
Combined analysis(d)	P = 0.9161				
Cochran—Armitage test(e)	P = 0.1869				
Fisher Exact test(e)		P = 0.4788	P = 0.4895	P = 0.1998	
mor rate	SITE : liver TUMOR : hepatocellular aden	oma,hepatocellular carcinoma			
umor rate	TUMOR : hepatocellular aden		9/50/ 18 0)	7/50( 14.0)	
Overall rates(a)	TUMOR : hepatocellular aden	12/49( 24.5)	9/50( 18.0) 15.56	7/50( 14.0) 15.38	
Overall rates(a) Adjusted rates(b)	TUMOR : hepatocellular aden 16/50(32.0) 42.86	12/49( 24.5) 25.00	15.56	15.38	
Overall rates(a) Adjusted rates(b) Terminal rates(c)	TUMOR : hepatocellular aden	12/49( 24.5)			
Overall rates(a) Adjusted rates(b) Terminal rates(c) tatistical analysis	TUMOR : hepatocellular aden 16/50(32.0) 42.86	12/49( 24.5) 25.00	15.56	15.38	
Overall rates(a) Adjusted rates(b) Terminal rates(c) tatistical analysis Peto test	TUMOR: hepatocellular aden 16/50(32.0) 42.86 15/35(42.9)	12/49( 24.5) 25.00	15.56	15.38	
Overall rates(a) Adjusted rates(b) Terminal rates(c) tatistical analysis Peto test Standard method(d)	TUMOR : hepatocellular aden 16/50(32.0) 42.86 15/35(42.9) P = 0.3303	12/49( 24.5) 25.00	15.56	15.38	
Overall rates(a) Adjusted rates(b) Terminal rates(c) tatistical analysis Peto test Standard method(d) Prevalence method(d)	TUMOR: hepatocellular aden 16/50(32.0) 42.86 15/35(42.9) P = 0.3303 P = 0.9922	12/49( 24.5) 25.00	15.56	15.38	
Overall rates(a) Adjusted rates(b) Terminal rates(c) tatistical analysis Peto test Standard method(d)	TUMOR : hepatocellular aden 16/50(32.0) 42.86 15/35(42.9) P = 0.3303	12/49( 24.5) 25.00	15.56	15.38	

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BAIS3

(HPT360A)

### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

ANIMAL : MOUSE BDF1
SEX : MALE

Group Name	Control	667ppm	2000ppm	6000ppm
	SITE : Harderian gland			
'umor rate	TUMOR : adenoma			
Overall rates(a)	0/50( 0.0)	5/50( 10.0)	2/48( 4.2)	0/50( 0.0)
Adjusted rates(b)	0.0	11.90	5.13	0.0
Terminal rates(c)	0/35( 0.0)	4/41( 9.8)	2/39(5.1)	0/39( 0.0)
tatistical analysis				
Peto test				
Standard method(d)	P =			
Prevalence method(d)	P = 0.9158			
Combined analysis(d)	P =			
Cochran-Armitage test(e)	P = 0.1969			
Fisher Exact test(e)		P = 0.0360*	P = 0.2475	P = 0.5000

(a): Number of tumor-bearing animals/number of animals examined at the site.

(b): Kaplan-Meire estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.

(c): Observed tumor incidence at terminal kill.

(d): Beneath the control incidence are the P-values associated with the trend test.

Standard method : Death analysis

Prevalence method: Incidental tumor test

Combined analysis: Death analysis + Incidental tumor test

(e): The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.

?: The conditional probabities of the largest and smallest possible out comes can not estimated or this P-value is beyond the estimated P-value.

-----: There is no data which should be statistical analysis.

Significant difference;  $*: P \le 0.05$   $**: P \le 0.01$ 

PAGE:

BAIS3

#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

ANIMAL : MOUSE BDF1

SEX	: MALE		PAGE:

Group Name	Control	667ppm	2000ppm	6000ppm	
	SITE : ALL SITE TUMOR : histiccytic sarcoma				
Tumor rate					
Overall rates(a)	5/50( 10.0)	5/50( 10.0)	4/50( 8.0)	2/50( 4.0)	
Adjusted rates(b)	<b>5.7</b> 1	7.32	7.32	0.0	
Terminal rates(c)	2/35(5.7)	3/41( 7.3)	3/41( 7.3)	0/39( 0.0)	
Statistical analysis					
Peta test					
Standard method(d)	P = 0.6127				
Prevalence method(d)	P = 0.9434				
Combined analysis(d)	P = 0.9064				
Cochran-Armitage test(e)	P = 0.2044		·		
Fisher Exact test(e)		P = 0.3710	P = 0.4883	P = 0.2425	
	SITE : ALL SITE				
iumor rate	TUMOR ; malignant lymphoma				
Overall rates(a)	6/50(12.0)	7/50( 14.0)	8/50(16.0)	10/50( 20.0)	
Adjusted rates(b)	11.11	13.64	14.63	17.95	
Terminal rates(c)	3/35(8,6)	5/41( 12.2)	6/41( 14.6)	7/39(17.9)	
Statistical analysis	0,000	0, 11 ( 1202)	0, 11( 1110)	1,00( 1110)	
Peto test					
Standard method(d)	P = 0.2173				
Prevalence method(d)	P = 0.2252				
Combined analysis(d)	P = 0.1482				
Cochran-Armitage test(e)	P = 0.2571				
Fisher Exact test(e)		P = 0.4863	P = 0.4157	P = 0.2557	

(HPT360A)

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Standard method : Death analysis

Prevalence method: Incidental tumor test

Combined analysis: Death analysis + Incidental tumor test

Significant difference;  $*: P \le 0.05$   $**: P \le 0.01$ 

<sup>(</sup>a): Number of tumor-bearing animals/number of animals examined at the site.

<sup>(</sup>b): Kaplan-Meire estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.

<sup>(</sup>c): Observed tumor incidence at terminal kill.

<sup>(</sup>d): Beneath the control incidence are the P-values associated with the trend test.

<sup>(</sup>e): The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.

<sup>?:</sup> The conditional probabities of the largest and smallest possible out comes can not estimated or this P-value is beyond the estimated P-value.

<sup>----:</sup> There is no data which should be statistical analysis.

# APPENDIX N 4

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

MOSUE :FEMALE

PAGE:

BAIS3

STUDY No. : 0206 ANIMAL : MOUSE BDF1

SEX : FEMALE

Group Name Control 667ppm 2000ppm 6000ppm SITE : lung TUMOR : bronchiolar-alveolar adenoma Tumor rate Overall rates(a) 3/50(6.0) 1/50( 2.0) 1/50( 2.0) 1/49( 2.0) Adjusted rates(b) 7.69 4.55 4.00 3.13 Terminal rates(c) 2/31(6.5) 1/22( 4.5) 1/25(4.0) 1/32( 3.1) Statistical analysis Peto test Standard method(d) Prevalence method(d) P = 0.7949Combined analysis(d) P = ----Cochran-Armitage test(e) P = 0.4505Fisher Exact test(e) P = 0.3235P = 0.3235P = 0.3312SITE : lung TUMOR : bronchiolar-alveolar carcinoma Tumor rate Overall rates(a) 4/50( 8.0) 2/50( 4.0) 1/50( 2.0) 2/49( 4.1) Adjusted rates(b) 11.76 2.50 3.57 6.25 Terminal rates(c) 3/31(9.7) 0/22( 0.0) 0/25( 0.0) 2/32(6.3) Statistical analysis Peto test Standard method(d) P = 0.5184Prevalence method(d) P = 0.6677Combined analysis(d) P = 0.7397Cochran-Armitage test(e) P = 0.5566Fisher Exact test(e) P = 0.3574P = 0.1998P = 0.3668SITE : lung TUMOR : bronchiolar-alveolar adenoma, bronchiolar-alveolar carcinoma Tumor rate Overall rates(a) 7/50(14.0) 3/50( 6.0) 2/50( 4.0) 3/49(6.1) Adjusted rates(b) 17.95 5.00 7.14 9.38 Terminal rates(c) 5/31(16.1) 1/22(4.5) 1/25( 4.0) 3/32( 9.4) Statistical analysis Peto test Standard method(d) P = 0.5184Prevalence method(d) P = 0.8161Combined analysis(d) P = 0.8548Cochran-Armitage test(e) P = 0.3413Fisher Exact test(e) P = 0.1917P = 0.1045P = 0.2004(IIPT360A)

STUDY No. : 0206 ANIMAL : MOUSE BDF1
SEX : FEMALE

Group Name	Control	667ppm	2000ppm	mqq0006	
	SITE : Lymph node				
Tumor rate	TUMOR : malignant lymphoma				
Overall rates(a)	14/50( 28.0)	15/50(30.0)	11/50( 22.0)	7/49( 14.3)	
Adjusted rates(b)	21.05	22.73	12.00	3.13	
Terminal rates(c)	6/31(19,4)	5/22( 22.7)	3/25(12.0)	1/32( 3.1)	
Peto test Standard method(d)	P = 0.7107				
Prevalence method(d)	P = 0.9972				
Combined analysis(d)	P = 0.9797				
Cochran-Armitage test(e)	P = 0.0524	5			
Fisher Exact test(e)		P = 0.4810	P = 0.3777	P = 0.1338	
	SITE : spleen				
	TUMOR : malignant lymphoma				
Cumor rate	0/50/ +0 0)	4/50/ 0.0	0.000		
Ouerall rates(a) Adjusted rates(b)	6/50( 12.0) 15.15	4/50( 8.0) 18.18	3/50( 6.0) 4.00	4/49( 8.2)	
Terminal rates(c)	4/31(12.9)	4/22( 18.2)	1/25( 4.0)	12.50 4/32( 12.5)	
Statistical analysis	1, 01 ( 11,0)	1, 22 (10.2)	1/20( 1.0)	4,04( 12.0)	
Peto test					
Standard method(d)	P = 0.6966				
Prevalence method(d) Combined analysis(d)	P = 0.6362 P = 0.7227				
Cochran-Armitage test(e)	P = 0.7227 P = 0.6743				
Fisher Exact test(e)	. 0.01.10	P = 0.3944	P = 0.2728	P = 0.4066	
	SITE : liver				
Tumor rate	TUMOR : hemangioma				
Overall rates(a)	0/50( 0.0)	1/50( 2.0)	3/50( 6.0)	1/49( 2.0)	
Adjusted rates(b)	0.0	4.55	12.00	2.56	
Terminal rates(c)	0/31( 0.0)	1/22( 4.5)	3/25( 12.0)	0/32( 0.0)	
Statistical analysis					
Peto test	D.				
Standard method(d) Prevalence method(d)	P = P = 0.4140				
Combined analysis(d)	P = 0.4140 P =				
Cochran-Armitage test(e)	P = 0.7060				
Fisher Exact test(e)		P = 0.4950	P = 0.1325	P = 0.5000	

(HPT360A)

ANIMAL : MOUSE BDF1
SEX : FEMALE

STUDY No. : 0206

Group Name Control 667ppm 2000ppm 6000ppm SITE : liver TUMOR : hepatocellular adenoma Tumor rate Overall rates(a) 2/50( 4.0) 3/50( 6.0) 12/50( 24.0) 10/49(20.4) Adjusted rates(b) 6.45 12.00 40.00 28.57 Terminal rates(c) 2/31(6.5) 2/22( 9.1) 10/25(40.0) 8/32(25.0) Statistical analysis Peto test Standard method(d) P = ----Prevalence method(d) P = 0.0178\*Combined analysis(d) P = ----Cochran-Armitage test(e) P = 0.0123\*Fisher Exact test(e) P = 0.4909P = 0.0106\*P = 0.0251\*SITE : liver TUMOR : hemangiosarcoma Tumor rate Overall rates(a) 2/50( 4.0) 0/50(0.0)1/50( 2.0) 4/49( 8,2) Adjusted rates(b) 0.0 0.0 0.0 12.50 Terminal rates(c) 0/31( 0.0) 0/22( 0.0) 0/25( 0.0) 4/32(12.5) Statistical analysis Peto test Standard method(d) P = 0.8757Prevalence method(d) P = 0.0013\*\*Combined analysis(d) P = 0.0714Cochran-Armitage test(e) P = 0.0686Fisher Exact test(e) P = 0.2574P = 0.4926P = 0.3483SITE : Liver TUMOR : hepatocellular carcinoma Tumor rate Overall rates(a) 1/50( 2.0) 5/50(10.0) 7/50(14.0) 5/49(10.2) Adjusted rates(b) 3.23 9,68 24.00 15,63 Terminal rates(c) 1/31(3.2) 2/22( 9.1) 6/25(24.0) 5/32(15.6) Statistical analysis Peto test Standard method(d) P = 0.7586Prevalence method(d) P = 0.1597Combined analysis(d) P = 0.2776Cochran-Armitage test(e) P = 0.3545Fisher Exact test(e) P = 0.1210P = 0.0430\*P = 0.1163

(HPT360A)

STUDY No.: 0206 NEOPLASTIC LESIONS-INCI ANIMAL : MOUSE BDF1 SEX : FEMALE

Group Name Control 667ppm 2000ppm 6000ppm SITE : liver TUMOR : hemangioma, hemangiosarcoma Tumor rate Overall rates(a) 2/50( 4.0) 1/50( 2.0) 4/50( 8.0) 5/49(10.2) Adjusted rates(b) 0.0 4.55 12.00 12.82 Terminal rates(c) 0/31( 0.0) 1/22( 4.5) 3/25(12.0) 4/32(12.5) Statistical analysis Peto test Standard method(d) P = 0.8757Prevalence method(d) P = 0.0190\*Combined analysis(d) P = 0.1049Cochran-Armitage test(e) P = 0.0974Fisher Exact test(e) P = 0.4926P = 0.3574P = 0.2345SITE : Liver TUMOR : hepatocellular adenoma, hepatocellular carcinoma Tumor rate Ouerall rates(a) 3/50( 6.0) 8/50(16.0) 16/50(32.0) 14/49(28.6) Adjusted rates(b) 9.68 20.00 52.00 40.00 Terminal rates(c) 3/31(9.7) 4/22(18.2) 13/25(52.0) 12/32(37.5) Statistical analysis Peto test Standard method(d) P = 0.7586Prevalence method(d) P = 0.0091\*\*Combined analysis(d) P = 0.0222\*Cochran-Armitage test(e) P = 0.0118\*Fisher Exact test(e) P = 0.1322P = 0.0049\*\*P = 0.0104\*SITE : pituitary gland TUMOR : adenoma Tumor rate Ouerall rates(a) 5/50(10.0) 6/49(12.2) 5/50(10.0) 4/49( 8.2) Adjusted rates(b) 16.13 22.73 20.00 9.38 Terminal rates(c) 5/31(16.1) 5/22(22.7) 5/25(20.0) 3/32(9.4) Statistical analysis Peto test Standard method(d) P = 0.2817Prevalence method(d) P = 0.8671Combined analysis(d) P = 0.7989Cochran-Armitage test(e) P = 0.6045Fisher Exact test(e) P = 0.5000P = 0.3710P = 0.4763

(HPT360A)

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## NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

ANIMAL : MOUSE BDF1
SEX : FEMALE

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Group Name	Contral	667ppm	2000ppm	6000ppm
	SITE : ovary			
mor rate	TUMOR : cystadenoma			
'umor rate Overall rates(a)	3/50( 6.0)	1/50/ 0.0)	1/50/ 0.0)	0/40/ 0.0)
Adjusted rates(b)	9.68	1/50( 2.0) 4.55	1/50( 2.0)	0/49( 0.0)
Terminal rates(c)	3/31(9.7)	1/22( 4.5)	4.00 1/25( 4.0)	0.0
Statistical analysis	0,01( 0.1)	1/22( 4.0)	1/20( 4.0)	0/32( 0.0)
Peto test				
Standard method(d)	P =			
Prevalence method(d)	P = 0.9654			
Combined analysis(d)	P =			
Cochran-Armitage test(e)	P = 0.1147			
Fisher Exact test(e)		P = 0.3235	P = 0.3235	P = 0.1364
			***************************************	
	SITE : uterus			
	TUMOR : histiocytic sarcoma			
umor rate	- 45-4			
Overall rates(a)	8/50(16.0)	13/50( 26.0)	12/50( 24.0)	15/49(30.6)
Adjusted rates(b)	5.71	14.29	12.50	18.92
Terminal rates(c) Statistical analysis	1/31( 3.2)	2/22( 9.1)	3/25(12.0)	5/32( 15.6)
Peto test				
Standard method(d)	P = 0.4010			
Prevalence method(d)	P = 0.0638			
Combined analysis(d)	P = 0.1357			
	P = 0.1612			
Cochran-Armitage test(e)	$F = V_{-}101Z$			

(HPT360A)

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#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

ANIMAL : MOUSE BDF1

SEX : FEMALE

Group Name	Control	667ppm	2000ppm	6000ppm	
	SITE : Harderian gland				
Tumor rate	TUMOR : adenoma				
Overall rates(a)	1/50( 2.0)	4/50( 8.0)	1/50( 2,0)	1/49( 2.0)	
Adjusted rates(b)	3.23	18.18	4.00	3,13	
Terminal rates(c)	1/31( 3.2)	4/22( 18.2)	1/25( 4.0)	1/32( 3.1)	
tatistical analysis	1/01( 0.2)	4/22(10.2)	1/20( 4.0)	1/02( 0,1)	
Peto test					
Standard method(d)	P =				
Prevalence method(d)	P = 0.8072				
Combined analysis(d)	P =				
Cochran-Armitage test(e)	P = 0.4686				
Fisher Exact test(e)	. 0, 2000	P = 0.1998	P = 0.2475	P = 0.2525	
			,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,		
PT360A)					BA

(a): Number of tumor-bearing animals/number of animals examined at the site.

(b): Kaplan-Meire estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.

(c): Observed tumor incidence at terminal kill.

(d): Beneath the control incidence are the P-values associated with the trend test.

Standard method : Death analysis

Prevalence method: Incidental tumor test

Combined analysis: Death analysis + Incidental tumor test

(e): The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.

?: The conditional probabities of the largest and smallest possible out comes can not estimated or this P-value is beyond the estimated P-value.

----: There is no data which should be statistical analysis.

Significant difference;  $*: P \le 0.05$   $**: P \le 0.01$ 

#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

ANIMAL : MOUSE BDF1
SEX : FEMALE

Group Name	Control	667ppm	2000ppm	6000pm
	SITE : ALL SITE			
T .	TUMOR : histiocytic sarcoma			•
Tumor rate	10/50( 20.0)	15/50/ 20 0)	10/50/ 20 0)	17/40/ 04 7)
Overall rates(a) Adjusted rates(b)	8.57	15/50( 30.0)	16/50( 32.0)	17/49( 34.7)
Terminal rates(c)	2/31( 6.5)	14.81	16.22	24.32 7/32( 21.9)
Statistical analysis	2/31( 0.5)	2/22( 9.1)	4/25( 16.0)	7/32( 21.9)
Peto test				
Standard method(d)	P = 0.5816			
Prevalence method(d)	P = 0.0358*			
Combined analysis(d)	P = 0.1823			
Cochran-Armitage test(e)	P = 0.1904			
Fisher Exact test(e)		P = 0.2516	P = 0.2039	P = 0.1527
	SITE : ALL SITE TUMOR : malignant lymphoma			
Tumor rate	TOTOM • INACTORIBITE COMPIDINA			
Overall rates(a)	21/50( 42.0)	19/50( 38.0)	14/50( 28.0)	11/49( 22.4)
Adjusted rates(b)	34.29	40.91	16.00	15.63
Terminal rates(c)	10/31(32.3)	9/22( 40.9)	4/25( 16.0)	5/32( 15.6)
Statistical analysis		, , ,	, , ,	, , , , ,
Peto test				
Standard method(d)	P = 0.8096			
Prevalence method(d)	P = 0.9923			
Combined analysis(d)	P = 0.9885			
Cochran-Armitage test(e)	P = 0.0318*			
Fisher Exact test(e)		P = 0.4682	P = 0.2055	P = 0.0983

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PAGE:

Prevalence method: Incidental tumor test

Combined analysis: Death analysis + Incidental tumor test

Significant difference;  $*:P \le 0.05$  \*\*:  $P \le 0.01$ 

<sup>(</sup>a): Number of tumor-bearing animals/number of animals examined at the site.

<sup>(</sup>b): Kaplan-Meire estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.

<sup>(</sup>c): Observed tumor incidence at terminal kill.

<sup>(</sup>d): Beneath the control incidence are the P-values associated with the trend test.

Standard method : Death analysis

<sup>(</sup>e): The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.

<sup>?:</sup> The conditional probabities of the largest and smallest possible out comes can not estimated or this P-value is beyond the estimated P-value.

<sup>-----:</sup> There is no data which should be statistical analysis.

## APPENDIX O 1

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

RAT: MALE: DEAD AND MORIBUND ANIMALS

HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

: RAT F344 ANIMAL REPORT TYPE : A1 SEX

(JPT150)

STUDY NO. : 0205

: MALE

Group Name Control 500ppm 1500ppm 4500ppm 12 19 No. of Animals on Study 13 Findings\_ [Respiratory system] nasal cavit <13> < 9> <12> <19> leukemic cell infiltration 0 1 lung <13> < 9> <12> <19> leukemic cell infiltration metastasis:adrenal tumor metastasis:pancreas tumor metastasis:kidney tumor [Hematopoietic system] < 9> <12> (19) bone marrow <13> leukemic cell infiltration 2 2 lymph nade <13> < 9> <12> <19> leukemic cell infiltration [Circulatory system] <13> < 9> <12> <19> heart leukemic cell infiltration [Digestive system] <13> < 9> <12> <19> tongue leukemic cell infiltration stomach <13> < 9> <12> **<19>** leukemic cell infiltration 1 0 (a) a: Number of animals examined at the site b b: Number of animals with lesion

## HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR (SUMMARY)

STUDY NO. : 0205 : RAT F344 DEAD AND MORIBUND ANIMALS (0-105W)

REPORT TYPE : A1 : MALE SEX

ANIMAL

4500ppm Control 500ppm 1500ppm Group Name 12 19 13 No. of Animals on Study Findings\_ [Digestive system] < 9> <12> <19> <13> small intes 1 0 leukemic cell infiltration <12> <19> <13> (9) large intes 1 leukemic cell infiltration <19> <12> (13) ( 9> liver 4 leukemic cell infiltration 2 (12) <19> <13> < 9> pancreas 1 leukemic cell infiltration [Urinary system] <12> <19> < 9> kidney <13> leukemic cell infiltration 2 2 1 metastasis:pancreas tumor [Endocrine system] < 9> <12> <19> <13> thyroid 0 0 leukemic cell infiltration < 9> <12> <19> <13> adrenal leukemic cell infiltration [Reproductive system] <13> < 9> <12> <19> mammary gl 1 leukemic cell infiltration [Nervous system] <19> <13> < 9> <12> brain 0 leukemic cell infiltration (a) a: Number of animals examined at the site

(JPT150)

b: Number of animals with lesion

b

BAIS3

STUDY NO. : 0205 ANIMAL : RAT F344 HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR (SUMMARY)

REPORT TYPE : A1 SEX : MALE

DEAD AND MORIBUND ANIMALS (0-105W)

0rgan		Group Name No. of Animals on Study 	Control 13	500ppm 9	1500ppm 12	4500ppm 19
[Nervous syste	em]					
brain	metastasis:kidney tumor		<13> 0	0	<12> 0	<19> 1
spinal cord	leukemic cell infiltration		<13> 0	0	<12> 1	<19> 0
(a) b	a : Number of animals examined at the si b : Number of animals with lesion	te				
(JPT150)	:	,				BA

## APPENDIX O 2

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

RAT: FEMALE: DEAD AND MORIBUND ANIMALS

STUDY NO. : 0205 ANIMAL : RAT F344 HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

REPORT TYPE : A1 SEX : FEMALE

rgan		Group Name No. of Animals on Study	Control 6	500ppm 12	1500ppm 6	4500ppm 13
Respiratory s	system]					
asal cavit	leukemic cell infiltration		< 6> 0	<12> 0	< 6> 0	<13> 1
ung	leukemic cell infiltration		< 6> 1	<12> 6	< 6>	<13> 0
	metastasis:bone tumor		0	0	1	0
lematopoietic	c system]					
one marrow	leukemic cell infiltration		< 6>	<12> 5	< 6> 4	<13> 2
	metastasis:liver tumor		1	0	0	0
vmph nade	leukemic cell infiltration		< 6> 0	<12> 3	< 6> 1	<13> 1
	metastasis:tongue tumor		0	1	0	0
	metastasis:ovary tumor		0	1	0	0
	metastasis:oral cavity tumor		0	0	0	1
oleen	metastasis:bone marrow tumor		< 6>	<12> 0	< 6> 0	<13> 1
Circulatory s	system]					
eart	leukemic cell infiltration		< 6>	<12> 3	< 6> 1	<13> 0
Digestive sys	stem]		·			
angue	leukemic cell infiltration		< 6> 0	<12> 2	< 6> 0	<13> 0
a > b	a: Number of animals examined at the si b: Number of animals with lesion	te				

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

ANIMAL : RAT F344 REPORT TYPE : A1

SEX : FEMALE

(JPT150)

STUDY NO. : 0205

rgan	Findings	Group Name No. of Animals on Study	Control 6	500ppm 12	1500ppm 6	4500ppn 13
						W. **** **** *** *** *** *** *** *** ***
oigestive sy	rstem]					
ongue	metastasis:oral cavity tumor		< 6> 0	<12> 0	< 6>	<13> 1
livary gl	leukemic cell infiltration		< 6> 0	<12> 0	< 6> 0	<13> 1
omach	leukemic cell infiltration		< 6> 1	<12> 2	< 6>	<13> 1
all intes	leukemic cell infiltration		< 6> 1	<12> 0	< 6>	<13> 0
rge intes	leukemic cell infiltration		< 6> 1	<12> 0	< 6>	<13> 0
ver	leukemic cell infiltration		< 6> 2	<12> 6	< 6>	<13> 2
	metastasis:bone marrow tumor		0	0	0	1
ncreas	leukemic cell infiltration		< 6> 1	<12> 3	< 6> 0	<13> 0
rinary syst	tem]					
dney	leukemic cell infiltration		< 6> 1	<12> 5	< 6> 1	<13> 1
	metastasis:ovary tumor		0	1	0	0
Endocrine s	vstem]					
tui tary	leukemic cell infiltration		< 6>	<12> 1	< 6>	<13> 0

STUDY NO. : 0205 ANIMAL : RAT F344 HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR (SUMMARY)
DEAD AND MORIBUND ANIMALS (0-105W)

REPORT TYPE : A1 SEX : FEMALE

(JPT150)

0rgan	Findings	Group Name No. of Animals on Study	Control 6	500ppm 12	1500ppm 6	4500ppm 13
(Endocrine sy	stem]					
adrena l	leukemic cell infiltration		< 6>	<12> 5	< 6>	<13>
	metastasis:ovary tumor		0	1	0	0
Reproductive	system]					
vary	leukemic cell infiltration		< 6> 0	<12> 3	< 6> 1	<13> 1
terus	leukemic cell infiltration		< 6> 1	<12> 2	< 6> 0	<13>
	metastasis:ovary tumor		0	1	0	0
ammary gl	leukemic cell infiltration		< 6> 0	<12> 1	< 6> 0	<13> 0
Nervous syst	em]					
rain	leukemic cell infiltration		< 6> 1	<12> 4	< 6> 1	<13> 1
oinal cord	leukemic cell infiltration		< 6> 0	<12> 3	< 6> 1	<13> 0
Special sens	e organs/appandage]					
arder gl	leukemic cell infiltration		< 6> 0	<12> 2	< 6> 0	<13>
	metastasis:oral cavity tumor		0 .	0	0	1

ANIMAL : RAT F344

REPORT TYPE : A1
SEX : FEMALE

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

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0rgan		Group Name No. of Animals on Study	Control 6	500ppm 12	1500ppm 6	4500ppm 13
Musculaskele	tal system]					
nuscle	leukemic cell infiltration		< 6> 0	<12> 0	< 6> 0	<13> 1
Body cauities	[8					
ediastinum	leukemic cell infiltration		< 6>	<12> 0	< 6>	<13> 2
etroperit	leukemic cell infiltration		< 6> 0	<12> 0	< 6> 0	<13> 1
	metastasis:ouary tumor		0	1	0	0
a> b	a: Number of animals examined at the sib: Number of animals with lesion	te				
(JPT150)						

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# APPENDIX O 3

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

RAT: MALE: SACRIFICED ANIMALS

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

STUDY NO. : 0205 ANIMAL : RAT F344 REPORT TYPE : A1

SEX : MALE

Organ	Findings	Group Name No. of Animals on Study	Control 37	500ppm 41	1500ppm 38	4500ppm 31
December						
[Respiratory	Systemį					
lung	leukemic cell infiltration		<37> 1	<41> 1	<38> 4	<31> 1
	metastasis:liver tumor		0	0	1	0
	metastasis:bone tumor		0	1	0	0
	metastasis:spleen tumor		0	1	0	0
[Hematopoieti	ic system]					
one marrow	leukemic cell infiltration		<37> 0	<41> 0	<38> 1	<31> 0
	metastasis:liver tumor		0	0	ī	0
	metastasis:spleen tumor		0	1	0	0
lymph nade	leukemic cell infiltration		<37> 0	<41> 1	<38> 1	<31>
	metastasis:liver tumor		0	0	1	0
	metastasis:urinary bladder tumor		0	0	0	1
[Digestive s	vstem]					
liver	leukemic cell infiltration		<37> 0	<41> 2	<38> 5	<31> 0
	metastasis:spleen tumor		0	1	0	0
[Urinary syst	tem]					
<idney< td=""><td>leukemic cell infiltration</td><td></td><td>&lt;37&gt;</td><td>&lt;41&gt;</td><td>&lt;38&gt;</td><td>&lt;31&gt; 0</td></idney<>	leukemic cell infiltration		<37>	<41>	<38>	<31> 0

(JPT150)

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STUDY NO. : 0205 ANIMAL : RAT F344

HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR (SUMMARY)

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SACRIFICED ANIMALS (105W)

REPORT TYPE : A1 SEX : MALE

Group Name Control 500ppm 1500ppm 4500ppm No. of Animals on Study 37 38 31 Findings\_ [Endocrine system] ⟨37⟩ adrenal <41> ⟨38⟩ ⟨31⟩ leukemic cell infiltration 0 0 1 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 (TOW-YERA STUDY: SUMMARY)

RAT: FEMALE: SACRIFICED ANIMALS

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

STUDY NO. : 0205 ANIMAL : RAT F344

REPORT TYPE : A1

: FEMALE SEX

Organ	Findings	Group Name No. of Animals on Study	Control 44	500ppm 38	1500ppm 44	4500ppm 37
, sait	i mumgs					· · · · · · · · · · · · · · · · · · ·
[Respiratory	system]					
trachea	metastasis:thyroid tumor		<44>	<38> 0	<44> 0	<37> 0
lung	leukemic cell infiltration		<44> 1	<38> 1	<44> 2	<37> 1
[Hematopoieti	c system]					
bone marrow	leukemic cell infiltration		<44>	<38> 0	<44> 1	<37> 1
lymph node	leukemic cell infiltration		<44> 1	<38> 0	<44> 0	<37> 2
(Circulatory	system]					
heart	leukemic cell infiltration		<44> 0	<38> 1	<44> 0	<37> 0
[Digestive sy	stem]					
liver	leukemic cell infiltration		<44> 3	<38> 2	<44> 3	<37> 2
	metastasis:uterus tumor		0	1	0	0
[Urinary syst	em]					
kidney	leukemic cell infiltration		<44> 1	<38> 0	<44> 0	<37> 0
(Reproductive	system]					
ovary	leukemic cell infiltration		<44>	<38>	<44>	<37>

(JPT150)

BAIS3

STUDY NO. : 0205 ANIMAL : RAT F344 REPORT TYPE : A1

: FEMALE

SEX

HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR (SUMMARY)

PAGE: 4

SACRIFICED ANIMALS (105W)

Group Name Contral 500ppm 1500ppm 4500ppm No. of Animals on Study 44 37 44 Findings\_ [Nervous system] brain <44> ⟨38⟩ <44> ⟨37⟩ metastasis:pituitary tumor 1 1 0 <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 (TOW-YERA STUDY: SUMMARY)

MOUSE: MALE: DEAD AND MORIBUND ANIMALS

## HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

STUDY NO. : 0206

Group Name 667ppm 2000ppm 6000ppm Control No. of Animals on Study 15 11 Findings\_ [Respiratory system] nasal cavit <15> < 9> < 9> <11> leukemic cell infiltration 2 metastasis:periferal nerve tumor 0 1 <15> < 9> < 9> <11> trachea leukemic cell infiltration 0 < 9> <11> <15> < 9> lung leukemic cell infiltration 3 1 1 metastasis:liver tumor [Hematopoietic system] <15> < 9> (11) bone marrow < 9> leukemic cell infiltration 1 < 9> < 9> (11) lymph nade <15> leukemic cell infiltration 0 0 metastasis:subcutis tumor <15> < 9> < 9> (11) spleen leukemic cell infiltration 2 2 1 1 0 0 metastasis:liver tumor 1 [Circulatory system] <15> < 9> < 9> (11) heart 2 leukemic cell infiltration [Digestive system] <15> < 9> < 9> <11> salivary gl leukemic cell infiltration 1

(JPT150)

<sup>&</sup>lt; a > a: Number of animals examined at the site

b b: Number of animals with lesion

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

ANIMAL : MOUSE BDF1

E BDF1 DEAD AND

REPORT TYPE : A1
SEX : MALE

Organ		Group Name No. of Animals on Study	Control 15	667ppm 9	2000ppm 9	6000ppm 11
<u> </u>						
Digestive sy	stem]					
salivary gl	metastasis:liver tumor		<15> 0	< 9> 1	< 9>	<11>> 0
tomach	leukemic cell infiltration		<15> 0	0	< 9>	<11> 1
	metastasis:liver tumor		1	0	0	0
iver	leukemic cell infiltration		<15> 0	< 9> 1	< 9> 2	<11> 2
	metastasis:epididymis tumor		0	0	1	0
pancreas	leukemic cell infiltration		<15> 0	< 9>	< 9> 1	<11> 0
Urinary syst	cem]					
tidney	leukemic cell infiltration		<15> 0	0 0	0 0 9>	<11> 2
rin bladd	leukemic cell infiltration		<15> 0	0 0	< 9> 0	<11> 1
	metastasis:liver tumor		0	1	0	0
Endocrine sy	vstem]					
drenal	leukemic cell infiltration		<15> 0	0	< 9> 1	<11> 0
[Reproductive	e system]					
testis	leukemic cell infiltration		<15> 0	0 0	0 0	<11> 1
(a) b	a: Number of animals examined at the s b: Number of animals with lesion	ite				
(JPT150)				1		

STUDY NO. : 0206 ANIMAL : MOUSE BDF1

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

REPORT TYPE : A1

SEX : MALE

		Group Name No. of Animals on Study	Control 15	667ppm 9	2000ppm 9	6000ppm 11
rgan	Findings					
Reproductive	system]					
epididymis	leukemic cell infiltration		<15> 0	<b>〈</b> 9 <b>〉</b> 0	< 9> 1	<11> 1
rostate	leukemic cell infiltration		<15> 0	< 9>	< 9> 0	<11> 1
Nervous syste	em]					
xain	metastasis:periferal nerve tumor		<15> 1	< 9> 0	< 9>	<11> 1
Special sense	e organs/appandage]					
э <b>у</b> ө	leukemic cell infiltration		<15> 0	< 9>	< 9> .0	<11> 1
larder gl	leukemic cell infiltration		<15> 0	0 0	0 0	<11> 1
	metastasis:periferal nerve tumor		0	0	0	1
Musculoskele	tal system]					
ouscle	leukemic cell infiltration		<15> 0	0 0	0	<11> 1
[Body cavities	s]					
oleura	leukemic cell infiltration		<15> 0	< 9> 0	< 9> 0	<11> 1
(a) b	a: Number of animals examined at the s b: Number of animals with lesion	ite				
(JPT150)					<del> </del>	

## APPENDIX O 6

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

MOUSE: FEMALE: DEAD AND MORIBUND ANIMALS

HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

STUDY NO. : 0206 ANIMAL : MOUSE BDF1

REPORT TYPE : A1
SEX : FEMALE

2000ppm 6000ppm Group Name Control 667ppm No. of Animals on Study 19 25 17 Findings\_ 0rgan\_ [Integumentary system/appandage] skin/app <19> ⟨28⟩ <25> <17> 2 leukemic cell infiltration 2 [Respiratory system] (17) (19) ⟨28⟩ <25> nasal cavit leukemic cell infiltration 2 1 1 0 0 metastasis:periferal nerve tumor 1 (25) <17> <19> <28> trachea leukemic cell infiltration (28) <25> (17) <19> lung 7 7 9 leukemic cell infiltration 4 2 metastasis:liver tumor 1 1 2 3 metastasis:uterus tumor [Hematopoietic system] <19> ⟨28⟩ ⟨25⟩ (17) bone marrow leukemic cell infiltration 5 metastasis:liver tumor 2 2 metastasis:uterus tumor <19> ⟨28⟩ ⟨25⟩ (17) lymph node metastasis:uterus tumor 1 0 1 <19> ⟨28⟩ ⟨25⟩ <17> spleen leukemic cell infiltration 6 5 8 6 (a)

(JPT150)

BAIS3

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

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : FEMALE HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

}rgan	Findings	Group Name No. of Animals on Study	Control 19	667.ppm 28	2000ppm 25	6000ppm 17
Hematopoieti	c system]					
spleen	metastasis:liver tumor		<19> 0	<28> 1	<25> 1	<17> 0
	metastasis:uterus tumor		0	2	0	0
Circulatory	system]					
neart	leukemic cell infiltration		<19> 4	<28>	<25> 2	<17> 1
	metastasis:uterus tumor		1	0	1	0
Digestive sy	stem]					
congue	leukemic cell infiltration		<19> 2	<28> 1	<25> 2	<17> 1
salivary gl	leukemic cell infiltration		<19> 4	<28> 3	<25> 6	<17> 0
	metastasis:uterus tumor		1	0	0	0
esophagus	leukemic cell infiltration		<19> 0	<28> 0	<25> 0	<17>
stomach	leukemic cell infiltration		<19> 5	<28> 4	<25> 3	<17>
	metastasis:uterus tumor		1	1	1	3
small intes	leukemic cell infiltration		<19> 1	<28> 0	<25> 0	<17> 0
arge intes	leukemic cell infiltration		<19> 1	<28> 0	<25> 0	<17> 0
(a) b	a : Number of animals examined at b : Number of animals with lesion	the site	,,	and the control of th		the state of the s

STUDY NO. : 0206 ANIMAL : MOUSE BDF1 UNISTOLOGICAL FINDINGS: METASTASIS OF TUMOR (SUMMARY)
DEAD AND MORIBUND ANIMALS (0-105W)

REPORT TYPE : A1

SEX : FEMALE

rgan	Findings	Group Name No. of Animals on Study	Control 19	667ppm 28	2000ppm 25	6000ppm 17
Digestive sy	rstem!					
iver.	leukemic cell infiltration		<19> 5	<28> 4	<25> 8	<17> 3
	metastasis:uterus tumor		5	7	5	7
eancreas	leukemic cell infiltration		<19> 2	<28> 3	<25> 5	<17> 1
	metastasis:uterus tumor		1	1	3	0
[Urinary syst	tem]					
cidney	leukemic cell infiltration		<19> 6	<28> 5	<25> 8	<17> 4
	metastasis:uterus tumor		1	3	1	4
rin bladd	leukemic cell infiltration		<19> 3	<28> 3	<25> 4	<17> 0
	metastasis:uterus tumor		1	4	0	0
Endocrine sy	/stem]					
pituitary	leukemic cell infiltration		<19> 1	<28> 0	<25> 0	<17> 0
thyroid	leukemic cell infiltration		<19> 1	<28> 0	<25> 1	<17>. 0
adrenal	leukemic cell infiltration		<19> 3	<28> 1	<25> 5	<17> 1
[Reproductive	e system]					
ovary	leukemic cell infiltration		<19>	<28> 4	<25> 6	<17> 5
(a) b	a: Number of animals examined at the s b: Number of animals with lesion	ite				

ANIMAL : MOUSE BDF1

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

REPORT TYPE : A1 : FEMALE SEX

PAGE: 7

6 Organ	Findings	Group Name No. of Animals on Study	Control 19	667ppm 28	2000ppm 25	6000ppm 17
[Reproductive	system]					
avary	metastasis:liver tumor		<19> 1	<28> 0	<25> 0	<17> 0
	metastasis:uterus tumor		4	4	4	7
	metastasis:retroperitoneum tumor		0	0	1	0
uterus	leukemic cell infiltration		<19> 2	<28> 2	<25> 5	<17> 0
vagina	leukemic cell infiltration		<19> 2	<28> 1	<25> 2	<17> 0
mammary gl	leukemic cell infiltration		<19> 1	<28> 0	<25> 2	<17> 0
[Nervous syste	em]					
brain	leukemic cell infiltration		<19> 1	<28> 0	<25> 1	<17> 0
	metastasis:periferal nerve tumor		0	1	0	0
spinal cord	leukemic cell infiltration		<19>	<28> 0	<25> 1	<17> 0
[Special sense	e organs/appandage]					
өуө	leukemic cell infiltration		<19> 3	<28> 0	<25> 2	<17> 0
Harder gl	leukemic cell infiltration		<19> 2	<28> 3	<25> 3	<17> 0
(a)	a: Number of animals examined at the b: Number of animals with lesion	site	· · · · · · · · · · · · · · · · · · ·			

HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

ANIMAL : MOUSE BDF1

REPORT TYPE : A1
SEX : FEMALE

Organ		Group Name No. of Animals on Study	Control 19	667.ppm 28	2000ppm 25	6000ppm 17
Musculaskele	tal system]					
muscle	leukemic cell infiltration		<19> 2	<28> 4	<25> 3	<17> 1
	metastasis:retroperitoneum tumor		0	0	1	0
Body cavitie	[s					
nediastinum	leukemic cell infiltration		<19> 1	<28> 0	<25> 0	<17> 0
peritoneum	leukemic cell infiltration		<19> 1	<28> 0	<25> 1	<17> 0
(a) b	a: Number of animals examined at the si b: Number of animals with lesion	te			4444-11-0444-19-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1-1	
(JPT150)						

### APPENDIX O 7

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

MOUSE: MALE: SACRIFICED ANIMALS

STUDY NO. : 0206 ANIMAL : MOUSE BDF1 HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY) SACRIFICED ANIMALS (105W)

REPORT TYPE : A1
SEX : MALE

(JPT150)

Organ	Findings	Group Name No. of Animals on Study	Control 35	667ppm 41	2000ppm 41	6000ppm 39
	. 1			The second secon		·
[Respiratory	systemj					
lung	leukemic cell infiltration		<35> 1	<41> 1	<41> 2	<39> 1
	metastasis:liver tumor		1	0	0	1
(Hematopoieti	c system]					
bone marrow	leukemic cell infiltration		<35> 0	<41> 1	<41> 1	<39> 0
spleen	leukemic cell infiltration		<35> 0	<40> 4	<41> 3	<39> 3
[Digestive sy	stem]					
stomach	leukemic cell infiltration		<35> 0	<41> 0	<41> 1	<39> 0
small intes	leukemic cell infiltration		<35> 0	<41> 0	<41> 0	<39> 1
liver	leukemic cell infiltration		<35> 1	<41> 2	<41> 3	<39> 1
pancreas	leukemic cell infiltration		<35> 0	<41> 0	<41> 1	<39> 0
[Urinary syst	cem]					
kidney	leukemic cell infiltration		<35> 1	<41> 1	<41> 1	<39> 2
urin bladd	leukemic cell infiltration		<35> 0	<41>	<41> 0	<39>

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

ANIMAL : MOUSE BDF1
REPORT TYPE : A1

REPORT TYPE : A1
SEX : MALE

Organ	Findings	Group Name No. of Animals on Study	Contral 35	667ppm 41	2000ppm 41	6000ppm 39
Reproductive	eveteml					
	5,500,17					
rostate	leukemic cell infiltration		<35> 0	<41> 0	<41> 1	<39> 0
rep/cli gl	metastasis:salivary gland tumor		<35> 0	<41> 0	<41>	<39> 0
a >	a: Number of animals examined at the b: Number of animals with lesion	site				
(JPT150)						

#### APPENDIX O 8

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

MOUSE: FEMALE: SACRIFICED ANIMALS

ANIMAL : MOUSE BDF1

REPORT TYPE : A1
SEX : FEMALE

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

Organ		Group Name No. of Animals on Study	Control 31	667ppm 22	2000:ppm 25	6000ppm 32
[Integumentary	y system/appandage]					
skin/app	leukemic cell infiltration		<31> 0	<22> 1	<25> 0	<32> 0
[Respiratory :	system]					
trachea	leukemic cell infiltration		<31> 0	<22> 0	<25> 0	<32> 1
ung	leukemic cell infiltration		<31> 4	<22> 4	<25> 1	<32> 1
	metastasis:liver tumor		0	0	0	1
[Hematopoietio	c system]					
oone marrow	leukemic cell infiltration		<31> 3	<22> 3	<25> 1	<32> 1
spleen	leukemic cell infiltration		<31> 2	<22> 4	<25> 3	<32> 1
	metastasis:liver tumor		0	0	0	1
Digestive sy:	stem]					
tongue	metastasis:subcutis tumor		<31> 0	<22> 0	<25> 1	<32> 0
salivary gl	leukemic cell infiltration		<31> 6	<22> 7	<25> 2	<32> 0
	metastasis:uterus tumor		0	0	1	0
⟨a⟩ b	a: Number of animals examined at the si b: Number of animals with lesion	te				

- HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR (SUMMARY)

ANIMAL : MOUSE BDF1 REPORT TYPE : A1

(JPT150)

SEX : FEMALE SACRIFICED ANIMALS (105W)

PAGE: 4 Group Name Control 667ppm 2000ppm 6000ppm 22 25 32 No. of Animals on Study 31 Findings\_ 0rgan\_ [Digestive system] ⟨31⟩ ⟨22⟩ ⟨25⟩ ⟨32⟩ stomach 1 1 leukemic cell infiltration 2 metastasis:uterus tumor 0 1 <31> (22> ⟨25⟩ ⟨32⟩ small intes metastasis:uterus tumor 0 liver ⟨31⟩ (22) ⟨25⟩ ⟨32⟩ leukemic cell infiltration 3 1 1 metastasis:uterus tumor 1 pancreas ⟨31⟩ ⟨22⟩ ⟨25⟩ ⟨32⟩ leukemic cell infiltration 0 0 0 1 metastasis:uterus tumor [Urinary system] kidney (31) <22> (25) <32> leukemic cell infiltration 1 0 1 0 metastasis:uterus tumor ⟨31⟩ (22) ⟨32⟩ urin bladd <25> leukemic cell infiltration 3 1 1 [Endocrine system] ⟨31⟩ ⟨22⟩ <25> <32> pituitary leukemic cell infiltration 0 adrenal ⟨31⟩ <22> <25> ⟨32⟩ leukemic cell infiltration 0 1 0 (a) a: Number of animals examined at the site b b: Number of animals with lesion

BAIS3

ANIMAL : MOUSE BDF1

REPORT TYPE : A1

SEX : FEMALE

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

	i	Group Name No. of Animals on Study	Control 31	667ppm 22	2000ppm 25	6000ppm 32
Organ	Findings					
fn i i						
[Reproductive	systemj					
DUary			⟨31⟩	<22>	<25>	⟨32⟩
	leukemic cell infiltration		0	1	1	0
	metastasis:uterus tumor		0	1	0	1
					4000	(00)
uterus	landamia and indidentia		<31>	<22> 4	<25>	<32>
	leukemic cell infiltration		V	4	1	1
vagina			⟨31⟩	<22>	<25>	⟨32⟩
	leukemic cell infiltration		0	3	0	0
[Body cavities	s]					
mediastinum			⟨31⟩	⟨22⟩	⟨25⟩	⟨32⟩
HOU! 45 LIFIUIII	leukemic cell infiltration		0	1	0	0
			4043	(00)	(05)	(00)
adipose	metastasis:uterus tumor		<31>	<22> 0	<25> 0	<32> 0
	metastasis•uterus tumor			V	V	V
(a)	a : Number of animals examined at the si	te				
b	b: Number of animals with lesion					
(JPT150)				P		

# APPENDIX P 1 IDENTITY OF BIPHENYL (TOW-YERA STUDY)

#### IDENTITY OF BIPHENYL (TWO-YEAR STUDIES)

Test Substance Lot No. TWN6529

1. Spectral data

#### (1) Mass Spectrometry

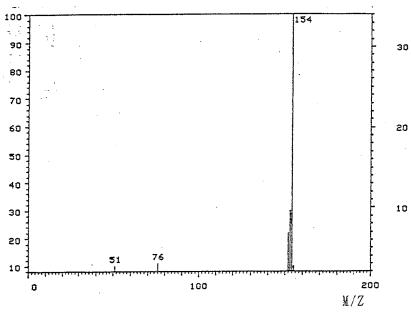
Instrument

: Hitachi M-80B Mass Spectrometer

Ionization

: EI(Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Results: The mass spectrum was consistent with Literature spectrum.

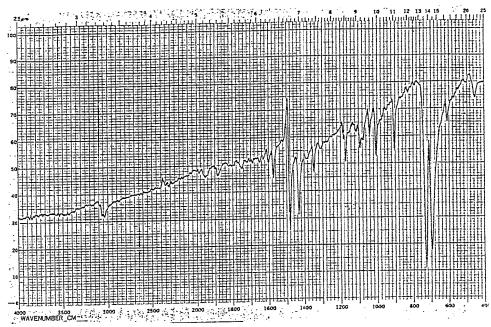
<u>Determined</u>	<u>Literature Value*</u>			
Molecular and Fragment Peak(M/Z)	Molecular and Fragment Peak(M/Z)			
154	154			
76	76			
51	51			
	(*EPA/NIH Mass Spectral			
	Data Base (1978) V. 1,			
	p. 529.)			

#### (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(cm <sup>-1</sup> )	Wave Number(cm <sup>-1</sup> )
440~ 480	430~ 480
600~ 620	600~ 620
650~ 710	650~ 710
710~ 750	710~ 750
880~ 910	890~ 910
990~1020	990~1010
1020~1050	$1020 \sim 1050$
1050~1100	1050~1120
1150~1180	1150~1170
1330~1360	$1330 \sim 1350$
1400~1450	$1400 \sim 1450$
1460~1490	$1460 \sim 1490$
1550~1580	1550~1580
$1730 \sim 1770$	$1730 \sim 1770$
1870~1890	1860~1890
1930~1970	1930~1970
2990~3100	2990~3100
	3300~3500
	(*Sadtler Handbook
	by Sadtler Research
	Laboratories, Inc.
	(1978) p. 68.)

2. Conclusions: The result of the mass spectrum and the infrared spectrum agreed with the literature values.

Consequently, the test substance was identified as Biphenyl.

### APPENDIX P 2

STABILITY OF 1BIPHENYL
(TOW-YERA STUDY)

#### STABILITY OF BIPHENYL (TWO-YEAR STUDIES)

#### Test Substance Lot No. TWN6529

1. Sample storage: This lot was used from 1992.6.1 to 1994.6.29. Test substance was stored in the dark at room temperature.

#### 2. Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell

: KBr

Slit

: Medium

Results

: The result of the infrared spectrum did not change when

before and after studies.

1992.05.29(date analyzed)	1994.07.01(date analyzed)
Wave Number(cm <sup>-1</sup> )	Wave Number(cm <sup>-1</sup> )
440~ 480	440~ 480
600~ 620	600~ 620
650~ 710	650~ 710
710~ 750	710~ 750
880~ 910	880~ 910
990~1020	990~1020
1020~1050	$1020 \sim 1050$
1050~1100	$1050 \sim 1100$
1150~1180	1150~1180
1330~1360	1330~1360
1400~1450	$1400 \sim 1450$
1460~1490	$1460 \sim 1490$
1550~1580	1550~1580
1730~1770	$1730 \sim 1770$
1870~1890	1870~1890
1930~1970	$1930 \sim 1970$
2990~3100	2990~3100

#### 3. Gas Chromatography

Instrument : Hewlett Packard 5890A Gass Chromatograph

Column

)

: Methyl Silicone(0.2mm $\phi imes50$ m)

Column Temperature : 180°C

Flow Rate : 1 ml/min

Detector

: FID(Flame Ionization Detector)

Injection Volume : 1  $\mu$ 1

Results: Chromatogram indicated one major peak analyzed except solvent peak (acetone) at 1992.5.29 and one major peak analyzed except solvent peak(acetone) at 1994.7.1. No new trace impurity peak in the test substance analyzed at 1994.7.1 was detected.

Date	Retention Time(min)	AREA	
1992.05.29 (date analyzed)	3. 752	682	
1994.07.01 (date analyzed)	3. 752	675	

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

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# APPENDIX P 3 CONCENTRATION OF BIPHENYL IN FORMULATED DIETS IN RAT (TOW-YERA STUDY)

#### CONCENTRATION OF BIPHENYL IN FORMULATED DIETS(TWO-YEAR STUDIES)

(Rat)

	Target Concentration(ppm)			
Date analyzed	500	1500	4500	
1992.05.29	444( 88.8)*	1513(100.9)	4146(-92.1)	
1992. 08. 31	434( 86.8)	1362( 90.8)	4198( 93.3)	
1992. 11. 17	484( 96.8)	1425( 95.0)	4245( 94.3)	
1993. 02. 25	467( 93.4)	1438( 95.9)	4229( 94.0)	
1993. 05. 24	470( 94.0)	1371( 91.4)	4103( 91.2)	
1993.09.10	455( 91.0)	1380( 92.0)	4232( 94.0)	
1993. 12. 13	431( 86.2)	1417( 94.5)	4426( 98.4)	
1994.03.30	473( 94.6)	1436( 95.7)	4234( 94.1)	

<sup>\* : %</sup> of target concentration

Analytical method: The samples were analyzed by the GC.

Instrument : Hewlett Packard 5890A

Column : METHYL SILICONE(0.2mm $\phi \times 50$ m)

Detector

Flow Rate

: 1ml/min : FID(Flame Ionization detector)

Column Temperature: 180°C

Carrier

: He

Injection Volume

 $: 1 \mu 1$ 

# APPENDIX P 4 CONCENTRATION OF BIPHENYL IN FORMULATED DIETS IN MOUSE (TOW-YERA STUDY)

#### CONCENTRATION OF BIPHENYL IN FORMULATED DIETS(TWO-YEAR STUDIES)

#### (Mouse)

	Target C		
Date analyzed	667	2000	6000
1992.06.17	621( 93.1)*	2236(111.8)	5575( 92.9)
1992.08.31	567( 85.0)	1814( 90.7)	5585( 93.1)
1992.11.17	602( 90.3)	1774( 88.7)	5280( 88.0)
1993.02.25	528( 79.2)	1955( 97.8)	5838( 97.3)
1993.05.24	608( 91.2)	1836( 91.8)	5443( 90.7)
1993.09.10	596( 89.4)	1868( 93.4)	5603( 93.4)
1993.12.13	566( 84.9)	1865( 93.3)	5736( 95.6)
1994.03.30	629( 94.3)	1874( 93.7)	5803( 96.7)

<sup>\* : %</sup> of target concentration

Analytical method: The samples were analyzed by the GC.

: Hewlett Packard 5890A Instrument

Column : METHYL SILICONE(0.2mm $\phi \times 50$ m) Flow Rate : lml/min

Detector

: FID(Flame Ionization Detector)

Column Temperature: 180°C Carrier

: He

Injection Volume  $: 1 \mu 1$ 

# APPENDIX P 5 STABILITY OF BIPHENYL IN FORMULATED DIETS (TOW-YERA STUDY)

#### STABILITY OF BIPHENYL IN FORMULATED DIETS(TWO-YEAR STUDIES)

#### (Rat)

_	Target Concentration(ppm)			
Date analyzed	500	1500	4500	
1992.05.29(a)	444	1513	4146	
1992.10.23(b)	458	1412	4181	

#### (Mouse)

_		Target Concentration(ppm)	ration(ppm)	
Date analyzed	667	2000	6000	
1992.06.17(a)	621	2236	5575	
1992.11.24(b)	556	2152	5485	

<sup>(</sup>a) Date of preparation

Analytical method: The samples were analyzed by the GC.

Instrument

: Hewlett Packard 5890A

Flow Rate

: lml/min

Column

: METHYL SILICONE(0.2mm $\phi \times 50$ m)

Detector

: FID(Flame Ionization Detector)

Column Temperature: 180°C

Injection Volume

 $: 1 \mu 1$ 

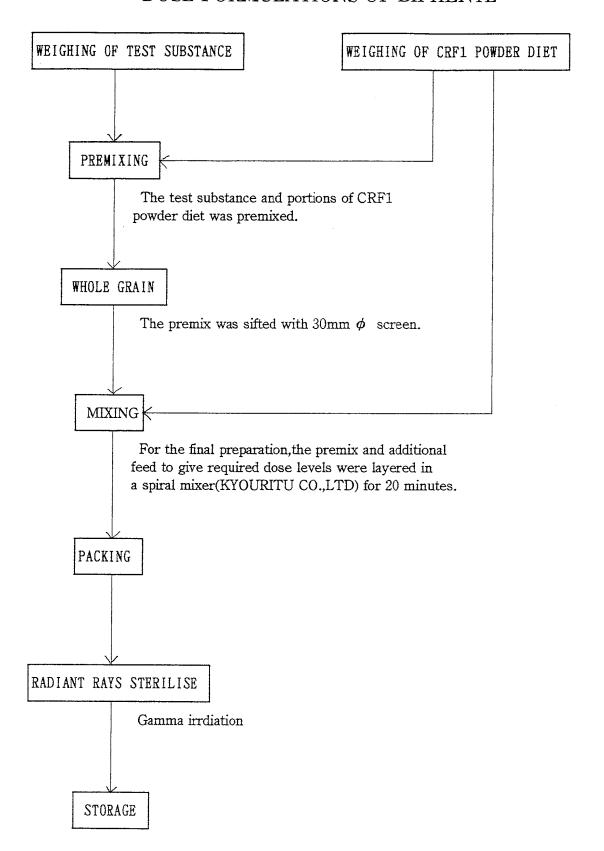
Carrier

: He

<sup>(</sup>b) The stability of biphenyl in formulated diets was established for 5 months when stored at 5°C.

## APPENDIX Q 1 DOSE FORMULATIONS IN BIPHENYL

#### DOSE FORMULATIONS OF BIPHENYL



### APPENDIX R 1

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS

#### METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS

Item	Method	Unit
Hematology		
Red blood cell(RBC)	Light scattering method <sup>1)</sup>	$\times 10^6/\mu$
Hemoglobin(Hgb)	Cyanmethohemoglobin method <sup>1)</sup>	g/dl
Hematocrit(Hct)	Calculated as RBC $\times$ MCV/10 <sup>1)</sup>	%
Mean corpuscular volume(MCV)	Light scattering method <sup>1)</sup>	fl
Mean corpuscular hemoglobin(MCHC)	Calculated as Hgb / RBC $ imes$ $10^{1)}$	pg
Mean corpuscular hemoglobin concentration(MCHC)	Calculated as Hgb / Hct $\times$ 100 <sup>1)</sup>	g/dl
Platelet	Light scattering method <sup>1)</sup>	$\times 10^3/\mu$ 1
Reticulocyte	Pattern recognition method <sup>3)</sup>	%
	(New methyleneblue staining)	
Prothrombin time	Quick one stage method <sup>2)</sup>	sec.
Activated partial thromboplastin time(APTT)	Ellagic acid activated method <sup>2)</sup>	sec.
White blood cell(WBC)	Light scattering method <sup>1)</sup>	$\times 10^3/\mu 1$
Differential WBC	Pattern recognition method <sup>3)</sup>	%
	(May-Grunwald-Giemsa staining)	
Biochemistry	V-1	<del>                                     </del>
Total protein(TP)	Biuret method <sup>4)</sup>	g/dl
Albumin(Alb)	BCG method <sup>4)</sup>	g/dl
A/G ratio	Calculated as Alb / (TP-Alb)4)	
T-bilirubin	Alkaline azobilirubin method <sup>4)</sup>	mg/dl
Glucose	Enzymatic method(GLK·G-6-PDH) <sup>4)</sup>	mg/dl
T-cholesterol	Enzymatic method(CE·COD·POD) <sup>4)</sup>	mg/dl
Triglyceride	Enzymatic method(LPL·GK·GPO·POD) <sup>4)</sup>	mg/dl
Phospholipid	Enzymatic method(PLD·COD·POD) <sup>4)</sup>	mg/dl
Glutamic oxaloacetic transaminase(GOT)	IFCC Method <sup>4)</sup>	IU/I
Glutamic pyruvic transaminase(GPT)	IFCC Method <sup>4)</sup>	IU/l
Lactate dehydrogenase(LDH)	Wroblewski-Ladue method4)	IU/I
Alkaline phosphatase(ALP)	GSCC method <sup>4)</sup>	IU/I
$\gamma$ -Glutamyl transpeptidase(G-GTP)	L-γ-Glutamyl-p-nitroaniline substrate method <sup>4)</sup>	IU/I
Creatine phosphokinase(CPK)	GSCC method <sup>4)</sup>	IU/I
Urea nitrogen	Enzymatic method(Urease · GLDH) <sup>4)</sup>	mg/dl
Creatinine	Jaffe method <sup>4)</sup>	mg/dl
Sodium	Ion selective electrode method <sup>4)</sup>	mEq/l
Potassium	Ion selective electrode method <sup>4)</sup>	mEq/I
Chloride	Ion selective electrode method <sup>4)</sup>	mEq/I
Calcium	OCPC method <sup>4)</sup>	mg/dl
Inorganic phosphorus	Enzymatic method(PNP·XOD·POD) <sup>4)</sup>	mg/dl
Urinalysis		
pH, Protein, Glucose, Ketone body	Urinalysis reagent paper method <sup>5)</sup>	
Bilirubin, Occult blood, Urobilinogen		
Automatic blood cell analyzer (Technicon H.1 · Techni		

<sup>1)</sup>Automatic blood cell analyzer (Technicon H·1: Technicon Instruments Corporation, USA)

<sup>2)</sup> Automatic coagulometer (Sysmex Ca-500 : Toa Medical Electronics Co., Ltd. , Japan)

<sup>3)</sup>Automatic blood cell differential analyzer (Hitachi 8200 : Hitachi, LTD., Japan)

<sup>4)</sup> Automatic analyzer (Hitachi 7070 : Hitachi, LTD., Japan)

<sup>5)</sup>Ames reagent strips for urinalysis (Multistix, Uro-Labstix: Bayer-Sankyo Co., LTD., Japan)

### APPENDIX R 2

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

#### UNIT AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

	TEST ITEM	DECIMAL PLACE	UNIT
HEMATOLOGY	Red blood cell	2	$\times 10^{6}/\mu 1$
	Hemoglobin	1	g/dl
	Hematorcit	1	%
	MCV	1	fl
	MCH	1	pg
	MCHC	1	g/dl
	Platelet	0	$\times 10^3/\mu$
	Prothorombin time	1	sec.
	APTT	1	sec.
	White blood cell	2	$\times 10^{3}/\mu 1$
	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/I
	GPT	0	IU/I
	LDH	0	IU/I
	ALP	0	IU/I
	γ-GTP	0	IU/I
	СРК	0	IU/I
	Urea nitrogen	1	mEq/l
	Creatinine	1	mg/dl
	Sodium	0	mEq/l
	Potassium	1	mEq/I
	Chloride	0	mEq/l
	Calcium	1	mEq/l
	Inorganic phosphorus	. 1	mEq/l