1,3,5,7-テトラアザトリシクロ [3.3.1.1^{3,7}] デカンの ラット及びマウスを用いた経口投与による が ん 原 性 試 験 (混 水 試 験) 報 告 書

APPENDIX

 $(L1\sim R2)$

APPENDIXES (CONTINUED)

- APPENDIX L 1 HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (TOW-YEAR STUDY : SUMMARY)

 RAT : MALE : DEAD AND MORIBUND ANIMALS
- APPENDIX L 3 HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (TOW-YEAR STUDY : SUMMARY)
 RAT :MALE SACRIFICED ANIMALS
- APPENDIX L 4 HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (TOW-YEAR STUDY : SUMMARY)

 RAT : FEMALE : SACRIFICED ANIMALS
- APPENDIX L 5 HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (TOW-YEAR STUDY : SUMMARY)

 MOUSE : MALE : DEAD AND MORIBUND ANIMALS
- APPENDIX L 6 HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (TOW-YEAR STUDY : SUMMARY)

 MOUSE : FEMALE : DEAD AND MORIBUND ANIMALS
- APPENDIX L 8 HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (TOW-YEAR STUDY : SUMMARY STUDY)

 MOUSE : FEMALE : SACRIFICED ANIMALS
- APPENDIX M 1 NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS-TIME RELATED ${\rm RAT: MALE}$
- APPENDIX M 2 NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS-TIME RELATED RAT : FEMALE
- APPENDIX M 3 NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS-TIME RELATED MOUSE : MALE
- APPENDIX M 4 NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS-TIME RELATED MOUSE: FEMALE

APPENDIXES (CONTINUED)

- APPENDIX N 1 HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (TOW-YEAR STUDY : SUMMARY)

 RAT : MALE
- APPENDIX N 2 HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (TOW-YEAR STUDY : SUMMARY)
 RAT : FEMALE
- APPENDIX M 3 HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS(TOW-YEAR STUDY : SUMMARY)

 MOUSE : MALE
- APPENDIX M 4 HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (TOW-YEAR STUDY : SUMMARY)

 MOUSE : FEMALE
- APPENDIX O 1 NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS, RAT: MALE
- APPENDIX O 2 NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS, RAT: FEMALE
- APPENDIX O 3 NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS, MOUSE: MALE
- APPENDIX O 4 NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS, MOUSE: FEMALE
- APPENDIX P 1 HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR(TOW-YEAR STUDY : SUMMARY)

 RAT : MALE : DEAD AND MORIBUND ANIMALS
- APPENDIX P 2 HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (TOW-YEAR STUDY : SUMMARY)

 RAT : FEMALE : DEAD AND MORIBUND ANIMALS
- APPENDIX P 3 HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (TOW-YEAR STUDY : SUMMARY)

 RAT : MALE : SACRIFICED ANIMALS
- APPENDIX P 4 HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (TOW-YEAR STUDY : SUMMARY)

 RAT : FEMALE : SACRIFICED ANIMALS
- APPENDIX P 5 HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (TOW-YEAR STUDY : SUMMARY)

 MOUSE : MALE : DEAD AND MORIBUN ANIMALS
- APPENDIX P 6 HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (TOW-YEAR STUDY : SUMMARY)

 MOUSE : FEMALE : DEAD AND MORIBUN ANIMALS

APPENDIXES (CONTINUED)

- APPENDIX P 7 HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (TOW-YEAR STUDY : SUMMARY)

 MOUSE : MALE : SACRJFICED ANIMALS
- APPENDIX P 8 HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR(TOW-YEAR STUDY : SUMMARY)

 MOUSE : FEMALE : SACRIFICED ANIMALS
- APPENDIX Q 1 IDENTITY OF UROTROPIN (TOW-YEAR STUDIES)
- APPENDIX Q 2 STABILITY OF UROTROPIN (TOW-YEAR STUDIES)
- APPENDIX Q 3 CONCENTRATION OF UROTROPIN IN DRINKING WATER (TOW-YEAR STUDIES:RAT)
- APPENDIX Q 4 CONCENTRATION OF UROTROPIN IN DRINKING WATER (TOW-YEAR STUDIES:MOUSE)
- APPENDIX Q 5 STABILITY OF UROTROPIN IN DRINKING WATER (TOW-YEAR STUDIES)
- APPENDIX R 1 METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS
- APPENDIX R 2 UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

APPENDIX L 1

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

RAT: MALE: DEAD AND MORIBUND ANIMALS

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

: MALE

SEX

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

PAGE: 1

0rgan	Group No. of Grade Findings	Name Control Animals on Study 12 1 2 3 4 (%) (%) (%) (%)	7500 ppm 11 1 2 3 4 (%) (%) (%) (%)	15000 ppm 16 1 2 3 4 (%) (%) (%) (%)	30000 ppm 20 1 2 3 4 (%) (%) (%) (%)
[Respiratory :	system]				
nasal cavit	ulcer	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	(16) 0 1 0 0 (0) (6) (0) (0)	<20> 0 0 0 0 0 0 0 0 0 0 0
	thrombus	0 0 1 0, (0) (8) (0)	1 0 0 0 0 (9) (0) (0)	0 4 1 0 (0) (25) (6) (0)	0 4 4 0 (0) (20) (20) (0)
	mineralization	5 0 0 0 (42) (0) (0) (0)	9 0 0 0 (82) (0) (0) (0)	4 0 0 0 0 (25) (0) (0) (0)	11 0 0 0 (55) (0) (0) (0)
	eosinophilic change:alfactory epithelium	7 1 0 0 (58) (8) (0) (0)	8 0 0 0 (73) (0) (0) (0)	7 0 0 0 (44) (0) (0) (0)	4 0 0 0 * (20) (0) (0)
	eosinophilic change:respiratory epithelium	2 0 0 0 (17) (0) (0) (0)	2 0 0 0 (18) (0) (0) (0)	5 0 0 0 (31) (0) (0) (0)	2 0 0 0 (10) (0) (0) (0)
	inflammation:foreign body	4 2 0 0 (33) (17) (0) (0)	1 0 0 0 0 (9) (0) (0)	3 0 0 0 0 (19) (0) (0) (0)	3 0 1 0 (15) (0) (5) (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)	1 0 0 0 (5) (0) (0) (0)
	respiratory metaplasia:olfactory epithelium	2 0 0 0 0 (17) (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 (13) (0) (0) (0)	(0) (0) (0) (0)

Grade 1 : Slight 2 : Moderate <a>>

a : Number of animals examined at the site

b b: Number of animals with lesion (c) c:b/a*100

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

3 : Marked

4 : Severe

(HPT150)

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

SEX : MALE

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

DEAD AND MORIBUND AND

Organ	Findings	Group Name Control No. of Animals on Study 12 Grade 1 2 3 4 (%) (%) (%) (%)	7500 ppm 11 1 2 3 4 (%) (%) (%) (%)	15000 ppm 16 1 2 3 4 (%) (%) (%) (%)	30000 ppm 20 1 2 3 4 (%) (%) (%) (%)
[Respiratory	system]				
nasal cavit	respiratory metaplasia:gland	\$\begin{array}{cccccccccccccccccccccccccccccccccccc	<pre></pre>	\(\langle 16 > \) \(\begin{array}{cccccccccccccccccccccccccccccccccccc	(20) 14 0 0 0 (70) (0) (0) (0)
nasopharynx	inflammation	<12> 0 0 1 0 (0) (0) (8) (0)	<11> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<16> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<20> 0 0 0 0 (0) (0) (0) (0)
Larynx	inflammation	<12> 0 0 0 0 0 0 0 0 0 0 0	<11> 0 0 0 0 0 0 0 0 0 0 0 0	<16> 0 1 0 0 (0) (6) (0) (0)	<20> 0 1 0 0 (0) (5) (0) (0)
trachea	inflammation	(12) 0 1 0 0 (0) (8) (0) (0)	0 0 0 0 (0) (0) (0) (0)	<16> 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<20> 0 0 0 0 0 0 0 0 0 0 0
lung	hemorrhage	(12) 0 0 0 0 (0) (0) (0) (0)	0 0 1 0 (0) (0) (9) (0)	\(\lambda \) \(<20> 0 1 0 0 (0) (5) (0) (0)
	edema	0 0 0 0 0 (0) (0)	0 0 0 0	0 1 0 0 (0) (6) (0) (0)	0 0 0 0 0 (0) (0)
	thrombus	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0) (0)	0 0 1 0 (0) (6) (0)	0 0 0 0 0 (0) (0)
Grade	1: Slight 2: Moderate	3 : Marked 4 : Severe			

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

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

b b: Number of animals with lesion

(c) c:b/a*100

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

(HPT150)

BAIS3

REPORT TYPE : A1 SEX : MALE HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

PAGE: 3

Organ	Findings	Group Name Contro No. of Animals on Study 12 Grade 1 2 (%) (%)	\(\frac{3}{\%}\) \(\frac{4}{\%}\) \(\frac{1}{\%}\)	7500 ppm 11 2 3 4 (%) (%) (%)	15000 ppm 16 1 2 3 4 (%) (%) (%) (%)	30000 ppm 20 1 2 3 4 (%) (%) (%) (%)
[Respiratory s	system]					
ung	inflammation	(12> 0 0 (0) (0) (0 0 2	<11> 0 1 0 (0) (9) (0)	<pre></pre>	<20> 0 0 0 0 0 0 0 0 0 0 0
	accumulation of foamy cells	1 0 (8) (0) (0 0 1 0) (9)	0 0 0 0 (0) (0)	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
	bronchiolar-alveolar cell hyperplasi	0 0 (0) (0) (0 0 1 0 (9)	0 0 0 0 (0)	0 0 0 0 0 (0) (0)	0 1 0 0 (0) (5) (0) (0)
Hematopoieti	c system]					
one marrow	necrosis:focal	(12) 0 0 (0) (0) (0 0 0	<11> 0 0 0 0 (0) (0) (0)	<16> 0 1 0 0 (0) (6) (0) (0)	<20> 0 0 0 0 0 0 0 0 0 0 0 0 0
	increased hematopoiesis	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)
	erythropoiesis:increased	2 0 (17) (0) (0 0 0 0	4 0 0 * (36) (0) (0)	1 3 0 0 (6) (19) (0) (0)	1 3 0 0 (5) (15) (0) (0)
	granulopoiesis:increased	(0) (0) (0 0 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) (6) (0)	0 0 0 0 0 0 (0) (0)
Grade (a > b (c) Significant d	1: Slight 2: Moderate a: Number of animals examined at the b: Number of animals with lesion c: b / a * 100 lifference; *: P ≤ 0.05 **: P					

(HPT150)

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

REPORT TYPE : A1

SEX : MALE

PAGE: 4

0rgan	Findings	Group Name Control No. of Animals on Study 12 Grade 1 2 3 4 (%) (%) (%) (%) (%)	7500 ppm 11 1 2 3 4 (%) (%) (%) (%)	15000 ppm 16 1 2 3 4 (%) (%) (%) (%)	30000 ppm 20 1 2 3 4 (%) (%) (%) (%)
[Hematopoieti	c system]				
lymph node	granulation	2 0 0 0 0 (17) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	<20> 0 0 0 0 0 0 0 0 0 0 0
	lymphadenitis	(0) (0) (0) (0)	0 0 0 0 0 0 (0) (0)	0 0 1 0 (0) (6) (0)	0 0 0 0 0 0 (0) (0)
spleen	atrophy	<12> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 (0) (0) (0) (0)	<16> 1 0 0 0 (6) (0) (0) (0)	<20> 0 1 0 0 (0) (5) (0) (0)
	deposit of hemosiderin	0 2 0 0 (0) (17) (0) (0)	0 2 0 0 (0) (18) (0) (0)	0 3 0 0 (0) (19) (0) (0)	0 8 0 0 (0) (40) (0) (0)
	fibrosis	0 0 0 0 0 (0)	1 0 0 0 0 (9) (0) (0)	0 0 0 0 0 0 (0) (0)	1 0 0 0 0 (5) (0) (0)
	SCAF .	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 1 0 (0) (6) (0)	0 0 0 0 0 (0) (0)
	extramedullary hematopoiesis	0 0 0 0 0 (0) (0)	0 2 1 0 (0) (18) (9) (0)	1 1 3 0 (6) (6) (19) (0)	0 1 1 0 (0) (5) (5) (0)
[Circulatory	system]				
heart	thrombus	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	0 1 0 0 (0) (6) (0) (0)	20> 1 0 0 0 (5) (0) (0) (0)

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

b b: Number of animals with lesion

(c) c:b/a*100

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

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

SEX : MALE

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

PAGE: 5

Organ		O Name Control of Animals on Study 12 of 1 2 3 4 of (%) (%) (%) (%)	7500 ppm 11 1 2 3 4 (%) (%) (%) (%)	15000 ppm 16 1 2 3 4 (%) (%) (%) (%)	30000 ppm 20 1 2 3 4 (%) (%) (%) (%)
(Circulatory	system]				
neart	mineralization	1 1 0 0 (8) (8) (0) (0)	0 0 0 0 (0) (0) (0) (0)	\(\lambda 1 \) \(0 \) \(6 \) \(0 \) \(0 \) \(0 \) \(0 \)	3 6 2 0 (15) (30) (10) (0)
	myocardial fibrosis	5 6 0 0 (42) (50) (0) (0)	4 7 0 0 (36) (64) (0) (0)	1 12 1 0 (6) (75) (6) (0)	2 16 1 0 (10) (80) (5) (0)
Digestive s	ystem]				
esophagus	necrosis	0 0 0 0 (0) (0) (0) (0)	0 0 1 0 (0) (0) (9) (0)	0 0 0 0 (0) (0) (0) (0)	<20> 0 0 0 0 0 0 0 0 0 0 0
stomach	edema	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	<16> 0 1 0 0 (0) (6) (0) (0)	<pre></pre>
	mineralization	0 1 1 0 (0) (8) (8) (0)	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	3 2 0 0 (15) (10) (0) (0)
	erosion:forestomach	0 1 0 0 (0) (8) (0) (0)	0 0 1 0 (0) (0) (0)	0 0 0 0 0 0 (0) (0)	0 0 0 0 0
Grade (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	rked 4 : Severe			**

(HPT150)

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

REPORT TYPE : A1
SEX : MALE

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

(HPT150)

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

⁽c) c:b/a*100 Significant difference: *:P < 0.05

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

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

SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

PAGE: 7

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

(HPT150)

c:b/a * 100

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

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

: MALE

SEX

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

PAGE: 8

Organ	Findings	Group Name Control No. of Animals on Study 12 Grade 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	15000 ppm 16 1 2 3 4 (%) (%) (%) (%)	30000 ppm 20 1 2 3 4 (%) (%) (%) (%)
[Digestive s	system]				
liver	acidophilic cell focus	2 0 0 0 (17) (0) (0) (0)	1 0 0 0 (9) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	\(\lambda 20 \rangle \) \[1 0 0 0 \\ (5) (0) (0) (0) \]
	basophilic cell focus	1 1 0 0 (8) (8) (0) (0)	1 0 0 0 (9) (9) (0) (0)	2 0 0 0 (13) (0) (0) (0)	2 0 0 0 0 (10) (10) (10) (10)
	vacuolated cell focus	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (6) (6) (0) (0)	1 0 0 0 (5) (0) (0) (0)
	spongiosis hepatis	0 0 0 0 0	0 0 0 0 0 (0) (0)	1 0 0 0 (6) (0) (0) (0)	2 1 0 0 (10) (5) (0) (0)
	bile duct hyperplasia	9 3 0 0 (75) (25) (0) (0)	7 2 0 0 (64) (18) (0) (0)	6 8 0 0 (38) (50) (0) (0)	14 4 1 0 (70) (20) (5) (0)
	bile ductular proliferation	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)
	biliary cyst	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 (0)	0 0 0 0 0 0 (0) (0)	1 0 0 0 0 (5) (0) (0) (0)
pancreas	atrophy	<12> 0 0 0 0 0 0 0 0 0 0 0	2 0 0 0 (18) (0) (0) (0)	<16> 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 (0) (0) (0) (0)

(HPT150)

Grade

<a>> b

(c)

1: Slight

c:b/a*100

2 : Moderate

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

a: Number of animals examined at the site

b: Number of animals with lesion

3 : Marked

4 : Severe

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

REPORT TYPE : A1
SEX : MALE

A1

PAGE: 9

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

(HPT150)

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

REPORT TYPE : A1 : MALE SEX

PAGE: 10

	No	oup Name . of Animals on Study	Control 12	7500 ppm	15000 ppm 16	30000 ppm 20
0rgan	Findings	ade <u>1</u> (%)	2 3 4 (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)
[Urinary syst	cem]					
kidney	mineralization:papilla	1 (8) (<12> 0 0 0 0) (0) (0)	<11> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<16> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<20> 0 0 0 0 0 0 0 0 0 0 0
	mineralization:cortex	1 (8) (1 0 0 8) (0) (0)	0 0 0 0 0 (0) (0)	2 0 0 0 (13) (0) (0) (0)	8 3 0 0 (40) (15) (0) (0)
	urothelial hyperplasia:pelivis	(0) (0 0 0 0 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)	1 2 0 0 (5) (10) (0) (0)
urin bladd	simple hyperplasia:transitional epitheli		<12> 1 0 0 8) (0) (0)	0 0 0 0 (0) (0) (0) (0)	(16) 0 1 0 0 (0) (6) (0) (0)	<pre></pre>
	nodular hyperplasia:transitional epithel		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 (9) (0) (0)	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
[Endocrine sy	vstem]					
pituitary	hyperplasia	(0) (<12> 0 0 0 0) (0) (0)	0 1 0 0 (0) (9) (0) (0)	0 1 0 0 (0) (6) (0) (0)	20> 1 0 0 0 (5) (0) (0) (0)
Grade <a>> b (c) Significant of	1: Slight 2: Moderate 3: a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 difference; *: P ≤ 0.05 **: P ≤ 0					

(HPT150)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

REPORT TYPE : A1
SEX : MALE

0rgan	Findings	Group Name Control No. of Animals on Study 12 Grade 1 2 3 4 (%) (%) (%) (%)	7500 ppm 111 1 2 3 4 (%) (%) (%) (%)	15000 ppm 16 1 2 3 4 (%) (%) (%) (%)	30000 ppm 20 1 2 3 4 (%) (%) (%) (%)
(Endocrine s	vstem]				
pituitary	Rathke pouch	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	(16) 1 0 0 0 (6) (0) (0) (0)	<20> 0 0 0 0 (0) (0) (0) (0)
thyroid	ultimibranchial body remanet	0 0 0 0 (0) (0) (0) (0)	<11> 0 0 0 0 0 0 0 0 0 0 0 0	<16> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<20> 2 0 0 0 (10) (0) (0) (0)
	C-cell hyperplasia	0 0 0 0 0 0 (0) (0)	2 0 0 0 0 (18) (0) (0) (0)	2 0 0 0 (13) (0) (0) (0)	1 1 0 0 (5) (5) (0) (0)
adrenal	hyperplasia:cortical cell	(12> 0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	(16) 1 0 0 0 (6) (0) (0) (0)	(20) (0)(0)(0)(0)(0)
	hyperplasia:medulla	0 0 0 0 0 0 (0) (0)	1 0 0 0 0 (9). (0) (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (5) (0) (0) (0)
	focal fatty change:cortex	1 0 0 0 0 (8) (0) (0)	1 0 0 0 0 (9) (0) (0)	3 0 0 0 0 (19) (0) (0)	1 1 0 0 (5) (5) (0) (0)
[Reproductive	e system]				
testis	atrophy	1 1 5 0 (8) (8) (42) (0)	0 1 6 0 (0) (9) (55) (0)	(16) 1 2 8 0 (6) (13) (50) (0)	<20> 1 1 11 0 (5) (5) (55) (0)

(c) Significa (HPT150)

Grade

< a >

b

1: Slight

c:b/a*100

2 : Moderate

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

a : Number of animals examined at the site

b: Number of animals with lesion

3 : Marked

4 : Severe

BAIS3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

ANIMAL : RAT F344 REPORT TYPE : A1

STUDY NO. : 0224

SEX : MALE

0rgan	Findings	Group Name Control No. of Animals on Study 12 Grade 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	15000 ppm 16 1 2 3 4 (%) (%) (%) (%)	30000 ppm 20 1 2 3 4 (%) (%) (%) (%)
[Reproductive	e system]				
testis	mineralization	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	(16) 2 0 0 0 (13) (0) (0) (0)	6 0 0 0 (30) (0) (0) (0)
	arteritis	0 0 0 0 0 (0) (0)	1 0 0 0 0 (9) (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
	interstitial cell hyperplasia	5 0 0 0 (42)(0)(0)(0)	3 0 0 0 (27) (0) (0) (0)	7 0 0 0 (44) (0) (0) (0)	1 0 0 0 *
prostate	inflammation	1 0 0 0 (8) (0) (0) (0)	<11> 2 1 0 0 (18) (9) (0) (0)	(16) 1 2 0 0 (6) (13) (0) (0)	<pre></pre>
	hyperplasia	1 0 0 0 (8) (0) (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 (6) (0) (0) (0)	1 0 0 0 0 (5) (0) (0)
nammary gl	duct ectasia	0 0 0 0 (0) (0) (0) (0)	<11> 0 0 0 0 (0) (0) (0) (0)	<16> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<20> 1 0 0 0 (5) (0) (0) (0)
	galactocele	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 (5)(0)(0)(0)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

REPORT TYPE : A1 SEX : MALE

0rgan	Findings	Group Name Control No. of Animals on Study 12 Grade 1 2 3 4 (%) (%) (%) (%)	7500 ppm 11 12 3 4 (%) (%) (%) (%)	15000 ppm 16 1 2 3 4 (%) (%) (%) (%)	30000 ppm 20 1 2 3 4 (%) (%) (%) (%)
[Reproductive	system]				
prep/cligl	duct ectasia	0 0 1 0 (0) (0) (8) (0)	0 0 0 0 (0) (0) (0) (0)	(16) 0 0 0 0 (0) (0) (0) (0)	(20) 0 0 0 0 (0) (0) (0) (0)
(Nervous syste	em]				
brain	hemorrhage	<12> 0 0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	1 0 0 0 (6) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)
	gliosis	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 (6) (0) (0) (0)	0 0 0 0 0 (0) (0)
spinal cord	hemorrhage ·	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	<16> 0 1 0 0 (0) (6) (0) (0)	<pre></pre>
[Special sens	e organs/appandage]				
эуө	hemorrhage	<pre></pre>	0 0 0 0 (0) (0) (0) (0)	<16> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<20> 0 0 0 0 0 0 0 0 0 0 0

(HPT150)

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

REPORT TYPE : A1 SEX

: MALE

Group Name Control 7500 ppm 15000 ppm 30000 ppm No. of Animals on Study 12 11 16 20 Findings Organ_ [Special sense organs/appandage] өуө <12> <11> <16> <20> cataract 0 1 0 0 0 0 0 0 1 0 0 1 0 0 (0) (8) (0) (0) (0)(0)(0)(0) (0)(6)(0)(0) (0)(5)(0)(0) retinal atrophy 0 12 5 7 (25) (50) (17) (0) (36) (45) (18) (0) (0)(75)(25)(0) (25) (35) (40) (0) keratitis 0 0 0 0 0 0 0 0 0 0 0 0 2 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(10)(0)(0) iritis 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(5)(0)(0) Harder al <12> <11> <16> <20> inflammatory infiltration 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(9)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) lymphocytic infiltration 0 0 0 0 (17) (0) (0) (0) (0)(0)(0)(0) (6)(0)(0)(0) (0)(5)(0)(0) [Musculoskeletal system] muscle <12> <11> atrophy 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 (8) (0) (0) (0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) Grade 1: Slight 2 : Moderate 3 : Marked 4 : Severe a: Number of animals examined at the site (a) b b: Number of animals with lesion (c) c:b/a*100

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

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

REPORT TYPE : A1 SEX : MALE

PAGE: 15

Organ	I	Group Name No. of Animals on Study Grade 1 (%)	Control 12 2 3 4 (%) (%) (%)	7500 ppm 11 1 2 3 4 (%) (%) (%) (%)	15000 ppm 16 1 2 3 4 (%) (%) (%) (%)	30000 ppm 20 1 2 3 4 (%) (%) (%) (%)
[Musculoske	eletal system]					
muscle	mineralization	0 (0)	<12> 1 0 0 (8) (0) (0)	<pre></pre>	<16> 0 0 0 0 0 0 0 0 0 0 0	(20) 0 0 0 0 (0) (0) (0) (0)
Grade <a>> b (c) Significant	1: Slight 2: Moderate 3 a: Number of animals examined at the sib: Number of animals with lesion c: b / a * 100 t difference; *: P ≤ 0.05 **: P ≤					
(HPT150)						RAT

(HPT150)

BA1S3

APPENDIX L 2

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

RAT: FEMALE: DEAD AND MORIBUND ANIMALS

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

: FEMALE

SEX

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

T 1011

PAGE: 16

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

(HPT150)

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

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

SEX	: FEMALE				

0rgan	Findings	Group Name Control No. of Animals on Study 3 Grade 1 2 3 4 (%) (%) (%) (%)	7500 ppm 11 1 2 3 4 (%) (%) (%) (%)	15000 ppm 15 1 2 3 4 (%) (%) (%) (%)	30000 ppm 36 1 2 3 4 (%) (%) (%) (%)
[Respiratory	system]				
nasal cavit	respiratory metaplasia:gland	\(\langle 3 \) \(\begin{array}{ccccc} 1 & 0 & 0 & 0 \\ (33) & (0) & (0) & (0) \end{array}	7 0 0 0 (64) (0) (0) (0)	(15) 13 0 0 0 (87) (0) (0) (0)	<36> 31 0 0 0 (86) (0) (0) (0)
	erythropoiesis:increased	0 0 0 0 0 (0) (0)	1 0 0 0 0 (9) (9) (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
lung	hemorrhage	(3) 0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	<15> 0 0 0 0 (0) (0) (0) (0)	<36> 1 0 0 0 (3) (0) (0) (0)
	edema	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)
	thrombus	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 1 0 0 (0) (7) (0) (0)	0 0 0 0 0 (0) (0)
	osseous metaplasia	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 (7) (0) (0) (0)	0 0 0 0 0 (0) (0)
	accumulation of foamy cells	0 0 0 0 0 (0) (0) (0)	1 0 0 0 (9) (0) (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (3) (0) (0) (0)
	bronchiolar-alveolar cell hyperplas	0 0 0 0 0 (0) (0) (0)	2 0 0 0 0 (18) (0) (0) (0)	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0)

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

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

b: Number of animals with lesion b

⁽c) c:b/a*100

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

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

STUDY NO. : 0224 ANIMAL : RAT F344

REPORT TYPE : A1 SEX : FEMALE

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

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

b b : Number of animals with lesion

⁽c) c:b/a*100

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

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

REPORT TYPE : A1 SEX : FEMALE

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

(HPT150)

BAIS3

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

SEX : FEMALE

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

4 : Severe

Grade 1: Slight 2: Moderate 3: Marked

⁽a) a: Number of animals examined at the site

b b: Number of animals with lesion

⁽c) c:b/a*100

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

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

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

PORT TYPE: AI

n	No	roup Name Control i. of Animals on Study 3 rade 1 2 3 4 (%) (%) (%) (%)	7500 ppm 11 1 2 3 4 (%) (%) (%) (%)	15000 ppm 15 15 (%) (%) (%) (%)	30000 ppm 36 1 2 3 4 (%) (%) (%) (%)
estive s	system]				
r	herniation	33) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	36> 1 0 0 0 (3) (0) (0) (0)
	hemorrhage	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (3) (0) (0) (0)
	necrosis:central	0 0 0 0 0 (0) (0)	1 0 0 0 0 (9) (0) (0) (0)	2 0 0 0 (13) (0) (0) (0)	0 0 0 0 0 (0) (0)
	necrosis:focal	1 0 0 0 0 (33) (0) (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 (7) (0) (0) (0)	3 0 0 0 0 (8) (0) (0) (0)
	fatty change	0 0 0 0 0 (0) (0)	2 0 0 0 (18) (0) (0) (0)	0 1 0 0 (0) (7) (0) (0)	1 0 0 0 0 (3) (3) (0) (0) (0)
	fatty change:central	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 1 0 0 (0) (7) (0) (0)	3 0 1 0 (8) (0) (3) (0)
	fatty change:peripheral	0 1 0 0 (0) (33) (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 0 (0) (0)
	deposit of hemosiderin	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)
de >		(0) (0) (0) (0) Marked 4: Severe			

(IIPT150)

BAIS3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

REPORT TYPE : A1
SEX : FEMALE

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

4 : Severe

(HPT150)

Grade 1: Slight 2: Moderate 3: Marked

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

b b: Number of animals with lesion

⁽c) c:b/a*100

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

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

REPORT TYPE : AI SEX : FEMALE

Organ	Group Na No. of A Grade Findings	me Control nimals on Study 3 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	15000 ppm 15 1 2 3 4 (%) (%) (%) (%)	30000 ppm 36 1 2 3 4 (%) (%) (%) (%)
[Digestive s	system]				
liver	bile duct hyperplasia	<pre></pre>	4 0 0 0 (36) (0) (0) (0)	<15> 0 0 0 0 0 0 0 0 0 0 0	<36> 4 0 0 0 (11) (0) (0) (0)
pancreas	atrophy	<pre></pre>	0 0 0 0 (0) (0) (0) (0)	1 0 0 0 (7) (0) (0) (0)	<36> 1 0 0 0 (3) (0) (0) (0)
[Urinary sys	stem]				
kidney	deposit of hemosiderin	3> 0 0 0 0 (0) (0) (0) (0)	0 1 0 0 (0) (9) (0) (0)	\(\lambda 15 \) \[1 1 0 0 \\ (7) (7) (0) (0) \]	<36> 2 0 0 0 (6) (0) (0) (0)
	chronic nephropathy	1 0 1 1 (33) (0) (33) (33)	2 2 1 1 (18) (18) (9) (9)	4 2 2 1 (27) (13) (13) (7)	7 4 4 0 ** (19) (11) (11) (0)
	hydronephrosis	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 0 (0) (0)	0 0 1 0 (0) (7) (0)	0 0 0 0 0 (0) (0) (0)
	tubular 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 1 0 (0) (3) (0)
Grade <a>> b (c) Significant	1: Slight 2: Moderate 3: Marked a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 difference; *: $P \le 0.05$ **: $P \le 0.01$				

(HPT150)

REPORT TYPE : AI
SEX : FEMALE

0rgan	Group Name No. of Anio Grade Findings	Control mals on Study 3 1 2 3 4 (%) (%) (%) (%)	7500 ppm 11 1 2 3 4 (%) (%) (%) (%)	15000 ppm 15 1 2 3 4 (%) (%) (%) (%)	30000 ppm 36 1 2 3 4 (%) (%) (%) (%)
[Urinary syst	tem]				
kidney	mineralization:cortico-medullary junction	3> 1 0 0 0 (33) (0) (0) (0)	7 0 0 0 (64) (0) (0) (0)	7 1 0 0 (47) (7) (0) (0)	<36> 12 1 1 0 (33) (3) (3) (0)
	mineralization:papilla	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) (0)	0 0 0 0 0 0 (0) (0)	1 0 0 0 0 (3) (0) (0) (0)
	mineralization:cortex	1 0 0 0 0 (33) (0) (0) (0)	1 0 0 0 0 (9) (0) (0)	0 0 1 0 (0) (7) (0)	10 9 6 1 (28) (25) (17) (3)
	urothelial hyperplasia:pelivis	0 0 0 0 0 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) (7) (0) (0)	0 1 0 0 (0) (3) (0) (0)
urin bladd	simple hyperplasia:transitional epithelium	<pre></pre>	<11> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<15> 1 0 0 0 (7) (0) (0) (0)	<36> 1 0 0 0 (3) (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 0 0 0 0	0 0 0 0 0 0 (0) (0)	1 0 0 0 0 (3) (0) (0)
(Endocrine s	ystem]				
pituitary	angiectasis	<pre></pre>	0 0 0 0 (0) (0) (0) (0)	2 0 0 0 (13) (0) (0) (0)	<36> 0 3 0 0 (0) (8) (0) (0)
Grade <a>> b (c) Significant (1: Slight 2: Moderate 3: Marked a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 difference: *: P ≤ 0.05 **: P ≤ 0.01 T	4 : Severe			

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

ANIMAL : RAT F344
REPORT TYPE : A1

STUDY NO. : 0224

SEX : FEMALE

Organ		up Name Control of Animals on Study 3 de <u>1 2 3 4</u> (%) (%) (%) (%)	7500 ppm 11 1 2 3 4 (%) (%) (%) (%)	15000 ppm 15 1 2 3 4 (%) (%) (%) (%)	30000 ppm 36 1 2 3 4 (%) (%) (%) (%)
(Endocrine s	system]				
pituitary	cyst	3> 1 0 0 0 (33) (0) (0) (0)	3 0 0 0 (27) (0) (0) (0)	5 1 0 0 (33) (7) (0) (0)	36> 2 1 0 0 (6) (3) (0) (0)
	hyperplasia	0 1 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 1 0 0	2 3 0 0 (6) (8) (0) (0)
	Rathke pouch	0 0 0 0 0 (0)	0 0 0 0 0 0 (0) (0)	1 0 0 0 0 (7) (0) (0)	2 0 0 0 0 (6) (6) (0) (0)
hyroid	C-cell hyperplasia	<pre></pre>	2 0 0 0 (20) (0) (0) (0)	<15> 1 0 0 0 (7) (0) (0) (0)	<36> 1 0 0 0 (3) (0) (0) (0)
	focal follicular 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 (3) (0) (0) (0)
adrenal	peliosis-like lesion	(33) (0) (0) (0)	2 1 0 0 (18) (9) (0) (0)	2 1 0 0 (13) (7) (0) (0)	<36> 6 2 0 0 (17) (6) (0) (0)
	necrasis	0 0 1 0 (0) (33) (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	1: Slight 2: Moderate 3: Mae: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100	arked 4: Severe			

(HPT150)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

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

: FEMALE

Group Name 15000 ppm 30000 ppm Control 7500 ppm No. of Animals on Study 3 11 15 36 Grade 3 3 2 3 (%) (%) (%) (%) (%) (%) (%) (%) (%) Organ_ Findings [Endocrine system] adrenat < 3> <11> <15> 0 0 0 extramedullary hematopoiesis 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (7)(0)(0)(0) (0)(0)(0)(0) hyperplasia:cortical cell (0)(0)(0)(0) (0)(0)(0)(0) (7)(0)(0)(0) (6)(0)(0)(0) hyperplasia:medulla 0 0 1 0 0 0 1 (0)(0)(0)(0) (9)(0)(0)(0) (0)(0)(0)(0) (3)(0)(0)(0) focal fatty change:cortex (0)(0)(0)(0) (0)(0)(0)(0) (7)(0)(0)(0) (3)(0)(0)(0) increased lipid:cortex 0 (0)(0)(0)(0) (0)(0)(0)(0) (7)(0)(0)(0) (3)(0)(0)(0) [Reproductive system] ovary < 3> <11> <15> ⟨36⟩ 0 0 0 0 0 0 0 cyst (0)(0)(0)(0) (0)(0)(0)(0) (13) (0) (0) (0) (0)(3)(0)(0) uterus < 3> <11> <15> <36> hemorrhage 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(3)(0)(0) Grade 1: Slight 2 : Moderate 3 : Marked 4 : Severe < a > a: Number of animals examined at the site

b

(c)

b: Number of animals with lesion

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

c:b/a*100

⁽HPT150)

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

DEAD AND MORIBUND ANIMALS (0-105W)

PAGE: 27

Organ		p Name Control of Animals on Study 3 e 1 2 3 4 (%) (%) (%) (%)	7500 ppm 11 1 2 3 4 (%) (%) (%) (%)	15000 ppm 15 1 2 3 4 (%) (%) (%) (%)	30000 ppm 36 1 2 3 4 (%) (%) (%) (%)
[Reproductive	e system]				
uterus	cystic endometrial hyperplasia	(0) (0) (0) (0)	1 0 0 0 (9) (0) (0) (0)	(15) 0 1 0 0 (0) (7) (0) (0)	36> 2 0 0 0 (6) (0) (0) (0)
mammary gl	hyperplasia	(33) (0) (0) (0)	1 0 0 0 (9) (0) (0) (0)	<15> 0 0 0 0 0 0 0 0 0 0 0	<36> 0 0 0 0 0 0 0 0 0 0 0
(Nervous syst	tem]				
orain	∪acuolic change	1 0 0 0 (33) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	<15> 0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)
	mineralization	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 (7) (0) (0) (0)	0 0 0 0 0 (0) (0)
[Special sens	se organs/appandage]				
өуө	hemorrhage	(0) (0) (0) (0)		(15) 0 0 1 0 (0) (0) (7) (0)	36> 0 0 0 0 (0) (0) (0) (0)
Grade <a>> b (c) Significant (1: Slight 2: Moderate 3: Ma a: Number of animals examined at the site b: Number of animals with lesion c:b/a*100 difference; *: P ≤ 0.05 **: P ≤ 0.0				

(HPT150)

PAGE: 28

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

SEX : FEMALE

DEAD AND MORIBUND ANIMALS (0-105W)

					rage · Zo
Organ	Findings	Group Name Control No. of Animals on Study 3 Grade 1 2 3 4 (%) (%) (%) (%)	7500 ppm 111 1 2 3 4 (%) (%) (%) (%)	15000 ppm 15 1 2 3 4 (%) (%) (%) (%)	30000 ppm 36 1 2 3 4 (%) (%) (%) (%)
[Special sens	se organs/appandage]				
еуе	cataract	<pre></pre>	0 1 0 0 (0) (9) (0) (0)	(15) 0 0 1 0 (0) (0) (7) (0)	<pre></pre>
	retinal atrophy	0 2 1 0 (0) (67) (33) (0)	0 6 3 1 (0) (55) (27) (9)	4 4 6 1 (27) (27) (40) (7)	8 7 16 1 (22) (19) (44) (3)
	keratitis	0 0 1 0 (0) (33) (0)	0 0 0 0 0 0 (0) (0)	0 1 0 0 (0) (7) (0) (0)	1 1 1 0 (3) (3) (0)
	iritis	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 1 0 (6) (3) (3) (0)
Harder gl	degeneration	<pre></pre>	0 0 0 0 (0) (0) (0) (0)	<15> 0 1 0 0 (0) (7) (0) (0)	<36> 0 1 0 0 (0) (3) (0) (0)
	inflammatory infiltration	0 0 1 0 (0) (0) (33) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
	lymphocytic infiltration	0 0 0 0 0 (0)	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (3) (0) (0)
[Musculaskele	etal system]				
bane	osteosclerosis	\(\langle 3 \rangle \) \(1 0 0 0 \) \((33) (0) (0) (0) \)	0 2 0 0 (0) (18) (0) (0)	3 1 0 0 (20) (7) (0) (0)	<36> 4 2 2 0 (11) (6) (6) (0)

Grade 1: Slight <a> a: Number

2 : Moderate

3 : Marked

4 : Severe

a : Number of animals examined at the site

b b: Number of animals with lesion

(c) c:b/a*100

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

APPENDIX L 3

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

RAT: MALE: SACRIFICED ANIMALS

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

REPORT TYPE: A1

SEX : MALE

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

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

(HPT150)

BAIS3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

REPORT TYPE : A1
SEX : MALE

: MALE

0rgan	Group Name No. of Ani Grade Findings	Control mals on Study 38 1 2 3 4 (%) (%) (%) (%)	7500 ppm 39 1 2 3 4 (%) (%) (%) (%)	15000 ppm 34 1 2 3 4 (%) (%) (%) (%)	30000 ppm 30 1 2 3 4 (%) (%) (%) (%)
[Respiratory	system]				
nasal cavit	inflammation:respiratory epithelium	38> 3 0 0 0 (8) (0) (0) (0)	<39> 0 0 0 0 0 0 0 0 0 0 0	2 0 0 0 (6) (0) (0) (0)	30> 1 0 0 0 (3) (0) (0) (0)
	respiratory metaplasia:olfactory epithelium	7 0 0 0 (18) (0) (0) (0)	3 0 0 0 0 (8) (0) (0) (0)	5 0 0 0 (15) (0) (0) (0)	4 0 0 0 (13) (0) (0) (0)
	respiratory metaplasia:gland	35 0 0 0 (92) (0) (0) (0)	34 0 0 0 (87) (0) (0) (0)	29 0 0 0 (85) (0) (0) (0)	29 0 0 0 (97) (0) (0) (0)
larynx	inflammation	<38> 1 0 0 0 (3) (0) (0) (0)	<39> 0 1 0 0 (0) (3) (0) (0)	2 0 0 0 (6) (0) (0) (0)	30> 1 0 0 0 (3) (0) (0) (0)
trachea	inflammation	<38> 0 0 0 0 (0) (0) (0) (0)	<39> 0 0 0 0 (0) (0) (0) (0)	<34> 0 0 1 0 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)
lung	inflammation	<38> 0 0 0 0 (0) (0) (0) (0)	<39> 0 0 0 0 (0) (0) (0) (0)	<34> 1 0 0 0 (3) (0) (0) (0)	<30> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
	osseous metaplasia	1 0 0 0 0 (3) (0) (0) (0)	0 0 0 0 0 (0) (0)	2 0 0 0 0 (6) (6) (7)	1 0 0 0 0 (3) (0) (0) (0)
Grade <a>a> b (c) Significant	1: Slight 2: Moderate 3: Marked a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 difference; $*: P \le 0.05$ **: $P \le 0.01$	4 : Severe Test of Chi Square			

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

REPORT TYPE : A1 SEX : MALE PAGE: 3

Organ	Findings	Group Name Control No. of Animals on Study 38 Grade 1 2 3 4 (%) (%) (%) (%)	7500 ppm 39 1 2 3 4 (%) (%) (%) (%)	15000 ppm 34 1 2 3 4 (%) (%) (%) (%)	30000 ppm 30 1 2 3 4 (%) (%) (%) (%)
[Respiratory :	system]				
lung	accumulation of foamy cells	38> 1 0 0 0 (3) (0) (0) (0)	<pre></pre>	34> 1 0 0 0 (3) (0) (0) (0)	30> 2 0 0 0 (7) (0) (0) (0)
	branchapneumania	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)
	bronchiolar—alveolar cell hyperplasia	2 0 0 0 0 (5) (0) (0)	7 0 0 0 (18) (0) (0) (0)	2 2 0 0 (6) (6) (6) (0)	1 2 0 0 (3) (7) (0) (0)
[Hematopoieti	c system]				
bone marrow	atrophy	<pre></pre>	39> 0 1 0 0 (0) (3) (0) (0)	0 0 0 0 (0) (0) (0) (0)	30> 0 0 0 0 (0) (0) (0) (0)
	necrosis:focal	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0) (0)	0 1 0 0 (0) (0)
	granulation	1 1 0 0 (3) (3) (0) (0)	(0) (0) (0) (0)	1 0 0 0 0 (3) (0) (0) (0)	1 0 0 0 (3) (0) (0) (0)
	fibrosis	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)
Grade <a>> b (c) Significant d	a: Number of animals examined at theb: Number of animals with lesionc: b / a * 100				

(HPT150)

BAIS3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

REPORT TYPE : A1 : MALE

Group Name Control 7500 ppm 15000 ppm 30000 ppm No. of Animals on Study 38 39 34 30 Grade Findings_ (%) (%) [Hematopoietic system] bone marrow ⟨38⟩ <39> ⟨34⟩ <30> 0 0 0 0 0 0 0 increased hematopoiesis 0 0 0 0 0 (0)(0)(0)(0) (3)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) erythropoiesis:increased 2 1 0 0 1 0 0 0 1 (5)(3)(0)(0) (3)(3)(0)(0) (0)(3)(0)(0) (3)(3)(0)(0) lymph nade <38> ⟨39⟩ ⟨34⟩ ⟨30⟩ dilatation 0 0 0 0 0 0 0 0 0 0 (0)(3)(0)(0) (3)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) granulation 1 0 0 0 0 3 0 0 3 0 3 2 0 0 (3)(0)(0)(0) (0)(8)(0)(0) (9)(0)(0)(0) (10) (7) (0) (0) spleen ⟨38⟩ <39> 0 0 ectopic tissue 0 0 0 0 0 0 1 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (3)(0)(0)(0) deposit of hemosiderin 2 0 0 0 0 0 0 0 0 0 1 0 0 0 (5)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(3)(0)(0) granulation 0 0 0 0 0 0 0 1 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (3)(0)(0)(0) (0)(0)(0)(0) Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe < a > a: Number of animals examined at the site b b: Number of animals with lesion

(HPT150)

(c)

c:b/a*100

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

BAIS3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

REPORT TYPE : A1 SEX : MALE

indings	Grade 1 2 3 4 (%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)
stem]				
ibrosis	<38> 1 0 0 0 (3) (0) (0) (0)	39> 5 0 0 0 (13) (0) (0) (0)	34> 2 1 0 0 (6) (3) (0) (0)	30> 1 0 0 0 (3) (0) (0) (0)
xtramedullary hematopoiesis	2 0 1 0 (5) (0) (3) (0)	0 1 0 0 (0) (0)	1 0 0 0 0 (3) (0) (0) (0)	0 0 1 0 (0) (3) (0)
apsule 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 0 (3) (0) (0) (0)	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 0 (0) (0)
em]				
ineralization	<38> 0 0 0 0 (0) (0) (0) (0)	39> 0 0 0 0 (0) (0) (0) (0)	34> 0 0 0 0 (0) (0) (0) (0)	<pre></pre>
yocardial fibrosis	8 29 1 0 (21) (76) (3) (0)	8 31 0 0 (21) (79) (0) (0)	3 30 1 0 (9) (88) (3) (0)	5 24 1 0 (17) (80) (3) (0)
rteritis	<38> 0 0 0 0 (0) (0) (0) (0)	<pre></pre>	<34> 0 0 0 0 (0) (0) (0) (0)	<30> 0 2 0 0 0 0 7) (0) (0)
i :	stem] ibrosis xtramedullary hematopoiesis apsule hyperplasia em] ineralization yocardial fibrosis rteritis Slight 2: Moderate	ibrosis	ibrosis	Stramedullary hematonoiesis 1

(HPT150)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

REPORT TYPE : A1 SEX : MALE

Group Name Control 7500 ppm 15000 ppm 30000 ppm No. of Animals on Study 39 38 34 30 Grade 3 Findings_ (%) (%) [Digestive system] tooth ⟨38⟩ ⟨39⟩ <34> <30> dysplasia 0 1 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(3)(0) (0)(0)(0)(0) (0)(0)(0)(0) stomach ⟨38⟩ ⟨39⟩ (34) <30> atrophy 0 0 0 0 0 0 0 (0)(0)(3)(0) (0)(0)(0)(0). (0)(0)(0)(0) (0)(0)(0)(0) ulcer:forestomach (3)(0)(3)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(3)(0)(0) erosion:glandular stomach 0 0 0 0 0 (3)(0)(0)(0) (5)(0)(0)(0) (3)(0)(0)(0) (10) (0) (0) (0) Liver ⟨38⟩ herniation 0 0 0 0 0 1 1 0 0 0 0 0 0 (0)(0)(0)(0) (3)(0)(0)(0) (3)(0)(0)(0) (3)(0)(0)(0) peliosis-like lesion 0 0 1 0 0 0 0 0 0 0 0 (3)(0)(0)(0) (3)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) necrosis:zonal 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(3)(0)(0) (0)(0)(0)(0) Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe <a>> a: Number of animals examined at the site b b: Number of animals with lesion (c) c:b/a*100

(HPT150)

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

BAIS3

SEX : MALE

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

ANIMAL : KAI F344 SACR
REPORT TYPE : A1

a: Number of animals examined at the siteb: Number of animals with lesion

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

c:b/a * 100

PAGE: 7

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

(c) Significa (NPT150)

< a >

BAIS3

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

REPORT TYPE : A1 SEX : MALE

0rgan	Group Name No. of Ani Grade Findings	Cantrol mals on Study 38 1 2 3 4 (%) (%) (%) (%)	7500 ppm 39 1 2 3 4 (%) (%) (%) (%)	15000 ppm 34 1 2 3 4 (%) (%) (%) (%)	30000 ppm 30 1 2 3 4 (%) (%) (%) (%)
[Digestive s	system]				
liver	mixed cell focus	(38) 1 0 0 0 (3) (0) (0) (0)	39> 2 0 0 0 (5) (0) (0) (0)	(34) 0 0 0 0 (0) (0) (0) (0)	<30> 0 0 0 0 (0) (0) (0) (0)
	spongiosis hepatis	3 1 0 0 (8) (3) (0) (0)	5 0 0 0 (13) (0) (0) (0)	7 0 0 0 (21) (0) (0) (0)	4 0 0 0 (13) (0) (0) (0)
	bile duct hyperplasia	23 15 0 0 (61) (39) (0) (0)	23 16 0 0 (59) (41) (0) (0)	17 17 0 0 (50) (50) (0) (0)	16 14 0 0 (53) (47) (0) (0)
pancreas	atrophy	<38> 6 0 0 0 (16) (0) (0) (0)	<pre></pre>	34> 10 0 0 0 (29) (0) (0) (0)	30> 3 0 0 0 (10) (0) (0) (0)
	basophilic change	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 (3) (0) (0) (0)
[Urinary sys	stem]				
kidney	deposit of hemosiderin	<38> 1 0 0 0 (3) (0) (0) (0)	<39> 0 0 0 0 0 0 0 0 0 0 0	34> 0 0 0 0 (0) (0) (0) (0)	<30> 0 1 0 0 (0) (3) (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		1.00	

(HPT150)

BAIS3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

REPORT TYPE : A1 : MALE SEX

Group Name Control No. of Animals on Study 38 Grade 1 2 3 4 (%) (%) (%) (%)	7500 ppm 39 1 2 3 4 (%) (%) (%) (%)	15000 ppm 34 1 2 3 4 (%) (%) (%) (%)	30000 ppm 30 1 2 3 4 (%) (%) (%) (%)
an (38) (0) (0) (0) (0)	<39> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	34> 1 0 0 0 (3) (0) (0) (0)	<30> 0 0 0 0 (0) (0) (0) (0)
1 16 17 4 (3) (42) (45) (11)	0 14 22 3 (0) (36) (56) (8)	2 12 20 0 (6) (35) (59) (0)	4 17 9 0 (13) (57) (30) (0)
1 0 0 0 (3) (0) (0) (0)	0 0 1 0 (0) (0) (0)	0 0 0 0 0 (0) (0)	2 0 0 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)	2 0 0 0 0 (7) (0) (0) (0)
peliuis 1 2 0 0 (3) (5) (0) (0)	0 1 0 0 (0) (0)	0 2 0 0 (0) (6) (0) (0)	1 3 0 0 (3) (10) (0) (0)
\langle 38 \rangle asitional epithelium 0 0 0 \rangle (0) (0) (0) (0)	39> 0 1 0 0 (0) (3) (0) (0)	0 0 0 0 (0) (0) (0) (0)	<30> 0 0 0 0 0 0 0 0 0 0 0
<38> 0 0 0 0 (0) (0) (0) (0)	39> 1 0 1 0 (3) (0) (3) (0)	<34> 0 0 0 0 (0) (0) (0) (0)	\(\lambda 0 \) \(\begin{array}{ccccc} \delta 0 & 0 & 0 \\ (\delta) & (\delta) & (\delta) \end{array} \)
th les	0 0 0 0 (0)(0)(0)(0)	0 0 0 0 1 0 1 0 (0)(0)(0)(0)(3)(0)(3)(0)	0 0 0 0 1 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

REPORT TYPE : A1 SEX : MALE

1 AIF

		up Name Control of Animals on Study 38 de 1 2 3 4	7500 ppm 39 1 2 3 4	15000 ppm 34 1 2 3 4	30000 ppm 30 1 2 3 4
Organ	Findings	(%) (%) (%) (%)	(%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)
Endocrine s	system]				
ituitary	cyst	<38> 1 1 0 0 (3) (3) (0) (0)	2 0 0 0 (5) (0) (0) (0)	<34> 0 0 0 0 (0) (0) (0) (0)	30> 0 0 0 0 (0) (0) (0) (0)
	hyperplasia	4 5 0 0 (11) (13) (0) (0)	10 3 0 0 (26) (8) (0) (0)	2 2 0 0 (6) (6) (6) (0) (0)	11 2 0 0 ** (37) (7) (0) (0)
	Rathke pouch	0 0 0 0 0 0 (0) (0)	2 1 0 0 (5) (3) (0) (0)	1 1 0 0 (3) (3) (0) (0)	0 0 0 0 0 0 (0) (0)
nyroid	ultimibranchial body remanet	<38> 0 0 0 0 0 0 0 0 0 0 0 0 0	<pre></pre>	<34> 0 0 0 0 (0) (0) (0) (0)	<30> 0 0 0 0 0 0 0 0 0 0 0
	C-cell hyperplasia	8 1 0 0 (21) (3) (0) (0)	7 0 0 0 (18) (0) (0) (0)	6 2 0 0 (18) (6) (0) (0)	4 0 0 0 (13) (0) (0) (0)
	focal follicular cell hyperplasia	0 0 0 0 0 0 (0) (0)	1 1 0 0 (3) (3) (0) (0)	0 1 0 0 (0) (3) (0) (0)	0 0 0 0 0 0 (0) (0)
idrena L	hemorrhage	<38> 0 1 0 0 (0) (3) (0) (0)	<39> 0 0 0 0 0 0 0 0 0 0 0	<34> 0 0 0 0 (0) (0) (0) (0)	<30> 0 0 0 0 0 0 0 0 0 0 0
Grade (a> b	1: Slight 2: Moderate 3: Maa: Number of animals examined at the site b: Number of animals with lesion c: b/a*100	arked 4: Severe			

(HPT150)

BAIS3

SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

PAGE: 11

0rgan	Group Nam No. of Ar Grade Findings	e Control imals on Study 38 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	30000 ppm 30 1 2 3 4 (%) (%) (%) (%)
Endocrine s	system]				
drenal	cyst	<38> 0 0 0 0 0 0 0 0 0 0 0	<39> 0 0 0 0 (0) (0) (0) (0)	<34> 0 1 0 0 (0) (3) (0) (0)	<pre></pre>
	hyperplasia:cortical cell	1 0 0 0 (3) (0) (0) (0)	3 0 0 0 0 (8) (0) (0) (0)	1 1 0 0 (3) (3) (0) (0)	2 0 0 0 0 (7) (0) (0) (0)
	hyperplasia:medulla	3 1 0 0 (8) (3) (0) (0)	3 4 0 0 (8) (10) (0) (0)	1 2 0 0 (3) (6) (0) (0)	3 0 0 0 0 (10) (0) (0)
	focal fatty change:cortex	7 0 0 0 (18) (0) (0) (0)	5 0 0 0 (13) (0) (0) (0)	8 0 0 0 (24) (0) (0) (0)	3 0 0 0 (10) (0) (0) (0)
Reproductiv	ve system]				
estis	atrophy	<pre></pre>	39> 3 3 31 0 (8) (8) (79) (0)	<34> 2 3 28 0 (6) (9) (82) (0)	30> 3 1 22 0 (10) (3) (73) (0)
	mineralization	3 1 0 0 (8) (3) (0) (0)	2 0 0 0 (5) (0) (0) (0)	3 0 0 0 0 (9) (0) (0)	3 0 0 0 (10) (0) (0) (0)
	arteritis	1 0 0 0 0 (3) (0) (0)	2 2 0 0 (5) (5) (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: Marked a: Number of animals examined at the site b: Number of animals with Lesion c: b / a * 100 difference; *: $P \le 0.05$ **: $P \le 0.01$	4 : Severe Test of Chi Square			

(HPT150)

BAIS3

SEX

: MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

PAGE: 12

0rgan	Findings	Group Name	7500 ppm 39 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	30000 ppm 30 1 2 3 4 (%) (%) (%) (%)
[Reproductive	o system]				
testis	interstitial cell hyperplasia	38> 3 0 0 0 (8) (0) (0) (0)		<34> 4 1 0 0 (12) (3) (0) (0)	30> 3 0 0 0 (10) (0) (0) (0)
epididymis	inflammation	<38> 0 0 1 0 (0) (0) (3) (0)		<34> 0 0 0 0 (0) (0) (0) (0)	<30> 0 0 0 0 0 0 0 0 0 0 0
prostate	inflammation	<38> 9 3 0 0 (24) (8) (0) (0)		<34> 8 3 0 0 (24) (9) (0) (0)	<pre></pre>
	hyperplasia	4 0 0 0 0 (11) (0) (0) (0)		4 0 0 0 (12) (0) (0) (0)	1 0 0 0 0 (3) (0) (0) (0)
mammary gl	duct ectasia	<38> 0 0 0 0 0 (0) (0) (0) (0)		<34> 0 1 0 0 (0) (3) (0) (0)	<30> 0 0 0 0 (0) (0) (0) (0)
	hyperplasia	1 0 0 0 0 (3) (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)
	galactocele	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)

4 : Severe

Grade 1: Slight 2: Moderate 3: Marked

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

b: Number of animals with lesion

(c) c:b/a*100

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

(HPT150)

b

SEX : MALE

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

44 SACRIFICA

0rgan	Findings	Group Name Control No. of Animals on Study 38 Grade 1 2 3 4 (%) (%) (%) (%)	7500 ppm 39 1 2 3 4 (%) (%) (%) (%)	15000 ppm 34 1 2 3 4 (%) (%) (%) (%)	30000 ppm 30 1 2 3 4 (%) (%) (%) (%)
[Reproductive	system]				
prep/cli gl	duct ectasia	\(\lambda 88 \) \[\begin{pmatrix} 1 & 0 & 0 & 0 \\ (& 3) & (& 0) & (& 0) & (& 0) \end{pmatrix}	(0) (0) (0) (0) (0) (0) (0) (0)	<34> 0 0 0 0 0 0 0 0 0 0 0	<30> 0 0 0 0 (0) (0) (0) (0)
(Nervous syste	em}				
brain	necrosis:focal	38> 0 0 0 0 (0) (0) (0) (0)	(0) (0) (0) (0) (0) (0) (0) (0)	(34) 0 1 0 0 (0) (3) (0) (0)	30> 0 0 0 0 (0) (0) (0) (0)
(Special sense	e organs/appandage]				
уө	cataract	\(\lambda 38 \rangle \) \(\begin{pmatrix} 1 & 2 & 0 & 0 \\ (& 3) & (& 5) & (& 0) & (& 0) \end{pmatrix}	39> 0 3 1 0 0 0) (8) (3) (0)	34> 0 5 0 0 (0) (15) (0) (0)	<30> 0 0 0 0 (0) (0) (0) (0)
	retinal atrophy	7 14 15 1 (18) (37) (39) (3)	2 14 23 0 (5) (36) (59) (0)	0 13 20 1 (0) (38) (59) (3)	2 12 16 0 (7) (40) (53) (0)
	keratitis	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 (0) (0)

SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

PAGE: 14

Organ	Group Group No. of Grade Findings	Name Control Animals on Study 38 1 2 3 4 (%) (%) (%) (%)	7500 ppm 39 1 2 3 4 (%) (%) (%) (%)	15000 ppm 34 1 2 3 4 (%) (%) (%) (%)	30000 ppm 30 1 2 3 4 (%) (%) (%) (%)
[Special ser	nse organs/appandage]				
еуе	iritis	\(\lambda 38 \rangle \) \[1 2 0 0 \\ (3) (5) (0) (0) \]	39> 0 1 0 0 (0) (3) (0) (0)	34> 0 0 0 0 (0) (0) (0) (0)	30> 0 0 0 0 (0) (0) (0) (0)
Harder gl	degeneration	<38> 0 1 0 0 (0) (3) (0) (0)	<39> 0 0 0 0 (0) (0) (0) (0)	<34> 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 0 0 0
	inflammatory infiltration	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)
	lymphocytic infiltration	2 1 0 0 (5) (3) (0) (0)	1 1 0 0 (3) (3) (0) (0)	1 0 0 0 0 (3) (0) (0) (0)	1 0 0 0 0 (3) (0) (0) (0)
[Musculaske	letal system]				
muscle	atrophy	<38> 0 0 0 0 0 0 0 0 0 0 0 0	<39> 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<34> 0 0 0 0 (0) (0) (0) (0)	30> 1 0 0 0 (3) (0) (0) (0)
Grade <a>> b (c) Significant	1: Slight 2: Moderate 3: Mark a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 difference; *: $P \le 0.05$ **: $P \le 0.01$				

(HPT150)

APPENDIX L 4

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

RAT: FEMALE: SACRIFICED ANIMALS

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

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

Organ	Group Name No. of Anima Grade	Control uls on Study 47 1 2 3 4 (%) (%) (%) (%)	7500 ppm 39 1 2 3 4 (%) (%) (%) (%)	15000 ppm 35 1 2 3 4 (%) (%) (%) (%)	30000 ppm 14 1 2 3 4 (%) (%) (%) (%)
[Integumentar:	y system/appandage]				
skin/app	ulcer	<47> 0 1 0 0 (0) (2) (0) (0)	<pre></pre>	<35> 0 0 0 0 (0) (0) (0) (0)	<14> 0 0 0 0 0 0 0 0 0 0 0 0 0 0
	inflammation	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 1 0 0 (0) (3) (0) (0)	0 0 0 0 0 (0) (0)
	scab	0 1 0 0 (0) (2) (0) (0)	0 1 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 1 0 0 (0) (7) (0) (0)
[Respiratory	system]				
nasal cavit	mineralization	447> 6 0 0 0 (13) (0) (0) (0)	\(\lambda 39 \) 15	35> 2 0 0 0 (6) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)
	eosinophilic change:alfactory epithelium	18 16 3 0 (38) (34) (6) (0)	20 10 1 0 (51) (26) (3) (0)	12 15 3 0 (34) (43) (9) (0)	2 6 4 0 (14) (43) (29) (0)
	eosinophilic change:respiratory epithelium	15 0 0 0 (32) (0) (0) (0)	16 0 0 0 (41) (0) (0) (0)	14 0 0 0 (40) (0) (0) (0)	4 0 0 0 (29) (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 lifference; *: P ≤ 0.05 **: P ≤ 0.01 Tes	4 : Severe			

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

REPORT TYPE : A1

SEX : FEMALE

0rgan	Findings	Group Name Control No. of Animals on Study 47 Grade 1 2 3 4 (%) (%) (%) (%)	7500 ppm 39 1 2 3 4 (%) (%) (%) (%)	15000 ppm 35 1 2 3 4 (%) (%) (%) (%)	30000 ppm 14 1 2 3 4 (%) (%) (%) (%)
[Respiratory s	system]				
nasal ca∪it	inflammation:foreign body	5 0 0 0 (11) (0) (0) (0)	<pre></pre>	<35> 0 0 0 0 (0) (0) (0) (0)	1 0 0 0 (7) (0) (0) (0)
	respiratory metaplasia:olfactory epit	helium 1 0 0 0 (2) (0) (0) (0)	1 0 0 0 0 (3) (0) (0) (0)	1 0 0 0 0 (3) (0) (0) (0)	0 0 0 0 0 (0) (0)
	respiratory metaplasia:gland	43 0 0 0 (91) (0) (0) (0)	35 0 0 0 (90) (0) (0) (0)	34 0 0 0 (97) (0) (0) (0)	14 0 0 0 (100) (0) (0) (0)
larynx	inflammation	3 0 0 0 (6) (0) (0) (0)	<39> 0 0 0 0 0 0 0 0 0 0 0	<35> 2 0 0 0 (6) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)
lung	accumulation of foamy cells	3 0 0 0 (6) (0) (0) (0)	39> 3 0 0 0 (8) (0) (0) (0)	<35> 4 0 0 0 (11) (0) (0) (0)	1 0 0 0 (7) (0) (0) (0)
	bronchiolar—alueolar cell hyperplasia	1 1 0 0 (2) (2) (0) (0)	0 1 0 0 (0) (3) (0) (0)	0 1 0 0 (0) (0)	0 0 0 0 0 (0) (0)
[Hematopoieti	c system]				
bone marrow	deposit of hemosiderin	<47> 0 0 0 0 (0) (0) (0) (0)	<pre></pre>	35> 2 0 0 0 (6) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)
Grade (a) b (c) Significant d	1: Slight 2: Moderate 3 a: Number of animals examined at the s b: Number of animals with lesion c: b / a * 100 ifference; *: P ≤ 0.05 **: P:				

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

REPORT TYPE : A1

SEX : FEMALE PAGE : 17

Organ	Group Name No. of Anima Grade Findings	Control als on Study 47 1 2 3 4 (%) (%) (%) (%) (%)	7500 ppm 39 1 2 3 4 (%) (%) (%) (%)	15000 ppm 35 1 2 3 4 (%) (%) (%) (%)	30000 ppm 14 1 2 3 4 (%) (%) (%) (%)
[Hematopoieti	c system]				
bone marrow	granulation	<47> 2 1 0 0 (4) (2) (0) (0)	3 2 0 0 (8) (5) (0) (0)	35> 1 2 0 0 (3) (6) (0) (0)	1 0 0 0 (7) (0) (0) (0)
	histiocytosis	1 0 0 0 0 (2) (0) (0) (0)	1 0 0 0 0 (3) (0) (0) (0)	3 1 0 0 (9) (3) (0) (0)	0 0 0 0 0 (0) (0)
	increased hematopoiesis	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (3) (0) (0) (0)	0 0 0 0 0 (0) (0)
	erythropoiesis:increased	1 0 0 0 0 (2) (0) (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 1 0 0 (0) (7) (0) (0)
lymph node	granulation	<47> 0 1 0 0 (0) (2) (0) (0)	<39> 0 0 0 0 0 0 0 0 0 0 0	<35> 1 0 0 0 (3) (0) (0) (0)	1 0 0 0 (7) (0) (0) (0)
thymus	glandular metaplasia	<47> 0 0 0 0 (0) (0) (0) (0)	<39> 0 1 0 0 (0) (3) (0) (0)	<35> 0 0 0 0 0 0 0 0 0 0 0	<14> 0 0 0 0 0 0 0 0 0 0 0 0
spleen	hyaline droplet	<47> 0 1 0 0 (0) (2) (0) (0)	<39> 0 0 0 0 0 0 0 0 0 0 0	<35> 0 0 0 0 (0) (0) (0) (0)	<14> 0 0 0 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 difference; *: P ≤ 0.05 **: P ≤ 0.01 Te	4: Severe st of Chi Square			

(HPT150)

BAIS3

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 47 Grade 1 2 3 4 (%) (%) (%) (%)	7500 ppm 39 1 2 3 4 (%) (%) (%) (%)	15000 ppm 35 1 2 3 4 (%) (%) (%) (%)	30000 ppm 14 1 2 3 4 (%) (%) (%) (%)
[Hematopoieti	c system]				
spleen	deposit of hemosiderin	<47> 0 22 0 0 (0) (47) (0) (0)	<pre></pre>	<35> 1 11 0 0 (3) (31) (0) (0)	<14> 0 6 0 0 0 (43) (0) (0)
	extramedullary hematopoiesis	0 2 1 0 (0) (4) (2) (0)	0 0 0 0 0 (0) (0) (0)	0 2 0 0 (0) (6) (0) (0)	0 0 0 0 0 (0) (0)
	capsule 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)
[Circulatory	system]				
heart	mineralization	<47> 0 0 0 0 (0) (0) (0) (0)	<39> 0 0 0 0 0 0 0 0 0 0 0	35> 0 0 1 0 (0) (0) (3) (0)	0 0 0 0 (0) (0) (0) (0)
	myocardial fibrosis	24 12 0 0 (51) (26) (0) (0)	23 7 0 0 (59) (18) (0) (0)	22 4 0 0 (63) (11) (0) (0)	13 0 0 0 * (93) (0) (0) (0)
artery/aort	arteritis	<47> 0 0 0 0 (0) (0) (0) (0)	<pre></pre>	<35> 1 1 0 0 (3) (3) (0) (0)	<14> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
Grade <a>> b (c) Significant o	1: Slight 2: Moderate a: Number of animals examined at t b: Number of animals with lesion c: b / a * 100 difference; *: P ≤ 0.05 **:	3: Marked 4: Severe he site P≤ 0.01 Test of Chi Square			

(HPT150)

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

REPORT TYPE : A1

SEX : FEMALE

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

Grade

1 : Slight

2 : Moderate

3 : Marked

4 : Severe

(a)

a: Number of animals examined at the site

b

b: Number of animals with lesion

(c)

c:b/a*100

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

(HPT150)

BAIS3

: FEMALE

SEX

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

PAGE: 20

Organ	Findings	Group Name Control No. of Animals on Study 47 Grade 1 2 3 4 (%) (%) (%) (%)	7500 ppm 39 1 2 3 4 (%) (%) (%) (%)	15000 ppm 35 1 2 3 4 (%) (%) (%) (%)	30000 ppm 14 1 2 3 4 (%) (%) (%) (%)
[Digestive s	ystem]				
liver	clear cell focus	<47> 2 1 0 0 (4) (2) (0) (0)	<39> 4 0 0 0 (10) (0) (0) (0)	<35> 3 0 0 0 (9) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)
	acidophilic cell focus	2 0 0 0 (4) (0) (0) (0)	0 1 0 0 (0) (3) (0) (0)	1 0 0 0 0 (3) (0) (0)	0 0 0 0 0 (0) (0)
	basophilic cell focus	20 0 0 0 (43) (0) (0) (0)	21 0 0 0 (54) (0) (0) (0)	19 1 0 0 (54) (3) (0) (0)	6 1 0 0 (43) (7) (0) (0)
	vacuolated cell focus	4 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)
	mixed cell focus	1 0 0 0 0 (2) (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)
	bile duct hyperplasia	12 0 0 0 (26) (0) (0) (0)	14 0 0 0 (36) (0) (0) (0)	13 0 0 0 (37) (0) (0) (0)	5 0 0 0 (36) (0) (0) (0)
	cholangiofibrosis	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	447> 4 0 0 0 (9) (0) (0) (0)	<39> 5 0 0 0 (13) (0) (0) (0)	<35> 2 0 0 0 (6) (0) (0) (0)	2 0 0 0 (14) (0) (0) (0)

(HPT150)

(c)

c:b/a * 100

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

BAIS3

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

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

SEX : FEMALE

					I NGD .
Organ	N	roup Name Control 0. of Animals on Study 47 rade 1 2 3 4 (%) (%) (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	15000 ppm 35 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
[Urinary sys	rtem]				
kidney	necrosis:zonal	0 0 0 0 (0) (0) (0) (0)	<pre></pre>	<pre></pre>	(14) 0 1 0 0 (0) (7) (0) (0)
	cyst	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)
	deposit of hemosiderin	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) (0)
	chronic nephropathy	12 20 8 2 (26) (43) (17) (4)	9 17 7 2 (23) (44) (18) (5)	4 22 9 0 * (11) (63) (26) (0)	4 8 0 0 (29) (57) (0) (0)
	mineralization:cortico-medullary juncti	on 16 1 0 0 (34) (2) (0) (0)	24 0 1 0 * (62) (0) (3) (0)	22 0 0 0 * (63) (0) (0) (0)	13 0 0 0 ** (93) (0) (0) (0)
	mineralization:papilla	2 0 0 0 0 (4) (0) (0) (0)	1 0 0 0 0 (3) (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (7) (0) (0) (0)
	mineralization:cortex	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)
[Endocrine s	system]				
pituitary	angiectasis	\(\langle 46> \) \(1 2 0 0 \) \(2) \((4) (0) (0) \)	39> 0 0 1 0 (0) (0) (3) (0)	<35> 0 0 0 0 (0) (0) (0) (0)	0 1 0 0 (0) (7) (0) (0)

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

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

b : Number of animals with lesion

(c) c:b/a*100

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

/----·

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

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

SEX : FEMALE

0rgan	Findings	Group Name No. of Animals on Stud Grade	iy 1	Contro 47 2 (%)	3	4 (%)	2	39 39 3 (%	<u>4</u>) (%)	<u>1</u> (%)	1500 2 (%)) ppm 35 3 (%)	<u>4</u> (%)	<u> </u>	l	0000 r 14 2 (%)		<u>4</u> (%)
Endocrine s	vstem]																	
ituitary	cyst	(6 13) (<46> 2 4) (0	0 9		(39 > 1) (3	0 (0)	7 (20)	1		0 (0)			<147 1 7) () 0 0) (0
	hyperplasia		9 20) (6 13) (0 (0 :	5 (13)	0 (0	0 (0)	6 (17)	8 (23)	0 (0)	0 (0)		3 1) (1	2 14) (0 0) (0
	Rathke pouch	(1 2) (0		0 :	: 0 b) (0)	0 (0	0 (0)	1 (3)	0 (0)	(0)	0 (0)	(1	1 7) (1 7) (0	0 0)
thyroid	ultimibranchial body remanet	(1 2) (<47> 0 0) (0	0 (0	<39> 0) (0	0 (0)	0 (0)	0	35> 0 (0)	0 (0)			<147 0 0) () 0 0) (0 0)
	C-cell hyperplasia	(4 9) (0 (0	0 (10	0) (0)	0 (0	0 (0)	4 (11)	0 (0)	(0)	0 (0)	(?		0 (0	0 (0)
	focal follicular cell hyperplasia	(0 (1 2) (0 (0 0)	0 (0	0 (0)	0 (0)	0 (0)	(0)	0 (0)		0 0) (0 (0	0 (0)
drenal	peliasis-like lesian		23 49) (<47> 6 13) (1	0 1.0) (4	8		0 (0)	18 (51)	6	35> 0 (0)	0 (0)			<14: 1 7) () 0 0) (0

(HPT150)

BAIS3

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

REPORT TYPE : A1 SEX

: FEMALE

PAGE: 23

Organ	Findings	Group Name Control No. of Animals on Study 47 Grade 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	15000 ppm 35 1 2 3 4 (%) (%) (%) (%)	30000 ppm 14 1 2 3 4 (%) (%) (%) (%)
[Endocrine s	ystem]				
adrenal	hyperplasia:cortical cell	<47> 4 2 0 0 (9) (4) (0) (0)	<pre></pre>	<pre></pre>	<14> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
	hyperplasia:medulla	0 0 0 0 0 (0) (0)	0 1 0 0 (0) (3) (0) (0)	1 0 0 0 0 (3) (0) (0) (0)	0 0 0 0 0 (0) (0)
	focal fatty change:cortex	7 0 0 0 (15) (0) (0) (0)	5 0 0 0 (13) (0) (0) (0)	0 1 0 0 * (0) (0)	1 0 0 0 0 (7) (0) (0) (0)
[Reproductiv	e system]				
ovary	cyst	<47> 1 1 0 0 (2) (2) (0) (0)	<38> 0 0 0 0 (0) (0) (0) (0)	35> 0 1 0 0 (0) (3) (0) (0)	0 0 0 0 (0) (0) (0) (0)
uterus	cystic endometrial hyperplasia	<47> 1 1 2 0 (2) (2) (4) (0)	<pre></pre>	<pre></pre>	\(\lambda 14 \rangle \) \(1 0 0 0 (7) (0) \q
mammary gl	hyperplasia	<47> 1 0 0 0 (2) (0) (0) (0)	<39> 0 0 0 0 (0) (0) (0) (0)	<35> 1 0 0 0 (3) (0) (0) (0)	<14> 0 0 0 0 0 0 0 0 0 0 0
Grade <a>> b (c) Significant	1: Slight 2: Moderate a: Number of animals examined at th b: Number of animals with lesion c: b / a * 100 difference; *: P ≤ 0.05 **:	3: Marked 4: Severe e site P ≤ 0.01 Test of Chi Square			

(HPT150)

: FEMALE

SEX

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

PAGE: 24

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

(HPT150)

b

(c)

b: Number of animals with lesion

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

c:b/a*100

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

REPORT TYPE : A1 : FEMALE

Group Name Control 7500 ppm 15000 ppm 30000 ppm No. of Animals on Study 47 39 35 14 Grade 2 3 0rgan_ Findings (%) (%) (%) (%) (%) (%) (%) [Special sense organs/appandage] Harder gl (47) ⟨35⟩ lymphocytic infiltration 4 0 0 0 0 0 0 0 4 0 0 0 0 (9)(0)(0)(0) (11) (0) (0) (0) (0)(0)(0)(0) (0)(0)(0)(0) 0 0 0 0 granulation 2 0 0 0 0 0 0 1 1 0 0 (4)(0)(0)(0) (15) (0) (0) (0) (3)(3)(0)(0) (0)(0)(0)(0) hyperplasia 1 0 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (3)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) [Musculoskeletal system] bane <14> osteosclerosis 3 3 2 0 7 3 0 0 4 3 3 0 2 2 1 0 (6)(6)(4)(0) (18) (8) (0) (0) (11) (9) (9) (0) (14) (14) (7) (0)

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

(a) a: Number of animals examined at the site

b b: Number of animals with Lesion

(c) c:b/a*100

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

(HPT150)

BAIS3

APPENDIX L 5

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

MOSUE: MALE: DEAD AND MORIBUND ANIMALS

STUDY NO. : 0225 ANIMAL : MOUSE BDF1 HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

REPORT TYPE : A1
SEX : MALE

PAGE: 1

0rgan	Group No. o Grade Findings_	f Animals on Study 16	10000 ppm 15 15 (%) (%) (%) (%)	20000 ppm 20 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$
[Integumentar	y system/appandage]				
skin/app	inflammation	<16> 0 0 0 0 0 0 0 0 0 0 0	\(\lambda 15 \) \(0 2 0 \) \(0 \rangle (13) (0) (0) \)	<pre></pre>	<25> 0 1 0 0 (0) (4) (0) (0)
subcutis	xanthogranuloma	<16> 0 0 0 0 0 0 0 0 0 0 0	<15> 0 0 0 0 (0) (0) (0) (0)	<20> 0 0 0 0 0 0 0 0 0 0 0	<pre></pre>
[Respiratory	system]				
nasal cavit	inflammation	<16> 0 0 0 0 (0) (0) (0) (0)	(15) 0 1 0 0 (0) (7) (0) (0)	<20> 0 0 0 0 0 0 0 0 0 0 0	<25> 0 0 0 0 0 0 0 0 0 0 0 0
	easinophilic change:olfactory epithelium	2 0 0 0 (13) (0) (0) (0)	4 0 0 0 (27) (0) (0) (0)	5 0 0 0 (25) (0) (0) (0)	4 0 0 0 0 (16) (0) (0) (0)
	eosinophilic change:respiratory epithelium	5 1 0 0 (31) (6) (0) (0)	3 2 0 0 (20) (13) (0) (0)	2 1 0 0 (10) (5) (0) (0)	4 2 0 0 (16) (8) (0) (0)
	respiratory metaplasia:olfactory epithelium	2 0 0 0 0 (13) (0) (0) (0)	1 0 0 0 0 (7) (0) (0)	8 0 0 0 0 (40) (0) (0)	12 2 0 0 * (48) (8) (0) (0)
Grade <a>> b (c) Significant o	1: Slight 2: Moderate 3: Mar a: Number of animals examined at the site b: Number of animals with lesion c:b/a*100 difference; *: P ≤ 0.05 **: P ≤ 0.01				

(HPT150)

STUDY NO. : 0225

SEX

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

ANIMAL : MOUSE BDF1
REPORT TYPE : A1

: MALE

Group Name Control 10000 ppm 20000 ppm 40000 ppm No. of Animals on Study 16 15 20 25 3 Findings (%) (%) (%) (%) (%) (%) (%) (%) (%) Organ___ [Respiratory system] nasal cavit <16> <20> respiratory metaplasia:gland 3 1 0 0 0 0 2 0 0 * 14 (19) (6) (0) (0) (35) (5) (0) (0) (27) (0) (0) (0) (56) (8) (0) (0) duct ectasia:olfactory gland 0 0 0 0 0 0 1 0 0 18 0 0 0 ** (0)(0)(0)(0) (0)(0)(0)(0) (5)(0)(0)(0) (72) (0) (0) (0) nasopharynx <16> <15> <20> eosinophilic change 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(4)(0)(0) lung <16> deposit of hemosiderin 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(4)(0)(0) [Hematopoietic system] bone marrow <16> <15> <20> atrophy 0 0 0 0 0 0 0 0 1 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (5)(0)(0)(0) (0)(0)(0)(0) erythropoiesis:increased 1 0 0 0 (6)(0)(0)(0) (7)(0)(0)(0) (0)(0)(0)(0) (4)(0)(0)(0) Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe <a>> a: Number of animals examined at the site b b: Number of animals with lesion c:b/a*100

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

STUDY NO. : 0225 ANIMAL : MOUSE BDF1 HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

REPORT TYPE : A1
SEX : MALE

PAGE: 3

Organ	i de la companya de	Firoup Name Control In of Animals on Study 16 Firade 1 2 3 4 (%) (%) (%) (%) (%)	10000 ppm 15 1 2 3 4 (%) (%) (%) (%)	20000 ppm 20 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
[Hematopoieti	c system]				
warrom enoc	hyperplasia:uascular	<16> 0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	<20> 0 2 0 0 0 10) (0) (0)	<25> 0 0 0 0 (0) (0) (0) (0)
spleen	thrombus	0 1 0 0 (0) (6) (0) (0)	<15> 0 0 0 0 0 0 0 0 0 0 0	<20> 0 0 0 0 (0) (0) (0) (0)	<25> 0 0 0 0 0 (0) (0) (0)
	deposit of melanin	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (4) (0) (0) (0)
	extramedullary hematopoiesis	2 2 2 0 (13) (13) (13) (0)	1 4 3 0 (7) (27) (20) (0)	0 3 4 0 (0) (15) (20) (0)	1 1 2 0 (4) (4) (8) (0)
	hyperplasia:vascular	(0) (0) (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (5) (0) (0) (0)	0 0 0 0 0 (0) (0)
Circulatory :	system]				
neart	necrosis	<16> 0 1 0 0 (0) (6) (0) (0)	0 0 0 0 (0) (0) (0) (0)	<20> 0 1 0 0 (0) (5) (0) (0)	225> 0 0 0 0 (0) (0) (0) (0)
Grade (a > b (c) Significant d	1: Slight 2: Moderate 3: a: Number of animals examined at the sit b: Number of animals with lesion c: b / a * 100 ifference; $*: P \le 0.05$ **: $P \le 0.05$	-			

(HPT150)

STUDY NO. : 0225

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : MALE HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

Organ	No	coup Name Control . of Animals on Study 16 ade 1 2 3 4 (%) (%) (%) (%)	10000 ppm 15 1 2 3 4 (%) (%) (%) (%)	20000 ppm 20 1 2 3 4 (%) (%) (%) (%)	40000 ppm 25 1 2 3 4 (%) (%) (%) (%)
[Circulatory	system]				
neart	mineralization	<16> 0 1 0 0 (0) (6) (0) (0)	<15> 0 0 0 0 0 0 0 0 0 0 0 0	20> 2 0 0 0 (10) (0) (0) (0)	25> 1 0 0 0 (4) (0) (0) (0)
Digestive sy	vstem]				
toath	dysplasia	5 1 0 0 (31) (6) (0) (0)	<15> 6 0 0 0 (40) (0) (0) (0)	<20> 7	<25> 8 1 0 0 (32) (4) (0) (0)
tangue	arteritis	(16) 0 0 0 0 (0) (0) (0) (0)	<15> 0 0 0 0 0 0 0 0 0 0 0	<20> 0 0 0 0 (0) (0) (0) (0)	<25> 1 0 0 0 (4) (0) (0) (0)
alivary gl	mineralization	<16> 0 1 0 0 (0) (6) (0) (0)	<15> 0 0 0 0 (0) (0) (0) (0)	<20> 0 0 0 0 0 0 0 0 0 0 0	<25> 0 0 0 0 0 0 0 0 0 0 0
tomach	mineralization	<16> 1 0 0 0 (6) (0) (0) (0)	<15> 1 0 0 0 (7) (0) (0) (0)	<20> 0 0 0 0 0 0 0 0 0 0 0	<25> 0 0 0 0 (0) (0) (0) (0)
	erosion:forestomach	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)
Grade (a> b	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. : 0225 ANIMAL : MOUSE BDF1

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

REPORT TYPE : A1

SEX : MALE

PAGE: 5

0rgan	Findings	Group Name Control No. of Animals on Study 16 Grade 1 2 3 4 (%)	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
[Digestive s	system]				
stomach	erosion:glandular stomach	<16> 1 0 0 0 (6) (0) (0) (0		<20> 0 0 0 0 0 0 0 0 0 0 0	<25> 2 0 0 0 (8) (0) (0) (0)
	ulcer:glandular stomach	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)
	hyperplasia:glandular stomach	1 2 0 0 (6) (13) (0) (0	1 0 0 0 0 (7) (0) (0) (0)	4 1 0 0 (20) (5) (0) (0)	2 0 0 0 0 (8) (0) (0) (0)
Liver	angiectasis	<16> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		<20> 0 0 0 0 (0) (0) (0) (0)	<25> 0 1 0 0 (0) (4) (0) (0)
	necrosis:central	0 0 0 0 0		0 1 0 0 (0) (5) (0) (0)	0 1 1 0 (0) (4) (4) (0)
	necrosis:focal	0 1 0 0 (0) (6) (0) (0	1 0 0 0 0 (7) (0) (0) (0)	0 0 1 0 (0) (5) (0)	0 0 1 0 (0) (4) (0)
	fatty change	0 0 0 0 (0 0 1 0 (0) (5) (0)	0 0 0 0 0 (0) (0)
	fatty change:central	0 0 0 0 (1 0 0 0 (5) (0) (0) (0)	0 0 0 0 (0) (0) (0)

<a>>

b

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

(c) c:b/a*100

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

STUDY NO. : 0225

ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

PAGE: 6

Organ	Group Name No. of Ani Grade Findings	Control mals on Study 16 16 (%) (%) (%) (%) (%)	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	20000 ppm 20 1 2 3 4 (%) (%) (%) (%)	40000 ppm 25 1 2 3 4 (%) (%) (%) (%)
[Digestive s	system]				
Liver	deposit of hemosiderin	<16> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	(15) 0 0 0 0 (0) (0) (0) (0)	<20> 0 0 0 0 (0) (0) (0) (0)	<25> 1 0 0 0 (4) (0) (0) (0)
pancreas	granulation	0 0 0 0 0 (0) (0)	1 0 0 0 (7) (0) (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
	basophilic cell focus	0 0 0 0 0 0 (0)	1 0 0 0 0 (7) (0) (0) (0)	1 0 0 0 0 (5) (0) (0) (0)	0 0 0 0 0 (0) (0)
	necrosis	<16> 0 1 0 0 (0) (6) (0) (0)	(15) 0 0 0 0 (0) (0) (0) (0)	<20> 0 0 0 0 0 0 0 0 0 0 0	<pre></pre>
	islet cell hyperplasia	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 (5) (0) (0) (0)	1 0 0 0 0 (4) (0) (0)
Urinary sys	stem]				
idney	cyst	<16> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	(15) 0 0 0 0 (0) (0) (0) (0)	(20) 0 0 0 0 (0) (0) (0) (0)	<pre></pre>
Grade (a > b (c) Significant	1: Slight 2: Moderate 3: Marked a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 difference; *: $P \le 0.05$ **: $P \le 0.01$ 7	4 : Severe Test of Chi Square			

(HPT150)

STUDY NO. : 0225

SEX

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL : MOUSE BDF1

REPORT TYPE : A1

: MALE

DEAD AND MORIBUND ANIMALS (0-105W)

)rgan		Group Name Control No. of Animals on Study 16 Grade 1 2 3 4 (%) (%) (%) (%)	10000 ppm 15 1 2 3 4 (%) (%) (%) (%)	20000 ppm 20 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$
Urinary sy			(10) (10) (10)	(10) (10) (10)	(10) (10) (10)
idney	hyaline droplet	<16> 0 0 0 0 0 0 0 0 0 0 0	<15> 2 0 0 0 (13) (0) (0) (0)	<20> 1 0 0 0 (5) (0) (0) (0)	<25> 1 1 0 0 (4) (4) (0) (0)
	basophilic change	0 0 0 0 0 (0) (0)	0 1 0 0 (0) (7) (0) (0)	0 1 2 0 (0) (5) (10) (0)	0 0 0 0 0 (0) (0)
	deposit of hemosiderin	1 0 0 0 (6) (0) (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0)
	inflammatory infiltration	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)
	hydronephrosis	0 1 1 0 (0) (6) (6) (0)	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0) (0)	0 0 1 0 (0) (4) (0)
	tubular 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 1 0 (0) (4) (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 1 0 (0) (5) (0)	0 1 0 0 (0) (4) (0) (0)
	mineralization:cortico-medullary junct	ion 6 0 0 0 (38) (0) (0) (0)	8 0 0 0 (53) (0) (0) (0)	8 0 0 0 (40) (0) (0) (0)	13 0 0 0 (52) (0) (0) (0)

4 : Severe

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

b b: Number of animals with lesion (c) c:b/a * 100

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

(HPT150)

BAISS

STUDY NO. : 0225 ANIMAL : MOUSE BDF1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

REPORT TYPE : A1 SEX

: MALE

Group Name Control 10000 ppm 20000 ppm 40000 ppm 25 No. of Animals on Study 16 15 20 3 0rgan_ Findings (%) (%) (%) (%) (%) (%) (%) (%) (%) [Urinary system] kidney <16> <15> <20> <25> mineralization:papilla 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (7)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) mineralization:cortex 0 0 0 0 0 1 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(4)(0) glomerulosclerosis (0)(0)(6)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) urethra <16> <15> ⟨20⟩ inflammation 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 (0)(0)(7)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) [Endocrine system] pituitary <16> <15> <20> <24> 0 0 1 0 0 0 0 0 0 angiectasis (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(4)(0) Rathke pouch 0 0 0 0 0 0 0 0 1 0 0 0 1 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (5)(0)(0)(0) (4)(0)(0)(0) Grade 1: Slight 2 : Moderate 3 : Marked 4 : Severe (a) a: Number of animals examined at the site b b: Number of animals with lesion (c) c:b/a*100Significant difference; *: $P \le 0.05$ **: $P \le 0.01$ Test of Chi Square

(HPT150)

BAIS3

STUDY NO. : 0225

• UZZO

ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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

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

(HPT150)

BAIS3

STUDY NO. : 0225

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

ANIMAL : MOUSE BDF1

REPORT TYPE : A1
SEX : MALE

DOIND WILLINGS (A-100M)

Organ		p Name	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	20000 ppm 20 1 2 3 4 (%) (%) (%) (%)	40000 ppm 25 1 2 3 4 (%) (%) (%) (%)
[Reproductive	system]				
prostate	inflammation	· 0 0 0 0 0 (0) (0) (0)	2 0 1 0 (13) (0) (7) (0)	<pre></pre>	<25> 0 0 0 0 0 (0) (0) (0) (0)
prep/cli gl	duct ectasia	0 0 0 0 (0) (0) (0) (0)	<15> 0 2 0 0 (0) (13) (0) (0)	(20) 0 3 1 0 (0) (15) (5) (0)	<25> 0 2 0 0 (0) (8) (0) (0)
[Nervous syste	em]				
brain	hemorrhage	1 1 0 0 (6) (6) (0) (0)	<15> 0 0 0 0 0 0 0 0 0 0 0	<20> 0 1 0 0 (0) (5) (0) (0)	<25> 0 0 0 0 0 (0) (0) (0) (0)
	mineralization	7 0 0 0 0 (44) (0) (0) (0)	8 0 0 0 (53) (0) (0) (0)	11 0 0 0 (55) (0) (0) (0)	11 0 0 0 (44) (0) (0) (0)
spinal cord	hemorrhage	0 0 0 0 (0) (0) (0) (0)	(15) 0 0 0 0 (0) (0) (0) (0)	<20> 0 1 0 0 (0) (5) (0) (0)	<pre></pre>
[Special sense	e organs/appandage]				
Harder gl	hyperplasia	<16> 0 1 0 0 (0) (6) (0) (0)	<15> 0 0 0 0 0 0 0 0 0 0 0 0	<20> 0 0 0 0 0 0 0 0 0 0 0	<pre></pre>
Grade (a > b (c) Significant d	1: Slight 2: Moderate 3: Ma a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 ifference: $*: P \le 0.05$ **: $P \le 0.0$				

STUDY NO. : 0225 ANIMAL : MOUSE BDF1 HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0-105W)

REPORT TYPE : A1

SEX : MALE

DEAD AND MONIDOND ANIMALS (0-100

Organ		up Name Control of Animals on Study 16 de 1 2 3 4 (%) (%) (%) (%)	10000 ppm 15 1 2 3 4 (%) (%) (%) (%)	20000 ppm 20 1 2 3 4 (%) (%) (%) (%)	40000 ppm 25 1 2 3 4 (%) (%) (%) (%)
Musculaskele	otal system]				
nuscle	mineralization	(16) 2 0 0 0 (13) (0) (0) (0)	<15> 2 0 0 0 (13) (0) (0) (0)	<20> 0 0 0 0 0 0 0 0 0 0 0	(25) 1 0 0 0 (4) (0) (0) (0)
Body cavitie	es]				
eritoneum	inflammation	(16) 0 0 0 0 (0) (0) (0) (0)	(15) 0 0 1 0 (0) (0) (7) (0)	<20> 0 0 0 0 0 0 0 0 0 0 0	<25> 0 0 0 0 0 0 0 0 0 0 0 0
rade a > b c)	1: Slight 2: Moderate 3: M a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 difference; *: P ≤ 0.05 **: P ≤ 0.				

APPENDIX L 6

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

MOSUE: FEMALE: DEAD AND MORIBUND ANIMALS

STUDY NO. : 0225 ANIMAL : MOUSE BDF1 HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

REPORT TYPE : A1

SEX : FEMALE

DEAD AND MORIBUND ANIMALS (0-105W)

Group Name Control 10000 ppm 20000 ppm mag 00004 No. of Animals on Study 21 26 31 22 2 3 3 2 3 Organ Findings (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) [Integumentary system/appandage] subcutis (21) <26> ⟨31⟩ inflammation 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(4)(0) (0)(0)(0)(0) (0)(0)(0)(0) [Respiratory system] nasal cavit ⟨21⟩ (26) <31> <22> bacteria 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(5)(0) embalus 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(5)(0)(0) mineralization 0 0 0 0 1 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (5)(0)(0)(0) eosinophilic change:olfactory epithelium 0 0 1 0 0 1 0 0 2 1 0 0 3 1 0 0 (0)(0)(5)(0) (0)(4)(0)(0) (6)(3)(0)(0) (14) (5) (0) (0) easinophilic change:respiratory epithelium (19) (5) (0) (0) (27) (4) (4) (0) (26) (6) (0) (0) (41) (5) (0) (0) respiratory metaplasia:olfactory epithelium 1 0 0 0 0 3 0 0 0 4 0 0 0 (5)(0)(0)(0) (8)(0)(0)(0) (10) (0) (0) (0) (18) (0) (0) (0)

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

b b: Number of animals with lesion

(c) c:b/a*100

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

(HPT150)

BAIS3

STUDY NO. : 0225 ANIMAL

: MOUSE BDF1

REPORT TYPE : A1

SEX : FEMALE

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

PAGE: 13

Organ		up Name Control of Animals on Study 21 de 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	40000 ppm 22 1 2 3 4 (%) (%) (%) (%)
[Respiratory s	system]				
nasal cavit	respiratory metaplasia:gland	\(\frac{\lambda}{21} \rangle \) \(1 0 0 0 \tag{5} (0) (0) (0) \tag{5} \)	200 0 0 (8)(0)(0)(0)	31> 2 0 0 0 (6) (0) (0) (0)	<22> 4 0 0 0 (18) (0) (0) (0)
	atrophy:olfactory epithelium	0 1 0 0 (0) (5) (0) (0)	1 0 0 0 0 (4) (0) (0) (0)	1 0 0 0 (3) (0) (0) (0)	0 0 0 0 0 (0) (0)
	duct ectasia:olfactory gland	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	2 0 0 0 0 (6) (6) (0) (0)	16 0 0 0 ** (73) (0) (0) (0)
nasopharynx	eosinophilic change	(21) 1 1 0 0 (5) (5) (0) (0)	3 1 0 0 (12) (4) (0) (0)	31> 1 0 0 0 (3) (0) (0) (0)	\(\lambda 22 \rangle \) \(1 0 0 0 \\ (5) (0) (0) (0) \)
lung	inflammatory infiltration	<21> 0 1 0 0 (0) (5) (0) (0)	<26> 0 0 0 0 (0) (0) (0) (0)	31> 0 0 0 0 (0) (0) (0) (0)	<22> 1 0 0 0 (5) (0) (0) (0)
	lymphocytic infiltration	0 0 0 0 0 (0) (0)	0 1 0 0 (0) (0)	1 0 0 0 0 (3) (0) (0) (0)	0 0 0 0 0 (0)
[Hematopoieti	c system]				
bone marrow	myelofibrosis	\(\langle 21 \rangle \) \(1 0 0 0 \\ (5) (0) (0) (0) \)	<26> 0 1 0 0 (0) (4) (0) (0)	31> 1 0 0 0 (3) (0) (0) (0)	<pre></pre>
Grade <a>> b (c) Significant d	a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100	farked 4: Severe 01 Test of Chi Square			

(HPT150)

BAIS3

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

PAGE: 14 Group Name Control 10000 ppm 20000 ppm 40000 ppm No. of Animals on Study 21 26 31 22 3 3 0rgan Findings_ (%) (%) (%) (%) (%) (%) (%) (%) (%) [Hematopoietic system] bone marrow (21) ⟨31⟩ erythropoiesis:increased 0 0 0 0 0 0 0 0 0 0 0 (0)(5)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) hyperplasia:vascular 0 0 0 0 0 0 0 0 0 0 0 1 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(5)(0)(0) spleen <21> <26> ⟨31⟩ thrombus 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(4)(0) (0)(0)(0)(0) (0)(0)(0)(0) deposit of hemosiderin 0 0 (0)(5)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) deposit of melanin (0)(0)(0)(0) (0)(0)(0)(0) (3)(0)(0)(0) (0)(0)(0)(0) extramedullary hematopoiesis 0 5 5 0 (5) (19) (33) (0) (4)(12)(8)(0) (0)(19)(16)(0) (0)(23)(23)(0) follicular hyperplasia 0 0 0 0 0 1 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (3)(0)(0)(0) (5)(0)(0)(0) [Circulatory system] heart ⟨21⟩ thrombus 0 0 0 0 1 0 0 0 1 0 0 0 0 0 0 (0)(-0)(0)(0) (0)(4)(0)(0) (0)(3)(0)(0) (0)(0)(0)(0)

4 : Severe

Grade 1: Slight 2 : Moderate (a)

3 : Marked a: Number of animals examined at the site

b b: Number of animals with lesion c:b/a*100

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

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

ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : FEMALE

0rgan	Findings	Group Name Control No. of Animals on Study 21 Grade 1 2 3 4 (%) (%) (%) (%)	10000 ppm 26 1 2 3 4 (%) (%) (%) (%)	20000 ppm 31 1 2 3 4 (%) (%) (%) (%)	40000 ppm 22 1 2 3 4 (%) (%) (%) (%)
[Circulatory :	system]				
neart	necrosis	\(\langle 21 \rangle \) \[\begin{pmatrix} 1 & 1 & 0 & 0 \\ (5) & (5) & (0) & (0) \end{pmatrix} \]	<26> 0 1 0 0 (0) (4) (0) (0)	(31) 0 0 0 0 (0) (0) (0) (0)	<pre></pre>
	mineralization	3 0 0 0 (14)(0)(0)(0)	1 0 0 0 0 (4) (0) (0) (0)	0 1 0 0 (0) (0)	2 0 0 0 0 (9) (0) (0) (0)
	arteritis	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 1 1 0 (0) (3) (3) (0)	0 0 0 0 0 (0) (0)
rtery/aort	arteritis	(21) 0 0 0 0 (0) (0) (0) (0)	<26> 0 0 0 0 (0) (0) (0) (0)	(31) 0 0 1 0 (0) (0) (3) (0)	\(\langle 22 \rangle \) \(0 \) \(0 \) \(0 \) \(0 \) \(0 \)
)igesti∪e sy	stem]				
ooth	dysplasia	(21) 1 0 0 0 (5) (0) (0) (0)	<26> 0 0 0 0 (0) (0) (0) (0)	31> 0 0 0 0 (0) (0) (0) (0)	<pre></pre>
congue	arteritis	<21> 0 0 0 0 (0) (0) (0) (0)	<26> 0 0 0 0 (0) (0) (0) (0)	<pre></pre>	<22> 0 0 0 0 0 (0) (0) (0) (0)
(a) (c)	1: Slight 2: Moderate a: Number of animals examined at the b: Number of animals with lesion c: b / a * 100 lifference; *: P ≤ 0.05 **: P				

STUDY NO. : 0225 ANIMAL : MOUSE BDF1

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

REPORT TYPE : A1

SEX : FEMALE

1	Findings	Group Name Control No. of Animals on Study 21 Grade 1 2 3 4 (%) (%) (%) (%)	10000 ppm 26 1 2 3 4 (%) (%) (%) (%)	20000 ppm 31 1 2 3 4 (%) (%) (%) (%)	40000 ppm 22 1 2 3 4 (%) (%) (%) (%)
stive syste	eem]				
vary gl	lymphocytic infiltration	2 0 0 0 (10) (0) (0) (0)	<26> 0 0 0 0 (0) (0) (0) (0)	<pre></pre>	2 0 0 0 (9) (0) (0) (0)
ach	mineralization	<21> 0 0 0 0 (0) (0) (0) (0)	<26> 1 0 0 0 (4) (0) (0) (0)	31> 1 0 0 0 (3) (0) (0) (0)	222> 1 0 0 0 (5) (0) (0) (0)
	ulcer:forestomach	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)
	erosion:glandular stomach	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (3) (0) (0)	1 0 0 0 0 (5) (0) (0) (0)
	hyperplasia:glandular stomach	2 0 0 0 (10) (0) (0) (0)	2 1 0 0 (8) (4) (0) (0)	5 0 0 0 (16) (0) (0) (0)	2 0 0 0 0 (9) (0) (0)
-	angiectasis	21> 2 0 0 0 (10) (0) (0) (0)	<26> 1 0 1 0 (4) (0) (4) (0)	<31> 0 1 0 0 (0) (3) (0) (0)	222> 2 2 0 0 (9) (9) (0) (0)
	necrosis:focal	0 0 1 0 (0) (5) (0)	0 0 0 0 0 (0) (0) (0)	1 0 0 0 0 (3) (0) (0) (0)	0 0 0 0 0 (0) (0)
9 1 9 a b	: Slight 2: Moderate a: Number of animals examined at th b: Number of animals with lesion b: b/a * 100	(0) (0) (5) (0) 3: Marked 4: Severe	0 0 0 0 0 (0) (0)	1 0 0 0 0 (3) (0) (0)	

(HPT150)

ANIMAL : MOUSE BDF1

REPORT TYPE : A1

SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

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

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

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

b b: Number of animals with lesion (c) c: b/a * 100

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

(HPT150)

BAIS3

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

ANIMAL : MOUSE BDF1
REPORT TYPE : A1

SEX : FEMALE

Organ	Findings	Group Name Control No. of Animals on Study 21 Grade 1 2 3 4 (%) (%) (%) (%)	10000 ppm 26 1 2 3 4 (%) (%) (%) (%)	20000 ppm 31 1 2 3 4 (%) (%) (%) (%)	40000 ppm 22 1 2 3 4 (%) (%) (%) (%)
(Digestive s	system]				
liver	basophilic cell focus	<21> 0 0 0 0 0 0 0 0 0 0 0 0	0 1 0 0 (0) (4) (0) (0)	(31) 1 1 0 0 (3) (3) (0) (0)	<222> 0 0 0 0 0 0 0 0 0 0 0
pancreas	lymphocytic infiltration	<21> 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<26> 0 0 0 0 0 0 0 0 0 0 0	31> 0 1 0 0 (0) (3) (0) (0)	<22> 0 0 0 0 0 0 0 0 0
Urinary sys	stem]				
ridney	necrosis:central	<21> 0 0 0 0 0 0 0 0 0 0 0 0 0	<26> 0 0 0 0 (0) (0) (0) (0)	(31) 0 1 0 0 (0) (3) (0) (0)	<pre></pre>
	hyaline droplet	6 4 0 0 (29) (19) (0) (0)	6 2 0 0 (23) (8) (0) (0)	3 6 1 0 (10) (19) (3) (0)	0 5 1 0 * (0) (23) (5) (0)
	deposit of hemosiderin	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 0 (0) (0)	0 1 0 0 (0) (5) (0) (0)
	hyaline cast	0 1 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)
Grade <a>> b (c) Significant	1: Slight 2: Moderate a: Number of animals examined at b: Number of animals with lesion c: b / a * 100 difference; *: P ≤ 0.05 **				

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

REPORT TYPE : A1
SEX : FEMALE

PAGE: 19

Organ	Findings	No. of Animals on Study	Control 21 3 4 (%) (%)	10000 ppm 26 1 2 3 4 (%) (%) (%) (%)	20000 ppm 31 1 2 3 4 (%) (%) (%) (%)	40000 ppm 22 1 2 3 4 (%) (%) (%) (%)
[Urinary syst	tem]					
kidney	lymphocytic infiltration	0 (<21>) 0 0)) (0) (0)	<26> 1 0 0 0 (4) (0) (0) (0)	<31> 0 0 0 0 0 0 0 0 0 0 0 0	<22> 1 0 0 0 (5) (0) (0) (0)
	granulation	1 (5) ((0 0 0	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
	inflammatory polyp	1 1 1 (5) (5	0 0	0 0 0 0	0 1 0 0 (0) (3) (0) (0)	0 1 0 0 (0) (5) (0) (0)
	hydronephrosis	0 1	2 0	0 0 0 0 0 (0) (0)	0 0 1 0 (0) (3) (0)	0 0 1 0 (0) (5) (0)
	tubular necrosis	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)
	mineralization:cortico-medullary junc		0 0 0	0 0 0 0 0 (0) (0)	2 0 0 0 0 (6) (6) (7) (7)	1 0 0 0 (5) (0) (0) (0)
urin bladd	inflammation	0 (<21> 0 0 0 0) (0) (0)	(26) 1 0 0 0 (4) (0) (0) (0)	(31) 0 0 0 0 (0) (0) (0) (0)	<22> 0 0 0 0 0 0 0 0 0
[Endocrine sy	vstem]					
pituitary	angiectasis	0 (<20> 0 0 0 0) (0) (0)	<26> 0 1 0 0 0 0 4) (0) (0)	<31> 0 0 0 0 (0) (0) (0) (0)	<21> 0 0 0 0 0 0 0 0 0 0 0 0

Grade 1: Slight 2: Moderate 3: Marked 4: Severe
(a) a: Number of animals examined at the site
b: Number of animals with lesion
(c) c: b/a * 100

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

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : FEMALE

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

PAGE: 20

Organ		Group Name Control No. of Animals on Study 21 Grade $\frac{1}{(\%)}$ $\frac{2}{(\%)}$ $\frac{3}{(\%)}$ $\frac{4}{(\%)}$	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	20000 ppm 31 1 2 3 4 (%) (%) (%) (%)	40000 ppm 22 1 2 3 4 (%) (%) (%) (%)
[Endocrine s	ystem]				
pituitary	hyperplasia	<20> 0 1 0 0 (0) (5) (0) (0)	<26> 1 0 0 0 (4) (0) (0) (0)	\(\lambda 31 \rangle \) \[1 1 0 0 \\ (3) (0) (0) \]	<21> 1 0 0 0 (5) (0) (0) (0)
adrenal	fatty change	<20> 0 0 0 0 (0) (0) (0) (0)	<26> 0 1 0 0 (0) (4) (0) (0)	<pre></pre>	<22> 0 0 0 0 0 (0) (0) (0) (0)
	extramedullary hematopoiesis	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (5) (0) (0) (0)
	spindle-cell hyperplasia	15 5 0 0 (75) (25) (0) (0)	21 4 0 0 (81) (15) (0) (0)	22 5 0 0 (71) (16) (0) (0)	19 2 0 0 (86) (9) (0) (0)
[Reproductiv	e system]				
DUALY	angiectasis	(20) 0 0 0 0 (0) (0) (0) (0)	<26> 0 0 0 0 0 0 0 0 0 0 0	(31) 0 1 1 0 (0) (3) (3) (0)	<pre></pre>
	hemorrhage	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 1 0 (0) (3) (0)	0 0 0 0 0 (0) (0)
Grade <a> b (c) Significant	1: Slight 2: Moderate 3 a: Number of animals examined at the si b: Number of animals with lesion c: b / a * 100 difference; *: P ≤ 0.05 **: P ≤				

(HPT150)

SEX

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

ANIMAL : MOUSE BDF1 REPORT TYPE : A1

: FEMALE

Group Name Control 10000 ppm 20000 ppm 40000 ppm No. of Animals on Study

0rgan	Findings	No. of Animals on Study 21 Grade 1 2 3 4 (%) (%) (%) (%)	26 1 2 3 4 (%) (%) (%) (%)	31 (%) (%) (%) (%)	22 (%) (%) (%) (%) (%)
[Reproductive	e system]				
ovary	thrombus	<20> 0 0 0 0 (0) (0) (0) (0)	<26> 0 0 0 0 (0) (0) (0) (0)	0 1 0 0 (0) (3) (0) (0)	0 0 1 0 (0) (0) (5) (0)
	cyst	0 1 0 0 (0) (0)	0 4 0 0 (0) (15) (0) (0)	1 1 0 0 0 (3) (3) (0) (0)	0 0 1 0 (0) (5) (0)
uterus	thrombus	<21> 0 0 0 0 0 0 0 0 0 0 0	(26) 0 0 1 0 (0) (0) (4) (0)	31> 0 0 0 0 (0) (0) (0) (0)	<222> 0 0 0 0 (0) (0) (0) (0)
	cystic endometrial hyperplasia	3 1 0 0 (14) (5) (0) (0)	7 1 0 0 (27) (4) (0) (0)	6 1 0 0 (19) (3) (0) (0)	3 1 0 0 (14) (5) (0) (0)
mammary gl	hyperplasia	1 0 0 0 (5) (0) (0) (0)	<26> 0 0 0 0 0 0 0 0 0 0 0	31> 1 1 0 0 (3) (3) (0) (0)	222> 1 0 0 0 (5) (0) (0) (0)
	galactocele	1 0 0 0 (5) (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)
prep/cli gl	duct ectasia	<21> 0 0 0 0 (0) (0) (0) (0)	<26> 0 0 0 0 0 0 0 0 0 0 0	1 0 0 0 (3) (0) (0) (0)	<22> 0 0 0 0 0 0 0 0 0 0 0

Grade 1 : Slight 2 : Moderate

3 : Marked

4 : Severe

a: Number of animals examined at the site

b b: Number of animals with lesion (c)

c:b/a*100

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

(HPT150)

< a >

BAIS3

ANIMAL : MOUSE BDF1

REPORT TYPE : A1
SEX : FEMALE

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

PAGE: 22

		Group Name Control No. of Animals on Study 21	10000 ppm 26	20000 ppm 31	40000 ppm 22
Organ	Findings	Grade <u>1 2 3 4</u> (%) (%) (%) (%)	1 2 3 4 (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)
[Nervous sy	stem]				
brain	hemorrhage	<21> 0 1 0 0 (0) (5) (0) (0)		31> 0 0 0 0 (0) (0) (0) (0)	0 0 0 0 0 0 (0) (0) (0)
	mineralization	6 0 0 0 0 (29) (0) (0) (0		8 0 0 0 (29)(0)(0)(0)	9 0 0 0 0 (41) (0) (0) (0)
[Special se	nse organs/appandage]				
llarder gl	lymphocytic infiltration	21> 1 0 0 0 (5) (0) (0) (0		31> 1 0 0 0 (3) (0) (0) (0)	222> 1 0 0 0 (5) (0) (0) (0)
[Musculoske	letal system]				
muscle	mineralization	21> 1 0 0 0 (5) (0) (0) (0		31> 1 0 0 0 (3) (0) (0) (0)	222> 1 0 0 0 (5) (0) (0) (0)
[Body cavit	ies]				
pleura	inflammation	<21> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		<31> 0 0 0 0 (0) (0) (0) (0)	<22> 0 1 0 0 (0) (5) (0) (0)
Grade <a>> b (c) Significant	1: Slight 2: Moderate a: Number of animals examined at the b: Number of animals with lesion c: b / a * 100 difference; *: P ≤ 0.05 **: P				

(HPT150)

BAISS

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX

: FEMALE

DEAD AND MORIBUND ANIMALS (0-105W)

Organ	Findings	Group Name No. of Animals on Study Grade 1 (%)	Control 21 2 3 (%) (%)	4 (%)		000 ppm 66 3 4 (%) (%)	1(%)	20000 ppr 31 2 3 (%) (%)	4 (%)	<u>1</u> (%)	40000 ppm 22 2 3 (%) (%)	<u>4</u> (%)
[Body cavitie	[z											
eritoneum	inflammation	0 (0) (<21> 1 0 5) (0)	0 (0) (0 0	26> 0 0 (0)(0)	(0) (<31> 0 0 0) (0)	0 (0)	0 (0) (<22> 0 0 0) (0) (0 ()
lipose	granulation	0 (0) (<21> 0 0 0) (0)	0 (0) (0 0 (0) (0)	1 (3) (<31> 0 0 0) (0)	0 (0)	0 (0) (<22> 0 0 0) (0) (0
	1: Slight 2: Moderate 3 a: Number of animals examined at the s b: Number of animals with lesion c: b / a * 100 ifference; *: P ≤ 0.05 **: P ≤											

APPENDIX L 7

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

MOSUE: MALE: SACRIFICED ANIMALS

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL REPORT TYPE : A1

: MALE

SEX

: MOUSE BDF1 SACRIFICED ANIMALS (105W)

PAGE: 1 Group Name Control 10000 ppm 20000 ppm 40000 ppm No. of Animals on Study 34 35 30 25 Grade 3 Findings [Integumentary system/appandage] skin/app <34> <35> <30> <25> erosion 1 0 0 0 0 0 0 0 0 0 0 (0)(3)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) inflammation 0 (0)(3)(0)(0) (0)(0)(0)(0) (0)(3)(0)(0) (0)(0)(0)(0) hyperplasia:epidermis 0 1 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(3)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) epidermal cyst 0 0 0 0 (0)(0)(0)(0) (3)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) [Respiratory system] nasal cavit <34> ⟨30⟩ <25> eosinophilic change:olfactory epithelium 13 0 0 0 0 0 0 15 0 6 (38) (0) (0) (0) (23) (0) (0) (0) (50) (0) (0) (0) (24) (0) (0) (0) eosinophilic change:respiratory epithelium 11 2 0 0 3 1 0 7 0 0 0 (32) (6) (0) (0) (17) (9) (3) (0) (47) (3) (0) (0) (28) (0) (0) (0) respiratory metaplasia:olfactory epithelium 11 10 18 0 ** (32) (0) (0) (0) (29) (0) (0) (0) (57) (0) (0) (0) (72) (0) (0) (0) Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe <a>> a: Number of animals examined at the site b b: Number of animals with lesion (c) c : b / a * 100Significant difference; * : $P \le 0.05$ ** : $P \le 0.01$ Test of Chi Square

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

PAGE: 2

Organ	Group Name No. of Anim Grade Findings	Control als on Study 34 1 2 3 4 (%) (%) (%) (%)	10000 ppm 35 1 2 3 4 (%) (%) (%) (%)	20000 ppm 30 1 2 3 4 (%) (%) (%) (%)	40000 ppm 25 1 2 3 4 (%) (%) (%) (%)
[Respiratory	system]				
nasal cavit	respiratory metaplasia:gland	34> 5 5 0 0 (15) (15) (0) (0)	<35> 15 7 0 0 * (43) (20) (0) (0)	<30> 10 3 0 0 (33) (10) (0) (0)	<pre></pre>
	duct ectasia:olfactory gland	0 0 0 0 0 (0) (0)	0 0 0 0 0 0 (0)	9 0 0 0 *** (30) (0) (0) (0)	21 0 0 0 ** (84) (0) (0) (0)
nasopharynx	eosinophilic change	34> 0 0 0 0 (0) (0) (0) (0)	(35) 0 0 1 0 (0) (0) (3) (0)	30> 0 0 0 0 (0) (0) (0) (0)	<25> 0 0 0 0 (0) (0) (0) (0)
lung	bronchiolar-alveolar cell hyperplasia	<34> 0 0 0 0 0 0 0 0 0 0 0	(35) 1 2 0 0 (3) (6) (0) (0)	<30> 0 0 0 0 0 0 0 0 0 0 0	<25> 0 0 0 0 0 0 0 0 0
[Hematopoieti	ic system]				
bone marrow	myelofibrosis	(34) 0 0 0 0 (0) (0) (0) (0)	<35> 0 0 0 0 (0) (0) (0) (0)	30> 0 0 0 0 (0) (0) (0) (0)	<25> 1 0 0 0 (4) (0) (0) (0)
spleen	thrombus	34> 0 1 0 0 (0) (3) (0) (0)	<35> 0 0 0 0 0 0 0 0 0 0 0	<30> 0 0 0 0 (0) (0) (0) (0)	<25> 0 0 0 0 0 0 0 0 0 0
Grade <a>> b <a>Co Significant o	1: Slight 2: Moderate 3: Marked a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 difference; *: P ≤ 0.05 **: P ≤ 0.01 Te	4 : Severe st of Chi Square			DIVO

(HPT150)

BAIS3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : MALE SACRIFICED ANIMALS (105W)

PAGE: 3

Organ	Findings	Group Name Control No. of Animals on Study 34 Grade 1 2 3 (%) (%) (%) (%) (%)	10000 ppm 35 4 1 2 3 4 (%) (%) (%) (%)	20000 ppm 30 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
[Hematopoie	tic system]				
spleen	ero systemy	⟨34⟩	⟨35⟩	<30>	⟨25⟩
	deposit of melanin		0 4 0 0 0	2 0 0 0 0 (7) (0) (0) (0)	1 0 0 0 0 (4) (0) (0) (0)
	extramedullary hematopoiesis	3 1 0 (9) (3) (0) (0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	2 1 0 0 (7) (3) (0) (0)	1 2 0 0 (4) (8) (0) (0)
	hyperplasia:vascular	1 0 0 (3) (0) (0) (0 0 0 0 0 (0) (0)	1 1 0 0 (4) (4) (0) (0)
	follicular hyperplasia	2 2 1 (6) (6) (3) (0 2 1 1 0 0 0 (6) (3) (3) (0)	4 3 0 0 (13) (10) (0) (0)	1 1 0 0 (4) (4) (0) (0)
[Circulator	y system]				
neart	necrasis	<34> 0 0 0 (0) (0) (0) (355> 0 0 0 0 0 0) (0) (0) (0) (0)	30> 1 0 0 0 (3) (0) (0) (0)	<25> 0 0 0 0 0 0 0 0 0 0 0
	mineralization	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)
[Digestive	system]				
tooth	dysplasia	<34> 22 3 2 (65) (9) (6) (35> 1 21 6 0 0 3) (60)(17)(0)(0)	<30> 9 6 2 0 * (30) (20) (7) (0)	<25> 15 2 1 0 (60) (8) (4) (0)

(11000-00)

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

b: Number of animals with lesion b

(c) c:b/a*100

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

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

PAGE: 4

Organ		Group Name Control No. of Animals on Study 34 Grade 1 2 3 4 (%) (%) (%) (%)	10000 ppm 35 1 2 3 4 (%) (%) (%) (%)	20000 ppm 30 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$
[Digestive sy:	stem]				
tongue	arteritis	(34) 1 0 0 0 (3) (0) (0) (0)	<35> 0 0 0 0 (0) (0) (0) (0)	<30> 0 0 0 0 (0) (0) (0) (0)	<25> 0 0 0 0 0 0 0 0 0 0
salivary gl	atrophy	34> 0 0 0 0 (0) (0) (0) (0)	<35> 0 0 0 0 0 0 0 0 0 0 0	<30> 0 0 0 0 (0) (0) (0) (0)	<25> 0 1 0 0 (0) (4) (0) (0)
tomach	hyperplasia:forestomach	34> 0 0 0 0 (0) (0) (0) (0)	<35> 0 0 0 0 0 0 0 0 0 0 0 0	<30> 1 1 0 0 (3) (3) (0) (0)	<25> 0 0 0 0 0 0 0 0 0 0 0
	erosion:glandular stomach	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 (3) (0) (0) (0)	1 0 0 0 (4) (0) (0) (0)
	hyperplasia:glandular stomach	14 5 0 0 (41) (15) (0) (0)	14 4 0 0 (40) (11) (0) (0)	9 3 0 0 (30) (10) (0) (0)	7 1 0 0 (28) (4) (0) (0)
mall intes	thrombus	<34> 0 1 0 0 (0) (3) (0) (0)	<35> 0 0 0 0 0 0 0 0 0 0 0	<30> 0 0 0 0 (0) (0) (0) (0)	<25> 0 0 0 0 0 0 0 0 0 0 0
liver	angiectasis	(34) 0 1 0 0 (0) (3) (0) (0)	<pre></pre>	<30> 0 1 1 0 (0) (3) (3) (0)	<25> 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 lifference; *: P ≤ 0.05 **: P ≤				

(HPT150)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL : MOUSE BDF1

: MALE

REPORT TYPE : A1

SEX

SACRIFICED ANIMALS (105W)

PAGE: 5

Organ	Findings	Group Name Control No. of Animals on Study 34 Grade 1 2 3 4 (%) (%) (%) (%)	10000 ppm 35 1 2 3 4 (%) (%) (%) (%)	20000 ppm 30 1 2 3 4 (%) (%) (%) (%)	40000 ppm 25 1 2 3 4 (%) (%) (%) (%)
[Digestive	system]				
liver	necrosis:central	<34> 0 0 0 0 (0) (0) (0) (0)	35> 0 0 0 0 (0) (0) (0) (0)	(30) 0 1 0 0 (0) (3) (0) (0)	<25> 0 0 0 0 0 0 0 0 0 0 0 0
	nocrosis:facal	2 0 2 0 (6) (0) (6) (0)	3 1 0 0 (9) (3) (0) (0)	3 1 0 0 (10) (3) (0) (0)	1 0 0 0 0 (4) (0) (0)
	fatty change:central	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 0 0 0 0 0 0 0 0 0 0 0 0 0
	lymphocytic infiltration	1 0 0 0 0 (3) (0) (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (3) (0) (0) (0)	0 0 0 0 0 (0) (0)
	granulation	11 1 0 0 (32) (3) (0) (0)	21 0 1 0 (60) (0) (3) (0)	15 1 0 0 (50) (3) (0) (0)	16 0 0 0 * (64) (0) (0) (0)
	clear cell focus	3 1 0 0 (9) (3) (0) (0)	2 0 0 0 0 (6) (0) (0)	1 0 0 0 0 (3) (0) (0) (0)	0 0 0 0 0 0 (0) (0)
	acidophilic cell focus	1 0 0 0 0 (3) (0) (0)	2 0 0 0 0 (6) (6) (7) (7)	1 0 0 0 0 (3) (0) (0) (0)	0 0 0 0 0 0 (0) (0)
	basophilic cell focus	2 1 0 0 (6)(3)(0)(0)	1 0 0 0 0 (3) (0) (0) (0)	3 1 0 0 (10) (3) (0) (0)	2 0 1 0 (8) (0) (4) (0)

Grade

1 : Slight

2 : Moderate

3 : Marked

4 : Severe

<a>>

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

b (c)

c:b/a*100

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

(HPT150)

BAIS3

STUDY NO. : 0225 ANIMAL : MOUSE BDF1 HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

REPORT TYPE : A1 SEX

: MALE

*** * * * * * * * * * * * * * * * * * *					
gan	Findings	Group Name Control No. of Animals on Study 34 Grade 1 2 3 (%) (%) (%)	10000 ppm 35 4 (%) (%) (%) (%)	20000 ppm 30 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
Digestive sy	vstem]				
iver	biliary cyst	(34) 1 0 0 (3) (0) (0) (0 0 0 0 0 0) (0) (0) (0) (0)	<30> 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<25> 0 0 0 0 (0) (0) (0) (0)
ancreas	islet cell hyperplasia	(34) 1	0 0 0 0 0 0) (0) (0) (0) (0)	<30> 0 1 0 0 (0) (3) (0) (0)	<25> 1 0 0 0 (4) (0) (0) (0)
Urinary syst	tem]				
idney	infarct	(34) 0 0 0 (0) (0) (0) (0 1 0 0 0 0) (3) (0) (0) (0)	<30> 0 0 0 0 (0) (0) (0) (0)	<25> 2 0 0 0 (8) (0) (0) (0)
	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)	1 0 0 0 (4) (0) (0) (0)
	basophilic change	0 0 0 (0) (0) (1 0 0 0 0 (3) (0) (0) (0)	0 1 0 0 (0) (0)
	hyaline cast	1 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)

(a)

a : Number of animals examined at the site

b

b: Number of animals with lesion

(c)

c:b/a*100

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

(HPT150)

BAIS3

STUDY NO. : 0225 ANIMAL : MOUSE BDF1 HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

REPORT TYPE : A1 SEX

: MALE

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

2 : Moderate

3 : Marked

4 : Severe

<a>>

a : Number of animals examined at the site

b (c) b: Number of animals with lesion

c:b/a*100 Significant difference; $*:P \le 0.05$ $**:P \le 0.01$ Test of Chi Square

(HPT150)

BAIS3

: MOUSE BDF1 ANIMAL

REPORT TYPE : A1 SEX : MALE HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

PAGE: 8

)rgan	Group Name No. of Anim Grade Findings	Control als on Study 34 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	20000 ppm 30 1 2 3 4 (%) (%) (%) (%)	40000 ppm 25 1 2 3 4 (%) (%) (%) (%)
Endocrine s	system]				
ituitary	hyperplasia	0 0 0 0 (0) (0) (0) (0)	35> 1 0 0 0 (3) (0) (0) (0)	30> 0 0 0 0 (0) (0) (0) (0)	25> 1 0 0 0 (4) (0) (0) (0)
	Rathke pouch	6 0 0 0 (18) (0) (0) (0)	4 0 0 0 (11) (0) (0) (0)	6 0 0 0 0 (20) (0) (0) (0)	2 0 0 0 0 (8) (0) (0) (0)
drena l	spindle-cell hyperplasia	20 0 0 0 (59) (0) (0) (0)	35> 16 0 0 0 (46) (0) (0) (0)	30> 11 1 0 0 (37) (3) (0) (0)	\(\langle 25 \) 12
	hyperplasia:cortical cell	2 0 0 0 0 (6) (6) (0) (0)	1 0 0 0 0 (3) (0) (0)	1 0 0 0 0 (3) (0) (0) (0)	0 0 0 0 0 (0) (0) (0)
Reproductiv	ve system]				
estis	atrophy	343 15 4 0 0 (44) (12) (0) (0)	35> 12 5 0 0 (34) (14) (0) (0)	30> 9 3 0 0 (30) (10) (0) (0)	(25) 11 0 0 0 (44) (0) (0) (0)
	mineralization	31 0 0 0 (91) (0) (0) (0)	32 1 0 0 (91) (3) (0) (0)	26 4 0 0 * (87) (13) (0) (0)	23 0 1 0 (92) (0) (4) (0)
rade 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 difference; *: $P \le 0.05$ **: $P \le 0.01$ Te	4 : Severe est of Chi Square			

(HPT150)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

Group Name Control 10000 ppm 20000 ppm 40000 ppm No. of Animals on Study 34 35 30 25 2 3 2 3 4 (%) Findings_ Organ___ (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) [Reproductive system] epididymis <34> inflammation 1 1 0 0 0 0 1 0 1 0 0 0 (3)(3)(0)(0) (0)(0)(3)(0) (3)(0)(0)(0) (0)(0)(0)(0) 0 1 0 0 spermatogenic granuloma 0 3 0 0 0 3 0 0 1 1 0 0 (0)(3)(0)(0) (0)(9)(0)(0) (0) (10) (0) (0) (4)(4)(0)(0) semin ves <30> mineralization 0 1 0 0 0 0 0 0 1 0 0 0 0 0 0 0 (0)(3)(0)(0) (0)(0)(0)(0) (3)(0)(0)(0) (0)(0)(0)(0) inflammation 0 0 0 0 1 0 0 0 0 0 0 0 (0)(0)(0)(0) (3)(0)(0)(0) (3)(0)(0)(0) (0)(0)(0)(0) prep/cli gl <30> duct ectasia 0 1 0 0 0 0 0 0 0 0 0 0 0 1 0 0 (0)(3)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(4)(0)(0) [Nervous system] brain <34> mineralization 0 0 0 0 0 0 20 22 0 0 0 14 0 0 0 (71) (0) (0) (0) (57) (0) (0) (0) (73) (0) (0) (0) (56) (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 b c:b/a*100

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

STUDY NO. : 0225 ANIMAL : MOUSE BDF1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

REPORT TYPE : A1 SEX : MALE

Group Name Control 10000 ppm 20000 ppm 40000 ppm No. of Animals on Study 34 35 30 25 3 2 3 0rgan Findings (%) (%) (%) (%) (%) (%) (%) (%) (%) [Special sense organs/appandage] еуе <34> cataract 0 0 0 0 0 0 0 0 0 (3)(0)(0)(0) (3)(0)(0)(0) (3)(0)(0)(0) (0)(0)(0)(0) keratitis 0 0 0 1 0 0 0 0 0 0 0 1 0 0 (0)(0)(0)(0) (3)(0)(0)(0) (0) (0) (0) (0) (0)(4)(0)(0) Harder gl <34> ⟨30⟩ lymphocytic infiltration 0 0 0 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (3)(0)(0)(0) (3)(0)(0)(0) (0)(0)(0)(0) hyperplasia 1 0 0 0 0 0 0 0 0 0 0 0 (3)(0)(0)(0) (3)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) [Body cavities] mesenterium <34> inflammation 0 1 0 0 0 0 0 0 0 0 0 (0)(3)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) adipose <34> ⟨35⟩ <30> granulation 1 0 0 0 0 0 0 1 0 0 0 0 0 0 0 (0)(3)(0)(0) (0)(0)(0)(0) (3)(0)(0)(0) (0)(0)(0)(0) Grade 1: Slight 2 : Moderate 3 : Marked 4 : Severe (a) a: Number of animals examined at the site b: Number of animals with lesion (c) c:b/a*100

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

APPENDIX L 8

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

MOSUE: FEMALE: SACRIFICED ANIMALS

ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

PAGE: 11

0rgan	No		3 4 %) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	20000 ppm 19 1 2 3 4 (%) (%) (%)	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$
[Integumentar	y system/appandage]					
skin/app	inflammation	<29> 0 1 (0) (3) (0 0 0) (0)	<24> 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	<28> 0 0 0 0 0 0 0 0 0 0 0 0 0 0
	scab	0 0 0 (0 0 0 0 0) (0)	0 0 0 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)
[Respiratory	system]					
nasal cavit	embolus	<29> 0 0 (0) (0) (0 0 0) (0)	0 0 0 0 (0) (0) (0) (0)	<pre></pre>	<pre></pre>
	easinophilic change:alfactory epithelium	1 0 (3) (0) (1 0 3) (0)	1 1 0 0 (4) (4) (0) (0)	0 0 0 0 0 (0) (0)	11 0 0 0 *** (39) (0) (0) (0)
	easinophilic change:respiratory epitheli	um 16 3 (55) (10) (0 0 0 0) (0)	14 4 1 0 (58) (17) (4) (0)	12 2 0 0 (63) (11) (0) (0)	18 5 0 0 (64) (18) (0) (0)
	inflammation:respiratory epithelium	0 0 0	0 0 0 0) (0)	1 0 0 0 0 (4) (0) (0)	1 0 0 0 0 (5) (0) (0)	0 0 0 0
	disarrangement:olfactory 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 0 (4) (0) (0) (0)

Grade 1: Slight

2 : Moderate

3 : Marked

4 : Severe

(a)

a: Number of animals examined at the site

b

b: Number of animals with lesion

(c) c:b/a*100

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

STUDY NO. : 0225 ANIMAL : MOUSE BDF1 HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

REPORT TYPE : A1 SEX : FEMALE

PAGE: 12

0rgan	Group Name No. of Anim Grade Findings	Control mals on Study 29 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	20000 ppm 19 12 3 4 (%) (%) (%) (%)	40000 ppm 28 1 2 3 4 (%) (%) (%) (%)
[Respiratory	system]				
nasal cavit	respiratory metaplasia:olfactory epithelium	29> 1 1 0 0 (3) (3) (0) (0)	0 0 0 0 (0) (0) (0) (0)	7 0 0 0 ** (37) (0) (0) (0)	<pre></pre>
	respiratory metaplasia:gland	0 0 0 0 0 (0) (0)	4 0 0 0 (17) (0) (0) (0)	7 0 0 0 *** (37) (0) (0) (0)	9 1 0 0 ** (32) (4) (0) (0)
	duct ectasia:olfactory gland	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	3 0 0 0 (16) (0) (0) (0)	24 0 0 0 *** (86) (0) (0) (0)
nasopharynx	eosinophilic change	(29) 1 2 0 0 (3) (7) (0) (0)	24> 1 2 0 0 (4) (8) (0) (0)	2 1 0 0 (11) (5) (0) (0)	<28> 1 1 0 0 (4) (4) (0) (0)
lung	hemorrhage	<29> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<24> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	(19) 0 0 1 0 (0) (0) (5) (0)	<28> 0 0 0 0 0 0 0 0 0 0 0
	lymphocytic infiltration	5 1 0 0 (17) (3) (0) (0)	3 0 0 0 0 (13) (0) (0) (0)	5 0 0 0 (26) (0) (0) (0)	4 2 0 0 (14) (7) (0) (0)
	bronchiolar—alveolar cell hyperplasia	1 0 0 0 (3) (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)
Grade < a > b (c) Significant d	1: Slight 2: Moderate 3: Marked a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 lifference; $*: P \le 0.05$ **: $P \le 0.01$ To	4 : Severe est of Chi Square			

(HPT150)

BAIS3

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

ANIMAL : MOUSE BDF1 REPORT TYPE : A1

SEX : FEMALE

PAGE: 13

Organ	Findings	Group Name Control No. of Animals on Study 29 Grade 1 2 3 (%) (%) (%)	10000 ppm 24 4 (%) 1 2 3 4 (%) (%) (%) (%)	20000 ppm 19 1 2 3 4 (%) (%) (%) (%)	40000 ppm 28 1 2 3 4 (%) (%) (%) (%)
Nematopoieti	c system]				
one marrow	myelofibrosis	(29) 1 0 0 (3) (0) (0)	C24> C 2 0 0 0 C 8) (0) (0) (0)	<19> 0 0 0 0 0 0 0 0 0 0 0 0 0 0	28> 1 0 0 0 (4) (0) (0) (0)
.ymph nade	deposit of melanin	<29> 0 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	<28> 0 1 0 0 (0) (4) (0) (0)
	lymphadenitis	0 0 0 0 (0)	0 0 2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 1 0 0 (5) (0) (0)	0 1 0 0 (0) (0)
pleen	deposit of melanin	29> 1 0 0 (3) (0) (0)	C24> C 2 0 0 0 C 8) (0) (0) (0)	(0) (0) (0) (0)	<28> 0 0 0 0 0 0 0 0 0 0 0
	extramedullary hematopoiesis	0 0 0 0 (0)	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	1 1 0 0 (5) (5) (0) (0)	0 2 0 0 (0) (7) (0) (0)
	follicular hyperplasia	1 1 0 (3) (3) (0)	0 2 2 0 0 (8) (8) (0) (0)	3 1 1 0 (16) (5) (5) (0)	1 1 0 0 (4) (4) (0) (0)
	capsule 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 1 0 0 (0) (4) (0) (0)

(HPT150)

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

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

ANIMAL : MOUSE BDF1 REPORT TYPE : A1

SEX : FEMALE

Organ	Findings	Group Name Control No. of Animals on Study 29 Grade 1 2 3 4 (%) (%) (%) (%)	10000 ppm 24 1 2 3 4 (%) (%) (%) (%)	20000 ppm 19 1 2 3 4 (%) (%) (%) (%)	40000 ppm 28 1 2 3 4 (%) (%) (%) (%)
[Circulatory	system]				
heart	inflammation	<29> 0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	1 0 0 0 (5) (0) (0) (0)	<28> 0 0 0 0 0 (0) (0) (0) (0)
[Digestive sy	stem]				
tooth	dysplasia	\$29> 5 0 0 0 (17) (0) (0) (0)	24> 2 0 0 0 (8) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	<pre></pre>
tangue	arteritis	<29> 0 0 0 0 (0) (0) (0) (0)	<24> 0 0 0 0 0 0 0 0 0 0 0	1 0 0 0 (5) (0) (0) (0)	<28> 0 0 0 0 0 (0) (0) (0) (0)
alivary gl	inflammation	<29> 0 1 0 0 (0) (3) (0) (0)	<24> 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	<28> 0 0 0 0 0 (0) (0) (0) (0)
	lymphocytic infiltration	9 0 0 0 (31) (0) (0) (0)	8 0 0 0 (33) (0) (0) (0)	4 0 0 0 0 (21) (0) (0)	6 1 0 0 (21) (4) (0) (0)
stomach	mineralization	29> 2 0 0 0 (7) (0) (0) (0)	<24> 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	<28> 0 0 0 0 0 0 0 0 0 0 0 0

b b: Number of ani (c) c:b/a * 100

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

(HPT150)

BAIS3

STUDY NO. : 0225 ANIMAL

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

REPORT TYPE : A1 SEX : FEMALE

: MOUSE BDF1 SACRIFICED ANIMALS (105W)

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

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

(HPT150)

BAIS3

STUDY NO. : 0225 ANIMAL

: MOUSE BDF1

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

Organ	Group Nam No. of An Grade Findings	Control imals on Study 29 1 2 3 4 (%) (%) (%) (%)	10000 ppm 24 1 2 3 4 (%) (%) (%) (%)	20000 ppm 19 1 2 3 4 (%) (%) (%) (%)	40000 ppm 28 1 2 3 4 (%) (%) (%) (%)
[Digestive	system]				
liver	lymphocytic infiltration	<29> 0 0 0 0 (0) (0) (0) (0)	<24> 0 0 0 0 (0) (0) (0) (0)	<19> 0 0 0 0 (0) (0) (0) (0)	<28> 2 0 0 0 (7) (0) (0) (0)
	granulation	22 0 0 0 (76) (0) (0) (0)	17 2 0 0 (71) (8) (0) (0)	11 0 0 0 (58) (0) (0) (0)	17 2 0 0 (61) (7) (0) (0)
	clear cell focus	1 0 0 0 0 (3) (0) (0)	2 0 0 0 0 (8) (0) (0) (0)	2 0 0 0 (11) (0) (0) (0)	2 0 1 0 (7) (0) (4) (0)
	acidophilic cell focus	0 0 0 0 0 (0)	0 0 0 0 0 (0) (0)	1 1 0 0 (5) (5) (0) (0)	0 0 0 0 0 (0) (0) (0)
	basophilic cell focus	1 0 0 0 0 (3) (0) (0)	0 0 0 0 0 (0) (0) (0)	1 0 0 0 (5) (0) (0) (0)	1 0 0 0 (4) (0) (0) (0)
	biliary cyst	1 0 0 0 0 (3) (0) (0)	1 0 0 0 0 (4) (0) (0)	1 0 0 0 0 (5) (0) (0) (0)	0 0 0 0 0 (0) (0)
[Urinary s	ystem]			•	
kidney	hyaline droplet	<29> 0 1 0 0 (0) (3) (0) (0)	(24) 0 0 0 0 (0) (0) (0) (0)	3 0 0 0 (16) (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 t difference; *: P ≤ 0.05 **: P ≤ 0.01	4 : Severe			

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 : FEMALE SEX

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

PAGE: 17 Group Name Control 10000 ppm 20000 ppm 40000 ppm No. of Animals on Study 29 24 19 28 2 3 3 3 2 3 0rgan_ Findings_ (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) [Urinary system] kidney ⟨29⟩ <24> <19> deposit of hemosiderin 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) hyaline cast 0 0 0 0 0 0 0 1 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (5)(0)(0)(0) (0)(0)(0)(0) lymphocytic infiltration 0 0 (10) (3) (0) (0) (21) (0) (0) (0) (16) (0) (0) (0) (21) (0) (0) (0) granulation (3)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) inflammatory polyp 0 0 0 0 (0)(0)(0)(0) (0)(4)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) hydronephrosis 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(4)(0) urin bladd <29> <24> <19> inflammation 1 0 0 0 0 0 0 1 0 0 0 0 1 1 0 (3)(0)(0)(0) (4)(0)(0)(0) (5)(0)(0)(0) (0)(4)(4)(0) [Endocrine system] pituitary ⟨29⟩ <24> <18> 0 0 0 0 angiectasis 0 0 0 0 0 0 1 0 0 0 (3)(0)(0)(0) (0) (0) (0) (0) (0)(0)(0)(0) (4)(0)(0)(0)

Grade 1: Slight (a)

3 : Marked 2 : Moderate

4 : Severe

a: Number of animals examined at the site

b b: Number of animals with lesion

(c) c:b/a*100

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

: MOUSE BDF1 ANIMAL.

REPORT TYPE : A1 : FEMALE SEX

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

PAGE: 18

0rgan	Group No. o Grade Findings	f Animals on Study 29	10000 ppm 24 1 2 3 4 (%) (%) (%) (%)	20000 ppm 19 12 3 4 (%) (%) (%) (%)	40000 ppm 28 1 2 3 4 (%) (%) (%) (%)
[Endocrine s	ystem]				
pituitary	hyperplasia	3 2 0 0 (10) (7) (0) (0)	3 1 0 0 (13) (4) (0) (0)	2 1 0 0 (11) (6) (0) (0)	28> 2 3 0 0 (7) (11) (0) (0)
adrenal	Rathke pouch	<29> 0 0 0 0 (0) (0) (0) (0)	<24> 0 0 0 0 (0) (0) (0) (0)	1 0 0 0 (5) (0) (0) (0)	<28> 0 0 0 0 0 0 0 0 0
	gaiter	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)
	spindle-cell hyperplasia	18 11 0 0 (62) (38) (0) (0)	10 14 0 0 (42) (58) (0) (0)	11 6 0 0 (58) (32) (0) (0)	13 14 1 0 (46) (50) (4) (0)
	hyperplasia:cortical cell	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)
[Reproductive	e system]				
o∪ary	angiectasis	<29> 0 0 0 0 (0) (0) (0) (0)	<24> 0 0 0 0 (0) (0) (0) (0)	<19> 0 0 0 0 (0) (0) (0) (0)	<28> 0 0 1 0 (0) (0) (4) (0)
Grade <a>> b (c) Significant	1: Slight 2: Moderate 3: Marla: Number of animals examined at the site $b:$ Number of animals with lesion $c:b/a*100$ difference; $*:P \le 0.05$ **: $P \le 0.01$				

(HPT150)

ANIMAL : MOUSE BDF1

REPORT TYPE : A1
SEX : FEMA : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

PAGE: 19

Organ	Findings	Group Name Control No. of Animals on Study 29 Grade 1 2 3 4 (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	20000 ppm 19 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$
[Reproductive	ə systəm]				
ovary	cyst	3 6 0 0 (10) (21) (0) (0)	4 5 0 0 (17) (21) (0) (0)	<19> 1 3 0 0 (5) (16) (0) (0)	3 2 0 0 (11) (7) (0) (0)
uterus	thrombus	<29> 0 0 0 0 0 0 0 0 0 0 0	<24> 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	<28> 0 0 1 0 0 0 1 0 0 0 0 4 0 0
	decidual change	0 0 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)
	cystic endometrial hyperplasia	8 6 0 0 (28) (21) (0) (0)	5 12 0 0 (21) (50) (0) (0)	4 8 0 0 (21) (42) (0) (0)	8 7 0 0 (29) (25) (0) (0)
mammary gl	lymphocytic infiltration	<29> 0 0 0 0 0 0 0 0 0 0 0	<24> 0 0 0 0 (0) (0) (0) (0)	<19> 1 0 0 0 (5) (0) (0) (0)	<28> 1 0 0 0 (4) (0) (0) (0)
	hyperplasia	3 1 0 0 (10) (3) (0) (0)	5 0 0 0 (21) (0) (0) (0)	1 0 0 0 (5) (0) (0) (0)	2 0 0 0 0 (7) (0) (0) (0)
	atypical hyperplasia	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (4) (0) (0) (0)
Grade (a> b (c) Significant of	1: Slight 2: Moderate 3 a: Number of animals examined at the s b: Number of animals with lesion c: b / a * 100 difference; *: P ≤ 0.05 **: P:				

(HPT150)

BAIS3

STUDY NO. : 0225 ANIMAL : MOUSE BDF1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

REPORT TYPE : A1

SEX

: FEMALE

SACRIFICED ANIMALS (105W)

PAGE: 20 Group Name Control 10000 ppm 20000 ppm 40000 ppm No. of Animals on Study 29 24 19 28 Grade 3 Findings (%) Organ___ (%) [Nervous system] brain <19> mineralization 14 0 0 0 14 0 0 0 10 17 0 0 0 0 0 0 (48) (0) (0) (0) (58) (0) (0) (0) (53) (0) (0) (0) (61) (0) (0) (0) [Special sense organs/appandage] Harder gl <29> <24> degeneration 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(5)(0)(0) (0)(0)(0)(0) lymphocytic infiltration 0 (0)(0)(0)(0) (4)(0)(0)(0) (5)(0)(0)(0) (7)(0)(0)(0) hyperplasia 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(5)(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 Significant difference; * : P \leq 0.05 ** : P \leq 0.01 Test of Chi Square

(HPT150)

BAIS3

APPENDIX M 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. : 0224
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

me-related Weeks	Items	Group Name	Control	7500 ppm	15000 ppm	maa 00008	
0 - 52	NO. OF EXAMINED ANIMALS		0	0	0	0	
	NO. OF ANIMALS WITH TUMORS		0	0	0	0	
	NO. OF ANIMALS WITH SINGLE TUMORS		0	0	0	0	
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	0	0	0	
	NO. OF BENIGN TUMORS		0	0	0	0	
	NO. OF MALIGNANT TUMORS		0	0	0	0	
	NO. OF TOTAL TUMORS		0	0	0	0	
53 - 78	NO. OF EXAMINED ANIMALS		2	3	4	0	
	NO. OF ANIMALS WITH TUMORS		2	3	2	0	
	NO. OF ANIMALS WITH SINGLE TUMORS		2	2	2	0	
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	1	0	0	
	NO. OF BENIGN TUMORS		1	2	1	0	
	NO. OF MALIGNANT TUMORS		1	2	1	0	
-	NO. OF TOTAL TUMORS		2	4	2	0	
79 - 104	NO. OF EXAMINED ANIMALS		10	8	12	20	
	NO. OF ANIMALS WITH TUMORS		10	8	12	20	
	NO. OF ANIMALS WITH SINGLE TUMORS		4	2	0	6	
	NO. OF ANIMALS WITH MULTIPLE TUMORS		6	6	12	14	
	NO. OF BENIGN TUMORS		15	11	20	36	
	NO. OF MALIGNANT TUMORS NO. OF TOTAL TUMORS		6 21	6 17	11 31	11 47	
105 - 105	NO. OF EXAMINED ANIMALS		38	39	34	30	
100 100							
	NO. OF ANIMALS WITH TUMORS		38	39	34	30	
	NO. OF ANIMALS WITH SINGLE TUMORS NO. OF ANIMALS WITH MULTIPLE TUMORS		12 26	8 31	13 21	5 25	
	NO. OF MATHALS WITH MOLITICE TOMONS		20	01			
	NO. OF BENIGN TUMORS		76	80	62	65	
	NO. OF MALIGNANT TUMORS		9	12	5 67	7	
	NO. OF TOTAL TUMORS		85	92	67	72	

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

PAGE: 2

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

NO. OF BENIGN TUMORS

NO. OF TOTAL TUMORS

NO. OF MALIGNANT TUMORS

Time-related Weeks	Items	Group Name	Control	7500 ppm	15000 ppm	maa 00008	
0 - 105	NO. OF EXAMINED ANIMALS		50	50	50	50	
	NO. OF ANIMALS WITH TUMORS NO. OF ANIMALS WITH SINGLE TUMORS NO. OF ANIMALS WITH MULTIPLE TUMORS		50 18 32	50 12 38	48 15 33	50 11 39	

108 (HPT070) BAIS3

92

16

93

20

113

83

17

100

101

18

119

APPENDIX M 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. : 0224
ANIMAL : RAT F344
REPORT TYPE : A1
SEY : FEMALE

SEX : FEMALE

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

(HPT070)

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

ANIMAL : RAT F344 REPORT TYPE : A1

: FEMALE SEX PAGE: 4

Time-relatedWeeks	Items	Group Name	Control	7500 ppm	15000 ppm	maq 00008	
0 - 105	NO. OF EXAMINED ANIMALS		50	50	50	50	
	NO. OF ANIMALS WITH TUMORS		36	37	33	26	
	NO. OF ANIMALS WITH SINGLE TUMORS NO. OF ANIMALS WITH MULTIPLE TUMORS		19 17	20 17	19 14	17 9	
	NO. OF BENIGN TUMORS		54	48	36	28	
	NO. OF MALIGNANT TUMORS NO. OF TOTAL TUMORS		4 58	12 60	17 53	8 36	
(HPT070)							DATES

(HPT070)

BAIS3

APPENDIX M 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. : 0225 ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : MALE

SEX : MALE PAGE : 1

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

(HPT070)

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

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : MALE

PAGE: 2

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

(HPT070)

BAIS3

APPENDIX M 4

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. : 0225 ANIMAL : MOUSE BDF1

REPORT TYPE : A1

SEX : FEMALE

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

(HPT070)

ANIMAL : MOUSE BDF1

NO. OF MALIGNANT TUMORS

NO. OF TOTAL TUMORS

REPORT TYPE : A1

SEX : FEMALE

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

PAGE: 4

Time-related Items_ Group Name Control 10000 ppm 20000 ppm 40000 ppm ____Weeks NO. OF EXAMINED ANIMALS 0 - 10550 50 50 50 NO. OF ANIMALS WITH TUMORS 40 42 41 44 NO. OF ANIMALS WITH SINGLE TUMORS 28 26 27 24 NO. OF ANIMALS WITH MULTIPLE TUMORS 12 16 14 20 NO. OF BENIGN TUMORS 26 30 22 35

(HPT070) BAIS3

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APPENDIX N 1

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

RAT : MALE :

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

REPORT TYPE : A1 SEX : MALE

0rgan	Findings	Group Name No. of animals on Study	Control 50	7500 ppm 50	15000 ppm 50	30000 ppm 50
[Integumenta	ary system/appandage]					
skin/app	squamous cell papilloma		<50> 0 (0%)	<50> 0 (0%)	<50> 0 (0%)	<50> 2 (4%)
	trichoepithelioma		0 (0%)	1 (2%)	0 (0%)	2 (4%)
	keratoacanthoma		1 (2%)	3 (6%)	1 (2%)	4 (8%)
	sebaceous adenoma		0 (0%)	0 (0%)	0 (0%)	3 (6%)
	squamous cell carcinoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
subcutis	fibroma		<50> 4 (8%)	<50> 4 (8%)	<50> 4 (8%)	<50> 6 (12%)
	lipoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
	schwannoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
	chordona		0 (0%)	1 (2%)	0 (0%)	0 (0%)
	hemangioma		0 (0%)	1 (2%)	1 (2%)	0 (0%)
	fibrosarcoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
	schwannoma:malignant		0 (0%)	1 (2%)	0 (0%)	0 (0%)
	malignant fibrous histiocytoma		0 (0%)	1 (2%)	0 (0%)	1 (2%)
(a) b (c)	a: Number of animals examined at the site b: Number of animals with neoplasm c: b/a*	100				
(HPT085)						

(HPT085)

BAIS3

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

REPORT TYPE : A1 SEX : MALE

rgan	Findings Group No. of	Name Control animals on Study 50	7500 ppm 50	15000 ppm 50	30000 ppm 50
Respiratory s	ystem]				
asal cavit	adenoma	<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)	<50> 0 (0%)
una	bronchiolar-alveolar adenoma	<50> 3 (6%)	<50> 3 (6%)	<50> 3 (6%)	<50> 5 (10%)
	bronchiolar-alveolar carcinoma	0 (0%)	0 (0%)	0 (0%)	2 (4%)
Hematopoietic	system]				
.ymph node	malignant lymphoma	<50> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)
hymus	thymoma:malignant	<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)	<50> 1 (2%)
pleen	hemangioma	<50>. 0 (0%)	<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)
	mononuclear cell leukemia	6 (12%)	2 (4%)	2 (4%)	4 (8%)
Digestive sys	tem]				
tomach	squamous cell papilloma	<50> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)
mall intes	fibroma	<50> 0 (0%)	<49> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)
arge intes	adenocarcinoma	<50> 0 (0%)	<49> 1 (2%)	<50> 0 (0%)	<50> 0 (0%)
.iver	hepatocellular adenoma	<50> 1 (2%)	<50> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)

⁽IIPT085)

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

REPORT TYPE : A1 SEX : MALE

Organ	Findings_	Group Name (No. of animals on Study	Cont	trol 50	750	0 ppm 50	150	00 ppm 50	3000	0 ppm 50
(Digestive sys	tem]									
liver	histiocytic sarcoma			<50> (0%)	0	<50> (0%)	1	<50> (2%)	1	<50> (2%)
	hepatocellular carcinoma		0	(0%)	2	(4%)	0	(0%)	1	(2%)
pancreas	islet cell adenoma			<50> (8%)	3	<50> (6%)	4	<50> (8%)	3	<50> (6%)
	islet cell adenocarcinoma		1	(2%)	0	(0%)	0	(0%)	0	(0%)
[Urinary system	n]									
kidney	nephrablastoma			<50> (2%)	0	<50> (0%)	0	<50> (0%)	0	<50> (0%)
rin bladd	transitional cell papilloma			<50> (0%)	1	<50> (2%)	1	<50> (2%)	0	<50> (0%)
Endocrine sys	tem]									
pituitary	adenoma	:		<50> (28%)	14	<50> (28%)	11	<50> (22%)	18	<50> (36%)
	adenocarcinoma		3	(6%)	1	(2%)	3	(6%)	1	(2%)
thyroid	C-cell adenoma	:		<50> (24%)	5	<50> (10%)	5	<50> (10%)	4	<50> (8%)
	follicular adenocarcinoma		1	(2%)	1	(2%)	2	(4%)	1	(2%)
adrena l	pheochromocytoma			<50> (8%)	7	<50> (14%)	5	<50> (10%)	7	<50> (14%)

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

: MALE

SEX

(HPT085)

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0-105W)

Organ		p Name Control of animals on Study 50	7500 ppm 50	15000 ppm 50	30000 ppm 50
(Endocrine syst	tem]				
adrenal	ganglioneuroma	<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)	<50> 1 (2%)
	cortical adenoma	0 (0%)	1 (2%)	1 (2%)	0 (0%)
	pheochromocytoma:malignant	0 (0%)	0 (0%)	1 (2%)	1 (2%)
[Reproductive :	system]				
testis	interstitial cell tumor	<50> 44 (88%)	<50> 43 (86%)	<50> 42 (84%)	<50> 44 (88%)
	rete testis adenoma	1 (2%)	0 (0%)	0 (0%)	0 (0%)
nammary gl	adenoma	(50) 1 (2%)	<50> 0 (0%)	<50> 0 (0%)	<50> 0 (0%)
	fibroadenoma	2 (4%)	1 (2%)	0 (0%)	0 (0%)
	adenocarcinoma	0 (0%)	1 (2%)	0 (0%)	0 (0%)
orep/cligl	adenoma	<50> 1 (2%)	<50> 1 (2%)	<50> 1 (2%)	<50> 0 (0%)
	adenocarcinoma	1 (2%)	0 (0%)	0 (0%)	0 (0%)
(Nervous system	m]				
orain	malignant reticulosis	<50> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)	<50> 1 (2%)

ALL ANIMALS (0-105W) REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS: NEOPLASTIC LESIONS (SUMMARY)

PAGE: 5

Organ	Findings	Group Name No. of animals on Study	Control 50	7500 ppm 50	15000 ppm 50	30000 ppm 50
(Nervous syste	em]					
brain	glioma		<50> 1 (2%)	<50> 1 (2%)	<50> 1 (2%)	<50> 0 (0%)
spinal cord	glioma		<50> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)
[Special sense	e organs/appandage]					
Zymbal gl	adenoma		<50> 0 (0%)	<50> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)
(Musculoskele	tal system]					
cone	osteosarcoma		<50> 0 (0%)	<50> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)
[Body cavities	sl					
peritoneum	mesothelioma		<50> 1 (2%)	<50> 6 (12%)	<50> 4 (8%)	<50> 3 (6%)
	malignant fibrous histiocytoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
retroperit	paraganglioma:benign		<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)	<50> 0 (0%)
<a>><a> b (c)	a: Number of animals examined at the site b: Number of animals with neoplasm c:b/a*1	00	***********			
(HPT085)		7.00				

BAIS3

APPENDIX N 2

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

RAT: FEMALE:

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0-105W)

REPORT TYPE : A1
SEX : FEMALE

)rgan	Findings	Group Name No. of animals on Study	Cont	trol 50	750	00 ppm 50	1500	00 ppm 50	3000	0 ppm 50
[Integumentar)	v system/appandage]									
skin/app	squamous cell papilloma			<50> (2%)	1	<50> (2%)	1	<50> (2%)	1	<50> (2%)
subcutis	fibroma			<50> (4%)	1	<50> (2%)	0	<50> (0%)	1	<50> (2%)
	schwannoma		1	(2%)	0	(0%)	0	(0%)	0	(0%)
	hemangioma		0	(0%)	0	(0%)	0	(0%)	1	(2%)
	histiocytic sarcoma		0	(0%)	0	(0%)	1	(2%)	0	(0%)
[Respiratory:	system]									
lung	bronchiolar-alveolar adenoma		0	<50> (0%)	3	<50> (6%)	1	<50> (2%)	0	<50> (0%)
[Hematopoieti	c system]									
thymus	thymoma:benign		0	<50> (0%)	. 0	<50> (0%)	0	<50> (0%)	1	<50> (2%)
	thymoma:malignant		0	(0%)	1	(2%)	1	(2%)	0	(0%)
spleen	hemangioma		1	<50> (2%)	1	<50> (2%)	0	<50> (0%)	0	<50> (0%)
	mononuclear cell leukemia		1	(2%)	7	(14%)	3	(6%)	4	(8%)
[Digestive sy	stem]									
oral cavity	squamous cell carcinoma		1	<50> (2%)	0	<50> (0%)	0	<50> (0%)	0	<50> (0%)

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

SEX : FEMALE

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

Organ		oup Name Co of animals on Study	ntrol 50	750	00 ppm 50	1500	0 ppm 50	3000	0 ppm 50
Digestive sys	stem]								
tooth	ameloblastoma:malignant	C	<50> (0%)	1	<50> (2%)	0	<50> (0%)	0	<50> (0%)
small intes	fibroma	C	<50> (0%)	1	<50> (2%)	0	<50> (0%)	0	<50> (0%)
larse intes	leiomyosarcoma	C	<50> (0%)	0	<50> (0%)	1	<50> (2%)	0	<50> (0%)
liver	hepatocellular adenoma	1	<50> (2%)	0	<50> (0%)	0	<50> (0%)	0	<50> (0%)
	histiocytic sarcoma	C	(0%)	0	(0%)	1	(2%)	0	(0%)
pancreas	islet cell adenocarcinoma	1	<50> (2%)	0	<50> (0%)	0	<50> (0%)	0	<50> (0%)
[Urinary syste	m]								
rin bladd	transitional cell papilloma	0	<50> (0%)	1	<50> (2%)	1	<50> (2%)	0	<50> (0%)
	transitional cell carcinoma	0	(0%)	1	(2%)	0	(0%)	0	(0%)
[Endocrine sys	stem]								
pituitary	adenoma	18	<49> (37%)	14	<50> (28%)	12	<50> (24%)	6	<50> (12%)
	adenocarcinoma	1	(2%)	0	(0%)	2	(4%)	1	(2%)
thyroid	C-cell adenoma	6	<50> (12%)	4	<49> (8%)	5	<50> (10%)	4	<50> (8%)

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

SEX : FEMALE

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

Organ		roup Name o. of animals on Study	Control 50	7500 ppm 50	15000 ppm 50	30000 ppm 50
(Endocrine sys	stem]					
thyroid	C-cell carcinoma		<50> 0 (0%)	<49> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)
adrenal	pheochromocytoma		<50> 1 (2%)	<50> 5 (10%)	<50> 2 (4%)	<50> 0 (0%)
	cortical adenoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
[Reproductive	system]					
ovary	hemangioma		<50> 0 (0%)	<49> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)
	luteoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
	granulosa-theca cell tumor		1 (2%)	2 (4%)	0 (0%)	0 (0%)
uterus	adenoma		<50> 1 (2%)	<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)
	endometrial stromal polyp		14 (28%)	5 (10%)	7 (14%)	7 (14%)
	adenocarcinoma		0 (0%)	0 (0%)	2 (4%)	1 (2%)
	endometrial stromal sarcoma		0 (0%)	0 (0%)	2 (4%)	1 (2%)
mammary gl	adenoma		<50> 2 (4%)	<50> 1 (2%)	<50> 0 (0%)	<50> 1 (2%)
	fibroadenoma		3 (6%)	5 (10%)	3 (6%)	2 (4%)

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)

PAGE: 9

ALL ANIMALS (0-105W)

REPORT TYPE : A1

SEX : FEMALE

Group Name 7500 ppm 30000 ppm Control 15000 ppm Organ__ Findings No. of animals on Study 50 50 50 50 [Reproductive system] mammary gl <50> <50> <50> <50> adenocarcinoma 0 (0%) 1 (2%) 1 (2%) 0 (0%) prep/cli gl <50> <50> <50> <50> squamous cell papilloma 0 (0%) 1 (2%) 0 (0%) 0 (0%) adenoma 1 (2%) 3 (6%) 1 (2%) 3 (6%) [Nervous system] brain <50> <50> <50> <50> malignant reticulosis 1 (2%) 0 (0%) 1 (2%) 0 (0%) [Special sense organs/appandage] Zymbal gl <50> <50> <50> <50> adenoma 1 (2%) 0 (0%) 0 (0%) 0 (0%) squamous cell carcinoma 0 (0%) 0 (0%) 1 (2%) 0 (0%) [Body cavities] peritoneum <50> <50> <50> <50> mesothelioma 0 (0%) 0 (0%) 0 (0%) 1 (2%) (a) a: Number of animals examined at the site b (c) b: Number of animals with neoplasm c:b/a * 100 (HPT085) BAIS3

APPENDIX N 3

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

MOUSE: MALE

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : MALE

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

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

(HPT085)

STUDY NO. : 0225 ANIMAL : MOUSE BDF1

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

REPORT TYPE : A1

SEX : MALE

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

STUDY NO. : 0225 ANIMAL : MOUSE BDF1

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

REPORT TYPE : A1 SEX : MALE

)rgan	Findings	Group Name No. of animals on Study		ntrol 50	10	000 ppm 50	2	0000 ppm 50	40	000 ppm 50
Digestive sys	tem]									
liver	hemangiosarcoma			<50> (0%)	1	<50> (2%)	1	<50> (2%)	2	<50> (4%)
	hepatocellular carcinoma	1	14	(28%)	11	(22%)	13	(26%)	9	(18%)
	hepatoblastoma		1	(2%)	2	(4%)	0	(0%)	0	(0%)
(Endocrine sys:	tem]									
adrena L	pheochromocytoma			<50> (2%)	0	<50> (0%)	0	<50> (0%)	1	<50> (2%)
[Reproductive :	system]									
testis	xanthoma			<50> (2%)	0	<50> (0%)	0	<50> (0%)	0	<50> (0%)
epididymis	hemangioma			<50> (0%)	0	<50> (0%)	1	<50> (2%)	0	<50> (0%)
	histiocytic sarcoma		0	(0%)	1	(2%)	0	(0%)	1	(2%)
[Nervous system	m]									
orain	glioma			<50> (0%)	0	<50> (0%)	1	<50> (2%)	0	<50> (0%)
periph nerv	histiocytic sarcoma			<50> (0%)	0	<50> (0%)	0	<50> (0%)	1	<50> (2%)
[Special sense	organs/appandage]									
Harder gl	adenoma			<50> (6%)	1	<50> (2%)	4	<50> (8%)	1	<50> (2%)

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : MALE HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)

PAGE: 4

0rgan	Findings No. of	Name Control animals on Study 50	10000 ppm 50	20000 ppm 50	40000 ppm 50
(Musculoskelet	tal system]				
oone	osteosarcoma	<50> 0 (0%)	<50> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)
[Body cavities	5]				
pleura	hemangioma	<50> 0 (0%)	<50> 0 (0%)	<50> 0 (0%)	<50> 2 (4%)
peritoneum	hemangiosarcoma	<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)	<50> 0 (0%)
mesenterium	hemangioma	<50> 1 (2%)	<50> 0 (0%)	<50> 0 (0%)	<50> 0 (0%)
<a>><a> b (c)	a: Number of animals examined at the site b: Number of animals with neoplasm c:b/a*100				
(HPT085)					

(HPT085)

BAIS3

APPENDIX N 4

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

MOUSE: FEMALE

SEX

: MOUSE BDF1 ANIMAL REPORT TYPE : A1 : FEMALE

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0-105W)

PAGE: 5

Organ	Findings	Group Name No. of animals on Study	Control 50	10000 ppm 50	20000 ppm 50	40000 ppm 50
[Integumentar	y system/appandage]					
skin/app	squamous cell papilloma		<50> 1 (2%)	<50> 0 (0%)	<49> 0 (0%)	<50> 0 (0%)
	sebaceous adenoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
subcutis	hemangioma '		<50> 0 (0%)	<50> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)
	fibrosarcoma		2 (4%)	1 (2%)	0 (0%)	2 (4%)
	histiocytic sarcoma		0 (0%)	1 (2%)	0 (0%)	0 (0%)
	mastcytoma:malignant		0 (0%)	0 (0%)	0 (0%)	1 (2%)
[Respiratory	system]		,			
lung	bronchiolar-alveolar adenoma		<50> 2 (4%)	<50> 3 (6%)	<50> 2 (4%)	<50> 0 (0%)
	bronchiolar-alveolar carcinoma		1 (2%)	2 (4%)	0 (0%)	0 (0%)
[Hematopoieti	ic system]					
lymph node	hemangioma		<50> 0 (0%)	<50> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)
	histiocytic sarcoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
	malisnant lymphoma		9 (18%)	15 (30%)	11 (22%)	14 (28%)
(a) b (c)	a: Number of animals examined at the site b: Number of animals with neoplasm c:b/a*	100				

(HPT085)

HISTOLOGICAL FINDINGS: NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0-105W)

ANIMAL : MOUSE BDF1 REPORT TYPE : A1

SEX : FEMALE

rgan		Group Name Control No. of animals on Study 50	10000 ppm 50	20000 ppm 50	40000 ppm 50
[Hematopoietic	system]				
ymph nade	mastcytoma:malignant	<50> 0 (0%)	<50> 0 (0%)	<50> 2 (4%)	<50> 0 (0%)
thymus	malignant lymphoma	<50> 2 (4%)	<50> 0 (0%)	<50> 0 (0%)	<50> 0 (0%)
spleen	malisnant lymphoma	<50> 1 (2%)	<50> 1 (2%)	<50> 1 (2%)	<50> 2 (4%)
	hemangiosarcoma	0 (0%)	1 (2%)	0 (0%)	1 (2%)
[Digestive sys	rtem]				
tangue	squamous cell papilloma	<50> 0 (0%)	<50> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)
	squamous cell carcinoma	0 (0%)	0 (0%)	0 (0%)	1 (2%)
salivary gl	xanthoma	<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)	<50> 0 (0%)
stomach	squamous cell papilloma	<50> 1 (2%)	<50> 0 (0%)	<50> 0 (0%)	<50> 0 (0%)
small intes	adenoma	<50> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)	<50> 1 (2%)
iver.	hemangioma	<50> 0 (0%)	<50> 2 (4%)	<50> 1 (2%)	<50> 0 (0%)
	hepatocellular adenoma	5 (10%)	11 (22%)	5 (10%)	10 (20%)
	histiocytic sarcoma	1 (2%)	2 (4%)	2 (4%)	0 (0%)

STUDY NO. : 0225 ANIMAL : MOUSE BDF1 HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0-105W)

REPORT TYPE : A1

(HPT085)

SEX : FEMALE

rgan	Findings Group Na No. of a	ame Control animals on Study 50	10000 ppm 50	20000 ppm 50	40000 ppm 50
Digestive s	ystem]				
iver	hemangiosarcoma	<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)	<50> 0 (0%)
	hepatocellular carcinoma	0 (0%)	2 (4%)	1 (2%)	0 (0%)
Endocrine s	ystem]				
ituitary	adenoma	<49> 9 (18%)	<50> 7 (14%)	<49> 9 (18%)	<49> 8 (16%)
	adenocarcinoma	2 (4%)	1 (2%)	2 (4%)	1 (2%)
drenal	pheachramacytoma	<49> 0 (0%)	<50> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)
Reproductiv	e system]				
Jary	cystadenoma	<49> 1 (2%)	<50> 2 (4%)	<50> 3 (6%)	<49> 1 (2%)
	cystadenocarcinoma	1 (2%)	0 (0%)	0 (0%)	0 (0%)
terus	hemansioma	<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)	<50> 0 (0%)
	endometrial stromal polyp	5 (10%)	2 (4%)	0 (0%)	2 (4%)
	histiocytic sarcoma	9 (18%)	3 (6%)	14 (28%)	12 (24%)
ammary gl	adenoma	<50> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)	<50> 3 (6%)
	a. I. Wumban of animala avanimad at the aite				
<a>> (c)	a : Number of animals examined at the site b : Number of animals with neoplasm c : b / a * 100				

ANIMAL : MOUSE BDF1

REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0-105W)

)rgan	Findings No. of anim	Control mals on Study 50	10000 ppm 50	20000 ppm 50	40000 ppm 50
[Reproductive :	system]				
nammary gl	adenocarcinoma	<50> 1 (2%)	<50> 1 (2%)	<50> 2 (4%)	<50> 3 (6%)
Nervous syste	em]				
periph nerv	histiocytic sarcoma	<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)	<50> 0 (0%)
Special sense	e organs/appandage]				
arder gl	adenoma	<50> 2 (4%)	<50> 1 (2%)	<50> 0 (0%)	<50> 4 (8%)
Body cavities	5]				
peritoneum	hemangioma	<50> 0 (0%)	<50> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)
<a>> b (c)	a: Number of animals examined at the site b: Number of animals with neoplasm c:b/a*100				
(HPT085)					

APPENDIX O 1

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

RAT: MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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

Group Name Control 7500 ppm 15000 ppm 30000 ppm SITE : skin/appendage TUMOR : keratoacanthoma Tumor rate Overall rates(a) 1/50(2.0) 3/50(6.0) 1/50(2.0) 4/50(8.0) Adjusted rates(b) 2,27 7.69 2.94 10.81 Terminal rates(c) 0/38(0.0) 3/39(7,7) 1/34(2.9) 3/30(10.0) Statistical analysis Peto test Standard method(d) P = -----Prevalence method(d) P = 0.1022Combined analysis(d) P = -----Cochran-Armitage test(e) P = 0.2260Fisher Exact test(e) P = 0.3235P = 0.2475P = 0.1998SITE : skin/appendage TUMOR : sebaceous adenoma Tumor rate Overall rates(a) 0/50(0.0) 0/50(0.0) 0/50(0.0) 3/50(6.0) Adjusted rates(b) 0.0 0.0 0.0 8.82 Terminal rates(c) 0/38(0.0) 0/39(0.0) 0/34(0.0) 2/30(6.7) Statistical analysis Peto test Standard method(d) P = -----Prevalence method(d) P = 0.0025**?Combined analysis(d) P = ----Cochran-Armitage test(e) P = 0.0079**Fisher Exact test(e) P = 0.5000P = 0.5000P = 0.1325SITE : subcutis TUMOR : fibroma Tumor rate Overall rates(a) 4/50(8.0) 4/50(8.0) 4/50(8.0) 6/50(12.0) Adjusted rates(b) 10.53 7.69 8.89 13.64 Terminal rates(c) 4/38(10.5) 3/39(7.7) 3/34(8.8) 3/30(10.0) Statistical analysis Peto test Standard method(d) P = 0.5801Prevalence method(d) P = 0.1950Combined analysis(d) P = 0.2370Cochran-Armitage test(e) P = 0.4522Fisher Exact test(e) P = 0.3579P = 0.3579P = 0.3944

(HPT360A)

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

STUDY No. : 0224 ANIMAL : RAT F344

SEX : MALE

Group Name Control 7500 ppm 15000 ppm 30000 ppm SITE : subcutis TUMOR : fibroma, fibrosarcoma Tumor rate Overall rates(a) 5/50(10.0) 4/50(8.0) 4/50(8.0) 6/50(12.0) Adjusted rates(b) 10.53 7.69 8.89 13.64 Terminal rates(c) 4/38(10.5) 3/39(7.7) 3/34(8.8) 3/30(10.0) Statistical analysis Peto test Standard method(d) P = 0.8773Prevalence method(d) P = 0.1950Combined analysis(d) P = 0.3375Cochran-Armitage test(e) P = 0.6539Fisher Exact test(e) P = 0.4883P = 0.4883P = 0.4872SITE : lung TUMOR : bronchiolar-alveolar adenoma Tumor rate Overall rates(a) 3/50(6.0) 3/50(6.0) 3/50(6.0) 5/50(10.0) Adjusted rates(b) 7.89 6.52 8.82 16.67 Terminal rates(c) 3/38(7.9) 2/39(5.1) 3/34(8.8) 5/30(16.7) Statistical analysis Peto test Standard method(d) P = ----Prevalence method(d) P = 0.1328Combined analysis(d) P = ----Cochran-Armitage test(e) P = 0.3991Fisher Exact test(e) P = 0.3392P = 0.3392P = 0.3790SITE : lung TUMOR : bronchiolar-alveolar adenoma, bronchiolar-alveolar carcinoma Tumor rate Overall rates(a) 3/50(6.0) 3/50(6.0) 3/50(6.0) 6/50(12.0) Adjusted rates(b) 7.89 6.52 8.82 20.00 Terminal rates(c) 3/38(7.9) 2/39(5,1) 3/34(8.8) 6/30(20.0) Statistical analysis Peto test Standard method(d) Prevalence method(d) P = 0.0655Combined analysis(d) P = ----Cochran-Armitage test(e) P = 0.2205Fisher Exact test(e) P = 0.3392P = 0.3392P = 0.2728(HPT360A)

BAIS3

STUDY No. : 0224 ANIMAL : RAT F344

SEX : MALE

Group Name	Control	7500 ppm	15000 ppm	30000 ppm	
	SITE : spleen				
Cumor rate	TUMOR : mononuclear cell leuke	9M1 a			
Overall rates(a)	6/50(12.0)	2/50(4.0)	2/50(4.0)	4/50(8.0)	
Adjusted rates(b)	2.63	5.13	0.0	6.67	
Terminal rates(c)	1/38(2.6)	2/39(5.1)	0/34(0.0)	2/30(6.7)	
Statistical analysis					
Peto test					
Standard method(d) Prevalence method(d)	P = 0.7590 P = 0.2656				
Combined analysis(d)	P = 0.2809				
Cochran-Armitage test(e)	P = 0.6395				
Fisher Exact test(e)	. 0,000	P = 0.1606	P = 0.1606	P = 0.3944	
	SITE : pancreas				
	TUMOR : islet cell adenoma	•			
Tumor rate	1/50 / O O	0.170 (
Overall rates(a) Adjusted rates(b)	4/50(8.0) 8.00	3/50(6.0)	4/50(8.0)	3/50(6.0)	
Terminal rates(c)	3/38(7.9)	7.69 3/39(7.7)	8.89 1/34(2.9)	10.00	
Statistical analysis	3/38(7.9)	3/33(1.1)	1/34(2.9)	3/30(10.0)	
Peto test					
Standard method(d)	P =				
Prevalence method(d)	P = 0.6012				
Combined analysis(d)	P =				
Cochran-Armitage test(e)	P = 0.7787	D 0 400F	n		
Fisher Exact test(e)		P = 0.4895	P = 0.3579	P = 0.4895	
	SITE : pancreas				
	TUMOR : islet cell adenoma, is	Let cell adenocarcinoma			
Tumor rate					
Overall rates(a)	5/50(10.0)	3/50(6.0)	4/50(8.0)	3/50(6.0)	
Adjusted rates(b)	10.53	7.69	8.89	10.00	
Terminal rates(c)	4/38(10.5)	3/39(7.7)	1/34(2.9)	3/30(10.0)	
Statistical analysis Peto test					
Standard method(d)	P =				
Prevalence method(d)	P = 0.7109				
Combined analysis(d)	P =				
Cochran-Armitage test(e)	P = 0.5552				
Fisher Exact test(e)		P = 0.3790	P = 0.4883	P = 0.3790	

(HPT360A)

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

Group Name	Control	7500 ppm	15000 ppm	30000 ppm	
	SITE : pituitary gland TUMOR : adenoma				
'umor rate	TOTION - adelibilia	4			
Overall rates(a)	14/50(28.0)	14/50(28.0)	11/50(22.0)	18/50(36.0)	
Adjusted rates(b)	31.58	28.21	25.71	36.96	
Terminal rates(c)	12/38(31.6)	11/39(28.2)	8/34(23.5)	7/30(23.3)	
tatistical analysis					
Peto test Standard method(d)	P = 0.5341				
Prevalence method(d)	P = 0.5341 P = 0.1884				
Combined analysis(d)	P = 0.2148				
Cochran-Armitage test(e)	P = 0.3823				
Fisher Exact test(e)	. 0,0020	P = 0.4155	P = 0.3777	P = 0.3405	
	SITE : pituitary gland				
	TUMOR : adenocarcinoma				
'umor rate Overall rates(a)	3/50(6.0)	1/5/ 9.0)	2/50/ 5.0	1/50/ 0.0	
Adjusted rates(b)	5,26	1/50(2.0) .0.0	3/50(6.0) 2.94	1/50(2.0) 0.0	
Terminal rates(c)	2/38(5.3)	0/39(0.0)	1/34(2.9)	0/30(0.0)	
Statistical analysis	2700(0.0)	0,00(0:0)	1/04(2.0)	0/30(0.0/	
Peto test					
Standard method(d)	P = 0.4509				
Prevalence method(d)	P = 0.8729				
Combined analysis(d)	P = 0.7196				
Cochran-Armitage test(e)	P = 0.4642				
Fisher Exact test(e)		P = 0.3235	P = 0.3392	P = 0.3235	
	SITE : pituitary gland				
	TUMOR: adenoma, adenocarcinoma				
Cumor rate	10000 Tadas isina yadas isasa arrisina				
Overall rates(a)	17/50(34.0)	15/50(30.0)	14/50(28.0)	19/50(38.0)	
Adjusted rates(b)	36.84	28.21	28,57	37.78	
Terminal rates(c)	14/38(36.8)	11/39(28.2)	9/34(26.5)	7/30(23.3)	
Statistical analysis					
Peto test					
Standard method(d)	P = 0.5008				
Prevalence method(d)	P = 0.2855				
Combined analysis(d) Cochran—Armitage test(e)	P = 0.3101 P = 0.5920				
Fisher Exact test(e)	1 - 0.0020	P = 0.4586	P = 0.3959	P = 0.4638	
				1 - 0.4000	

ANIMAL : RAT F344
SEX : MALE

STUDY No. : 0224

*				1101	
Group Name	Control	7500 ppm	15000 ppm	30000 ppm	
	SITE : thyroid				
Tumor rate	TUMOR : C-cell adenoma				
Overall rates(a)	12/50(24.0)	5/50(10.0)	5/50(10.0)	4/50(8.0)	
Adjusted rates(b)	29.27	12.82	14.71	11.76	
Terminal rates(c) Statistical analysis Peto test	11/38(28.9)	5/39(12.8)	5/34(14.7)	3/30(10.0)	
Standard method(d)	P =				
Prevalence method(d)	P = 0.9671				
Combined analysis(d)	P =				
Cochran-Armitage test(e)	P = 0.0393*				
Fisher Exact test(e)		P = 0.0942	P = 0.0942	P = 0.0539	
	SITE : thyroid				
	TUMOR : C-cell adenoma, C-cell	carcinoma			
Tumor rate					
Overall rates(a)	12/50(24.0)	5/50(10.0)	5/50(10.0)	4/50(8.0)	
Adjusted rates(b)	29.27	12.82	14.71	11.76	
Terminal rates(c)	11/38(28.9)	5/39(12.8)	5/34(14.7)	3/30(10.0)	
Statistical analysis Peto test					
Standard method(d)	P =				
Prevalence method(d)	P = 0.9671				
Combined analysis(d)	P =				
Cochran-Armitage test(e)	P = 0.0393*				
Fisher Exact test(e)		P = 0.0942	P = 0.0942	P = 0.0539	
	SITE : adrenal gland				
There are the	TUMOR : pheochromocytoma				
Tumor rate Overall rates(a)	4/50(9.0)	7/50/ 14 0)	5/50/ 10 0)	- (- o (o o o o o o o o o o o o o o o o	
Adjusted rates(b)	4/50(8.0) 9.30	7/50(14.0) 17.95	5/50(10.0) 13.51	7/50(14.0)	
Terminal rates(c)	2/38(5.3)	7/39(17.9)	4/34(11.8)	21.88 6/30(20.0)	
Statistical analysis	_, 55(5.5)	7,00(17.0)	4/04(11.0)	0/30(20.0)	
Peto test					
Standard method(d)	P =				
Prevalence method(d)	P = 0.1540				
Combined analysis(d)	P =				
Cochran—Armitage test(e) Fisher Exact test(e)	P = 0.4766	P = 0.2958	D = 0.4000	D 4 00°C	
. IGIO, DAGOL LOSE(B)		i - 0,2350	P = 0.4883	P = 0.2958	

(HPT360A)

STUDY No. : 0224 ANIMAL : RAT F344

SEX : MALE

Group Name	Control	7500 ppm	15000 ppm	30000 ppm	
	SITE : adrenal gland				
ſumor rate	TUMOR : pheochromocytoma, pheochro	mocytoma:malignant			
Overall rates(a)	4/50(8.0)	7/50(14.0)	6/50(12.0)	9/50/ 16 0	
Adjusted rates(b)	9.30	17.95	13.51	8/50(16.0) 21.88	
Terminal rates(c)	2/38(5.3)	7/39(17.9)	4/34(11.8)	6/30(20.0)	
Statistical analysis	2,00(0,0)	1,00(11.0)	1,01(11,0)	5/50(ZV.V)	
Peto test					
Standard method(d)	P = 0.1343				
Prevalence method(d)	P = 0.1540				
Combined analysis(d)	P = 0.0912				
Cochran—Armitage test(e)	P = 0.2946				
Fisher Exact test(e)		P = 0.2958	P = 0.3944	P = 0.2169	
	SITE : testis TUMOR : interstitial cell tumor	***************************************			
Tumor rate					
Overall rates(a)	44/50(88.0)	43/50(86.0)	42/50(84.0)	44/50(88.0)	
Adjusted rates(b)	92.68	97.50	93.18	97,30	
Terminal rates(c)	35/38(92.1)	38/39(97.4)	31/34(91.2)	29/30(96.7)	
Statistical analysis			, , , ,	,	
Peto test					
Standard method(d)	P =				
Prevalence method(d)	P = 0.4513				
Combined analysis(d)	P =				
Cochran-Armitage test(e)	P = 0.9721				
Fisher Exact test(e)		P = 0.4728	P = 0.4956	P = 0.4419	
****	OTTE .	,			
	SITE : mammary gland				
Tumor rate	TUMOR : adenoma, fibroadenoma				
Overall rates(a)	3/50(6.0)	1/50(2.0)	0/50(0.0)	0/50/ 0.0)	
Adjusted rates(b)	7.89	2.44	0.0	0/50(0.0)	
Terminal rates(c)	3/38(7.9)	0/39(0.0)	0/34(0.0)	0.0 0/30(0.0)	
Statistical analysis	2,000	V/ V V V V V	0,01(0.0)	0,00(0.0)	
Peto test					
Standard method(d)	P =				
Prevalence method(d)	P = 0.9858				
Combined analysis(d)	P =				
Cochran-Armitage test(e)	P = 0.0405*				
Fisher Exact test(e)		P = 0.3235	P = 0.1325	P = 0.1325	

STUDY No. : 0224

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

ANIMAL : RAT F344 SEX : MALE

Group Name	Control	7500 ppm	15000 ppm	30000 ppm	
	SITE : peritoneum TUMOR : mesothelioma				
Tumor rate					
Overall rates(a)	1/50(2.0)	6/50(12.0)	4/50(8.0)	3/50(6.0)	
Adjusted rates(b)	2.63	10.42	4.55	3,33	
Terminal rates(c)	1/38(2.6)	3/39(7.7)	0/34(0.0)	1/30(3.3)	
Statistical analysis		, , ,	, , , , , , ,	_, _, _,	
Peto test					
Standard method(d)	P = 0.0972				
Prevalence method(d)	P = 0.7222				

P = 0.1998

(HPT360A)

Combined analysis(d)

Fisher Exact test(e)

Cochran-Armitage test(e)

BAIS3

P = 0.3235

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

P = 0.3710

P = 0.7787

- (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.

P = 0.0724

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

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

APPENDIX O 2

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

RAT: FEMALE

STUDY No. : 0224 ANIMAL : RAT F344

: FEMALE

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

(HPT360A)

STUDY No. : 0224 ANIMAL : RAT F344

SEX : FEMALE

Group Name	Control	7500 ppm	15000 ppm	30000 ppm	
,	SITE : pituitary gland				
S	TUMOR : adenoma				
`umor rate Overall rates(a)	18/49(36.7)	14/50(28.0)	12/50(24.0)	6/50(12.0)	
Adjusted rates(b)	35.42	25.64	25.71	21.43	
Terminal rates(c)	16/46(34.8)	10/39(25.6)	9/35(25.7)	3/14(21.4)	
Statistical analysis					
Peto test Standard method(d)	P = 0.4673				
Prevalence method(d)	P = 0.4673 P = 0.9411				
Combined analysis(d)	P = 0.9192				
Cochran-Armitage test(e)	P = 0.0041**				
Fisher Exact test(e)		P = 0.3228	P = 0.2121	P = 0.0201*	
			,	the transfer of the transfer o	
	SITE : pituitary gland TUMOR : adenoma,adenocarcinoma				
Tumor rate	1011011 • audi julia, audi juudi CTT julia				
Overall rates(a)	19/49(38.8)	14/50(28.0)	14/50(28.0)	7/50(14.0)	
Adjusted rates(b)	37.50	25.64	28.57	21.43	
Terminal rates(c)	17/46(37.0)	10/39(25.6)	10/35(28.6)	3/14(21.4)	
Statistical analysis Peto test					
Standard method(d)	P = 0.1912				
Prevalence method(d)	P = 0.9439				
Combined analysis(d)	P = 0.8365				
Cochran-Armitage test(e)	P = 0.0070**	D 0.0000			
Fisher Exact test(e)		P = 0.2736	P = 0.2736	P = 0.0256*	
	SITE : thyroid				•
	TUMOR : C-cell adenoma				
umor rate					
Overall rates(a)	6/50(12.0)	4/49(8.2)	5/50(10.0)	4/50(8.0)	
Adjusted rates(b) Terminal rates(c)	12.00 5/47(10.6)	9.52	12.82	10.71	
Statistical analysis	J/41 (10.0)	3/39(7.7)	3/35(8.6)	1/14(7.1)	
Peto test					
Standard method(d)	P =				
Prevalence method(d)	P = 0.4969				
Combined analysis(d)	P =				
Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.5887	P = 0.4066	P = 0.4872		

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ANIMAL : RAT F344
SEX : FEMALE

Group Name	Control	7500 ppm	15000 ppm	30000 ppm	
	SITE : thyroid	II samainana			
îumor rate	TUMOR : C-cell adenoma,C-ce	ell carcinoma			
Overall rates(a)	6/50(12.0)	4/49(8.2)	6/50(12.0)	4/50(8.0)	
Adjusted rates(b)	12.00	9.52	15.38	10.71	
Terminal rates(c) Statistical analysis	5/47(10.6)	3/39(7.7)	4/35(11.4)	1/14(7.1)	
Peto test					
Standard method(d)	P =				
Prevalence method(d)	P = 0.4602				
Combined analysis(d) Cochran-Armitage test(e)	P = P = 0.6246				
Fisher Exact test(e)	1 - 0.0240	P = 0.4066	P = 0.3807	P = 0.3944	
				. 0.0011	
	SITE : adrenal gland				
	TUMOR : pheochromocytoma				
Tumor rate	1/50(0.0)	# (#a (. a . a)			
Overall rates(a) Adjusted rates(b)	1/50(2.0) 2.13	5/50(10.0) 11.36	2/50(4.0) 5.71	0/50(0.0)	
Terminal rates(c)	1/47(2,1)	4/39(10.3)	2/35(5.7)	0.0 0/14(0.0)	
Statistical analysis	, ,	2, 22 (2,000,	2,00(011)	V/11(0.0)	
Peto test	•				
Standard method(d) Prevalence method(d)	P = P = 0.7056				
Combined analysis(d)	P =				
Cochran-Armitage test(e)	P = 0.2225				
Fisher Exact test(e)		P = 0.1210	P = 0.4926	P = 0.4950	
	CIPP				
	SITE : adrenal gland TUMOR : pheochromocytoma,ph	enchromocytoma:malignant			
Tumor rate	Total Prodor a dilady Edilary Pr	COSOTE CHICAGO ECHICAGO ECHICA			
Overall rates(a)	1/50(2.0)	5/50(10.0)	2/50(4.0)	0/50(0.0)	
Adjusted rates(b)	2.13	11.36	5.71	0.0	
Terminal rates(c) Statistical analysis	1/47(2.1)	4/39(10.3)	2/35(5.7)	0/14(0.0)	
Peto test					
Standard method(d)	P =				
Prevalence method(d)	P = 0.7056				
Combined analysis(d) Cochran-Armitage test(e)	P = P = 0.2225				

STUDY No. : 0224

ANIMAL : RAT F344
SEX : FEMALE
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				•	non .
Group Name	Control	7500 ppm	15000 ppm	30000 ppm	
	SITE : uterus				
mor rate	TUMOR : endometrial stromal	. polyp			
Overall rates(a)	14/50(28.0)	5/50(10.0)	7/50(14.0)	7/50(14.0)	
Adjusted rates(b)	28.00	12.82	13.04	29.41	
Cerminal rates(c) tatistical analysis Peto test	13/47(27.7)	5/39(12.8)	3/35(8.6)	4/14(28.6)	
Standard method(d)	P = 0.0621		•		
Prevalence method(d)	P = 0.6556				
Combined analysis(d)	P = 0.4651				
Cochran-Armitage test(e)	P = 0.1662				
Fisher Exact test(e)		P = 0.0481*	P = 0.1246	P = 0.1246	
	SITE : uterus				
	TUMOR : adenoma, adenocarcin	noma			
umor rate	1/50/ 0.0	0/50/ 0.0	0 (70 (0 0)	. (5.)	
Overall rates(a) Adjusted rates(b)	1/50(2.0) 2.13	0/50(0.0) 0.0	3/50(6.0)	1/50(2.0)	
Terminal rates(c)	1/47(2.1)	0.0	4.55 1/35(2.9)	7.14 1/14(7.1)	
tatistical analysis	1/4.(8.1)	0,00(0.0)	1/55(2.5)	1/14(7.1)	
Peto test					
Standard method(d)	P = 0.2722				
Prevalence method(d)	P = 0.1998				
Combined analysis(d)	P = 0.1642				
Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.7019	D 0.4050	D 0.0005	D 0.0455	
ISPER EXACT TEST(8)		P = 0.4950	P = 0.3235	P = 0.2475	
	SITE : uterus				
umor rate	TUMOR : endometrial stroma	l polyp,endometrial stromal sarcoma		•	
unur rate Overall rates(a)	14/50(28.0)	5/50(10.0)	9/50(18.0)	8/50(16.0)	
Adjusted rates(b)	28.00	12.82	13.33	8/50(15.0) 29.41	
Terminal rates(c)	13/47(27.7)	5/39(12.8)	3/35(8.6)	4/14(28.6)	
tatistical analysis			• • • • • •	-, \ \ \	
Peto test					
Standard method(d)	P = 0.0146*				
Prevalence method(d)	P = 0.6429				
Combined analysis(d) Cochran-Armitage test(e)	P = 0.2632 P = 0.3195				
vochran-Armitage test(e) Fisher Exact test(e)	L = A.91A9	P = 0.0481*	P = 0.2397	P = 0.1781	
LYACE TOST(A)		1 - 0.0401+	r - v.2381	r = 0.1101	

(HPT360A)

STUDY No. : 0224

STUDY No. : 0224

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

ANIMAL : RAT F344 SEX : FEMALE

Group Name	Control	7500 ppm	15000 ppm	30000 maa	
	SITE : mammary gland				
umor rate	TUMOR : fibroadenoma				
Overall rates(a)	3/50(6.0)	5/50(10.0)	3/50(6.0)	9/50/ 4.0)	
Adjusted rates(b)	6.38	11,90	8.57	2/50(4.0) 4.26	
Terminal rates(c)	3/47(6.4)	4/39(10.3)	3/35(8.6)	0/14(0.0)	
tatistical analysis	2, 2, (1,00(10.0)	0,00(0.0)	0/14(0.0)	
Peto test					
Standard method(d)	P =				
Prevalence method(d)	P = 0.6398				
Combined analysis(d)	P =				
Cochran-Armitage test(e)	P = 0.4671				
Fisher Exact test(e)		P = 0.3790	P = 0.3392	P = 0.4909	
	SITE : mammary gland TUMOR : adenoma,fibroadenoma				
'umor rate	· · · · · · · · · · · · · · · · · · ·				
Overall rates(a)	5/50(10.0)	6/50(12.0)	3/50(6.0)	3/50(6.0)	
Adjusted rates(b)	10.64	11.90	8.57	7.14	
	5/47(10.6)	4/39(10.3)	3/35(8.6)	1/14(7.1)	
	0/41 (10.0)	1,00(10.0)	0,00(0.0)	1/14(7.1)	
Terminal rates(c) Statistical analysis	0,4.(10.0)	1,00(10.0)	5/50/ 0.0/	1/14(1.1)	
tatistical analysis Peto test		1,00(10.0)	0,00(0.0)	1/14(1.1)	
tatistical analysis Peto test Standard method(d)	P = 0.5248	1,00(10.0)	0,00(0.0)	1/14(1.1)	
Statistical analysis Peto test Standard method(d) Prevalence method(d)	P = 0.5248 P = 0.6074	1,00(10.0)	5/30(3.5)	1/14(1.1)	
tatistical analysis Peto test Standard method(d)	P = 0.5248	1,00(10.0)	5/30(3.5)	1/14(1.1)	

(HPT360A)

BAIS3

STUDY No. : 0224

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

ANIMAL : RAT F344 SEX : FEMALE

Group Name	Control	7500 ppm	15000 ppm	30000 ppm
	SITE : preputial/clitoral gland			
C	TUMOR : adenoma			
fumor rate	1/50(0.0)	2/52/ 2.2	to the state of th	
Overall rates(a)	1/50(2.0)	3/50(6.0)	1/50(2.0)	3/50(6.0)
Adjusted rates(b)	2.13	5.13	0.0	7.14
Terminal rates(c)	1/47(2.1)	2/39(5.1)	0/35(0.0)	1/14(7.1)
Statistical analysis				· · ·
Peto test				
Standard method(d)	P = 0.1924			
Prevalence method(d)	P = 0.1824			
Combined analysis(d)	P = 0.1066			
Cochran-Armitage test(e)	P = 0.4642			
Fisher Exact test(e)	1 0.1014	D = A 2925	D - 0.047	D 0.0005
LIZHEL EXACT TERT(A)		P = 0.3235	P = 0.2475	P = 0.3235
IPT360A)				В

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

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

(c): Observed tumor incidence at terminal kill.

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

Standard method : Death analysis
Prevalence method : Incidental tumor test

Combined analysis: Death analysis + Incidental tumor test

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

?: The conditional 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; $*: P \le 0.05$ $**: P \le 0.01$

APPENDIX O 3

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

MOSUE: MALE

PAGE: 1

STUDY No. : 0225 ANIMAL : MOUSE BDF1

SEX : MALE

Group Name	Control	10000 ppm	20000 ppm	40000 ppm	
		- Marian de	- · · · · · · · · · · · · · · · · · · ·		
	SITE : lung TUMOR : bronchiolar—alveol	ar adenoma			
mor rate	m /m + (, , , , ,)				
Nerall rates(a) Adjusted rates(b)	5/50(10.0)	7/50(14.0)	8/50(16.0)	8/50(16.0)	
'erminal rates(c)	12.82 4/34(11.8)	14.29 4/35(11.4)	20.00 6/30(20.0)	18.18 4/25(16.0)	
atistical analysis	1,01(11,0)	4,00(11.4)	0/00(20.0)	4/23(10.0)	
'eto test Standard method(d)	P =				
Prevalence method(d)	P = 0.1435				
Combined analysis(d)	P =				
Cochran-Armitage test(e)	P = 0.4084				
Fisher Exact test(e)		P = 0.4062	P = 0.3141	P = 0.3141	
	SITE : Lung	***************************************	A de de de la constante de la		
	TUMOR : bronchiolar-alveol	ar carcinoma			
mor rate Vuerall rates(a)	7/50(14.0)	3/50(6.0)	6/50(12.0)	3/50(6.0)	
Adjusted rates(b)	14.71	6.67	13.33	12.00	
Germinal rates(c)	5/34(14.7)	2/35(5.7)	4/30(13.3)	3/25(12.0)	
tatistical analysis Peto test					
Standard method(d)	P = 0.8753				
Prevalence method(d)	P = 0.5613				
Combined analysis(d)	P = 0.7348				
Cochran-Armitage test(e)	P = 0.3082				
Fisher Exact test(e)		P = 0.1917	P = 0.4863	P = 0.1917	
	SITE : Lung				
mor roto	TUMOR : bronchiolar-alveol	ar adenoma,bronchiolar-alveolar carcinom	a		
mor rate Verall rates(a)	12/50(24.0)	10/50(20.0)	14/50(28.0)	11/50/ 22 0)	
Adjusted rates(b)	26.47	20.41	14/50(28.0) 33.33	11/50(22.0) 28.00	
Germinal rates(c)	9/34(26.5)	6/35(17.1)	10/30(33.3)	7/25(28.0)	
tatistical analysis	•				
Peto test Standard method(d)	P = 0.8753				
Prevalence method(d)	P = 0.2340				
Combined analysis(d)	P = 0.3564				
	P = 0.9775				
Cochran—Armitage test(e)	1 - 0.3110	P = 0.4406			

ANIMAL : MOUSE BDF1
SEX : MALE

O V					
Group Name	Control	10000 maa	20000 ppm	40000 ppm	
	SITE : bone marrow				
mor rate	TUMOR : hemangioma				
Overall rates(a)	2/50(4.0)	3/50(6.0)	0/50(0.0)	0/50(0.0)	
djusted rates(b)	5.88	6.12	0.0	0.0	
erminal rates(c) atistical analysis	2/34(5.9)	1/35(2.9)	0/30(0.0)	0/25(0.0)	
Peto test Standard method(d)	P =				
Prevalence method(d)	P = 0.9632				
Combined analysis(d) Cochran-Armitage test(e)	P = P = 0.0783				
Fisher Exact test(e)	1 - 0.0700	P = 0.4909	P = 0.2574	P = 0.2574	
	SITE : Lymph node				
	TUMOR : malignant lymphoma				
umor rate	7/50(14.0)	0 (50 (0 0 0)	2/24/ 22 2		
Overall rates(a) Adjusted rates(b)	7/50(14.0) 11.76	3/50(6.0) 5.71	6/50(12.0) 10.00	6/50(12.0) 10.00	
Terminal rates(c)	4/34(11.8)	2/35(5.7)	3/30(10.0)	2/25(8.0)	
tatistical analysis				, , ,	
Peto test Standard method(d)	P = 0.2716				
Prevalence method(d)	P = 0.4197				
Combined analysis(d)	P = 0.2899				
Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.9391	D 0 1016	D 0 4000	B 4 4000	
risher Exact Test(e)		P = 0.1917	P = 0.4863	P = 0.4863	
	SITE : spleen				
umor rate	TUMOR : hemangioma				
Overall rates(a)	1/50(2.0)	0/50(0.0)	3/50(6.0)	1/50(2.0)	
Adjusted rates(b)	2.94	0.0	6.52	4.00	
Terminal rates(c) tatistical analysis	1/34(2.9)	0/35(0.0)	1/30(3.3)	1/25(4.0)	
eto test					
Standard method(d)	P =				
Prevalence method(d)	P = 0.3127				
Combined analysis(d) Cochran-Armitage test(e)	P = P = 0.7019				
Fisher Exact test(e)	1 = 0.1019	P = 0.4950	P = 0.3235	P = 0.2475	

STUDY No. : 0225

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

Group Name	Control	10000 ppm	20000 ppm	40000 ppm	
	SITE : spleen				
T	TUMOR : malignant lymphoma				
Tumor rate Overall rates(a)	1/50(2.0)	0/50(0.0)	3/50/ 0.0	0/50/ (0.0)	
Adjusted rates(b)	2.94	0.0	3/50(6.0) 6.67	3/50(6.0) 0.0	
Terminal rates(c)	1/34(2.9)	0/35(0.0)	2/30(6.7)	0/25(0.0)	
Statistical analysis	-,,	5,000	2,00(0.1)	0/20(0.0)	
Peta test					
Standard method(d)	P = 0.0074**				
Prevalence method(d)	P = 0.5831				
Combined analysis(d)	P = 0.0462*				
Cochran-Armitage test(e)	P = 0.1347				
Fisher Exact test(e)		P = 0.4950	P = 0.3235	P = 0.3235	
•	SITE : spleen				
	TUMOR : hemangiosarcoma				
Tumor rate	101101 • Hellia 19103ai Collia				
Overall rates(a)	1/50(2.0)	3/50(6.0)	3/50(6.0)	1/50(2.0)	
Adjusted rates(b)	2,94	6.12	6.25	4.00	
Terminal rates(c)	1/34(2.9)	1/35(2.9)	1/30(3,3)	1/25(4.0)	
Statistical analysis			-, -,	4,400	
Peto test					
Standard method(d)	P = 0.3515				
Prevalence method(d)	P = 0.5632				
Combined analysis(d)	P = 0.5187				
Cochran-Armitage test(e)	P = 0.8073	D 0.000			
Fisher Exact test(e)		P = 0.3235	P = 0.3235	P = 0.2475	
	SITE : spleen				
	TUMOR : hemangioma, hemangiosarcoma				
l'umor rate					
Overall rates(a)	2/50(4.0)	3/50(6.0)	6/50(12.0)	2/50(4.0)	
Adjusted rates(b)	5.88	6.12	11.11	8.00	
Terminal rates(c)	2/34(5.9)	1/35(2.9)	2/30(6.7)	2/25(8.0)	
Statistical analysis					
Peto test	D 0.0515				
Standard method(d)	P = 0.3515				
Prevalence method(d) Combined analysis(d)	P = 0.4214				
oundined analysis(d)	P = 0.3930 P = 0.9613				
Coobson-Assistance test(s)	r = v. Mp i.3				
Cochran-Armitage test(e) Fisher Exact test(e)	. 0,0020	P = 0.4909	P = 0.1606	P = 0.3088	

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

·					
Group Name	Control	10000 ppm	20000 ppm	40000 ppm	
	SITE : Liver				
Tumor rate	TUMOR : hemangioma				
Overall rates(a)	5/50(10.0)	8/50(16.0)	1/50(2.0)	5/50(10.0)	
Adjusted rates(b)	13.16	18.60	0.0	10.81	
Terminal rates(c) Statistical analysis	4/34(11.8)	6/35(17.1)	0/30(0.0)	2/25(8.0)	
Peto test Standard method(d)	D - 0 1147				
Prevalence method(d)	P = 0.1147 P = 0.7526				
Combined analysis(d)	P = 0.5758				
Cochran-Armitage test(e)	P = 0.5962				
Fisher Exact test(e)		P = 0.3141	P = 0.1210	P = 0.3710	
	SITE : liver				
	TUMOR : hepatocellular adenoma				
fumor rate	0/50/ 10 0)	10/50/ 00 0			
Overall rates(a) Adjusted rates(b)	6/50(12.0) 14.71	13/50(26.0) 37.14	13/50(26.0)	7/50(14.0)	
Terminal rates(c)	5/34(14.7)	13/35(37.1)	36.67 11/30(36.7)	24.00 6/25(24.0)	
Statistical analysis	-,,	10,00 (0.11)	11/00(00:1/	0/20(24.0)	
Peto test					
Standard method(d)	P = 0.0866				
Prevalence method(d) Combined analysis(d)	P = 0.3780 P = 0.2711				
Cochran-Armitage test(e)	P = 0.8801				
Fisher Exact test(e)		P = 0.1099	P = 0.1099	P = 0.4863	
	SITE : Liver		W		
	TUMOR : histiocytic sarcoma				
Cumor rate					
Overall rates(a)	2/50(4.0)	3/50(6.0)	1/50(2.0)	4/50(8.0)	
Adjusted rates(b) Terminal rates(c)	0.0 0/34(0.0)	2.86	0.0	4.00	
Statistical analysis	V/04(0.0)	1/35(2.9)	0/30(0.0)	1/25(4.0)	
Peto test					
Standard method(d)	P = 0.2368				
Prevalence method(d)	P = 0.1900				
Combined analysis(d) Cochran-Armitage test(e)	P = 0.1505				
Fisher Exact test(e)	P = 0.4426	P = 0.4909	P = 0.4926	P = 0.3574	
		. 0.4000	1 - 0.4020	r - 0.5074	

(HPT360A)

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STUDY No. : 0225 ANIMAL : MOUSE BDF1

SEX : MALE

Group Name	Control	10000 ppm	20000 ppm	40000 ppm	
	SITE : liver				
umor rate	TUMOR : hepatocellular carcino	ňa			
Overali rates(a)	14/50(28.0)	11/50(22,0)	13/50(26.0)	9/50(18.0)	
Adjusted rates(b)	32.35	14.29	25.71	25,93	
Terminal rates(c)	11/34(32.4)	5/35(14.3)	7/30(23.3)	6/25(24.0)	
tatistical analysis				, , ,	
Peto test Standard method(d)	P = 0.6941				
Prevalence method(d)	P = 0.5612				
Combined analysis(d)	P = 0.6633				
Cochran-Armitage test(e)	P = 0.2969				
Fisher Exact test(e)		P = 0.3777	P = 0.4815	P = 0.2397	
	SITE : Liver				
umor rate	TUMOR : hemangioma,hemangiosar	coma			
Overall rates(a)	5/50(10.0)	9/50(18.0)	2/50(4.0)	7/50(14.0)	
Adjusted rates(b)	13.16	21.05	0.0	17.24	
Terminal rates(c)	4/34(11.8)	7/35(20.0)	0/30(0.0)	4/25(16.0)	
tatistical analysis				, , ,	
Peto test Standard method(d)	D 0.1004				
Prevalence method(d)	P = 0.1284 P = 0.4814				
Combined analysis(d)	P = 0.3112				
Cochran-Armitage test(e)	P = 0.9105				
Fisher Exact test(e)		P = 0.2379	P = 0.2425	P = 0.4062	
	SITE : liver				
umor rate	TUMUK : Nepatocellular adenoma	hepatocellular carcinoma,hepatoblas,	toma		
Overall rates(a)	19/50(38.0)	23/50(46.0)	23/50(46.0)	15/50(30.0)	
Adjusted rates(b)	44.12	48.57	53.33	44.44	
Terminal rates(c)	15/34(44.1)	17/35(48.6)	16/30(53.3)	11/25(44.0)	
tatistical analysis				• • •	
Peto test	D 0.5110				
Standard method(d) Prevalence method(d)	P = 0.5119 P = 0.5219				
Combined analysis(d)	P = 0.5219 P = 0.5292				
Cochran-Armitage test(e)	P = 0.2831				
Fisher Exact test(e)		P = 0.3695	P = 0.3695	P = 0.3472	

STUDY No. : 0225

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

10000 ppm

ANIMAL : MOUSE BDF1

Group Name

SEX : MALE

> 20000 ppm 40000 ppm

di DOD Mallia	COITE DE	10000 ppm	20000 ppm	40000 ppm	
	SITE : Harderian gland TUMOR : adenoma				
Tumor rate					
Overall rates(a)	3/50(6.0)	1/50(2.0)	4/50(8.0)	1/50(2.0)	
Adjusted rates(b)	4.44	2,86	9.09	4.00	
Terminal rates(c)	1/34(2.9)	1/35(2.9)	2/30(6.7)	1/25(4.0)	
Statistical analysis		, , ,	.,,	2,20(2,0)	
Peto test					
Standard method(d)	P = 0.9150 ?				
Prevalence method(d)	P = 0.5308				
Combined analysis(d)	P = 0.6801				
Cochran-Armitage test(e)	P = 0.5259				
Fisher Exact test(e)		P = 0.3235	P = 0.4895	P = 0.3235	
(HPT360A)			***************************************		

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PAGE:

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

Control

- (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; $*: P \le 0.05$ **: $P \le 0.01$

APPENDIX O 4

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

MOSUE :FEMALE

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

Group Name Control 10000 ppm 20000 ppm 40000 ppm SITE : lung TUMOR : bronchiolar-alveolar adenoma Tumor rate Overall rates(a) 2/50(4.0) 3/50(6.0) 2/50(4.0) 0/50(0.0) Adjusted rates(b) 6.90 9.38 9.09 0.0 Terminal rates(c) 2/24(8.3) 2/29(6.9) 1/19(5.3) 0/28(0.0) Statistical analysis Peto test Standard method(d) Prevalence method(d) P = 0.9246Combined analysis(d) P = -----Cochran-Armitage test(e) P = 0.1720Fisher Exact test(e) P = 0.4909P = 0.3088P = 0.2574SITE : lung TUMOR : bronchiolar-alveolar adenoma, bronchiolar-alveolar carcinoma Tumor rate Overall rates(a) 3/50(6.0) 5/50(10.0) 2/50(4.0) 0/50(0.0) Adjusted rates(b) 6.90 16.67 9.09 0.0 Terminal rates(c) 2/29(6.9) 4/24(16.7) 1/19(5.3) 0/28(0.0) Statistical analysis Peto test Standard method(d) P = 0.9204 ? Prevalence method(d) P = 0.9507Combined analysis(d) P = 0.9759Cochran-Armitage test(e) P = 0.0622Fisher Exact test(e) P = 0.3790P = 0.4909P = 0.1325SITE : Lymph node TUMOR : malignant lymphoma Tumor rate Overall rates(a) 9/50(18.0) 15/50(30,0) 11/50(22.0) 14/50(28.0) Adjusted rates(b) 13.79 16.67 15.79 28.57 Terminal rates(c) 4/29(13.8) 4/24(16.7) 3/19(15.8) 8/28(28.6) Statistical analysis Peto test Standard method(d) P = 0.6197Prevalence method(d) P = 0.0761Combined analysis(d) P = 0.2712Cochran-Armitage test(e) P = 0.4203Fisher Exact test(e) P = 0.1915P = 0.4357P = 0.2397

(HPT360A)

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

Group Name	Control	10000 ppm	20000 ppm	40000 ppm	
	SITE : liver				
`umor rate	TUMOR : hepatocellular adenoma				
Overall rates(a)	5/50(10.0)	11/50(22.0)	5/50(10.0)	10/50(20.0)	
Adjusted rates(b)	17.24	35.48	22.73	32.14	
Terminal rates(c) tatistical analysis Peto test	5/29(17.2)	8/24(33.3)	4/19(21.1)	9/28(32.1)	
Standard method(d)	P =				
Prevalence method(d) Combined analysis(d)	P = 0.2226 P =				
Cochran-Armitage test(e)	P = 0.3726				
Fisher Exact test(e)		P = 0.1300	P = 0.3710	P = 0.1771	
	SITE : Liver				
umor rate	TUMOR : hemangioma,hemangiosarco	na			
umor rate Overall rates(a)	0/50(0.0)	3/50(6.0)	1/50(2.0)	0/50(0.0)	
Adjusted rates(b)	0.0	8.33	5.26	0.0	
Terminal rates(c)	0/29(0.0)	2/24(8.3)	1/19(5.3)	0/28(0.0)	
Statistical analysis Peto test					
Standard method(d)	P = 0.5708				
Prevalence method(d)	P = 0.6483				
Combined analysis(d) Cochran-Armitage test(e)	P = 0.7247				
Fisher Exact test(e)	P = 0.4946	P = 0.1325	P = 0.4950	P = 0.5000	
		. 0,1020	1 - 0.1000	1 - 0.5000	
	SITE : Liver TUMOR : hepatocellular adenoma,he	enatacallular corainama hanatahlaa	toma		
'umor rate	1011011 1 1000 Edical duoy lottia y ti	opa to continuity ropa top tas	tona		
Overall rates(a)	5/50(10.0)	13/50(26.0)	5/50(10.0)	10/50(20.0)	
Adjusted rates(b) Terminal rates(c)	17.24 5/29(17.2)	41.94 8/24(33.3)	22.73	32.14	
Statistical analysis	0/20(11.2)	0/44(00.0)	4/19(21.1)	9/28(32.1)	
Peto test		•			
Standard method(d)	P =				
Prevalence method(d) Combined analysis(d)	P = 0.3131 P =				
Cochran—Armitage test(e)	P = 0.4989				
Fisher Exact test(e)		P = 0.0676	P = 0.3710	P = 0.1771	

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

				I AGE •
Group Name	Control	10000 ppm	20000 ppm	40000 ppm
	SITE : pituitary gland			
Tumor rate	TUMOR : adenoma			
Overall rates(a)	9/49(18.4)	7/50(14.0)	9/49(18.4)	9/40/ 16 9)
Adjusted rates(b)	27.59	25.00	23.81	8/49(16.3) 26.67
Terminal rates(c) Statistical analysis	8/29(27.6)	6/24(25.0)	3/18(16.7)	7/28(25.0)
Peto test Standard method(d)	P = 0.4236			
Prevalence method(d)	P = 0.6277			
Combined analysis(d)	P = 0.6058			
Cochran-Armitage test(e)	P = 0.9357			
Fisher Exact test(e)		P = 0.4089	P = 0.3991	P = 0.4843
	SITE : pituitary gland			
Tumor rate	TUMOR : adenoma, adenocarcinoma			
Overall rates(a)	11/49(22.4)	8/50(16.0)	11/49(22.4)	9/49(18.4)
Adjusted rates(b)	31.03	25.00	33,33	26.67
Terminal rates(c)	9/29(31.0)	- 6/24(25.0)	5/18(27.8)	7/28(25.0)
Statistical analysis				
Peto test	D = 0.5000			
Standard method(d) Prevalence method(d)	P = 0.5036 P = 0.6911			
Combined analysis(d)	P = 0.6811			
Cochran-Armitage test(e)	P = 0.7991			
Fisher Exact test(e)		P = 0.3379	P = 0.4070	P = 0.4361
	SITE : quary			
T	TUMOR : cystadenoma			
Tumor rate Overall rates(a)	1/49(2.0)	2/50/ 4.0)	0/50/ 0.0)	1/10/ 0.0
Adjusted rates(b)	3.45	2/50(4.0) 7.69	3/50(6.0) 8,57	1/49(2.0)
Terminal rates(c)	1/29(3.4)	1/24(4.2)	1/19(5.3)	3.57 1/28(3.6)
Statistical analysis Peto test		2,02(2.2)	1/10(0.0)	
Standard method(d)	P =			
Prevalence method(d)	P = 0.5488			
Combined analysis(d) Cochran-Armitage test(e)	P = P = 0.9516			
Fisher Exact test(e)	. ~ 0.0010	P = 0.4851	P = 0.3312	P = 0.2475
(HDT0001)				

(HPT360A)

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

Group Name	Control	10000 ppm	20000 ppm	40000 ppm	
	SITE : cuary TUMOR : cystadenoma,cystade	poored name			
mor rate	Tonon · Cystaderiuma, Cystade	nucai emuna			
verall rates(a)	2/49(4.1)	2/50(4.0)	3/50(6.0)	1/49(2.0)	
justed rates(b)	5.88	7.69	8.57	3.57	
rminal rates(c) tistical analysis to test	1/29(3.4)	1/24(4.2)	1/19(5.3)	1/28(3.6)	
tandard method(d)	P =				
revalence method(d)	P = 0.7029				
Combined analysis(d)	P =				
ochran-Armitage test(e) isher Exact test(e)	P = 0.6275	P = 0.3015	P = 0.4816	P = 0.4925	
		. 0.0010	0.1010	1 - 0.4320	
	SITE : uterus				-
nor rate	TUMOR : endometrial stroma	polyp			
werali rates(a)	5/50(10.0)	2/50(4.0)	0/50(0.0)	2/50(4.0)	
diusted rates(b)	17.24	8.33	0.0	4.76	
erminal rates(c)	5/29(17.2)	2/24(8.3)	0/19(0.0)	1/28(3.6)	
atistical analysis					
'eto test Standard method(d)	P =				
Prevalence method(d)	P = 0.9062				
Combined analysis(d)	P =				
ochran-Armitage test(e)	P = 0.1848				
isher Exact test(e)		P = 0.2425	P = 0.0360*	P = 0.2425	
	a.m.				
	SITE : uterus TUMOR : histiocytic sarcoma				
nor rate	Tonon V This Flady Cite Sai Come	•			
verall rates(a)	9/50(18.0)	3/50(6.0)	14/50(28.0)	12/50(24.0)	
diusted rates(b)	7.50	4.17	16,67	14.29	
erminal rates(c) atistical analysis	2/29(6.9)	1/24(4.2)	3/19(15.8)	4/28(14.3)	
eto test					
Standard method(d)	P = 0.2545				
Prevalence method(d)	P = 0.1165				
Combined analysis(d)	P = 0.1085				
ochran-Armitage test(e) isher Exact test(e)	P = 0.1277	D = 0.0000	D = 0.0007	D 0.0000	
PIE EXECT FERT(B)		P = 0.0899	P = 0.2397	P = 0.3620	

ANIMAL : MOUSE BDF1
SEX : FEMALE

STUDY No. : 0225

				1 10	
Group Name	Contral	10000 ppm	20000 ppm	40000 ppm	
	SITE : mammary gland TUMOR : adenoma				
Tumor rate	TUTOK • adenoma				
Overall rates(a)	0/50(0.0)	0/50(0.0)	1/50(2.0)	3/50(6.0)	
Adjusted rates(b)	0.0	0.0	5.26	7.69	
Terminal rates(c) Statistical analysis Peto test	0/29(0.0)	0/24(0.0)	1/19(5.3)	2/28(7.1)	
Standard method(d)	P =				
Prevalence method(d)	P = 0.0146*			·	
Combined analysis(d)	P =				
Cochran-Armitage test(e)	P = 0.0168*		_		
Fisher Exact test(e)		P = 0.5000	P = 0.4950	P = 0.1325	
	SITE : mammary gland				
Tumor rate	TUMOR : adenocarcinoma				
Overall rates(a)	1/50(2.0)	1/50(2.0)	2/50(4.0)	3/50(6.0)	
Adjusted rates(b)	2,94	0.0	0.0	5.41	
Terminal rates(c)	0/29(0.0)	0/24(0.0)	0/19(0.0)	1/28(3.6)	
Statistical analysis Peto test					
Standard method(d)	P = 0.2823				
Prevalence method(d)	P = 0.1702				
Combined analysis(d)	P = 0.1418				
Cochran-Armitage test(e)	P = 0.2166				
Fisher Exact test(e)		P = 0.2475	P = 0.4926	P = 0.3235	
	SITE : mammary gland				
Tumor rate	TUMOR : adenoma,adenocarcinoma				
Overall rates(a)	1/50(2.0)	1/50(2.0)	3/50(6.0)	6/50/ 19.0)	
Adjusted rates(b)	2.94	0.0	5.26	6/50(12.0) 13.16	
Terminal rates(c)	0/29(0.0)	0/24(0.0)	1/19(5.3)	3/28(10.7)	
Statistical analysis					
Peto test Standard method(d)	P = 0.2823				
Prevalence method(d)	P = 0.2823 P = 0.0098**				
Combined analysis(d)	P = 0.0142*				
Cochran-Armitage test(e)	P = 0.0137*				
Fisher Exact test(e)		P = 0.2475	P = 0.3235	P = 0.0724	

(HPT360A)

STUDY No. : 0225

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

ANIMAL : MOUSE BDF1 SEX : FEMALE

Group Name	Control	10000 ppm	20000 ppm	40000 ppm	
	SITE : Harderian gland				
	TUMOR : adenoma				
mor rate Vuerall rates(a)	0/50/ 4.0)	1/50/ 0.0)	0/50/ 0.0	. (=	
idjusted rates(b)	2/50(4.0)	1/50(2.0)	0/50(0.0)	4/50(8.0)	
	4.76	4.17	0.0	14.29	
Perminal rates(c)	0/29(0.0)	1/24(4.2)	0/19(0.0)	4/28(14.3)	
atistical analysis					
eto test	_				
Standard method(d)	P =				
Prevalence method(d)	P = 0.1320				
Combined analysis(d)	P =				
Cochran—Armitage test(e)	P = 0.2166				
isher Exact test(e)		P = 0.4926	P = 0.2574	P = 0.3574	

BAIS3

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Standard method : Death analysis

Prevalence method: Incidental tumor test

Combined analysis: Death analysis + Incidental tumor test

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

⁽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.

⁽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.

APPENDIX P 1

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

RAT: MALE: DEAD AND MORIBUND ANIMALS

HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE

STUDY NO. : 0224

Organ	Findings	Group Name Control No. of Animals on Study 12	7500 ppm 11	15000 ppm 16	30000 ppm 20
[Respiratory s	system]			·	
nasal cavit	leukemic cell infiltration	<12>	<11> 0	<16> 0	<20>
ung	leukemic cell infiltration	<12> 5	<11> 0	<16> 2	<20> 2
	metastasis:bone tumor	0	0	0	1
[Hematopoietio	system]				
oone marrow	leukemic cell infiltration	<12> 3	<11> 0	<16> 2	<20>
	metastasis:liver tumor	0	0	1	0
ymph nade	leukemic cell infiltration	<12> 3	<11> 0	<16> 2	<20>
	metastasis:liver tumor	0	0	1	0
Digestive sy:	stem]	,			
salivary gl	leukemic cell infiltration	<12> 1	<11> 0	<16> 0	<20> 0
stomach	leukemic cell infiltration	<12> 2	<11> 0	<16> 0	<20> 0
small intes	leukemic cell infiltration	<12>	<10> 0	<16> 0	<20>
Liver⁻	leukemic cell infiltration	<12> 5	<11> 0	<16>	<20>
(a)	a: Number of animals examined at th b: Number of animals with lesion	e site			

(JPT150)

BAIS3

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

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

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

(JPT150)

STUDY NO. : 0224 ANIMAL : RAT F344

: RAT F344 DEAD AND MORIBUND

REPORT TYPE : A1
SEX : MALE

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

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

APPENDIX P 2

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

RAT: FEMALE: DEAD AND MORIBUND ANIMALS

STUDY NO. : 0224 ANIMAL : RAT F344

REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name No. of Animals on Study	Control 3	7500 ppm 11	15000 ppm 15	30000 ppm 36
[Respiratory	systemi					
lung	5,5 25111		< 3>	<11>	/15\	(00)
tu is	leukemic cell infiltration		0	3	<15> 1	<36>
	metastasis:liver tumor		0	0	1	0
	metastasis:uterus tumor		0	0	1	0
[Hematopoiet	ic system]					
bone marrow	leukemic cell infiltration		< 3> 0	<11> 1	<15> 0	<36>
	metastasis:liver tumor		0	0	1	0
lymph node	leukemic cell infiltration		< 3> 0	<11> 4	<15> 1	<36>
	metastasis:liver tumor		0	0	1	0
	metastasis:uterus tumor		0	0	1	_ 0
[Digestive s	ystem]					
Liver	leukemic cell infiltration		< 3> 0	<11> 4	<15> 1	<36> 3
[Urinary sys	tem]					
kidney	leukemic cell infiltration		< 3> 0	<11> 1	<15> 0	<36> 0
(Nervous sys	tem]					
brain	leukemic cell infiltration		< 3> 0	<11>> 2	<15> 0	<36>

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

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

PAGE: 5

SEX : FEMALE

Organ		Group Name No. of Animals on Study	Control 3	7500 ppm 11	15000 ppm 15	30000 ppm 36
[Nervous syst	em]					
spinal cord	leukemic cell infiltration		< 3> 0	<11> 1	<15> 0	<36> 0
(Special sens	e organs/appandage]					
еуе	leukemic cell infiltration		< 3> 0	<11> 1	<15> 0	<36> 0
⟨a⟩ b	a: Number of animals examined at the si b: Number of animals with lesion	te			201	
(JPT150)						BAIS3

APPENDIX P 3

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

RAT: MALE: SACRIFICED ANIMALS

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

PAGE: 1

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

SEX

: MALE

)rgan	Findings	Group Name No. of Animals on Study	Control 38	7500 ppm 39	15000 ppm 34	30000 ppm 30
[Respiratory s	noton]					
	sys remi					
lung	leukemic cell infiltration		<38> 0	<39> 1	<34> 0	<30> 2
	metastasis:liver tumor		0	0	0	1
	metastasis:thyroid tumor		0	0	1	0
	metastasis:preputial/clitoral gland tumo	or-	1	0	0	0
[Hematopoietic	system]					
oone marrow	metastasis:liver tumor		<38> 0	<39> 0	<34> 0	<30> 1
lymph node	leukemic cell infiltration		<38> 0	<39> 0	<34> 0	<30> 1
	metastasis:liver tumor		0	0	0	1
spleen	metastasis:liver tumor		<38> 0	<39> 0	<34> 0	<30> 1
Digestive sys	etem]					
stomach	leukemic cell infiltration		<38> 0	<39> 0	<34>	<30> 0
small intes	leukemic cell infiltration		<38> 0	<39> 0	<34> 1	<30> 0
Liver	leukemic cell infiltration		<38> 0	<39> 0	<34> 0	<30> 1
(Endocrine sys	stem]					
pituitary	metastasis:liver tumor		<38> 0	<39> 0	<34>	<30> 1

⁽a) a: Number of animals examined at the site

b: Number of animals with lesion

STUDY NO. : 0224 ANIMAL

: RAT F344

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

PAGE: 2

SACRIFICED ANIMALS (105W)

7500 ppm 15000 ppm Group Name Control 30000 ppm 39 34 No. of Animals on Study 38 30 Organ____Findings_ [Endocrine system] ⟨38⟩ adrenal ⟨39⟩ <34> <30> leukemic cell infiltration 0 1 0 0 < a > a : Number of animals examined at the site b b: Number of animals with lesion (JPT150) BAIS3

APPENDIX P 4

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

RAT: FEMALE: SACRIFICED ANIMALS

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

: FEMALE

SEX

HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR (SUMMARY)

SACRIFICED ANIMALS (105W)

7500 ppm 15000 ppm 30000 ppm Group Name Control No. of Animals on Study 47 39 35 14 Findings_ [Respiratory system] lung <47> <39> ⟨35⟩ <14> leukemic cell infiltration 3 0 1 1 0 0 metastasis:uterus tumor 1 [Hematopoietic system] lymph node <47> <39> ⟨35⟩ <14> leukemic cell infiltration [Digestive system] liver <47> <39> <35> <14> leukemic cell infiltration 3 0 1 [Nervous system] brain <47> <39> <35> <14> leukemic cell infiltration 0 0 1 0 < a > a: Number of animals examined at the site b: Number of animals with lesion (JPT150) BAIS3

APPENDIX P 5

HISTOLOGICAL FINDINGS :METASTASIS OF TUMOR (TOW-YEAR 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. : 0225

Group Name 10000 ppm 20000 ppm 40000 ppm Control No. of Animals on Study 16 15 20 25 Findings_ [Integumentary system/appandage] subcutis <16> <15> ⟨20⟩ ⟨25⟩ leukemic cell infiltration 1 [Respiratory system] nasal cavit <16> <15> <20> ⟨25⟩ leukemic cell infiltration 1 lung <16> <15> ⟨20⟩ <25> leukemic cell infiltration 1 1 metastasis:liver tumor 3 1 0 [Hematopoietic system] bone marrow <16> <15> <20> <25> leukemic cell infiltration 1 metastasis:Liver tumor 1 0 0 1 lymph nade <16> <15> <20> <25> leukemic cell infiltration 0 3 metastasis:liver tumor 0 1 spleen <16> <15> <20> ⟨25⟩ leukemic cell infiltration 1 3 metastasis:Liver tumor 1 [Circulatory system] heart <16> <15> ⟨20⟩ <25> leukemic cell infiltration 1 1 (a) a: Number of animals examined at the site b: Number of animals with lesion

(JPT150)

BAIS3

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

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

SEX : MALE

Organ	Findings	Group Name No. of Animals on Study	Control 16	10000 ppm 15	2000 ppm 20	40000 ppm 25
[Circulatory	system]					
neart	metastasis:liver tumor		<16> 0	<15> 1	<20> 0	<25> 0
[Digestive sy	stem]					
tongue	leukemic cell infiltration		<16> 0	<15>	<20>	<25>
salivary gl	leukemic cell infiltration		<16> 0	<15> 0	<20> 1	<25> 2
	metastasis:liver tumor		0	0	0	1
stomach	leukemic cell infiltration		<16>	<15> 0	<20> 0	<25>
liver	leukemic cell infiltration		<16>	<15> 1	<20> 2	<25>
pancreas	leukemic cell infiltration		<16> 0	<15> 0	<20> 0	<25> 2
[Urinary syst	rem]					
kidney	leukemic cell infiltration		<16> 1	<15> 1	<20> 0	<25> 3
	metastasis:liver tumor		1	0	0	0
[Reproductive	system]					
epididymis	metastasis:liver tumor		<16> 0	<15> 0	<20> 1	<25>
(a)	a: Number of animals examined at b: Number of animals with lesion	the site				

(JPT150)

BAIS3

STUDY NO. : 0225

: MOUSE BDF1

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

DEAD AND MORIBUND ANIMALS (0-105W)

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

BAIS3

APPENDIX P 6

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

MOUSE: FEMALE: DEAD AND MORIBUND ANIMALS

HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR (SUMMARY)

DEAD AND MORIBUND ANIMALS (0-105W)

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

Group Name Control 10000 ppm 20000 ppm 40000 ppm No. of Animals on Study 26 31 22 Findings_ [Integumentary system/appandage] subcutis <21> <26> <31> <22> leukemic cell infiltration 0 1 1 [Respiratory system] nasal cavit ⟨21⟩ <26> ⟨31⟩ ⟨22⟩ leukemic cell infiltration 1 0 metastasis:uterus tumor 1 1 lung (21) <26> ⟨31⟩ <22> leukemic cell infiltration 10 8 metastasis:liver tumor metastasis:uterus tumor metastasis:subcutis tumor [Hematopoietic system] bone marrow <21> ⟨26⟩ <31> <22> leukemic cell infiltration 3 metastasis: Liver tumor 1 metastasis:uterus tumor 2 1 1

<21>

2

<26>

<31>

0

1

3

Leukemic cell infiltration

metastasis:liver tumor

metastasis:uterus tumor

(JPT150)

Lymph node

BAIS3

<22>

1

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

ANIMAL : MOUSE BDF1 REPORT TYPE : A1

STUDY NO. : 0225

SEX : FEMALE

0	5	Group Name No. of Animals on Study	Control 21	10000 ppm 26	20000 ppm 31	40000 ppm 22
Organ	Findings					
[Hematopoiet	ic system]					
			(01)	(0.0)		
lymph node	metastasis:subcutis tumor		<21> 1	<26> 0	<31> 0	<22> 0
thymus			⟨21⟩	<26>	<31>	⟨22⟩
	leukemic cell infiltration		0	0	1	0
spleen			<21>	<26>	<31>	<22>
	leukemic cell infiltration		4	7	4	5
	metastasis:liver tumor		1	0	1	0
	metastasis:uterus tumor		0	0	1	0
[Circulatory	system]					
neart			<21>	<26>	⟨31⟩	<22>
	leukemic cell infiltration		2	6	5	2
	metastasis:uterus tumor		1	0	0	0
Digestive s	ystem]					
tangue			<21>	⟨26⟩	⟨31⟩	<22>
	leukemic cell infiltration		1	3	2	2
salivary gl			<21>	⟨26⟩	⟨31⟩	<22>
	leukemic cell infiltration		1	4	5	2
stomach			<21>	<26>	⟨31⟩	<22>
	leukemic cell infiltration		0	3	3	0
	metastasis:uterus tumor		0	1	1	1
small intes			⟨21⟩	<26>	<31>	⟨22⟩
	leukemic cell infiltration		1	0	0	0

(JPT150)

BAIS3

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

ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : FEMALE

STUDY NO. : 0225

Organ	Findings	Group Name No. of Animals on Study	Control 21	10000 ppm 26	20000 ppm 31	40000 ppm 22
OI 9dII	r mangs					
Digestive s	vstem]					
liver			<21>	<26>	⟨31⟩	⟨22⟩
	leukemic cell infiltration		5	9	10	6
	metastasis:uterus tumor		6	2	7	6
pancreas	loukomia aall infiltration		<21>	<26>	<31>	⟨22⟩
	leukemic cell infiltration		1	2	0	3
	metastasis:liver tumor		0	0	1	0
	metastasis:uterus tumor		1	0	1	2
[Urinary sys	tem]					
kidney			⟨21⟩	<26>	<31>	⟨22⟩
	leukemic cell infiltration		1	9	7	2
	metastasis:liver tumor		1	0	0	0
	metastasis:uterus tumor		2	2	0	3
urin bladd			<21>	<26>	⟨31⟩	<22>
	leukemic cell infiltration		0	2	3	2
[Endocrine s	vstem]					
pituitary			<21>	<26>	⟨31⟩	<22>
	leukemic cell infiltration		1	0	0	0
adrena l	Sandarata and Confidences		<21>	<26>	⟨31⟩	<22>
	leukemic cell infiltration		0	3	3	0
	metastasis:uterus tumor		1	0	0	0

(JPT150)

BAIS3

STUDY NO. : 0225

ANIMAL : MOUSE BDF1

REPORT TYPE : A1

SEX : FEMALE

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

		Consulta Nassa	0	10000		
)rgan	Findings	Group Name No. of Animals on Study	Control 21	10000 ppm 26	20000 ppm 31	40000 ppm 22
Reproductive :	system]					
ovary	leukemic cell infiltration		<21> 3	<26> 8	<31> 5	<22> 3
	metastasis:uterus tumor		6	2	6	6
rterus	leukemic cell infiltration		<21> 1	<26> 2	<31> 3	<22>
	metastasis:lung tumor		1	0	0	0
nammary gl	metastasis:uterus tumor		<21> 1	<26>	<31> 0	<22> 0
Nervous syste	m]					
rain	leukemic cell infiltration		<21> 0	<26>	<31> 2	<22> 0
opinal cord	leukemic cell infiltration		<21> 0	<26>	<31> 1	<22> 0
Special sense	organs/appandage]					
Harder gl	leukemic cell infiltration		<21> 1	<26> 3	<31> 3	<22> 1
[Musculoskelet	al system]					
uscle	leukemic cell infiltration		<21> 1	<26> 1	<31> 2	<22>
[Body cavities]					
peritoneum	metastasis:uterus tumor		<21> 0	<26>	<31> 2	<22> 0

APPENDIX P 7

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

MOUSE: MALE: SACRIFICED ANIMALS

STUDY NO. : 0225

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)

SACRIFICED ANIMALS (105W)

ANIMAL : MOUSE BDF1
REPORT TYPE : A1

SEX : MALE

Group Name 10000 ppm 20000 ppm Control 40000 ppm No. of Animals on Study 34 35 25 Organ___ Findings_ [Respiratory system] <34> <35> ⟨30⟩ <25> lung leukemic cell infiltration metastasis:liver tumor 3 0 1 [Hematopoietic system] bone marrow ⟨34⟩ ⟨35⟩ ⟨30⟩ ⟨25⟩ leukemic cell infiltration thymus ⟨34⟩ <35> <30> ⟨25⟩ leukemic cell infiltration ⟨34⟩ ⟨35⟩ (25) <30> spleen leukemic cell infiltration [Circulatory system] <34> heart <35> ⟨30⟩ <25> leukemic cell infiltration 1 0 [Digestive system] ⟨34⟩ <35> tongue <30> <25> leukemic cell infiltration 0 0 1 salivary gl ⟨34⟩ <35> <30> <25> leukemic cell infiltration 1 0 liver <34> ⟨35⟩ <30> ⟨25⟩ leukemic cell infiltration 1 0 2 <34> ⟨35⟩ <30> <25> pancreas leukemic cell infiltration 0 0 0 1 (a) a: Number of animals examined at the site b: Number of animals with lesion

⁽JPT150)

STUDY NO. : 0225

: MOUSE BDF1 ANIMAL

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

SACRIFICED ANIMALS (105W)

Group Name Control 10000 ppm 20000 ppm 40000 ppm No. of Animals on Study 34 35 30 25 Organ____ Findings_ [Urinary system] <35> <30> kidney <25> <34> leukemic cell infiltration 1 0 2 0 ⟨a⟩ a : Number of animals examined at the site b b: Number of animals with lesion (JPT150) BAIS3

APPENDIX P 8

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

MOUSE: FEMALE: SACRIFICED ANIMALS

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

PAGE: 3

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

: FEMALE SEX

		Group Name No. of Animals on Study	Contral 29	10000 ppm 24	20000 ppm 19	40000 ppm 28
)rgan	Findings					
Respiratory	system]					
lung	leukemic cell infiltration		<29> 1	<24> 1	<19> 2	<28> 4
[Hematopoiet	ic system]					
oone marrow	leukemic cell infiltration		<29> 1	<24> 2	<19> 0	<28>
lymph node	leukemic cell infiltration		<29> 1	<24>	<19>	<28>
spleen	leukemic cell infiltration		<29> 1	<24> 2	<19>	<28> 2
[Circulatory	system]					
heart	leukemic cell infiltration		<29>	<24> 1	<19> 0	<28> 0
[Digestive s	eystem]					
salivary gl	leukemic cell infiltration		<29> 1	<24>	<19> 0	<28> 2
stomach	leukemic cell infiltration		<29> 1	<24> 0	<19> 0	<28>
liver	leukemic cell infiltration		<29> 3	<24> 3	<19> 3	<28>
	metastasis:uterus tumor		0	0	2	1
[Urinary sys	stem]					
kidney	leukemic cell infiltration		<29> 2	<24> 2	<19> 1	<28> 3

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

b: Number of animals with lesion

STUDY NO. : 0225

ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : FEMALE

HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR (SUMMARY)

SACRIFICED ANIMALS (105W)

0rgan		Group Name No. of Animals on Study	Control 29	10000 ppm 24	20000 ppm 19	40000 ppm 28
[Urinary system]					
urin bladd	leukemic cell infiltration		<29> 0	<24> 2	<19> 1	<28> 2
[Reproductive s	ystem]					
ovary	leukemic cell infiltration		<29> 0	<24> 2	<19> 0	<28> 1
uterus	leukemic cell infiltration		<29> 0	<24> 1	<19> 1	<28> 0
[Musculoskeleta	ol system]					
muscle	leukemic cell infiltration		<29> 0	<24> 2	<19> 0	<28> 0
[Body cavities]						
peritoneum	metastasis:subcutis tumor		<29> 1	<24> 0	<19> 0	<28> 0
⟨ a ⟩ b	a: Number of animals examined at the s b: Number of animals with lesion	te				
(JPT150)						

APPENDIX Q 1 IDENTITY OF UROTROPIN (TOW-YEAR STUDY)

IDENTITY OF 1, 3, 5, 7-TETRAAZATRICYCLO[3, 3, 1, 13, 7] DECANE(TWO-YEAR STUDIES)

A.Lot no. TWH2454

1. Spectral data

Mass Spectrometry

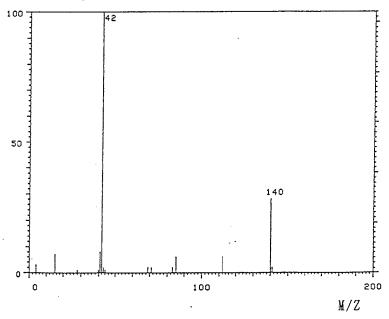
Instrument

: Hitachi M-80B Mass Spectrometer

Ionization

: EI(Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Results: The mass spectrum was consistent with literature spectrum.

<u>Determined Value</u> Fragment Peak(M/Z) <u>Literature Value*</u> Fragment Peak(M/Z)

42(Base Peak) 140

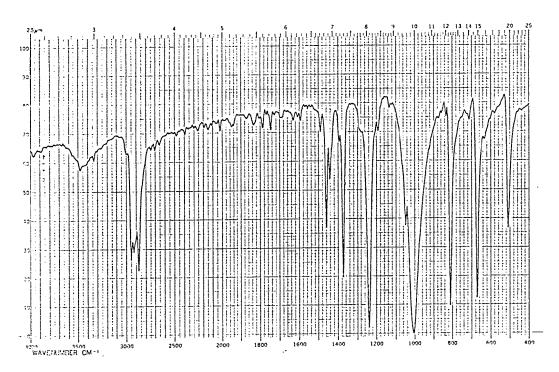
42(Base Peak) (*EPA/NIH Mass Spectral Data Base (1978) Vol. 1, p. 348.)

Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium



Infrared Spectrum of Test Substance

Results: The infrared spectrum was consistent with literature spectrum.

Determined Value	<u>Literature Value*</u>
Wave Number(cm ⁻¹)	Wave Number(cm ⁻¹)
480~ 530	480~ 530
640~ 700	640~ 700
780~ 830	780~ 830
910~1100	910~1100
1200~1270	1200 ~ 1270
1350~1420	$1350 \sim 1420$
1420~1490	$1420 \sim 1490$
2800~3000	2800~3000
	(Performed by the WAKO
	PURE CHEMICAL INDUSTRIES,
	LTD.)

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

Consequently, the test substance was identified as 1, 3, 5, 7-Tetraazatricyclo[$3.3.1.1^{3.7}$]decane.

B. Lot no. APR5276

1. Spectral data

Mass Spectrometry

Instrument

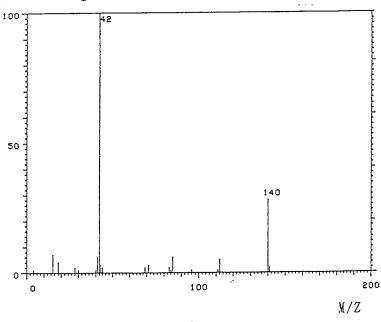
: Hitachi M-80B Mass Spectrometer

Ionization

: EI(Electron Ionization)

Ionization Voltage

: 70eV



Mass Spectrum of Test Substance

Results: The mass spectrum was consistent with literature spectrum.

Determined Value
Fragment Peak(M/Z)

<u>Literature Value*</u> Fragment Peak(M/Z)

42(Base Peak) 140

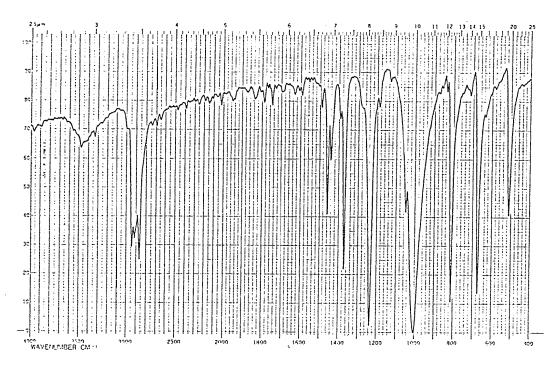
42(Base Peak) 140 (*EPA/NIH Mass Spectral Data Base (1978) Vol. 1, p. 348.)

Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium



Infrared Spectrum of Test Substance

Results: The infrared spectrum was consistent with literature spectrum.

<u>Determined Value</u>	<u>Literature Value*</u>
Wave Number(cm ⁻¹)	Wave Number(cm ⁻¹)
480~ 530	480~ 530
640~ 700	640~ 700
780~ 830	780~ 830
910~1100	910~1100
1200~1270	1200~1270
1350~1420	$1350 \sim 1420$
$1420 \sim 1490$	$1420 \sim 1490$
2800~3000	2800~3000
	(Performed by the WAKO
	PURE CHEMICAL INDUSTRIES,
	LTD.)

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

Consequently, the test substance was identified as 1, 3, 5, 7-Tetraazatricyclo[$3.3.1.1^{3.7}$]decane.

C. Lot no. APF5582

1. Spectral data

Mass Spectrometry

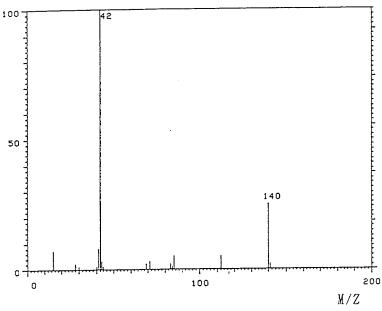
Instrument

: Hitachi M-80B Mass Spectrometer

Ionization

: EI(Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Results: The mass spectrum was consistent with literature spectrum.

Determined Value Fragment Peak(M/Z)

42(Base Peak)

140

<u>Literature Value*</u> Fragment Peak(M/Z)

42(Base Peak)

140

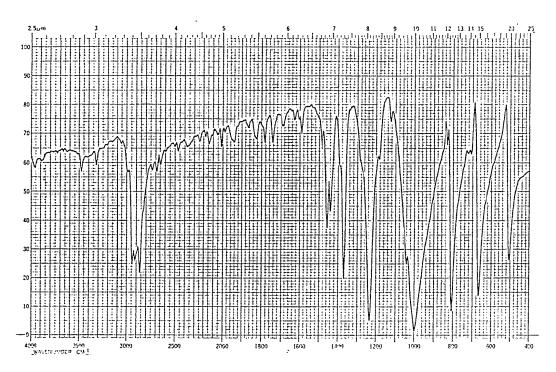
(*EPA/NIH Mass Spectral Data Base (1978) Vol. 1, p. 348.)

Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium



Infrared Spectrum of Test Substance

Results: The infrared spectrum was consistent with literature spectrum.

<u>Determined Value</u>	Literature Value*
Wave Number(cm ⁻¹)	Wave Number(cm ⁻¹)
480∼ 530	480~ 530
640~ 700	640~ 700
780∼ 830	780~ 830
910~1100	910~1100
$1200 \sim 1270$	1200~1270
$1350 \sim 1420$	1350~1420
$1420 \sim 1490$	$1420 \sim 1490$
2800~3000	2800~3000
	(Performed by the \AKO
	PURE CHEMICAL INDUSTRIES,
	LTD.)

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

Consequently, the test substance was identified as 1, 3, 5, 7-Tetraazatricyclo[3.3.1.1 $^{3, 7}$]decane.

D. Lot no. KCR6018

1. Spectral data

Mass Spectrometry

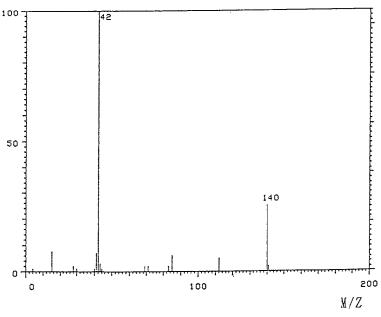
Instrument

: Hitachi M-80B Mass Spectrometer

Ionization

: EI(Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Results: The mass spectrum was consistent with literature spectrum.

<u>Determined Value</u> Fragment Peak(M/Z)

> 42(Base Peak) 140

Literature Value* Fragment Peak(M/Z)

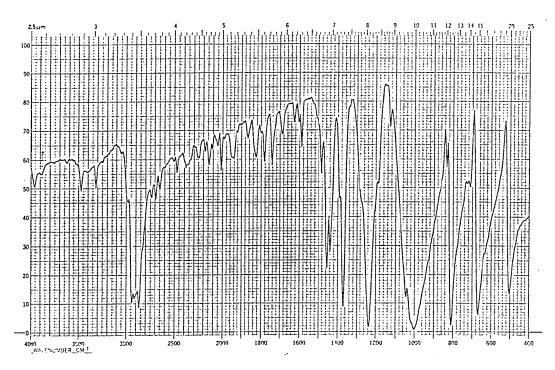
> 42(Base Peak) 140 (*EPA/NIH Mass Spectral Data Base (1978) Vol. 1, p. 348.)

Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium



Infrared Spectrum of Test Substance

Results: The infrared spectrum was consistent with literature spectrum.

<u>Determined Value</u>	<u>Literature Value*</u>
Wave Number(cm ⁻¹)	Wave Number(cm ⁻¹)
480~ 530	480~ 530
640~ 700	640~ 700
780~ 830	780~ 830
910~1100	910~1100
$1200 \sim 1270$	$1200 \sim 1270$
$1350 \sim 1420$	1350~1420
1420~1490	1420~1490
2800~3000	2800~3000
	(Performed by the WAKO
	PURE CHEMICAL INDUSTRIES,
	LTD.)

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

Consequently, the test substance was identified as 1, 3, 5, 7-Tetraazatricyclo[3.3.1.1 3 .7]decane.

APPENDIX Q 2
STABILITY OF UROTROPIN
(TOW-YEAR STUDY)

STABILITY OF 1, 3, 5, 7-TETRAAZATRICYCLO[3.3.1.13.7]DECANE(TWO-YEAR STUDIES)

A. Lot no. TWH2454

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

2. Gas Chromatography

Instrument:

Hewlett Packard 5890A Gas Chromatograph

Column:

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

Column Temperature:

215°C

Flow Rate:

35m1/min

Detector:

FID(Flame Ionization Detector)

Injection Volume:

 $1 \mu 1$

Results: Gas chromatography indicated one major peak(peak No.1) analyzed at

1992.10.21 and one major peak(peak No.1) analyzed at 1993.4.2. No new treace impurity peak in the test substance analyzed at

1993.4.2 was detected.

Date	Peak	No.	Retention Time(min)	Area Count	
1992.10.		1	5.957	140000	
1993.04.		1	5.962	140000	

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

B. Lot no. APR5276

1. Sample storage: This lot was used from 1993. 3.25 to 1994.1.20. Test substance was stored at room temperature.

2. Gas Chromatography

Instrument:

Hewlett Packard 5890A Gas Chromatograph

Column:

4% Carbowax 20M / 0.8% KOH(2mm ϕ × 2m)

Column Temperature:

215°C

Flow Rate:

35m1/min

Detector:

FID(Flame Ionization Detector)

Injection Volume:

 $1 \mu 1$

Results: Gas chromatography indicated one major peak(peak No.1) analyzed at

1993.3.1 and one major peak(peak No.1) analyzed at 1994.1.23. No new treace impurity peak in the test substance analyzed at

1994.1.23 was detected.

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

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

C. Lot no. APF5582

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

2. Gas Chromatography

Instrument:

Hewlett Packard 5890A Gas Chromatograph

Column:

4% Carbowax 20M / 0.8% KOH(2mm ϕ × 2m)

Column Temperature:

215°C

Flow Rate:

35ml/min

Detector:

FID(Flame Ionization Detector)

Injection Volume:

 $1 \mu 1$

Results: Gas chromatography indicated one major peak(peak No. 1) analyzed at 1994. 1.10 and one major peak(peak No. 1) analyzed at 1994. 3.24.

No new treace impurity peak in the test substance analyzed at

1994.3.24 was detected.

Date	Peak	No.	Retention Time(min)	Area Count	
1994.01.1 (date ana		1	5.988	141000	
1994.03.2 (date ana		1	5.990	140000	

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

D. Lot no. KCR6018

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

2. Gas Chromatography

Instrument:

Hewlett Packard 5890A Gas Chromatograph

Column:

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

Column Temperature:

215°C

Flow Rate:

35m1/min

Detector:

FID(Flame Ionization Detector)

Injection Volume:

 $1 \mu 1$

Results: Gas chromatography indicated one major peak(peak No.1) analyzed at

1994.1.27 and one major peak(peak No.1) analyzed at 1994.12.7. No new treace impurity peak in the test substance analyzed at

1994.12.7 was detected.

Date	Peak	No.	Retention Time(min)	Area Count	
1994.01. (date an		1	5.970	141000	
1994.12. (date an		1	5.987	141000	

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

APPENDIX Q 3

CONCENTRATION OF UROTROPIN IN DRINKING WATER

(TOW-YEAR STUDY: RAT)

CONCENTRATION OF 1, 3, 5, 7-TETRAAZATRICYCLO[3.3.1.13.7] DECANE IN DRINKING WATER(TWO-YEAR STUDY)

(Rat)

	Target Concentration(ppm)			
Date analyzed	7500	15000	30000	
1992.11.09	7146(95.3)*	14699(98.0)	29914(99.7)	
993.02.15	6993(93.2)	14292(95.3)	28822(96.1)	
1993-05-10	7228(96.4)	14533(96.9)	29366(97.9)	
993.08.23	7319(97.6)	14771(98.5)	29369(97.9)	
993.11.08	7382(98.4)	14784(98.6)	29521(98.4)	
994.02.09	7386(98.5)	14867(99.1)	29127(97.1)	
994.05.16	7415(98.9)	14775(98.5)	29879(99.6)	
994.08.15	7461(99.5)	15038(100.3)	30022(100.1)	
1994.11.07	7363(98.2)	14872(99.1)	29873(99.6)	

^{* : %} of target concentration

Analytical method: The samples were analyzed by the GC.

Instrument : Hewlett Packard 5890A

Column : 4% Carbowax 20M / 0.8% KOH

Flow Rate Detector

: 35m1/min

: FID(Hydrogen Flame Ionization)

/ 60/80 Carbopack B $(2mm\phi \times 2m)$ Injection Volume $: 1 \mu 1$

Column Temperature: 215°C

APPENDIX Q 4

CONCENTRATION OF UROTROPIN IN DRINKING WATER

(TOW-YEAR STUDY: MOUSE)

CONCENTRATION OF 1, 3, 5, 7-TETRAAZATRICYCLO[3.3.1.13.7] DECANE IN DRINKING WATER(TWO-YEAR STUDY)

(Mouse)

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

^{*} : % of target concentration

Analytical method: The samples were analyzed by the GC.

Instrument

: Hewlett Packard 5890A

Flow Rate

: 35ml/min

Column

: 4% Carbowax 20M / 0.8% KOH

Detector

: FID(Hydrogen Flame Ionization)

/ 60/80 Carbopack B $(2mm\phi \times 2m)$

Injection Volume

 $: 1 \mu 1$

Column Temperature: 215°C

APPENDIX Q 5 STABILITY OF UROTROPIN IN DRINKING WATER (TOW-YEAR STUDY)

STABILITY OF 1, 3, 5, 7-TETRAAZATRICYCLO[3.3.1.13.7] DECANE IN DRINKING WATER (TWO-YEAR STUDIES)

(Rat)

	Target Concen	tration(ppm)	
Date analyzed	7500	30000	
1992.11.02(a)	7276	28626	
1992.11.13(b)	7312	29463	
(Mouse)			
	Target Concentration(ppm)		
Date analyzed	10000	40000	
1992.11.02(a)	9429	37556	
1992.11.13(b)	9697	39154	

a : Date of preparation

Analytical method: The samples were analyzed by the GC.

Instrument

: Hewlett Packard 5890A

: 4% Carbowax 20M / 0.8% KOH

Flow Rate

: 35m1/min

Column

Detector

: FID(Hydrogen Flame Ionization)

/ 60/80 Carbopack B $(2mm\phi \times 2m)$

Injection Volume

 $: 1 \mu 1$

Column Temperature: 215°C

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

APPENDIX R 1

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS

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

- 1) Automatic blood cell analyzer (Technicon H-1: Technicon Instruments Corporation, USA)
- 2) Automatic blood cell differential analyzer (Hitachi 8200 : Hitachi, Ltd., Japan)
- 3) Automatic analyzer (Hitachi 7070 : Hitachi, Ltd., Japan)
- 4) Ames reagent strips for urinalysis (Multistix, Uro-Labstix: Bayer-Sankyo Co., Ltd., Japan)

APPENDIX R 2

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

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