アントラセンのラット及びマウスを用いた経口投与によるがん原性予備試験(混餌試験)報告書

試験番号: ラット/0242; マウス/0243

APPENDIXES

(K1~S4)

- APPENDIX K 1 HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY,
 RAT : MALE : ALL ANIMALS (2-YEAR STUDY)
- APPENDIX K 2 HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY, RAT : FEMALE : ALL ANIMALS (2-YEAR STUDY)
- APPENDIX K 3 HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY,
 RAT :MALE SACRIFICED ANIMALS (2-YEAR STUDY)
- APPENDIX K 4 HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY,
 RAT : FEMALE : SACRIFICED ANIMALS (2-YEAR STUDY)
- APPENDIX K 5 HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY,
 MOUSE : MALE : ALL ANIMALS (2-YEAR STUDY)
- APPENDIX K 6 HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS :SUMMARY,
 MOUSE : FEMALE : ALL ANIMALS (2-YEAR STUDY)
- APPENDIX K 7 HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY,
 MOUSE : MALE : SACRIFICED ANIMALS (2-YEAR STUDY)
- APPENDIX K 8 HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY,
 MOUSE : FEMALE : SACRIFICED ANJMALS (2-YEAR STUDY)
- APPENDIX L 1 NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS-TIME RELATED,
 RAT: MALE (2-YEAR STUDY)
- APPENDIX L 2 NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS-TIME RELATED,
 RAT: FEMALE (2-YEAR STUDY)
- APPENDIX L 3 NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS-TIME RELATED, MOUSE: MALE (2-YEAR STUDY)
- APPENDIX L 4 NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS-TIME RELATED, MOUSE : FEMALE (2-YEAR STUDY)

- APPENDIX M1 HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS : SUMMARY, RAT : MALE (2-YEAR STUDY)
- APPENDIX M 2 HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS : SUMMARY, RAT FEMALE (2-YEAR STUDY)
- APPENDIX M 3 HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS : SUMMARY, MOUSE : MALE (2-YEAR STUDY)
- APPENDIX M 4 HISTOLOGICAL FINDINGS : NEOPLASTIC SUMMARY, MOUSE : FEMALE (2-YEAR STUDY)
- APPENDIX N 1 NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS, RAT :MALE (2-YEAR STUDY)
- APPENDIX N 2 NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS, RAT :FEMALE (2-YEAR STUDY)
- APPENDIX N 3 NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS, MOUSE: MALE (2-YEAR STUDY)
- APPENDIX N 4 NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS, MOUSE : FEMALE (2-YEAR STUDY)
- APPENDIX O 1 HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR : SUMMARY,
 RAT : MALE : ALL ANIMALS (2-YEAR STUDY)
- APPENDIX O 2 HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR : SUMMARY, RAT : FEMALE : ALL ANIMALS (2-YEAR STUDY)
- APPENDIX O 3 HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR : SUMMARY,
 RAT : MALE : SACRIFICED ANIMALS (2-YEAR STUDY)
- APPENDIX O 4 HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR : SUMMARY, RAT : FEMALE : SACRIFICED ANIMALS (2-YEAR STUDY)

- APPENDIX O 5 HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR : SUMMARY, MOUSE : MALE : ALL ANIMALS (2-YEAR STUDY)
- APPENDIX O 6 HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR : SUMMARY,
 MOUSE : FEMALE : ALL ANIMALS (2-YEAR STUDY)
- APPENDIX O 7 HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR : SUMMARY,
 MOUSE : MALE : SACRJFICED ANIMALS (2-YEAR STUDY)
- APPENDIX O 8 HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR : SUMMARY,
 MOUSE : FEMALE : SACRIFICED ANIMALS (2-YEAR STUDY)
- APPENDIX P 1 IDENTITY AND IMPURITY OF ANTHRACENE IN THE 2-YEAR FEED STUDIES
- APPENDIX P 2 STABILITY OF ANTHRACENE IN THE 2-YEAR FEED STUDIES
- APPENDIX P 3 CONCENTRATION OF ANTHRACENE IN FORMULATED DIETS OF RATS IN THE 2-YEAR FEED STUDIES
- APPENDIX P 4 CONCENTRATION OF ANTHRACENE IN FORMULATED DIETS OF MICE IN THE 2-YEAR FEED STUDIES
- APPENDIX P 5 STABILITY OF ANTHRACENE IN FORMULATED DIETS IN THE 2-YEAR FEED STUDIES
- APPENDIX Q1 DOSE FORMULATION OF ANTHRACENE IN THE 2-YEAR FEED STUDIES (REPARED IN JAPAN BIOASSAY RESEARCH CENTER)
- APPENDIX Q 2 DOSE FORMULATION OF ANTHRACENE IN THE 2-YEAR FEED STUDIES (PREPARED BY ORIENTAL YEAST CO., LTD.)
- APPENDIX R 1 METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS
- APPENDIX R 2 UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

- APPENDIX S 1 Q PLOT GRAPH FOR RETICULOCYTE OF MALE RATS IN THE 2 YEAR FEED STUDY OF ANTHRACENE
- APPENDIX S 2 Q PLOT GRAPH FOR GLUTAMIC PYRUVIC TRANSAMINASE (GPT) OF MALE RATS IN THE 2-YEAR FEED STUDY OF ANTHRACENE
- APPENDIX S 3 Q PLOT GRAPH FOR TRIGLYCERIDE OF FEMALE RATS IN THE 2-YEAR FEED STUDY OF ANTHRACENE
- APPENDIX S 4 Q PLOT GRAPH FOR A/G RATIO OF MALE MICE IN THE 2-YEAR FEED STUDY OF ANTHRACENE

APPENDIX K 1

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

RAT: MALE: ALL ANIMALS

ANIMAL : RAT F344/DuCrj

: MALE

REPORT TYPE : A1

SEX

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0-105W)

PAGE: 1 Group Name Control 8000 ppm 20000 ppm 50000 ppm No. of Animals on Study 50 50 50 50 Grade 3 Organ Findings_ (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) [Integumentary system/appandage] skin/app <50> <50> <50> <50> hemorrhage 0 0 0 0 0 0 0 0 0 0 0 0 0 0 (2)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) epidermal cyst (0)(0)(0)(0) (0)(2)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) sebaceous hyperplasia 0 0 0 (0)(0)(0)(0) (0) (0) (0) (0) (0)(0)(0)(0) (0)(2)(0)(0) subcutis <50> <50> <50> <50> abscess 0 0 0 0 0 0 1 0 0 0 0 0 0 (0) (0) (0) (0) (0)(0)(0)(0) (0)(2)(0)(0) (0)(0)(0)(0) [Respiratory system] nasal cavit <50> hemorrhage 0 0 0 0 0 1 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(2)(0)(0) (0)(0)(0)(0) inflammation (2)(0)(0)(0) (0)(0)(0)(0) (2)(0)(0)(0) (6)(0)(0)(0) Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe (a) a: Number of animals examined at the site b b: Number of animals with lesion (c) c:b/a*100Significant difference : $*: P \leq 0.05$ **: $P \leq 0.01$ Test of Chi Square

(HPT150)

ANIMAL : RAT F344/DuCri

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

REPORT TYPE : A1 SEX : MALE ALL ANTINLO (U

Organ		p Name of Animals on Study de <u>1</u> (%)	Contr 50 2 (%)		<u>4</u> (%)	1 (%)	8000 5 2 (%)		<u>4</u> (%)	1 (%)	20000 50 2 (%)		<u>4</u> (%)	<u>1</u> (%	2		
[Respiratory	system]																
nasal cavit	ecsinophilic change:olfactory epithelium	22 (44)	<50 23 (46) (0	0 (0)			0	0 ** (0)	0 (0)		0	0 ** (0)	0 (0	0		0 **) (0)
	eosinophilic change:respiratory epithelium		1 (2)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 ** (0)	0 (0)		0			0 (0		0 **
	inflammation:foreign body		11 (22)			7 (14)	10 (20)		0 (0)	12 (24)			0 (0)			1 (2)	0 (0)
	respiratory metaplasia:olfactory epithelio		0 (0)	0 (0)		3 (6)	1 (2)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)	5 (10	0 (0	0 (0)	0 (0)
	respiratory metaplasia:gland	31 (62)	3 (6)	0 (0)		27 (54)	4 (8)		0 (0)	19 (38)	0 (0)		0 ** (0)	18 (36			0 **) (0)
larynx	inflammatory infiltration	1 (2)	(50 (0)	0		0 (0)	0	0 (0)		0 (0)	<5 0 (0)	0			0	<50> 0) (0	0 (0)
lung	consestion	3 (6)	(50 (0)	0	-	1 (2)	0	0 (0)		0 (0)	<5 0 (0)	0			0	<50> 0) (0	0) (0)
Grade (a > b (c)	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 : Sever	θ	-													

: RAT F344/DuCrj ANIMAL

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

REPORT TYPE : A1

: MALE SEX

Organ	Findings	Group Name Control No. of Animals on Study 50 Grade 1 2 3 4 (%) (%) (%) (%)	8000 ppm 50 1 2 3 4 (%) (%) (%) (%)	20000 ppm 50 1 2 3 4 (%) (%) (%) (%)	50000 ppm 50 1 2 3 4 (%) (%) (%) (%)
[Respiratory	system]				
lung	deposit of hemosiderin	<50> 0 0 0 0 (0) (0) (0) (0)	(50) 1 0 0 0 (2) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)
	inflammation	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 1 0 0 (0) (2) (0) (0)
	inflammatory infiltration	1 0 0 0 0 (2) (3) (4)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
	osseous metaplasia	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 (2) (0) (0) (0)	0 0 0 0 0 (0) (0)
	bronchiolar—alveolar cell hyperplasia	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 0 (0) (0)	0 1 0 0 (0) (0)
[Hematopoieti	c system]				
bone marrow	congestion	<50> 1 0 0 0 (2) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)
	granulation	1 2 0 0 (2) (4) (0) (0)	2 1 0 0 (4) (2) (0) (0)	0 0 0 0 0 (0) (0)	3 0 0 0 0 (6) (6) (7) (7)
Grade <a>\ 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 lifference; *: P ≤ 0.05 **: P ≤				

(HPT150)

BAIS3

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0-105W)

Organ	Graup No. a Grade Findings	Name Control F Animals on Study 50 1 2 3 4 (%) (%) (%) (%)	8000 ppm 50 1 2 3 4 (%) (%) (%) (%)	20000 ppm 50 1 2 3 4 (%) (%) (%) (%)	50000 ppm 50 1 2 3 4 (%) (%) (%) (%)
[Hematopoieti	c system]				
oone marrow	increased hematopolesis	2 0 0 0 (4) (0) (0) (0)	<50> 4 1 0 0 (8) (2) (0) (0)	<50> 4 1 0 0 (8) (2) (0) (0)	<50> 4 0 0 0 (8) (0) (0) (0)
	decreased hematopoiesis	0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	2 0 0 0 0 (4) (0) (0) (0)	0 2 0 0 (0) (4) (0) (0)	0 1 1 0 (0) (2) (2) (0)
	granulopoiesis:increased	2 0 0 0 0 (4) (6) (6)	2 0 0 0 0 (4) (0) (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (2) (0) (0) (0)
lymph node	lymphocytic infiltration	(50) 0 0 0 0 (0) (0) (0) (0)	(50) 1 0 0 0 (2) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)
spleen	atrophy	2 0 0 0 (4) (0) (0) (0)	(50) 1 0 1 0 (2) (0) (2) (0)	<50> 1 2 0 0 (2) (4) (0) (0)	<pre></pre>
	congestion	7 4 0 0 (14) (8) (0) (0)	8 1 0 0 (16) (2) (0) (0)	12 0 0 0 (24) (0) (0) (0)	6 0 0 0 (12) (0) (0) (0)
	deposit of hemosiderin	1 1 1 0 (2) (2) (2) (0)	4 1 0 0 (8) (2) (0) (0)	8 1 0 0 (16) (2) (0) (0)	9 5 0 0 **
Grade <a>> b (c)	1: Slight 2: Moderate 3: Mar a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	ked 4: Severe			

(HPT150)

BAIS3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0-105W)

ANIMAL : RAT F344/DuCrj REPORT TYPE : A1

SEX : MALE

Group Name 8000 ppm 20000 ppm 50000 ppm Control No. of Animals on Study 50 50 50 50 Grade 3 (%) (%) (%) (%) 0rgan Findings [Hematopoietic system] spleen <50> <50> <50> fibrosis 0 0 1 0 0 (0)(2)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) extramedullary hematopoiesis 2 5 0 (6)(4)(0)(0) (4)(4)(0)(0) (4)(4)(0)(0) (10) (6) (2) (0) engorgement of erythrocyte 0 0 0 0 13 2 0 0 ** 14 0 0 ** 0 10 0 ** (0)(0)(0)(0) (26) (4) (0) (0) (28) (0) (0) (0) (20) (0) (0) (0) [Circulatory system] heart ⟨50⟩ <50> <50> <50> thrombus 0 0 0 0 0 (0)(2)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) myocardial fibrosis 0 (6)(0)(0)(0) (4)(0)(0)(0) (6)(0)(0)(0) (8)(8)(0)(0) arteritis (0) (0) (0) (0) (0)(0)(0)(0) (2)(0)(0)(0) (0)(0)(0)(0) artery/aort mineralization 0 0 0 0 0 0 0 0 0 0 0 1 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(2)(0)(0)

(HPT150)

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

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)

STUDY NO. : 0242 ANIMAL : RAT F344/DuCrj

ALL ANIMALS (0-105W)

REPORT TYPE : A1 SEX : MALE

Organ		o Name	8000 ppm 50 1 2 3 4 (%) (%) (%)	20000 ppm 50 1 2 3 4 (%) (%) (%) (%)	50000 ppm 50 1 2 3 4 (%) (%) (%) (%)
[Circulatory :	system]				
artery/aort	arteritis	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)
Digestive sy	stem]				
tongue	arteritis	<50> 3 1 0 0 (6) (2) (0) (0)	3 0 0 0 (6) (0) (0) (0)	3 0 0 0 (6) (0) (0) (0)	2 1 0 0 (4) (2) (0) (0)
alivary gl	inflammation	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 0 1 0 0 (0) (2) (0) (0)
tomach	mineralization	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 0 1 0 0 (0) (2) (0) (0)
	ulcer:forestomach	1 1 0 0 (2) (2) (0) (0)	1 1 0 0 (2) (2) (0) (0)	1 2 0 0 (2) (4) (0) (0)	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
	hyperplasia:forestomach	1 0 0 0 0 (2) (0) (0) (0)	1 0 0 0 0 (2) (0) (0) (0)	0 1 0 0 (0) (2) (0) (0)	0 1 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			

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

STUDY NO. : 0242 ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1 SEX : MALE

PAGE: 7

Organ	Group No. c Grade Findings	f Animals on Study 50	8000 ppm 50 1 2 3 4 (%) (%) (%) (%)	20000 ppm 50 1 2 3 4 (%) (%) (%) (%)	50000 ppm 50 1 2 3 4 (%) (%) (%) (%)
[Digestive sy	stem]				
stomach	erosion:glandular stomach	(50) 1 0 0 0 (2) (0) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)	(50) 1 0 0 0 (2) (0) (0) (0)	<50> 2 0 0 0 (4) (0) (0) (0)
	ulcer:glandular stomach	4 3 0 0 (8) (6) (0) (0)	5 0 0 0 (10) (0) (0) (0)	2 1 0 0 (4) (2) (0) (0)	2 0 0 0 0 (4) (0) (0) (0)
	hyperplasia:glandular stomach	2 0 0 0 0 (4) (0) (0) (0)	2 0 0 0 0 (4) (0) (0) (0)	1 1 0 0 (2) (2) (0) (0)	3 1 0 0 (6) (6) (7) (7)
small intes	diverticula	(50) 0 0 0 0 (0) (0) (0) (0)	(50) 0 1 0 0 (0) (2) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)	<pre></pre>
iver	herniation	<50> 0 0 0 0 (0) (0) (0) (0)	3 0 0 0 (6) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)
	necrosis:central	1 1 0 0 (2) (2) (0) (0)	0 0 1 0 (0) (2) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
	necrosis:focal	1 0 0 0 0 (2) (0) (0) (0)	1 0 0 0 (2) (0) (0) (0)	0 1 0 0 (0) (0)	0 0 0 0 0 (0) (0)
Grade (a) b	1: Slight 2: Moderate 3: Mar a: Number of animals examined at the site $b:$ Number of animals with lesion $c:b/a*100$ lifference; $*:P \le 0.05$ **: $P \le 0.01$				

(HPT150)

BAIS3

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

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1 SEX : MALE

PAGE: 8

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

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)

ALL ANIMALS (0-105W)

ANIMAL : RAT F344/DuCrj REPORT TYPE : A1

SEX : MALE PAGE : 9

Organ	Group Name No. of Anima Grade	Control ls on Study 50 1 2 3 4 (%) (%) (%) (%)	8000 ppm 50 1 2 3 4 (%) (%) (%) (%)	20000 ppm 50 1 2 3 4 (%) (%) (%) (%)	50000 ppm 50 1 2 3 4 (%) (%) (%) (%)
[Digestive s	system]				
liver	bile duct hyperplasia	\(\frac{50}{10} \) \(\frac{10}{20} \) (\(\frac{36}{72} \) (\(0) \) (\(0) \)	(50) 10 37 0 0 (20) (74) (0) (0)	(50) 18 22 2 0 * (36) (44) (4) (0)	(50) 18 22 1 0 * (36) (44) (2) (0)
	cholangiofibrosis	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (2) (0) (0) (0)	2 0 0 0 (4) (0) (0) (0)
	biliary cyst	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 0 (0) (0)	0 1 0 0 (0) (0)	0 0 0 0 0 (0) (0)
pancreas	atrophy	<50> 3 3 0 0 (6) (6) (0) (0)	50> 5 7 2 0 (10) (14) (4) (0)	(50) 7 5 1 0 (14) (10) (2) (0)	(50) 10 6 0 0 * (20) (12) (0) (0)
	hyperplasia	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0) (0)	1 0 0 0 (2) (0) (0) (0)	0 0 0 0 0 (0) (0)
	arteritis	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 2 0 0 (0) (4) (0) (0)	0 0 0 0 0 (0) (0)
[Urinary sys	stem]				
kidney	hyperplasia:tubular epithelial cell	(50) 0 0 0 0 (0) (0) (0) (0)	<50> 4 0 0 0 (8) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 2 0 0 0 (4) (0) (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 Tes	4 : Severe			

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1 SEX : MALE

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

Organ	No	roup Name	8000 ppm 50 1 2 3 4 (%) (%) (%) (%)	20000 ppm 50 1 2 3 4 (%) (%) (%) (%)	50000 ppm 50 1 2 3 4 (%) (%) (%) (%)
[Urinary sy	stem]				
kidney	infarct	<50> 0 0 0 0 (0) (0) (0) (0)	(50) 1 0 0 0 (2) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)
	cyst	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 (2) (0) (0) (0)	0 0 0 0 0 (0) (0)
	deposit of hemosiderin	0 0 0 0 0 (0) (0)	1 0 0 0 0 (2) (0) (0) (0)	0 0 0 0 0 (0) (0)	0 1 0 0 (0) (2) (0) (0)
	eosinophilic body	0 0 0 0 0 (0) (0)	0 1 0 0 (0) (2) (0) (0)	0 0 0 0 0 (0) (0)	0 1 0 0 (0) (2) (0) (0)
	chronic nephropathy	6 12 17 10 (12) (24) (34) (20)	1 15 11 15 (2) (30) (22) (30)	3 13 14 15 (6) (26) (28) (30)	7 13 16 7 (14) (26) (32) (14)
	tubular necrosis	0 0 2 0 (0) (4) (0)	0 0 1 0 (0) (0) (2) (0)	0 0 2 0 (0) (4) (0)	0 1 1 0 (0) (2) (2) (0)
	papillary necrosis	0 1 0 0 (0) (0) (0)	4 0 0 0 0 (8) (0) (0) (0)	5 1 0 0 (10) (2) (0) (0)	1 1 0 0 (2) (2) (0) (0)
	mineralization:cortico-medullary junctio	0 2 0 0 (0) (4) (0) (0)	0 1 0 0 (0) (2) (0) (0)	0 0 0 0 0 (0) (0) (0)	0 1 0 0 (0) (2) (0) (0)

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

ANIMAL : RAT F344/DuCrj

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

REPORT TYPE : A1

SEX : MALE PAGE: 11

Organ	Group Name No. of Anim Grade	Control als on Study 50 1 2 3 4 (%) (%) (%) (%)	8000 ppm 50 1 2 3 4 (%) (%) (%) (%)	20000 ppm 50 1 2 3 4 (%) (%) (%) (%)	50000 ppm 50 1 2 3 4 (%) (%) (%) (%)
[Urinary syst	tem]				
kidney	mineralization:papilla	<50> 2 0 0 0 (4) (0) (0) (0)	<50> 4 2 0 0 (8) (4) (0) (0)	<50> 8 0 0 0 (16) (0) (0) (0)	(50) 6 1 0 0 (12) (2) (0) (0)
	mineralization:pelvis	0 0 0 0 0 (0) (0)	1 1 0 0 (2) (2) (0) (0)	1 1 0 0 (2) (2) (0) (0)	2 2 0 1 (4) (4) (0) (2)
	mineralization:cortex	0 1 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 1 0 0 (0) (2) (0) (0)	0 0 0 0 0 (0) (0)
	simple hyperplasia:transitional epithelium	2 0 0 0 0 (4) (0) (0) (0)	5 0 0 0 (10) (0) (0) (0)	4 1 0 0 (8) (2) (0) (0)	7 0 0 0 (14) (0) (0) (0)
	nodular hyperplasia:transitional epithelium	4 0 0 0 0 (8) (0) (0) (0)	5 3 0 0 (10) (6) (0) (0)	8 0 0 0 0 (16) (16) (10) (10)	5 0 0 0 (10) (0) (0) (0)
	eosinophilic droplet:proximal tubule	1 0 0 0 0 (2) (0) (0)	19 4 0 0 ** (38) (8) (0) (0)	27 5 0 0 ** (54) (10) (0) (0)	23 13 0 0 ** (46) (26) (0) (0)
urin bladd	hemorrhage	(50) 1 0 0 0 (2) (0) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)
	simple hyperplasia:transitional epithelium	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (2) (0) (0) (0)	1 0 0 0 (2) (0) (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; $*: P \le 0.05$ **: $P \le 0.01$ Te	4 : Severe st of Chi Square			

(HPT150)

BAIS3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1

ALL ANIMALS (0-105W)

SEX : MALE PAGE: 12

Organ	No	roup Name	8000 pp 50 4 1 2 (%) (%)	3 4 (%) (%) (%)	20000 ppm 50 2 3 4 (%) (%) (%)	50000 ppm 50 1 2 3 4 (%) (%) (%) (%)
[Urinary syst	rem]					
urin bladd	nodular hyperplasia:transitional epithe	<pre></pre>	(50) 0 0 0 0 0 (0) (0) (0) (0 0 1	<50> 0 0 0 (0) (0) (0)	2 0 0 0 (4) (0) (0) (0)
[Endocrine sy	vstem]					
pituitary	angiectasis	2 1 0 (4) (2) (0)	0 1 0 (0) (2) (0) (0 0 0	<50> 0 0 0 (0) (0) (0)	1 2 0 0 (2) (4) (0) (0)
	cyst	1 0 0 (2) (0) (0)	0 1 0 (2) (0) (0 0 1 0 (2)	0 0 0 0 (0) (0)	1 0 0 0 (2) (0) (0) (0)
	hyperplasia	6 2 0 (12) (4) (0)	0 5 1 (10) (2) (0 0 6 0 (12)	3 0 0 (6) (0) (0)	7 2 0 0 (14) (4) (0) (0)
	hyperplasia:gland	0 0 0 0 (0) (0)	0 1 0 (2) (0) (0 0 0 0	0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
	Rathke pouch	0 0 0 0 (0) (0)	0 2 0 (4) (0) (0 0 2 0) (0) (4)	0 0 0 0 (0) (0)	2 0 0 0 0 (4) (0) (0) (0)
thyroid	C-cell hyperplasia	<50> 1 2 0 (2) (4) (0)		0 0 3	<50> 0 0 0 (0) (0) (0)	<50> 2 3 0 0 (4) (6) (0) (0)

(a)

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

(HPT150)

BAIS3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0-105W)

ANIMAL : RAT F344/DuCrj REPORT TYPE : A1

: MALE

SEX PAGE: 13

Organ	N	roup Name Control b. of Animals on Study 50 rade 1 2 3 4 (%) (%) (%) (%)	8000 ppm 50 1 2 3 4 (%) (%) (%) (%)	20000 ppm 50 1 2 3 4 (%) (%) (%) (%)	50000 ppm 50 - 1 2 3 4 (%) (%) (%) (%)
(Endocrine s	system]				
thyroid	focal follicular cell hyperplasia	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	\(\lambda 50 \rangle \) \[\begin{pmatrix} 1 & 0 & 0 & 0 \\ (& 2) & (& 0) & (& 0) & (& 0) \end{pmatrix} \]
panc islet	islet cell hyperplasia	\(\frac{50}{1} \) \(1 \) \(1 \) \(0 \) \(2 \) \(2 \) \(0 \) \(0 \)	<50> 2 0 0 0 (4) (0) (0) (0)	<50> 1 1 0 0 (2) (2) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)
adrenal	peliosis-like lesion	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)	<50> 2 0 0 0 (4) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)
	hyperplasia:medulla	3 5 0 0 (6) (10) (0) (0)	4 7 0 0 (8) (14) (0) (0)	7 4 0 0 (14) (8) (0) (0)	5 1 0 0 (10) (2) (0) (0)
	focal fatty change:cortex	1 0 0 0 0 (2) (0) (0) (0)	1 0 0 0 0 (2) (0) (0) (0)	2 0 0 0 0 (4) (0) (0) (0)	0 0 0 0 0 (0) (0)
[Reproductiv	ve system]				
testis	atrophy	<50> 1 0 0 0 (2) (0) (0) (0)	\(\lambda 50 \rangle \) \[1 0 0 0 \\ (2) (0) (0) (0) (0) \]	<50> 1 0 0 0 (2) (0) (0) (0)	<50> 3 0 0 0 (6) (0) (0) (0)
Grade (a) b (c) Significant	1: Slight 2: Moderate 3: a: Number of animals examined at the sit b: Number of animals with lesion c: b/a * 100 difference; *: P ≤ 0.05 **: P ≤				

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

ANIMAL : RAT F344/DuCrj

ALL

REPORT TYPE : A1
SEX : MAI.

SEX : MALE

Organ	Findings	Group Name Control No. of Animals on Study 50 Grade 1 2 3 4 (%) (%) (%) (%)	8000 ppm 50 1 2 3 4 (%) (%) (%) (%)	20000 ppm 50 1 2 3 4 (%) (%) (%) (%)	50000 ppm 50 1 2 3 4 (%) (%) (%) (%)
[Reproductive	e system]				
testis	mineralization	<50> 6 0 0 0 (12) (0) (0) (0)	<50> 7 0 0 0 (14) (0) (0) (0)	\(\lambda 50 \rangle \) 14	<50> 16 1 0 0 * (32) (2) (0) (0)
	arteritis	5 0 0 0 (10) (0) (0) (0)	0 0 0 0 0 (0) (0)	3 0 0 0 0 (6) (6) (0) (0)	1 0 0 0 (2) (0) (0) (0)
	interstitial cell hyperplasia	8 0 0 0 (16) (0) (0) (0)	2 0 0 0 0 (4) (0) (0) (0)	2 0 0 0 0 (4) (0) (0) (0)	3 0 0 0 0 (6) (6) (0) (0)
prostate	inflammation	<50> 4 0 0 0 (8) (0) (0) (0)	7 0 0 0 (14)(0)(0)(0)	<50> 4 0 1 0 (8) (0) (2) (0)	7 0 0 0 (14) (0) (0) (0)
	hyperplasia	8 0 0 0 (16) (0) (0) (0)	6 0 0 0 (12) (0) (0) (0)	11 0 0 0 (22) (0) (0) (0)	11 0 0 0 (22) (0) (0) (0)
mammary gl	hyperplasia	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)
	galactocele	0 1 0 0 (0) (2) (0) (0)	0 1 0 0 (0) (2) (0) (0)	0 1 0 0 (0) (2) (0) (0)	0 0 0 0 0 (0) (0)
Grade (a) b (c) Significant	a: Number of animals examined at theb: Number of animals with lesionc: b / a * 100	3 : Marked 4 : Severe site ≤ 0.01 Test of Chi Square			

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0-105W)

ANIMAL : RAT F344/DuCrj REPORT TYPE : A1

: MALE SEX PAGE: 15

0rgan	Findings	Group Name No. of Animals on Study Grade Control 50 Grade 1 2 3 4 (%) (%) (%) (%)	8000 ppm 50 1 2 3 4 (%) (%) (%) (%)	20000 ppm 50 1 2 3 4 (%) (%) (%) (%)	50000 ppm 50 1 2 3 4 (%) (%) (%) (%)
[Nervous syst	cem]				
periph nerv	adhesion	(50) 0 0 0 0 (0) (0) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)	(50) 0 1 0 0 (0) (2) (0) (0)
[Special sens	se organs/appandage]				
еуе	hemorrhage	<50> 0 0 0 0 (0) (0) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)	(50) 1 0 0 0 (2) (0) (0) (0)	<pre></pre>
	inflammatory infiltration	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) (2) (0) (0)
	cataract	0 5 0 0 (0) (10) (0) (0)	0 4 0 0 (0) (8) (0) (0)	0 3 0 0 (0) (6) (0) (0)	0 4 0 0 (0) (8) (0) (0)
	retinal atrophy	2 10 0 0 (4) (20) (0) (0)	2 16 0 0 (4) (32) (0) (0)	0 9 0 0 (0) (18) (0) (0)	4 9 0 0 (8) (18) (0) (0)
	keratitis	0 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)
Harder gl	degeneration	<50> 2 0 0 0 (4) (0) (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 0 2 0 0 (0) (4) (0) (0)
Grade	1: Slight 2: Moderate	3: Marked 4: Severe			

<a>>

a : Number of animals examined at the site

b: Number of animals with lesion (c)

c:b/a*100

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

(HPT150)

BAIS3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL : RAT F344/DuCrj

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

Group Name mag 0008 Control 20000 ppm 50000 ppm No. of Animals on Study 50 50 50 50 Grade 3 2 3 Findings (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) [Special sense organs/appandage] Harder gl <50> inflammatory infiltration 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(2)(0)(0) lymphocytic infiltration (2)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) nasolacr d <50> <50> <50> inflammation 0 1 0 0 0 0 0 0 0 0 0 1 0 0 0 (0)(0)(0)(0) (0)(2)(0)(0) (0)(0)(0)(0) (2)(0)(0)(0) [Body cavities] retroperit <50> hemorrhage 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(2)(0)(0) adipose <50> ⟨50⟩ (50) <50> necrosis 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(2)(0)(0) (0)(0)(0)(0) Grade 1:Slight 2 : Moderate 3 : Marked 4 : Severe (a) a: Number of animals examined at the site b b: Number of animals with lesion (c) c:b/a*100Significant difference; $*: P \le 0.05$ $**: P \le 0.01$ Test of Chi Square

(HPT150)

APPENDIX K 2

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

RAT: FEMALE: ALL ANIMALS

ANIMAL : RAT F344/DuCrj

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

REPORT TYPE : A1 SEX

: FEMALE

PAGE: 1

	Group Nam No. of Ap	e Control imals on Study 50	8000 ppm 50	20000 ppm 50	50000 ppm 50
Organ	Grade Findings_	1 2 3 4 (%) (%) (%) (%)			
[Integumentar	y system/appandage]				
skin/app	inflammation	<50> 0 0 0 0 (0) (0) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 0 1 0 0 (0) (2) (0) (0)
[Respiratory	system]				
nasal cavit	follicle	(2) (0) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	(50) (0) (0) (0) (0)
	atrophy	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 (2) (0) (0) (0)
	eosinophilic change:olfactory epithelium	4 29 16 0 (8) (58) (32) (0)	0 0 0 0 ***	0 0 0 0 ***	0 0 0 0 *
	eosinophilic change:respiratory epithelium	36 0 0 0 (72) (0) (0) (0)	0 0 0 0 ***	0 0 0 0 ***	0 0 0 0 *
	inflammation:foreign body	5 2 0 0 (10) (4) (0) (0)	1 1 0 0 (2) (2) (0) (0)	2 1 0 0 (4) (2) (0) (0)	6 1 0 0 (12) (2) (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 (2) (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 Test of Chi Square			

(HPT150)

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

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1

SEX : FEMALE

0rgan	Group Name No. of Ani Grade	Control 50 1 2 3 4 (%) (%) (%) (%)	8000 ppm 50 1 2 3 4 (%) (%) (%) (%)	20000 ppm 50 1 2 3 4 (%) (%) (%) (%)	50000 ppm 50 1 2 3 4 (%) (%) (%) (%)
[Respiratory	system]				
nasal cavit	respiratory metaplasia:olfactory epithelium	<50> 0 0 0 0 (0) (0) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	<pre></pre>
	respiratory metaplasia:gland	30 2 0 0 (60) (4) (0) (0)	18 0 0 0 * (36) (0) (0) (0)	23 0 0 0 (46) (0) (0) (0)	15 0 0 0 *** (30) (0) (0) (0)
	necrosis:olfactory epithelium	0 0 0 0 0 0 (0) (0)	3 0 0 0 0 (6) (6) (0) (0)	14 0 0 0 *** (28) (0) (0) (0)	25 0 0 0 *** (50) (0) (0) (0)
lung	congestion	<50> 1 0 0 0 (2) (0) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)	<50> 2 0 0 0 (4) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)
	hemorrhage	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)
	inflammation.	0 0 0 0 0 0 (0) (0)	2 0 0 0 0 (4) (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)	1 0 0 0 0 (2) (0) (0)	3 0 0 0 0 (6) (6) (0) (0)	1 0 0 0 0 (2) (0) (0)
	lymphocytic 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)
Grade (a > b (c) Significant of	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 est of Chi Square			·

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

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1

SEX : FEMALE

		Group Name No. of Animals on Study	Contro					00 ppn 50					20000					5	0 ppm 50		
Organ	Findings	Grade <u>1</u> (%)	<u>2</u> (%)	3 (%)	<u>4</u> (%)	(%)	(%) (9	(3)	<u>4</u> (%)	(1 %)	2 (%)	(%)	(%)		(%)	(%)	(%)) (<u>4</u> (%)
Respiratory s	system]																				
lung	accumulation of foamy cells	(0)	<50 0 (0) (0	0 (0)	1 (2)	0	<50> (0 0)		0 0) (0 (0)	(0	1	50> 0 (0)		0
	bronchiolar-alveolar cell hyperplasia	1 (2)	(0) (0 0)	0 (0)	0 (0)	0	())) (0 0)	(2 4) (0	0	0 (0)	(0	0 (0)	(0)		0
[Hematopoietic	c system]																				
bone marrow	granulation	2 (4)	<50 4 (8)(0	0 (0)	2 (4)	5	<50> (0 0)		1 2) (<50 2 4)	0 (0)	0 (0)	(5 10)	5	50> 0 (0)		0 0)
	increased hematopoiesis	5 (10)	(0) (0 0)	0 (0)	2 (4)	0)) ((0		4 8) (0	0 0)	0 (0)	(4 8)	1 (2)	(0)		0
	decreased hematopoiesis	(0)	1 (2) (0 (0)	0 (0)	(0)	0 (0) ((0 0)		0 0) (0	0 0)	0 (0)	(0	2 (4)	(0)		0 0)
	granulopoiesis: increased	(0)	0 (0) (0 0)	0 (0)	(2)				0 0)		1 2) (0	0 (0)	0 (0)	(0	0 (0)	(0)		0 0)
spleen	atrophy	1 (2)	<50 0 (0) (0	0 (0)	(0)				0 0)		0 0) (<50 2 4)	0 (0)	0	(1	50> 0 (0)		0
(a) b	a : Number of animals examined at the s b : Number of animals with lesion c : b / a * 100				****																

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1
SEX : FEMALE

ALL ANIMALS (0-105W)

Group Name Control 8000 ppm 20000 ppm 50000 ppm No. of Animals on Study 50 50 50 50 Grade 0rgan Findings (%) (%) [Hematopoietic system] spleen <50> (50) <50> congestion 0 0 6 0 0 0 0 0 0 0 0 (12) (0) (0) (0) (12) (0) (0) (0) (4)(0)(0)(0) (14) (0) (0) (0) deposit of hemosiderin 9 0 8 1 0 7 1 0 * (30) (18) (0) (0) (44) (16) (2) (0) (56) (14) (2) (0) (42) (18) (0) (0) extramedullary hematopoiesis 3 3 0 0 0 0 2 2 3 0 0 0 (6)(6)(0)(0) (4)(2)(0)(0) (0)(4)(0)(0) (4)(6)(0)(0) engargement of erythracyte 0 6 0 ** 29 () ** 20 8 (0)(0)(0)(0) (44) (12) (0) (0) (58) (8) (0) (0) (40) (16) (0) (0) [Circulatory system] heart <50> thrombus 0 1 1 0 0 0 0 0 0 0 0 0 (0)(0)(2)(0) (0)(2)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) necrosis:focal 1 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) mineralization 0 1 0 0 0 0 (0)(2)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe (a) a: Number of animals examined at the site b b: Number of animals with lesion (c) c : b / a * 100

(HPT150)

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

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

ANIMAL : RAT F344/DuCrj REPORT TYPE : A1

EX : FEMALE

PAGE: 5

Organ	Group No. of No. of Grade	Sime Control Animals on Study 50 1 2 3 4 (%) (%) (%) (%)	8000 ppm 50 1 2 3 4 (%) (%) (%) (%)	20000 ppm 50 1 2 3 4 (%) (%) (%) (%)	50000 ppm 50 1 2 3 4 (%) (%) (%) (%)
[Circulatory :	system]				
heart	myocardial fibrosis	(50) 1 0 0 0 (2) (0) (0) (0)	2 0 0 0 (4) (0) (0) (0)	(50) 0 1 0 0 (0) (2) (0) (0)	3 0 0 0 (6) (0) (0) (0)
artery/aort	arteritis	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 0 1 0 0 (0) (2) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)
[Digestive sy	stem]		,		
tooth	epidermal cyst	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 0 1 0 0 (0) (2) (0) (0)	<pre></pre>
tongue	arteritis	<50> 1 0 0 0 (2) (0) (0) (0)	<50> 1 1 0 0 (2) (2) (0) (0)	<50> 2 1 0 0 (4) (2) (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)
stomach	mineralization	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)	<50> 1 1 0 0 (2) (2) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)
	arteritis	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 1 0 0 (0) (2) (0) (0)	1 0 0 0 0 (2) (0) (0) (0)
Grade < a > b (c) Significant d	1: Slight 2: Moderate 3: Marke a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 lifference; $*: P \le 0.05$ **: $P \le 0.01$	d 4: Severe Test of Chi Square			

(HPT150)

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1

SEX : FEMALE

ALL ANIMALS (0-105W)

Organ		Name Control of Animals on Study 50 \[\frac{1}{\lambda} \frac{2}{\lambda} \frac{3}{\lambda} \frac{4}{\lambda} \frac{1}{\lambda} \frac{2}{\lambda} \frac{3}{\lambda} \frac{4}{\lambda} \frac{4}{\lambda} \frac{1}{\lambda} \frac{1}		20000 ppm 50 1 2 3 4 (%) (%) (%) (%)	50000 ppm 50 1 2 3 4 (%) (%) (%) (%)
Digestive sy	stem]				
tomach	ulcer:forestomach	(50) 0 0 0 0 (0) (0) (0) (0)		<50> 0 0 1 0 (0) (0) (2) (0)	<50> 1 0 0 0 (2) (0) (0) (0)
	hyperplasia:forestomach	0 0 0 0 (0 1 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0) (0)
	erosion:glandular stomach	0 0 0 0 (1 0 0 0 0 (2) (0) (0) (0)	0 0 0 0 0 0 (0) (0)
	ulcer:glandular stomach	2 0 0 0 (0 0 0 1	0 0 0 0 0 0 (0) (0)	1 1 0 0 (2) (2) (0) (0)
	hyperplasia:glandular stomach	0 0 0 0 (0 0 0 0 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 (2) (0) (0)
mall intes	inflammation	(50) 0 0 0 0 (0)(0)(0)(<50> 0 1 0 0 (0) (2) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)
iver	herniation	3 0 0 ((6) (0) (0) (<50> 1 0 0 0 (2) (0) (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)
rade a > b c)	1 : Slight 2 : Moderate 3 : Mar a : Number of animals examined at the site b : Number of animals with lesion c : b / a * 100 difference ; * : $P \le 0.05$ ** : $P \le 0.0$				

(HPT150)

SEX

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1

: FEMALE

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

Group Name Control mag 0008 20000 ppm 50000 ppm No. of Animals on Study 50 50 50 50 Grade 0rgan Findings (%) (%) [Digestive system] liver <50> <50> <50> <50> peliosis-like lesion 2 0 0 0 0 0 0 1 0 0 0 0 (0)(0)(0)(0) (4)(0)(0)(0) (2)(0)(0)(0) (0)(0)(0)(0) necrosis:central 0 2 0 0 0 0 0 0 1 0 0 1 1 0 (0)(4)(0)(0) (0)(0)(0)(0) (0)(2)(0)(0) (0)(2)(2)(0) necrosis: focal 0 1 0 0 0 0 0 0 2 0 0 (0)(2)(0)(0) (0)(0)(0)(0) (4)(0)(0)(0) (0)(0)(0)(0) fatty change 0 0 (2)(0)(0)(0) (0)(0)(2)(0) (0)(2)(0)(0) (0)(0)(0)(0) lymphocytic infiltration 0 1 (0)(2)(0)(0) (0)(2)(0)(0) (2)(2)(0)(0) (0)(0)(0)(0) granulation 17 8 24 10 2 12 (34) (18) (0) (0) (40) (16) (2) (0) (48) (20) (4) (0) (40) (24) (4) (0) extramedullary hematopoiesis 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(2)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) clear cell focus () ** 5 6 0 ** (2)(0)(0)(0) (6) (12) (0) (0) (16) (14) (0) (0) (10) (12) (4) (0)

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

(a) a: Number of animals examined at the site b: Number of animals with Lesion b

c:b/a * 100 (c)

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

(HPT150)

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

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1

SEX : FEMALE

PAGE: 8

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

(HPT150)

(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)
ALL ANIMALS (0-105W)

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1

SEX : FEMALE

Organ	Group Na No. of A Grade Findings	me Control nimals on Study 50 \\ \[\frac{1}{(\chi)} & \frac{2}{(\chi)} & \frac{3}{(\chi)} & \frac{4}{(\chi)} \]	8000 ppm 50 1 2 3 4 (%) (%) (%)	20000 ppm 50 1 2 3 4 (%) (%) (%) (%)	50000 ppm 50 1 2 3 4 (%) (%) (%) (%)
[Urinary sy	vstem]				
cidney	infarct	(50) 0 0 0 0 (0) (0) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)	<50> 0 1 0 0 (0) (2) (0) (0)	(50) (0)(0)(0)(0)(0)
	cyst	0 1 0 0 (0) (0)	1 0 0 0 0 (2) (0) (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (2) (0) (0)
	chronic nephropathy	23 11 3 3 (46) (22) (6) (6)	10 15 15 4 ** (20) (30) (30) (8)	10 21 8 5 * (20) (42) (16) (10)	17 18 7 0 (34) (36) (14) (0)
	hydranephrasis	0 0 1 0 (0) (2) (0)	0 0 0 0 0 (0) (0)	0 1 0 0 (0) (2) (0) (0)	0 1 0 0 (0) (2) (0) (0)
	tubular necrosis	0 3 4 0 (0) (6) (8) (0)	0 1 3 0 (0) (2) (6) (0)	0 1 1 0 0 0 0 2 0 0 0	0 1 2 0 (0) (2) (4) (0)
	papillary necrosis	0 0 0 0 0 0 (0) (0)	0 1 0 0 (0) (2) (0) (0)	1 0 0 0 0 (2) (0) (0) (0)	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
	mineralization:cortico-medullary junction	21 2 0 0 (42) (4) (0) (0)	13 4 0 0 (26) (8) (0) (0)	15 0 0 0 (30) (0) (0) (0)	13 0 0 0 (26) (0) (0) (0)
	mineralization:papilla	2 0 0 0 0 (4) (0). (0) (0)	11 1 0 0 * (22) (2) (0) (0)	7 0 0 0 (14) (0) (0) (0)	5 0 0 0 (10) (0) (0) (0)
Grade (a> b	1: Slight 2: Moderate 3: Marked a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100	d 4 : Severe			

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1

SEX : FEMALE

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

Organ	No	roup Name	8000 ppm 50 1 2 3 4 (%) (%) (%) (%)	20000 ppm 50 1 2 3 4 (%) (%) (%) (%)	50000 ppm 50 1 2 3 4 (%) (%) (%) (%)
[Urinary syst	rem]				
kidney	mineralization:pelvis	50> 5 1 0 0 (10) (2) (0) (0	<50> 4 2 0 0 (8) (4) (0) (0)	7 0 0 0 (14) (0) (0) (0)	<50> 7 1 0 0 (14) (2) (0) (0)
	mineralization:cortex	0 0 0 0 0 0 (0) (0) (0)	0 1 0 0 (0) (2) (0) (0)	1 0 0 0 0 (2) (0) (0) (0)	0 0 0 0 0 (0) (0)
	dilatation:tubular lumen	0 0 0 0 0 0 (0) (0) (0	1 0 0 0 0 (2) (0) (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
	simple tubule hyperplasia	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 (0) (0) (0)	2 0 0 0 0 (4) (0) (0) (0)	0 0 0 0 0 (0) (0)
	atypical tubule hyperplasia	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	12 0 0 0 *** (24) (0) (0) (0)	13 0 0 0 *** (26) (0) (0) (0)	7 0 0 0 * (14) (0) (0) (0)
	eosinophilic droplet:proximal tubule	2 0 0 0 0 (4) (0) (0) (0)	14 32 0 0 *** (28) (64) (0) (0)	4 38 0 0 ***	8 37 0 0 *** (16) (74) (0) (0)
urin bladd	nodular hyperplasia:transitional epithe	<pre></pre>	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)
[Endocrine s	vstem]				
pituitary	angiectasis	<50> 6 5 0 0 (12) (10) (0) (0	<pre></pre>	\(\langle 50 \rangle \) \[1 0 0 ** \\ (2) (0) (0) (0) \]	<50> 4 0 0 0 (8) (0) (0) (0)

b

<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)

BAIS3

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

ANIMAL : RAT F344/DuCrj REPORT TYPE : A1

SEX : FEMALE

..._

)rgan	Findings	Croup Name Control	8000 ppm 50 1 2 3 4 (%) (%) (%) (%)	20000 ppm 50 1 2 3 4 (%) (%) (%) (%)	50000 ppm 50 1 2 3 4 (%) (%) (%) (%)
Endocrine sy	vstem]				
ituitary	cyst	<50> 3 0 0 0 (6) (0) (0) (0)	\$ 0 0 0 (16) (0) (0) (0)	(50) 1 1 0 0 (2) (2) (0) (0)	\$ 0 0 0 (18) (0) (0) (0)
	hyperplasia	6 0 0 0 0 (12) (0) (0) (0)	6 1 0 0 (12) (2) (0) (0)	4 1 0 0 (8) (2) (0) (0)	7 1 0 0 (14) (2) (0) (0)
	Rathke pouch	0 0 0 0 0 (0) (0)	1 0 0 0 0 (2) (0) (0)	1 0 0 0 0 (2) (0) (0) (0)	0 0 0 0 0 0 (0)
hугоid	cyst	<50> 0 0 0 0 (0) (0) (0) (0)	(50) 1 0 0 0 (2) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	<49> 0 0 0 0 (0) (0) (0) (0)
	ultimibranchial body remanet	0 0 0 0 0 (0) (0)	1 0 0 0 0 (2) (0) (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
	C-cell hyperplasia	4 0 0 0 0 (8) (0) (0) (0)	3 1 0 0 (6) (2) (0) (0)	2 0 0 0 0 (4) (0) (0)	1 0 0 0 0 (2) (0) (0)
	focal follicular cell hyperplasia	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0)	1 0 0 0 0 (2) (0) (0)	1 0 0 0 0 (2) (0) (0)
drenat	peliosis-like lesion	<50> 6 0 0 0 (12) (0) (0) (0)	5 0 0 0 (10) (0) (0) (0)	<50> 2 1 0 0 (4) (2) (0) (0)	50> 5 0 0 0 (10) (0) (0) (0)

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0-105W)

ANIMAL : RAT F344/DuCrj REPORT TYPE : A1

SEX

: FEMALE PAGE: 12

Organ	No	roup Name Control 50 add	8000 ppm 50 1 2 3 4 (%) (%) (%) (%)	20000 ppm 50 1 2 3 4 (%) (%) (%) (%)	50000 ppm 50 1 2 3 4 (%) (%) (%) (%)
[Endocrine	system]				
adrenal	cyst	0 0 0 0 (0) (0) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)	(50) 1 0 0 0 (2) (0) (0) (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)	1 0 0 0 0 (2) (0) (0) (0)
	hyperplasia:medulla	6 1 0 0 (12) (2) (0) (0)	6 0 0 0 0 (12) (0) (0) (0)	3 1 0 0 (6) (2) (0) (0)	9 2 0 0 (18) (4) (0) (0)
	focal fatty change:cortex	2 1 0 0 (4) (2) (0) (0)	3 0 0 0 0 (6) (6) (0) (0)	3 0 0 0 0 (6) (6) (0) (0)	0 0 0 0 0 (0) (0)
[Reproducti	ive system]				
DUALLA	cyst	<50> 0 0 0 0 (0) (0) (0) (0)	(50) 1 0 0 0 (2) (0) (0) (0)	(50) 0 2 0 0 (0) (4) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)
uterus	dilatation	<50> 1 0 0 0 (2) (0) (0) (0)	<50> 0 1 0 0 (0) (2) (0) (0)	(50) 1 0 0 0 (2) (0) (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)
Grade <a>> b (c) Significant	1: Slight 2: Moderate 3: 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				

(HPT150)

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

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1

SEX : FEMALE

PAGE: 13

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

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

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1 SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0-105W)

0rgan	Findings	Group Name Control No. of Animals on Study 50 Grade 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	20000 ppm 50 1 2 3 4 (%) (%) (%) (%)	50000 ppm 50 1 2 3 4 (%) (%) (%) (%)
(Special sens	se organs/appandage]				
эуө	retinal atrophy	<50> 9 4 0 0 (18) (8) (0) (0)	50> 5 4 1 0 (10) (8) (2) (0)	(50) 1 9 0 0 * (2) (18) (0) (0)	<50> 2 5 0 0 (4) (10) (0) (0)
	keratitis	0 0 0 0 0 0 (0) (0)	0 1 0 0 (0) (2) (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (2) (0) (0) (0)
	Vascularization:cornea	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 0 (0) (0)	1 0 0 0 0 (2) (3) (6) (7)	0 0 0 0 0 (0) (0)
Harder 9l	atrophy	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	(50) 0 1 0 0 (0) (2) (0) (0)	(50) 0 1 0 0 (0) (2) (0) (0)
	degeneration	0 1 0 0 (0) (2) (0) (0)	2 0 0 0 0 (4) (0) (0) (0)	0 0 0 0 0 (0) (0)	2 0 0 0 0 (4) (0) (0) (0)
	inflammatory infiltration	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 (2) (2) (0) (0)
	lymphocytic infiltration	3 1 0 0 (6) (2) (0) (0)	1 1 0 0 (2) (2) (0) (0)	0 1 0 0 (0) (0)	2 0 0 0 0 (4) (0) (0) (0)
nasolacr d	inflammation	<50> 1 0 0 0 (2) (0) (0) (0)	3 0 0 0 (6) (0) (0) (0)	(50) 1 0 0 0 (2) (0) (0) (0)	(50) 1 0 0 0 (2) (0) (0) (0)
Grade < a > b (c) Significant o	a: Number of animals examined at theb: Number of animals with lesionc: b / a * 100	•			

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

ANIMAL ANIMAL : RAT F344/DuCrj REPORT TYPE : A1

SEX

: FEMALE

PAGE: 15

Organ	Group Na No. of A Grade Findings	ne Control nimals on Study 50 1 2 3 4 (%) (%) (%) (%)	8000 ppm 50 1 2 3 4 (%) (%) (%) (%)	20000 ppm 50 $\frac{1}{(\%)}$ $\frac{2}{(\%)}$ $\frac{3}{(\%)}$ $\frac{4}{(\%)}$	50000 ppm 50 1 2 3 4 (%) (%) (%) (%)
7 3011	· mangs		(6) (6) (6)	(%) (%) (%)	(%) (%) (%)
[Musculaskele	tal system]				
nuscle	hematoma	0 0 0 1 (0) (0) (0) (2)	(50) 0 0 0 0 (0) (0) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)
	mineralization	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)
bone	asteasclerosis	(50) 5 6 0 0 (10) (12) (0) (0)	(50) 4 3 3 0 (8) (6) (6) (0)	2 4 1 0 (4) (8) (2) (0)	2 2 2 0 (4) (4) (4) (0)
[Body cavitie	s]				
leura	inflammation	(50) 0 0 0 0 (0) (0) (0) (0)	(50) 0 0 1 0 (0) (0) (2) (0)	(50) 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)
peritoneum	inflammation	<50> 0 0 0 0 (0) (0) (0) (0)	(50) 0 0 1 0 (0) (0) (2) (0)	<50> 0 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)
retroperit	hematoma	<50> 0 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 1 (0) (0) (0) (2)
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; $*: P \le 0.05$ **: $P \le 0.01$	4: Severe Test of Chi Square			

APPENDIX K 3

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

RAT: MALE: SACRIFICED ANIMALS

ANIMAL

SEX

: RAT F344/DuCrj

REPORT TYPE : A1

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

: MALE

Group Name Control 8000 ppm 20000 ppm 50000 ppm No. of Animals on Study 33 43 43 38 0rgan Findings_ (%) (%) (%) (%) [Integumentary system/appandage] skin/app ⟨33⟩ <43> ⟨43⟩ epidermal cyst 0 1 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(2)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) subcutis <33> <43> <43> ⟨38⟩ abscess Ó 0 0 0 0 0 1 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(2)(0)(0) (0)(0)(0)(0) [Respiratory system] nasal cavit <43> inflammation 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (2)(0)(0)(0) (5)(0)(0)(0) eosinophilic change:olfactory epithelium 15 18 1 0 0 ** 0 0 0 () ** 0 (45) (55) (0) (0) (2)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) eosinophilic change:respiratory epithelium 1 0 0 ** 0 0 0 ** 0 (79) (3) (0) (0) (2)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) inflammation: foreign body 0 7 10 0 0 12 10 2 2 7 1 0 (24) (21) (0) (0) (16) (23) (0) (0) (28) (23) (5) (0) (5)(18)(3)(0) Grade 1: Slight 2 : Moderate 3 : Marked 4 : Severe (a) a: Number of animals examined at the site

b

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

ANIMAL : RAT F344/DuCrj

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

PAGE: 2

Organ	Group Name No. of Anima Grade Findings	Control als on Study 33 1 2 3 4 (%) (%) (%) (%)	8000 ppm 43 1 2 3 4 (%) (%) (%) (%)	20000 ppm 43 1 2 3 4 (%) (%) (%) (%)	50000 ppm 38 1 2 3 4 (%) (%) (%) (%)
[Respiratory	system]				
nasal cavit	respiratory metaplasia:olfactory epithelium	<pre></pre>	2 0 0 0 (5) (0) (0) (0)	4 0 0 0 (9) (0) (0) (0)	4 0 0 0 (11) (0) (0) (0)
	respiratory metaplasia:gland	24 3 0 0 (73) (9) (0) (0)	25 3 0 0 (58) (7) (0) (0)	18 0 0 0 *** (42) (0) (0) (0)	15 1 0 0 ** (39) (3) (0) (0)
lung	osseous metaplasia	33> 0 0 0 0 (0) (0) (0) (0)	<43> 0 0 0 0 (0) (0) (0) (0)	<43> 1 0 0 0 (2) (0) (0) (0)	<pre></pre>
	bronchiolar-alveolar cell hyperplasia	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 1 0 0 (0) (3) (0) (0)
(Hematopoieti	c system]				
cone marrow	granulation	33> 1 2 0 0 (3) (6) (0) (0)	2 1 0 0 (5) (2) (0) (0)	<43> 0 0 0 0 (0) (0) (0) (0)	3 0 0 0 (8) (0) (0) (0)
	increased hematopoiesis	1 0 0 0 0 (3) (3) (6) (6)	2 1 0 0 (5) (2) (0) (0)	3 0 0 0 0 (7) (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 Nifference; *: P ≤ 0.05 **: P ≤ 0.01 Tes	4 : Severe			

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

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1

SEX : MALE

Organ	Findings	Group Name Control No. of Animals on Study 33 Grade 1 2 3 (%) (%) (%)	8000 ppm 43 1 2 3 4 (%) (%) (%) (%)	20000 ppm 43 1 2 3 4 (%) (%) (%) (%)	50000 ppm 38 1 2 3 4 (%) (%) (%) (%)
[Hematopoietio	c system]				
bone marrow	decreased hematopoiesis	33> 0 0 0 (0) (0) (0) (0 1 0 0 0 0) (2) (0) (0) (0)	0 1 0 0 (0) (2) (0) (0)	38> 0 1 0 0 (0) (3) (0) (0)
	granulopoiesis: increased	1 0 0 (3) (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)	0 0 0 0 0 (0)
lymph node	lymphocytic infiltration	33> 0 0 0 (0) (0) (0) (0 1 0 0 0 0) (2) (0) (0) (0)	<pre></pre>	<pre></pre>
spleen	atrophy	<33> 0 0 0 (0) (0) (0) (0 0 0 0 0 0) (0) (0) (0) (0)	<43> 0 1 0 0 (0) (2) (0) (0)	<38> 0 0 0 0 (0) (0) (0) (0)
	congestion	6 4 0 (18) (12) (0) (0 8 1 0 0 0) (19) (2) (0) (0)	12 0 0 0 (28) (0) (0) (0)	6 0 0 0 0 (16) (0) (0)
	deposit of hemosiderin	0 0 0 0 (0) (0) (0 2 1 0 0 0 0 5) (5) (2) (0) (0)	7 0 0 0 * (16) (0) (0) (0)	7 3 0 0 *** (18) (8) (0) (0)
	fibrosis	0 0 0 0 (0) (0) (0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 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:b/a*100

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

(HPT150)

BAIS3

ANIMAL : RAT F344/DuCrj

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

SACRIFICED ANIMALS (105W)

		Group Name No. of Animals on Study	Contr	}			8000 4	3				3			5	0000 p 38	mak	
Organ	Findings	Grade <u>1</u> (%)	2 (%)	(%)	(%)	(%)	(%)	3 (%)	(%)	<u>1</u> (%)	(%)	3 (%)	(%)	(1 %)	2 (%)	3 (%)	(%)
[Hematopoietic	: system]																	
spleen	extramedullary hematopoiesis	2 (6)	<33 0 (0) (0	0 (0)	2 (5)	<4 2 (5)	0	0 (0)	1 (2)	1		0 (0)	(-	2 5) (<382 2 5) (> 0 0) (0
	engargement of erythrocyte	0 (0)	0 (0) (0 (0)	0 (0)	12 (28)	2 (5)	0 (0) (0 **	14 (33)	0 (0)	0 (0)	0 ** (0)	1 (2		0 (0	0 ** 0)
[Circulatory s	system]																	
heart	myocardial fibrosis	3 (9)	<33 0 (0) (0	0	2 (5)	<4 0 (0)	0	0 (0)	1 (2)	0		0 (0)	(2 5) (<382 3 8) () 0 0) (0 0)
	arteritis	0 (0)	(0) (0 (0)	0 (0)	0 (0)	0 (0)	0 (0) (0 (0)	1 (2)	0 (0)	0 (0)	0 (0)		0 0) (0 (0 (0)	0 0)
artery/aort	arteritis	0 (0)	<33 0 (0) (0	0 (0)	0 (0)	<4 0 (0)	0	0 (0)	1 (2)	0		0 (0)		0 0) (<383 0 0) () 0 0) (0 0)
[Digestive sys	stem]																	
tongue	arteritis		<33 1 (3) (0	0 (0)	3 (7)	<4 0 (0)	0	0 (0)	3 (7)	0	0 (0)	0 (0)			<382 1 3) (0
⟨a⟩ b	 a: Number of animals examined at the b: Number of animals with lesion c: b / a * 100 	3 : Marked 4 : Severa site ≦ 0.01 Test of Chi Squal												······································				

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

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1

SEX : MALE

,...,

Organ	Findings	Group Name Control No. of Animals on Study 33 Grade 1 2 3 (%) (%) (%)	8000 ppm 43 4 1 2 3 4 (%) (%) (%) (%)	20000 ppm 43 1 2 3 4 (%) (%) (%) (%)	50000 ppm 38 1 2 3 4 (%) (%) (%) (%)
[Digestive sy	stem]				
salivary gl	inflammation	(33) 0 0 0 (0) (0) (0) (0 0 0 0 0 0) (0) (0) (0) (0)	<43> 0 0 0 0 (0) (0) (0) (0)	38> 0 1 0 0 (0) (3) (0) (0)
stomach	ulcer:forestomach	<33> 0 0 0 (0) (0) (0) (0 0 0 0 0 0) (0) (0) (0) (0)	43> 1 1 0 0 (2) (2) (0) (0)	<38> 0 0 0 0 0 0 0 0 0 0 0 0 0 0
	erosion:glandular stomach	1 0 0 (3) (0) (0) (0 0 0 0 0 0	0 0 0 0 0 (0) (0)	2 0 0 0 0 (5) (6) (6)
	ulcer:glandular stomach	2 0 0 (6) (0) (0) (0 5 0 0 0 0) (12) (0) (0) (0)	2 0 0 0 0 (5) (0) (0) (0)	2 0 0 0 0 (5) (6) (6) (7)
	hyperplasia:glandular stomach	1 0 0 (3) (0) (0) (0 2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	1 1 0 0 (2) (2) (0) (0)	2 1 0 0 (5)(3)(0)(0)
small intes	diverticula	<33> 0 0 0 (0) (0) (0) (0 0 1 0 0 0) (0) (2) (0) (0)	<43> 0 0 0 0 0 0 0 0 0 0 0 0	<38> 0 0 0 0 0 0 0 0 0 0 0 0 0 0
liver	herniation	<33> 0 0 0 (0) (0) (0) (0 2 0 0 0 0) (5) (0) (0) (0)	<43> 0 0 0 0 (0) (0) (0) (0)	<38> 0 0 0 0 0 0 0 0 0 0 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)

: RAT F344/DuCrj

ANIMAL REPORT TYPE : A1 SEX

: MALE

PAGE: 6

0rgan	_ Findings	Group Name No. of Animals on Study Grade 1 (%)	Cont 2 (%)	:rol :3 	<u>4</u> (%)	8000 ppm 43 1 2 3 4 (%) (%) (%) (%)	20000 ppm 43 1 2 3 4 (%) (%) (%) (%)	50000 ppm 38 1 2 3 4 (%) (%) (%) (%)
[Digestive	system]							
liver	necrosis:focal	1 (3)	0	33> 0 (0)	0 (0)	\(\lambda 43 \rangle \) \(\begin{picture} 1 & 0 & 0 & 0 \\ (& 2) & (& 0) & (& 0) & (& 0) \end{picture}	0 1 0 0 (0) (2) (0) (0)	<38> 0 0 0 0 0 0 0 0 0 0 0
	granulation	0 (0)	0 (0)	0 (0)	0 (0)	1 0 0 0 0 (2) (0) (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (3) (0) (0) (0)
	clear cell focus	6 (18)		1 (3)	0 (0)	2 10 17 11 ** (5) (23) (40) (26)	1 12 14 14 ** (2) (28) (33) (33)	2 19 8 5 ** (5) (50) (21) (13)
	acidophilic cell focus	4 (12)	0 (0)	0 (0)	0 (0)	4 13 14 7 ** (9) (30) (33) (16)	2 9 13 15 ** (5) (21) (30) (35)	2 5 8 15 ** (5) (13) (21) (39)
	basophilic cell focus	5 (15)	7 (21)	0 (0)	0 (0)	8 9 4 0 (19) (21) (9) (0)	6 13 0 1 (14) (30) (0) (2)	9 8 3 0 (24) (21) (8) (0)
	spongiosis hepatis	(0)		0 (0)	0 (0)	9 3 0 0 ** (21) (7) (0) (0)	7 3 1 0 * (16) (7) (2) (0)	9 5 0 0 ** (24) (13) (0) (0)
	bile duct hyperplasia	4 (12)		0 (0)	0 (0)	9 33 0 0 (21) (77) (0) (0)	16 22 2 0 * (37) (51) (5) (0)	15 19 1 0 * (39) (50) (3) (0)
	cholangiofibrosis	(0)		0 (0)	0 (0)	0 0 0 0 0 (0) (0) (0)	1 0 0 0 (2) (0) (0) (0)	2 0 0 0 (5) (0) (0) (0)

Grade

1 : Slight

2 : Moderate

3 : Marked

4 : Severe

(a)

a: Number of animals examined at the site

b

b: Number of animals with lesion c: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)

ANIMAL : RAT F344/DuCrj REPORT TYPE : A1

SEX

: MALE

PAGE: 7 Craun Name Control 2000 20000 50000

Organ	N	roup Name	8000 ppm 43 1 2 3 4 (%) (%) (%) (%)	20000 ppm 43 1 2 3 4 (%) (%) (%) (%)	50000 ppm 38 1 2 3 4 (%) (%) (%) (%)
[Digestive :	system]				
liver	biliary cyst	<33> 0 0 0 0 (0) (0) (0) (0)	<43> 0 0 0 0 (0) (0) (0) (0)	(43> 0 1 0 0 (0) (2) (0) (0)	<38> 0 0 0 0 (0) (0) (0) (0)
pandreas	atrophy	<33> 3 3 0 0 (9) (9) (0) (0)	<43> 5 6 2 0 (12) (14) (5) (0)	<43> 7 5 1 0 (16) (12) (2) (0)	38> 9 6 0 0 (24) (16) (0) (0)
	hyperplasia	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 (2) (0) (0) (0)	0 0 0 0 0 (0) (0)
	arteritis	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 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
[Urinary sy	rstem]				
kidney	hyperplasia:tubular epithelial cell	33> 0 0 0 0 (0) (0) (0) (0)	4 0 0 0 (9) (0) (0) (0)	<43> 0 0 0 0 (0) (0) (0) (0)	38> 2 0 0 0 (5) (0) (0) (0)
	infarct	0 0 0 0 0 (0) (0)	1 0 0 0 0 (2) (0) (0) (0)	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0) (0)
Grade <a>> b (c) Significant	1: Slight 2: Moderate 3: a: Number of animals examined at the sit b: Number of animals with lesion c: b / a * 100 difference; *: P ≤ 0.05 **: P ≤				

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1

SEX

: MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

Group Name Control Mag 0008 20000 ppm 50000 ppm No. of Animals on Study 33 43 43 38 Findings_ Organ (%) (%) (%) (%) [Urinary system] kidney <43> <43> <38> cyst 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (2)(0)(0)(0) (0)(0)(0)(0) deposit of hemosiderin 0 0 0 0 0 0 (0)(0)(0)(0) (2)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) easinaphilic body 1 0 0 0 0 0 0 1 0 0 (0)(0)(0)(0) (0)(2)(0)(0) (0)(0)(0)(0) (0)(3)(0)(0) chronic nephropathy 3 9 14 7 3 11 14 14 1 15 11 15 4 11 15 (9)(27)(42)(21) (2) (35) (26) (35) (7) (26) (33) (33) (11) (29) (39) (16) papillary necrosis 0 5 (0)(0)(0)(0) (9)(0)(0)(0) (12) (2) (0) (0) (3)(0)(0)(0) mineralization:cortico-medullary junction 0 0 0 0 (0)(0)(0)(0) (0)(2)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) mineralization:papilla 0 0 0 3 1 0 0 6 0 0 0 5 1 0 0 (6)(0)(0)(0) (7)(2)(0)(0) (14) (0) (0) (0) (13) (3) (0) (0) mineralization:pelvis (0)(0)(0)(0) (2)(2)(0)(0) (0)(2)(0)(0) (5)(3)(0)(3)

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

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

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1

SEX : MALE

. I F

PAGE: 9

0rgan	Group Name No. of Anim Grade	Control als on Study 33 4 (%) (%) (%) (%)	8000 ppm 43 1 2 3 4 (%) (%) (%) (%)	20000 ppm 43 1 2 3 4 (%) (%) (%) (%)	50000 ppm 38 1 2 3 4 (%) (%) (%) (%)
[Urinary syst	tem]				
kidney	simple hyperplasia:transitional epithelium	<pre></pre>	5 0 0 0 (12) (0) (0) (0)	4 1 0 0 (9) (2) (0) (0)	38> 7 0 0 0 (18) (0) (0) (0)
	nodular hyperplasia:transitional epithelium	3 0 0 0 0 (9) (0) (0)	5 3 0 0 (12) (7) (0) (0)	8 0 0 0 (19) (0) (0) (0)	4 0 0 0 (i1)(0)(0)(0)
	eosinophilic droplet:proximal tubule	1 0 0 0 0 (3) (0) (0)	19 4 0 0 ** (44) (9) (0) (0)	26 5 0 0 ** (60) (12) (0) (0)	20 13 0 0 ** (53) (34) (0) (0)
urin bladd	simple hyperplasia:transitional epithelium	<33> 0 0 0 0 (0) (0) (0) (0)	<43> 0 0 0 0 (0) (0) (0) (0)	<43> 1 0 0 0 (2) (0) (0) (0)	<38> 0 0 0 0 0 0 0 0 0
	nodular hyperplasia:transitional epithelium	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (2) (0) (0) (0)	2 0 0 0 (5) (0) (0) (0)
[Endocrine s	ystem]				
pituitary	angiectasis	32> 2 1 0 0 (6) (3) (0) (0)	\(\lambda 43 \rangle \) \(1 0 0 0 \) \(2) \((0) (0) (0) \)	<43> 0 0 0 0 (0) (0) (0) (0)	(38) 1 1 0 0 (3) (3) (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; *: $P \le 0.05$ **: $P \le 0.01$ Te	4 : Severe			

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

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1

SEX : MALE

PAGE: 10

0rgan	Findings	Group Name No. of Animals on Study Grade 1 (%)	Control 33 2 3 (%) (%)	<u>4</u> (%)	8000 ppm 43 1 2 3 4 (%) (%) (%) (%)	20000 ppm 43 1 2 3 4 (%) (%) (%) (%)	50000 ppm 38 1 2 3 4 (%) (%) (%) (%)
(Endocrine s	ystem]						
pituitary	cyst	1 (3)	<32> 0 0 (0) (0) (0	(43) 1 0 0 0 (2) (0) (0) (0)	(43) 1 0 0 0 (2) (0) (0) (0)	38> 1 0 0 0 (3) (0) (0) (0)
	hyperplasia	5 (16)	2 0 (6) (0) (0 (0)	4 1 0 0 (9) (2) (0) (0)	6 3 0 0 (14) (7) (0) (0)	7 2 0 0 (18) (5) (0) (0)
	hyperplasia:gland	(0)	0 0 (0) (0 (0)	1 0 0 0 0 (2) (0) (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
	Rathke pouch	(0)	0 0 (0) (0	2 0 0 0 0 (5) (0) (0) (0)	2 0 0 0 0 (5) (0) (0)	2 0 0 0 0 (5) (0) (0) (0)
thyroid	C-cell hyperplasia	0 (0)	<33> 1 0 (3) (0) (0 (0)	4 0 0 0 (9) (0) (0) (0)	3 0 0 0 (7) (0) (0) (0)	38> 1 3 0 0 (3) (8) (0) (0)
panc islet	islet cell hyperplasia	1 (3)	<33> 1 0 (3) (0) (0 (0)	<43> 2 0 0 0 (5) (0) (0) (0)	<43> 1 1 0 0 (2) (2) (0) (0)	<38> 0 0 0 0 0 0 0 0 0 0 0
adrena l	peliosis-like lesion	0 (0)	<33> 0 0 (0) (0) (0 (0)	(43) 1 0 0 0 (2) (0) (0) (0)	<43> 2 0 0 0 (5) (0) (0) (0)	<38> 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 the b: Number of animals with lesion c: b / a * 100 difference; *: P ≤ 0.05 **: F						

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

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1 SEX

: MALE

		Group Name Control No. of Animals on Study 33	8000 ppm 43	20000 ppm 43	50000 ppm 38	
Organ	Findings	Grade 1 2 3 4 (%) (%) (%) (%)	1 2 3 4 (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)	1 2 3 4	
Endocrine sy	rstem]					
adrena l	hyperplasia:medulla	333> 3 4 0 0 (9) (12) (0) (0)	<43> 4 7 0 0 (9) (16) (0) (0)	7 4 0 0 (16) (9) (0) (0)	<pre></pre>	
	focal fatty change:cortex	0 0 0 0 0 (0) (0)	1 0 0 0 0 (2) (0) (0)	1 0 0 0 0 (2) (0) (0)	0 0 0 0 0 (0) (0)	
[Reproductive	e system]					
testis	atrophy	\(\lambda 33 \rangle \) \(1 0 0 0 \) \((3) (0) (0) (0) (0) \)	<43> 1 0 0 0 (2) (0) (0) (0)	<43> 1 0 0 0 (2) (0) (0) (0)	<pre></pre>	
	mineralization	5 0 0 0 (15) (0) (0) (0)	7 0 0 0 (16) (0) (0) (0)	13 1 0 0 (30) (2) (0) (0)	10 0 0 0 (26) (0) (0) (0)	
	arteritis	3 0 0 0 0 (9) (0) (0)	0 0 0 0 0 0 (0) (0)	2 0 0 0 0 (5) (0) (0)	1 0 0 0 0 (3) (0) (0)	
	interstitial cell hyperplasia	3 0 0 0 0 (9) (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (2) (0) (0) (0)	0 0 0 0 0 (0) (0)	
prostate	inflammation	30000 (9)(0)(0)(0)	6 0 0 0 (14) (0) (0) (0)	2 0 1 0 (5) (0) (2) (0)	38> 7 0 0 0 (18) (0) (0) (0)	
Grade (a) b (c) Significant o	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 **: I	3: Marked 4: Severe e site P ≤ 0.01 Test of Chi Square				

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL : RAT F344/DuC-j SACRIFICED ANIMALS (105W)

REPORT TYPE : A1

SEX : MALE

Organ	Group Name No. of Anim Grade	Control nals on Study 33 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	50000 ppm 38 1 2 3 4 (%) (%) (%) (%)
[Reproductive	e system]	,			
prostate	hyperplasia	<pre></pre>	6 0 0 0 (14) (0) (0) (0)	<pre></pre>	<38> 11 0 0 0 (29) (0) (0) (0)
mammary gl	hyperplasia	<33> 0 0 0 0 (0) (0) (0) (0)	<43> 0 0 0 0 (0) (0) (0) (0)	<43> 1 0 0 0 (2) (0) (0) (0)	<38> 0 0 0 0 0 0 (0) (0) (0)
	galactocele	0 1 0 0 (0) (0)	0 1 0 0 (0) (2) (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
[Special sens	se organs/appandage]				
эуе	cataract	<33> 0 4 0 0 (0) (12) (0) (0)	0 4 0 0 (0) (9) (0) (0)	0 3 0 0 (0) (7) (0) (0)	<pre></pre>
	retinal atrophy	2 7 0 0 (6) (21) (0) (0)	1 16 0 0 (2) (37) (0) (0)	0 9 0 0 (0) (21) (0) (0)	4 9 0 0 (11) (24) (0) (0)
Harder gl	degeneration	<33> 0 0 0 0 (0) (0) (0) (0)	<pre></pre>	<43> 0 0 0 0 (0) (0) (0) (0)	<pre></pre>
Grade < a > b (c) 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; $*: P \le 0.05$ **: $P \le 0.01$ Te	4 : Severe est of Chi Square			

SEX

: RAT F344/DuCrj

ANIMAL REPORT TYPE : A1

: MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

Group Name Control mag 0008 20000 ppm mag 00003 No. of Animals on Study 33 43 43 38 Organ Findings_ [Special sense organs/appandage] Harder gl <43> <43> lymphocytic infiltration 0 0 0 0 0 0 0 0 0 0 0 0 0 0 (0) (0) (0) (0) (3)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) nasolacr d <33> <43> <43> ⟨38⟩ inflammation 0 0 0 0 0 1 0 0 0 0 0 0 1 0 0 0 (0)(0)(0)(0) (0)(2)(0)(0) (0)(0)(0)(0) (3)(0)(0)(0) [Body cavities] retroperit hemorrhage 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(3)(0)(0) adipose ⟨33⟩ <43> <43> necrosis 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(2)(0)(0) (0)(0)(0)(0)

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

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

b b: Number of animals with lesion

c:b/a*100(c)

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

(HPT150)

BAIS3

APPENDIX K 4

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

RAT: FEMALE: SACRIFICED ANIMALS

SEX : FEMALE

ANIMAL : RAT F344/DuCrj REPORT TYPE : A1

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

PAGE: 1

0rgan	Findings		trol 40 3 4 (%) (%) (%)	8000 ppm 40 2 3) (%) (%)	<u>4</u> (%)	1 (%)	20000 ; 40 2 (%)		4 (%)	1	0000 p 37 2 (%)	3	<u>4</u> (%)
[Integumentar	y system/appandage]												
skin/app	inflammation	0 0	40> 0 0 0 (0) (0) (0	<40> 0 0) (0) (0)	0 (0) (0 (<400 0 0) (0	0	0 (0) (<37> 1 3) (0	0 0)
[Respiratory:	system]												
nasal cavit	follicle	1 0		<40> 0 0) (0) (0)	0 (0) (0 (<40 0 0) (0	0	0 (0) (<37> 0 0) (0	0 0)
	atrophy	0 0	0 0 0 0	0 0	0 (0) (0 (0) (0 0) (0	0 0)	1 (3) (0 (0 0) (0 0)
	eosinophilic change:olfactory epith		15 0 0 (38) (0) (0	0 0	0 **	0 (0) (0 (0	0 ** 0)	0 (0) (0 (0 (0 ** 0)
	eosinophilic change:respiratory epi		0 0 0	0 0	0 **	0 (0 (0	0 ** 0)	0 (0) (0 (0 0) (0 ** 0)
	inflammation:foreign body	4 2 (10) (5)	0 0 1 (3	1 0	0 (0) (2 (5) (1 3) (0	0	4 (11) (1 3) (0	0 0)
	disarrangement:olfactory epithelium		0 0 0	0 0	0 (0) (0 (0) (0 (0	0	1 (3) (0	0	0
Grade (a) b (c)	1: Slight 2: Moderate a: Number of animals examined at the b: Number of animals with lesion c: b/a * 100												

(HPT150)

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

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

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

PAGE: 2

Organ	Findings	Group Name No. of Animals on Study Grade 1 (%	I :	ontro 40 2 %)	3 (%)	<u>4</u> (%)	1 (%)		0 ppm 40 3 (%)		<u>4</u> (%)	(1 %)	20000		<u>4</u> (%)		1 (%)			om 3 (%)	<u>4</u> (%)
[Respiratory s	system]																					
nasal cauit	respiratory metaplasia:olfactory ep))) (<40> 0 0) (0 0) (0 0)	0 (0)	0			0 0)		0 0) (<4 0 0)	0	0 (0)	(6 16)	0 (0)		0 0) (0 *
	respiratory metaplasia:gland	24 (60	1	1 3) (0 0) (0 0)	17 (43)	0 (0)	0 (0)		0 0)	2 (5		0 0)	0 (0)	0 (0)	(14 38)	(0)		0	0 0)
	necrosis:olfactory epithelium))) (0 0) (0	0 0)	3 (8)	0 (0)	0 (0)) (0 0)	1 (3	4 5) (0	0 (0)	0 ** (0)	(24 65)	0 (0)		0 0) (0 **
lung	hemorrhage	1 (3	i 3) (<40> 0 0) (0	0 0)	0 (0)	0	40> 0 (0)		0 0)		0 0) (<4 0 0)	0	0 (0)	(0	0 (0)		0 0) (0 ()
	inflammation))) (0 0) (0 0) (0 0)	1 (3)	0 (0)	0 (0)		0 0)		0 0) (0 0)	0 (0)	0 (0)	(0 0)	0 (0)		0 0) (0 (0)
	inflammatory infiltration	0 (0))) (0 0) (0 0) (0 0)	0 (0)	0 (0)	0 (0)) (0		1 3) (0 0)	0 (0)	0 (0)	(0 0)	0		0 (0 0)
	lymphocytic infiltration	1 (3	l 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)
	accumulation of foamy cells	0 (0))) (0 0) (0 0) (0 0)	1 (3)	0 (0)	0 (0)) (0 0)	(0 0) (0 0)	0 (0)	0 (0)	(0 0)	1 (3)) (0 (0 0)

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

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

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1 SEX

: FEMALE

Organ	Findings	Group Name Control No. of Animals on Study 40 Grade 1 2 3 (%) (%)	8000 ppm 40 1 2 3 4 (%) (%) (%) (%)	20000 ppm 40 1 2 3 4 (%) (%) (%) (%)	50000 ppm 37 1 2 3 4 (%) (%) (%) (%)
[Respiratory	system]				
lung	bronchiolar-alveolar cell hyperplasia	<40> 1 0 0 (3) (0) (0) (0 0 0 0 0 0) (0) (0) (0) (0)	2 0 0 0 (5) (0) (0) (0)	<37> 0 0 0 0 0 (0) (0) (0) (0)
[Hematopoieti	c system]				
bone marrow	granulation	2 3 0 (5) (8) (0) (0 2 5 0 0 0) (5) (13) (0) (0)	\(\lambda 40 \rangle \) \[1 2 0 0 \\ (3) (5) (0) (0) \]	<pre></pre>
	increased hematopoiesis	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	2 0 0 0 0 (5) (0) (0) (0)	1 0 0 0 0 (3) (0) (0) (0)
	granulopoiesis:increased	0 0 0 0 (0) (0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0) (0)
spleen	congestion	6 0 0 (15) (0) (0) (0 6 0 0 0 0) (15) (0) (0) (0)	2 0 0 0 (5) (0) (0) (0)	<37> 7 0 0 0 (19) (0) (0) (0)
	deposit of hemosiderin	14 8 0 (35) (20) (0) (0 21 7 0 0 0) (53) (18) (0) (0)	25 5 0 0 * (63) (13) (0) (0)	21 6 0 0 (57) (16) (0) (0)
<pre></pre>	1: Slight 2: Moderate 3 a: Number of animals examined at the s b: Number of animals with lesion c: b / a * 100 ifference; $*: P \leq 0.05$ **: $P \leq 0.05$				

(HPT150)

BAIS3

ANIMAL : RAT F344/DuCrj

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

REPORT TYPE : A1

SEX : FEMALE

Organ	Findings	Group Name No. of Animals on Study Grade 1 (%)	Control 40 2 3 4 (%) (%) (%)	8000 ppm 40 1 2 3 4 (%) (%) (%) (%)	20000 ppm 40 1 2 3 4 (%) (%) (%) (%)	50000 ppm 37 1 2 3 4 (%) (%) (%) (%)
[Hematopoieti	c system]					
spleen	extramedullary hematopoiesis	2 (5)	<40> 1 0 0 (3) (0) (0)	(40) 1 0 0 0 (3) (0) (0) (0)	<40> 0 0 0 0 0 0 0 0 0 0 0 0 0 0	37> 1 0 0 0 (3) (0) (0) (0)
	ensargement of erythracyte	0 (0)	0 0 0 0 (0) (0)	21 6 0 0 ** (53) (15) (0) (0)	27 4 0 0 ** (68) (10) (0) (0)	17 7 0 0 *** (46) (19) (0) (0)
[Circulatory	system]					
heart	thrombus	(0)	<40> 0 0 0 (0) (0) (0)	<40> 0 1 0 0 (0) (3) (0) (0)	<40> 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<pre></pre>
	myocardial fibrosis	0 (0)	0 0 0 0 (0) (0)	2 0 0 0 0 (5) (0) (0)	0 1 0 0 (0) (0)	3 0 0 0 0 (8) (0) (0) (0)
artery/aort	arteritis	(0)	<40> 0 0 0 (0) (0) (0)	(40) 0 0 0 0 (0) (0) (0) (0)	<40> 0 1 0 0 (0) (3) (0) (0)	<37> 0 0 0 0 0 0 0 0 0 0 0 0
[Digestive sy	stem]					
tongue	arteritis	(0)	<40> 0 0 0 (0) (0) (0)	(40) 1 1 0 0 (3) (3) (0) (0)	2 1 0 0 (5) (3) (0) (0)	37> 1 0 0 0 (3) (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

BAIS3

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

: RAT F344/DuCrj ANIMAL

REPORT TYPE : A1

SEX : FEMALE

Organ	Findings	Group Name Continuo of Animals on Study 40 Grade 1 2 (%) (%)		8000 ppm 40 1 2 3 4 (%) (%) (%) (%)	20000 ppm 40 1 2 3 4 (%) (%) (%) (%)	50000 ppm 37 1 2 3 4 (%) (%) (%) (%)
[Digestive s	system]					
stomach	arteritis	0 0 (0) (0)	0 0	(40) 0 0 0 0 (0) (0) (0) (0)	0 1 0 0 (0) (3) (0) (0)	<37> 0 0 0 0 0 0 0 0 0 0 0 0
	ulcer:forestomach	0 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)
	hyperplasia:forestomach	0 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)
	erosion:glandular stomach	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)
	ulcer:glandular stomach	0 0 (0) (0)	0 0	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (3) (0) (0) (0)
liver	herniation	3 0 (8) (0)	0 0	2 0 0 0 (5) (0) (0) (0)	<40> 1 0 0 0 (3) (0) (0) (0)	37> 1 0 0 0 (3) (0) (0) (0)
	peliosis-like lesion	0 0 (0) (0)	0 0 (0)	2 0 0 0 (5) (0) (0) (0)	1 0 0 0 (3) (0) (0) (0)	0 0 0 0 0 (0) (0)
	lymphocytic infiltration	0 1 (0) (3)	0 0	0 1 0 0 (0) (3) (0) (0)	1 1 0 0 (3) (3) (0) (0)	0 0 0 0 0 (0) (0) (0)

Grade 1 : Slight 2 : Moderate

3 : Marked

4 : Severe

< a >

a : Number of animals examined at the site

b

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

ANIMAL : RAT F344/DuCrj

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

REPORT TYPE : A1

SEX : FEMALE PAGE: 6

anulation Lear cell focus	<40> 15 9 0 0 (38) (23) (0) (0) 1 0 0 0	<40> 20 8 1 0 (50) (20) (3) (0)	<40> 21 9 2 0 (53) (23) (5) (0)	<37> 18 10 2 0
	15 9 0 0 (38) (23) (0) (0)	20 8 1 0	21 9 2 0	18 10 2 0
lear cell focus	1 0 0 0			(49) (27) (5) (0)
	(3) (0) (0) (0)	3 6 0 0 * (8) (15) (0) (0)	8 7 0 0 ** (20) (18) (0) (0)	5 6 2 0 ** (14) (16) (5) (0)
cidaphilic cell facus	0 0 0 0 0 (0) (0)	6 11 3 0 ** (15) (28) (8) (0)	6 10 3 1 ** (15) (25) (8) (3)	7 4 1 1 ** (19) (11) (3) (3)
asophilic cell focus	10 10 0 0 (25) (25) (0) (0)	7 10 0 0 (18) (25) (0) (0)	9 10 1 1 (23) (25) (3) (3)	8 4 1 0 (22) (11) (3) (0)
ixed cell focus	0 0 0 0 0 (0) (0)	1 1 0 0 (3) (3) (0) (0)	0 0 0 0 0 (0) (0)	0 1 0 0 (0) (3) (0) (0)
pongiosis hepatis	0 0 0 0 0 (0) (0)	1 0 0 0 0 (3) (0) (0) (0)	2 0 0 0 0 (5) (0) (0) (0)	0 0 0 0 0 (0) (0) (0)
ile duct hyperplasia	4 0 0 0 0 (10) (10) (10) (10)	3 1 0 0 (8) (3) (0) (0)	1 1 0 0 (3) (3) (0) (0)	1 0 0 0 0 (3) (0) (0) (0)
nolangiofibrosis	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)
i	xed cell focus xed cell focus congiosis hepatis le duct hyperplasia	(0) (0) (0) (0) (0) sophilic cell focus 10 10 0 0 0 (25) (25) (0) (0) xed cell focus 0 0 0 0 0 (0) (0) (0) congiosis hepatis 0 0 0 0 0 (0) (0) (0) le duct hyperplasia 4 0 0 0 (10) (0) (0) (0) collangiofibrosis 0 0 0 0 0	(0) (0) (0) (0) (15) (28) (8) (0) sophilic cell focus 10 10 0 0 7 10 0 0 0 (25) (25) (0) (0) (18) (25) (0) (0) xed cell focus 0 0 0 0 0 1 1 0 0 0 0 0 (0) (0) (0) (0) congiosis hepatis 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0	ridophilic cell focus \[\begin{array}{cccccccccccccccccccccccccccccccccccc

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)

: RAT F344/DuCrj

ANIMAL REPORT TYPE : A1 : FEMALE SEX

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

PAGE: 7 Group Name Control Mqq 0008 20000 ppm 50000 ppm No. of Animals on Study 40 40 40 37 Grade 3 3 Findings (%) (%) Organ (%) (%) (%) (%) (%) (%) [Digestive system] liver <40> <40> (40) biliary cyst 0 0 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (3)(0)(0)(0) (0)(0)(0)(0) pancreas <40> ⟨40⟩ ⟨37⟩ atrophy 0 0 0 3 2 0 0 7 0 0 * 3 0 0 (8)(0)(0)(0) (8)(5)(0)(0) (5)(18)(0)(0) (14) (8) (0) (0) [Urinary system] kidney <40> <40> <40> <37> infarct 0 0 0 0 0 0 1 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(3)(0)(0) (0)(0)(0)(0) cyst 0 1 0 0 1 0 0 0 0 0 (0)(3)(0)(0) (3)(0)(0)(0) (0)(0)(0)(0) (3)(0)(0)(0) chronic nephropathy 22 10 2 3 7 15 15 2 ** 8 20 7 4 ** 14 16 6 0 (55) (25) (5) (8) (18) (38) (38) (5) (20) (50) (18) (10) (38) (43) (16) (0) papillary necrosis 0 0 (0)(0)(0)(0) (0)(3)(0)(0) (3)(0)(0)(0) (0)(0)(0)(0) Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe <a>> a: Number of animals examined at the site b b: Number of animals with lesion (c) c:b/a*100Significant difference; $*:P \le 0.05$ $**:P \le 0.01$ Test of Chi Square

(HPT150)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL : RAT F344/DuCrj REPORT TYPE : A1

SACRIFICED ANIMALS (105W)

rgan	1	Group Name No. of Animals on Study Grade <u>1</u> (%)	2	rol 0 <u>3</u> (%)	<u>4</u> (%)	1 (%)	8000 40 2 (%)		1 (%)	20000 i 40 2 (%)		<u>4</u> (%)	1(%)	50000 3 2 (%)) ppm 37 3 (%)	<u>4</u> (%)
lrinary sy	rstem]															
idney	mineralization:cortico-medullary junct		<4 1) (3)	0	0 (0)	13 (33)	<40 2 (5) (13 (33)	<40 0 (0) (0	0 (0)	9 (24)	0	37> 0 (0)	-
	mineralization:papilla	1 (3)	0 (0)	0 (0)	0 (0)	10 (25)	0 (0) (0 0 **	6 (15)	0 (0) (0	0	3 (8)	0 (0)	0 (0)	0 (0)
	mineralization:pelvis	5 (13)	0 (0)	0 (0)	0 (0)	3 (8)	1 (3) (0 0	4 (10)	0 (0) (0	0 (0)	6 (16)	0 (0)	0 (0)	0 (0)
	mineralization:cortex	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0) (0 0	1 (3)	0 (0) (0	0	0 (0)	0 (0)		
	dilatation:tubular lumen	0 (0)	0 (0)		0 (0)	1 (3)	0 (0) (0 0	0 (0)	0 (0) (0	0	0 (0)			0 (0)
	simple tubule hyperplasia	0	0 (0)	0 (0)	0 (0)	0 (0)	0 (0) (0 0 (0) (0)	2 (5)	0 (0) (0 (0)	0 (0)		0 (0)	
	atypical tubule hyperplasia		0 (0)		0 (0)	10 (25)	0 (0) (0 0 **	13 (33)	0 (0) (0	0 ** (0)	7 (19)		0 (0)	0 (0)
	eosinophilic droplet:proximal tubule	2 (5	0 (0)	0 (0)	0 (0)	11 (28)	29 (73) (0 0 **	1 (3)	37 (93) (0	0 ** (0)	4 (11)	33 (89)	0 (0)	0 (0)

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

b : Number of animals with lesion

c:b/a*100 (c)

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

(HPT150)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

REPORT TYPE : A1

ANIMAL

SEX : FEMALE

: RAT F344/DuCrj

Group Name 8000 ppm Control 20000 ppm 50000 ppm No. of Animals on Study 40 40 40 37 Grade 3 (%) Organ_ Findings_ (%) (%) (%) (%) (%) (%) (%) [Urinary system] urin bladd <40> <40> ⟨37⟩ 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) (3)(0)(0)(0) (0)(0)(0)(0) [Endocrine system] pituitary <40> angiectasis 3 0 0 1 0 0 * 0 0 0 * 3 0 0 0 1 (15) (8) (0) (0) (0)(3)(0)(0) (3)(0)(0)(0) (8)(0)(0)(0) cyst 0 7 0 0 0 1 1 0 0 9 0 0 0 (8) (0) (0) (0) (18) (0) (0) (0) (3)(3)(0)(0) (24) (0) (0) (0) hyperplasia 6 4 1 0 0 7 1 0 0 (13) (0) (0) (0) (15) (3) (0) (0) (10) (3) (0) (0) (19) (3) (0) (0) Rathke pouch 1 0 0 0 0 0 0 (0)(0)(0)(0) (3)(0)(0)(0) (3)(0)(0)(0) (0)(0)(0)(0) thyroid <40> <40> <40> ⟨37⟩ ultimibranchial body remanet 0 0 0 1 0 0 0 0 0 0

(3)(0)(0)(0)

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

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

(HPT150)

0 0 0 0

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

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

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

b b: Number of animals with lesion

⁽c) c:b/a*100

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

__.ISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1 SEX : FEMALE

PAGE: 10

Organ	Findings	Group Name Control No. of Animals on Study 40 Grade 1 2 3 4 (%) (%) (%) (%)	8000 ppm 40 1 2 3 4 (%) (%) (%) (%)	20000 ppm 40 1 2 3 4 (%) (%) (%) (%)	50000 ppm 37 1 2 3 4 (%) (%) (%) (%)
(Endocrine s	system]				
thyroid	C-cell hyperplasia	40> 4 0 0 0 (10) (0) (0) (0)	3 1 0 0 (8) (3) (0) (0)	<pre></pre>	37> 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)	1 0 0 0 (3) (0) (0)	1 0 0 0 0 (3) (0) (0) (0)
adrenal	peliasis-like lesion	6 0 0 0 (15) (0) (0) (0)	5 0 0 0 (13) (0) (0) (0)	<pre></pre>	37> 5 0 0 0 (14) (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)	1 0 0 0 (3) (0) (0) (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)	1 0 0 0 0 (3) (0) (0) (0)
	hyperplasia:medulla	6 0 0 0 (15) (0) (0) (0)	5 0 0 0 (13) (0) (0) (0)	3 1 0 0 (8) (3) (0) (0)	8 2 0 0 (22) (5) (0) (0)
	focal fatty change:cortex	2 1 0 0 (5) (3) (0) (0)	1 0 0 0 0 (3) (0) (0)	3 0 0 0 0 (8) (0) (0)	0 0 0 0 0 0 (0) (0)
[Reproduction	ve system]				
ovary	cyst	<40> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	\(\lambda 40 \rangle \) \(1 0 0 0 \) \(3) \((0) (0) (0) \)	<pre></pre>	37> 0 0 0 0 (0) (0) (0) (0)
Grade <a>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 **: F	3 : Marked 4 : Severe site ≤ 0.01 Test of Chi Square			

(HPT150)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1 SEX

: FEMALE

Group Name Control 8000 ppm 20000 ppm 50000 ppm No. of Animals on Study 40 40 40 37 Grade 3 3 3 (%) (%) (%) (%) (%) (%) (%) (%) (%) Organ_ Findings_ [Reproductive system] uterus <40> <40> <40> ⟨37⟩ dilatation 0 0 0 1 0 0 0 0 0 1 0 0 0 (0)(0)(0)(0) (0)(3)(0)(0) (3)(0)(0)(0) (3)(0)(0)(0) cystic endometrial hyperplasia (8)(3)(0)(0) (10) (10) (0) (0) (8) (5) (0) (0) (19) (5) (0) (0) mammary gl <40> <40> <40> ⟨37⟩ duct ectasia 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 (3)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) hyperplasia 0 0 0 0 0 0 0 0 (8)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) [Special sense organs/appandage] <40> еуе <40> (37) cataract 1 0 0 0 1 0 0 2 0 0 0 0 1 0 0 (0)(3)(0)(0) (0)(3)(0)(0) (0)(5)(0)(0) (0)(3)(0)(0) retinal atrophy 8 3 0 4 0 * (20) (8) (0) (0) (13) (10) (3) (0) (3) (20) (0) (0) (5) (14) (0) (0) Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe (a) a: Number of animals examined at the site b b: Number of animals with lesion (c) c:b/a*100

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

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

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1

SEX : FEMALE PAGE: 12

Organ	No.	oup Name	8000 ppm 40 1 2 3 4 (%) (%) (%) (%)	20000 ppm 40 1 2 3 4 (%) (%) (%) (%)	50000 ppm 37 1 2 3 4 (%) (%) (%) (%)
[Special sens	se organs/appandage]				
еуе	keratitis	<pre></pre>	0 0 0 0 (0) (0) (0) (0)	<40> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	37> 1 0 0 0 (3) (0) (0) (0)
	vascularization:cornea	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)
Harder gl	atrophy	<pre></pre>	<40> 0 0 0 0 (0) (0) (0) (0)	<40> 0 1 0 0 (0) (3) (0) (0)	<37> 0 0 0 0 0 0 0 0 0
	degeneration	0 1 0 0 (0) (0)	2 0 0 0 0 (5) (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 0 0 0 0 (0) (0)	1 1 0 0 (3) (3) (0) (0)
	lymphocytic infiltration	3 1 0 0 (8) (3) (0) (0)	1 1 0 0 (3) (3) (0) (0)	0 1 0 0 (0) (0)	2 0 0 0 0 (5) (0) (0) (0)
nasolacr d	inflammation	\(\lambda \) \(\begin{array}{cccccccccccccccccccccccccccccccccccc	(40) 1 0 0 0 (3) (0) (0) (0)	(40) 1 0 0 0 (3) (0) (0) (0)	<37> 0 0 0 0 (0) (0) (0) (0)
Grade <a>> b (c) Significant c	1: Slight 2: Moderate 3: 1 a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100 difference: $*: P \le 0.05$ **: $P \le 0$	Marked 4 : Severe ,01 Test of Chi Square			

(HPT150)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL : RAT F344/DuCrj REPORT TYPE : A1

SEX : FEMALE

SACRIFICED ANIMALS (105W)

Organ	Findings	Group Name No. of Animals on Study Grade	2	rol .0 <u>3</u> (%)	<u>4</u> (%)	<u>1</u> (%)	8000 40 2 (%)		<u>4</u> (%)	<u>1</u> (%)	20000		<u>4</u> (%)	1 (%)		37 37 3 (%)	<u>4</u> (%)
Musculoske	letal system]																
one	osteosclerosis	(10		0 (0)	0 (0)	2 (5)	3 (8)	2	0 (0)	1 (3)	3	0> 1 (3)	0 (0)	2 (5)	2		0 (0)
rade a > b c) ignificant	1 : Slight 2 : Moderate a : Number of animals examined at b : Number of animals with lesion c : b / a * 100 difference : * : P ≤ 0.05 **																

APPENDIX K 5

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

MOSUE: MALE: ALL ANIMALS

ANIMAL : MOUSE Cri:BDF1

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

ALL ANIMALS (0-105W)

Group Name Control 3200 ppm Mqq 0008 20000 ppm No. of Animals on Study 50 49 50 50 Grade 3 3 3 0rgan_ Findings (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) [Integumentary system/appandage] subcutis <49> <50> <50> inflammation 0 0 0 1 0 (0)(0)(0)(0) (0)(0)(2)(0) (0)(0)(0)(0) (0)(0)(0)(0) [Respiratory system] nasal cavit <49> <50> inflammation 0 0 0 0 0 0 0 0 0 0 0 0 (2)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) inflammatory infiltration 0 0 0 0 0 0 0 (0)(2)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) eosinophilic change:plfactory epithelium 5 5 0 (6)(2)(0)(0) (14) (0) (0) (0) (10) (0) (0) (0) (10) (0) (0) (0) eosinophilic change:respiratory epithelium 0 2 1 6 (6)(4)(2)(0) (8)(0)(0)(0) (4)(4)(2)(0) (12) (2) (0) (0) respiratory metaplasia:olfactory epithelium 0 0 0 3 0 (12) (2) (0) (0) (14) (0) (0) (0) (2)(6)(0)(0) (22) (4) (0) (0) respiratory metaplasia:gland 7 2 0 0 12 2 0 0 5 3 1 11 2 1 0 (14) (4) (0) (0) (24) (4) (0) (0) (10) (6) (2) (0) (22) (4) (2) (0) Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

(HPT150)

<a>> b

(c)

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

c:b/a*100

BAIS3

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

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

SEX : MALE

Organ	Group N No. of Grade Findings_	ame Control Animals on Study 49 1 2 3 4 (%) (%) (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	20000 ppm 50 1 2 3 4 (%) (%) (%) (%)
Respirator	y system]				
.na	congestion	<49> 0 0 0 0 (0) (0) (0) (0)	<50> 0 1 0 0 (0) (2) (0) (0)	(50) 1 0 0 0 (2) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)
	hemorr'hage	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (2) (0) (0)	0 1 0 0 (0) (2) (0) (0)
	inflammatory infiltration	0 1 0 0 (0) (2) (0) (0)	2 0 0 0 0 (4) (0) (0) (0)	3 0 0 0 0 (6) (6) (70) (70)	0 1 0 0 (0) (2) (0) (0)
	bronchiolar-alveolar cell hyperplasia	1 0 0 0 0 (2) (0) (0) (0)	2 0 0 0 0 (4) (0) (0) (0)	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0) (0)
llematopoie	otic system]				
pleen	atrophy	<pre></pre>	<50> 0 0 0 0 (0) (0) (0) (0)	(50) 1 0 0 0 (2) (0) (0) (0)	<50> 0 0 1 0 (0) (0) (2) (0)
	deposit of melanin	0 3 0 0 (0) (6) (0) (0)	2 2 0 0 (4) (4) (6) (6)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (2) (0) (0) (0)
	extramedullary hematopoiesis	1 2 0 0 (2) (4) (0) (0)	0 5 2 0 (0) (10) (4) (0)	1 4 2 0 (2) (8) (4) (0)	1 3 1 0 (2) (6) (2) (0)
Grade (a > b (c)	1: Slight 2: Moderate 3: Marke a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 t difference; *: P ≤ 0.05 **: P ≤ 0.01	ed 4: Severe			

(HPT150)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

j:BDF1 ALL ANIMALS (0-105W)

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

1

PAGE: 3

Organ	Group No. of A No. of A Grade Findings	Animals on Study 49 1 2 3 4 (%) (%) (%) (%) (%)	3200 ppm 50 1 2 3 4 (%) (%) (%) (%)	8000 ppm 50 1 2 3 4 (%) (%) (%) (%)	20000 ppm 50 1 2 3 4 (%) (%) (%) (%)
[Hematopoie1	tic system]				
spleen	follicular hyperplasia	3 1 2 0 (6) (2) (4) (0)	(50) 1 0 2 0 (2) (0) (4) (0)	3 3 1 0 (6) (6) (2) (0)	3 2 1 0 (6) (4) (2) (0)
[Circulator)	v system]				
heart	arteritis	0 0 0 0 (0) (0) (0) (0)	\(\lambda 50 \rangle \) \[1 0 0 0 (2) (0) \qquad (0) (\qquad 0) (0) \	(50) 0 0 0 0 (0) (0) (0) (0)	(50) (0)(0)(0)(0)
[Digestive s	system]				
oral cavity	cyst	0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	(50) 0 1 0 0 (0) (2) (0) (0)
	inflammation	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)
tooth	cyst	0 2 0 0 (0) (4) (0) (0)	(50) 1 1 0 0 (2) (2) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)
Grade <a> b (c)	1: Slight 2: Moderate 3: Market a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 difference; *: $P \le 0.05$ **: $P \le 0.01$				

ANIMAL : MOUSE Crj:BDF1 REPORT TYPE : A1

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

SEX : MALE

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

PAGE: 4

0rgan	И	iroup Name Control to. of Animals on Study 49 irade 1 2 3 4 (%) (%) (%) (%)	3200 ppm 50 1 2 3 4 (%) (%) (%) (%)	8000 ppm 50 1 2 3 4 (%) (%) (%) (%)	20000 ppm 50 1 2 3 4 (%) (%) (%) (%)
[Digestive:	system]				
tooth	inflammation	<49> 0	(50) 0 0 0 0 (0) (0) (0) (0)	(50) 1 0 0 0 (2) (0) (0) (0)	5 0 0 0 (10) (0) (0) (0)
	foreign body granuloma	1 0 0 0 0 (2) (0) (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 (2) (0) (0) (0)	3 2 0 0 (6) (4) (0) (0)
	dysplasia	13 4 0 0 (27) (8) (0) (0)	7 2 0 0 (14) (4) (0) (0)	4 0 2 0 ** (8) (0) (4) (0)	8 5 0 0 (16) (10) (0) (0)
tongue	arteritis	<49> 0 0 0 0 (0) (0) (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)
stomach	ulcer:forestomach	\(\lambda 9 \) \[1 0 0 \\ (2) (0) (0) (0) \]	<50> 0 1 0 0 (0) (2) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)
	hyperplasia:forestomach	0 0 0 0 0 (0) (0)	1 1 0 0 (2) (2) (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (2) (0) (0)
	erosion:glandular stomach	0 0 0 0 0 (0) (0)	1 0 0 0 0 (2) (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
Grade (a) b (c)	a: Number of animals examined at the sit b: Number of animals with lesion c:b/a*100				

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL : MOUSE Crj:BDF1

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

PAGE: 5

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

(HPT150)

(a)

b

(c)

a : Number of animals examined at the site

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

b: Number of animals with lesion

c:b/a*100

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0-105W)

ANIMAL : MOUSE Crj:BDF1 REPORT TYPE : A1

SEX : MALE

PAGE: 6

Organ	Findings	Group Name Control No. of Animals on Study 49 Grade 1 2 3 4 (%) (%) (%) (%)	3200 ppm 50 1 2 3 4 (%) (%) (%) (%)	8000 ppm 50 1 2 3 4 (%) (%) (%) (%)	20000 ppm 50 1 2 3 4 (%) (%) (%) (%)
[Urinary sy	rstem]				
kidney	hyperplasia:tubular epithelial cell	<49> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	(50) 0 0 0 0 (0) (0) (0) (0)	(50) 1 0 0 0 (2) (0) (0) (0)	(50) 1 0 0 0 (2) (0) (0) (0)
	infarct	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)
	hyaline droplet	2 0 0 0 0 (4) (6) (6) (7)	3 0 0 0 0 (6) (6) (0) (0)	6 0 0 0 (12) (0) (0) (0)	3 0 0 0 0 (6) (6) (0) (0)
	basophilic change	16 0 0 0 (33) (0) (0) (0)	21 0 0 0 (42) (0) (0) (0)	21 0 0 0 (42) (0) (0) (0)	20 0 0 0 (40) (0) (0)
	inflammation	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 1 0 0 (0) (0)	0 0 0 0 0 (0) (0) (0)
	lymphocytic infiltration	(0) (2) (0) (0)	0 0 0 0 0 (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
	inflammatory polyp	0 0 0 0 0 (0) (0)	0 1 1 0 (0) (2) (2) (0)	0 0 1 0 (0) (2) (0)	0 0 1 0 (0) (2) (0)
	vacuolization of proximal tubule	21 1 0 0 (43) (2) (0) (0)	14 0 0 0 (28) (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 (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)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1

REPORT TYPE : A1
SEX : MALE

ALL ANIMALS (0-105W)

0rgan	Group Name No. of Animals on S Grade Findings	Study 1 (%)	Con 4 2 (%)	trol 9 3 (%)	<u>4</u> (%)	1 (%)		00 ppm 60 3 (%)	4 (%)	1 (%)	8000 50 2 (%)		4 (%)	1 (%)	20000 p 50 2 (%)	3 4 (%) (%)
[Urinary syst	cem]															
kidney	hydronephrosis	0 (0)	<4 0 (0)	0	0 (0)	1 (2)	0	50> 2 (4)	0 (0)	3 (6) (<50 2 (4) (1	0 (0)	1 (2)		2 0 4) (0)
	mineralization:papilla	1 (2)		0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	3 (6) (0 (0)	0 0)	0 (0)	3 (6)	0 (0) (0 0
	mineralization:pelvis	3 (6)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 0)	0 (0)	4 (8)		0 0
	mineralization:cortex	33 (67)	1 (2)	0 (0)	0 (0)	34 (68)	1 (2)	0 (0)	0 (0)	33 (66)	3 (6) (0 (0)	0 (0)	33 (66)	0 (0) (0 0
urin bladd	hyaline droplet degeneration:superficial cell of transit ional epithelium	0 (0)	0		0 (0)	28 (56)	0	50> 0 (0)	0 **	38 (76) +	<50 4 (8) (0	0 ** (0)	20 (40)		0 0 *
(Endocrine sy	vstem]															
pituitary	angiectasis	0 (0)	0	.9> 0 (0)	0 (0)	0 (0)	0	50> 0 (0)	0 (0)	1 (2)	<49 0 (0) (0	0 (0)	0 (0)	<50> 0 (0) (0 0
Grade <a>> b (c) Significant c	1: Slight 2: Moderate 3: Marked 4 a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 difference; *: $P \le 0.05$ **: $P \le 0.01$ Test of C	: Severe														

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0-105W)

ANIMAL : MOUSE Crj:BDF1 REPORT TYPE : A1 SEX

: MALE

PAGE: 8

Findings	Group Name No. of Animals on Study Grade 1 (%)	49 2	3 4	1(%)			<u>4</u> (%)	<u>_1</u>	<u>(</u>	50 2	9PM 3 (%)	<u>4</u> (%)	(1	50 2		<u>4</u> (%)
				··········		··· ··· ··											
etem]																	
cyst	4 (8)			3 (6)	0	0	0 (0)			0	0	0 0)			0	0	0 (0)
hyperplasia	0 (0)			1 (2)	0 (0)	0 (0)	0 (0)			0 0) (0	0 0)	(0 0) (0 0) (0 0)	0 (0)
Rathke pouch	1 (2)	0 (0) (0 0 0 0) (0)	1 (2)	0 (0)	0 (0)	0 (0)	(4) (0 (0 (0)	0 0)	(3 6) (0	0 0)	0
focal follicular cell hyperplasia	0 (0)			0 (0)	0	0	0 (0)	(())) (0	0	0 0)			0	0	0
extramedullary hematopoiesis	0 (0)			0 (0)	0	0	0 (0)			0	0	0 0)			0	0	0
spindle-cell hyperplasia				0 (0)	0 (0)	0 (0)	0 (0)			0 (0	0			0	0 0)	0
hyperplasia:cortical cell	5 (10)	3 (6) (0 0	5 (10)	3 (6)	0 (0)	0 (0)	(12	5 2) (1 2) (0	0 0)	(1	7 4) (4 8) (0 0)	0 (0)
	cyst hyperplasia Rathke pouch focal follicular cell hyperplasia extramedullary hematopoiesis spindle-cell hyperplasia	No. of Animals on Study Grade 1 (%) Stem] cyst 4 (8) hyperplasia 0 (0) Rathke pouch 1 (2) focal follicular cell hyperplasia 0 (0) extramedullary hematopoiesis 0 (0) spindle-cell hyperplasia 1 (2) hyperplasia:cortical cell 5	No. of Animals on Study	No. of Animats on Study	No. of Animals on Study 49 50 1 2 3 4 1 2 3 4 1 2 3 4 1 2 3 4 1 2 3 4 1 2 3 4 1 2 3 4 1 2 3 4 1 2 3 4 1 3 3 4 3 3 3 3 3 3 3	No. of Animals on Study	No. of Animals on Study 48 50 50 50 50 50 50 50 5	No. of Animals on Study	No. of Animats on Study	No. of Animats on Study	No. of Animals on Study	No. of Animals on Study 49 50 50 12 3 4 1 2					

(HPT150)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0-105W)

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

0rgan	Findings	Group Name No. of Animals on Study Grade 1 (%)	Contr 49 2 (%)		<u>4</u> (%)	1 (%)	3200 50 2 (%)) ppm) 3 (%)	4 (%)	1 (%)	8000 50 2 (%)) ppm) 3 (%)	<u>4</u> (%)	1 (%)	2000 5 2 (%)	0 ppm 0 3 (%)	<u>4</u> (%)
(Endocrine sy	vstem]																
adrena l	hyperplasia:medulla	(0)	<49: 0 (0) (0	0 (0)	1 (2)	<56 0 (0)	0	0 (0)	0 (0)	<50 0 (0)	0	0 (0)	0 (0)	0	0 (0)	0 (0)
[Reproductive	e system]																
testis	atrophy	0 (0)	<49 0 (0) (0	0	0 (0)	(5 0 (0)	0	0	1 (2)	<56 2 (4)	0	0 (0)	1 (2)	0	0 (0)	0 (0)
	mineralization	12 (24)	0 (0) (0 0)	0 (0)	6 (12)	0 (0)	0 (0)	0 (0)	7 (14)	1 (2)	0 (0)	(0)	11 (22)	0 (0)	0 (0)	0 (0)
epididymis	lymphocytic infiltration	0 (0)	<49 0 (0) (0	0 (0)	0 (0)	<5 1 (2)	0	0 (0)	0 (0)	<5 0 (0)	0	0 (0)	0 (0)	0		
	spermatogenic granuloma	0 (0)	3 (6) (0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)
prep/cli gl	duct ectasia	0 (0)	<49 5 (10) (0	0 (0)	0 (0)	<5 2 (4)	0	0	0 (0)	<5 1 (2)	0		0 (0)	2		0 (0)
Grade (a > b (c)	duct ectasia 1 : Slight 2 : Moderate a : Number of animals examined at b : Number of animals with lesion c : b / a * 100 difference ; * : P ≤ 0.05 **	3 : Marked 4 : Severe the site	5 (10) (0		(0)	2	0	0 (0)		1	0			2		0

ANIMAL : MOUSE Crj:BDF1

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

ALL ANIMALS (0-105W)

0rgan		Group Name Control No. of Animals on Study 49 Grade 1 2 3 4 (%) (%) (%) (%)	3200 ppm 50 1 2 3 4 (%) (%) (%) (%)	8000 ppm 50 1 2 3 4 (%) (%) (%) (%)	20000 ppm 50 1 2 3 4 (%) (%) (%) (%)
[Reproductive	ə system]				
prep/cli gl	inflammation	0 0 0 0 (0) (0) (0) (0)	(50) 0 1 0 0 (0) (2) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)
[Nervous sys	tem]				
brain	mineralization	449> 17 16 0 0 (35) (33) (0) (0)	(50) 18 24 0 0 (36) (48) (0) (0)	(50) 9 22 0 0 (18) (44) (0) (0)	<50> 14 29 0 0 * (28) (58) (0) (0)
[Special sens	se organs/appandage]				
Narder gl	degeneration	\(\lambda 49 \rangle \) \(1 0 0 0 \) \(2) \((0) (0) (0) \)	(50) 0 0 0 0 (0) (0) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)
	hyperplasia	0 0 0 0 0 (0) (0)	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 (0)	0 1 0 0 (0) (2) (0) (0)
[Musculoskele	etal system]				
muscle	mineralization	0 1 0 0 (0) (2) (0) (0)	(50) 1 0 0 0 (2) (0) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)	<50> 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 difference; *: P ≤ 0.05 **: P ≤				
(HPT150)					BAI

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0-105W)

ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1

SEX : MALE

·

0rgan	Group Name No. of Ani Grade Findings	Control mals on Study 49 1 2 3 4 (%) (%) (%) (%)	3200 ppm 50 1 2 3 4 (%) (%) (%) (%)	8000 ppm 50 1 2 3 4 (%) (%) (%) (%)	20000 ppm 50 1 2 3 4 (%) (%) (%) (%)
(Musculoske	letal system]				
muscle	inflammatory infiltration	0 0 0 0 (0) (0) (0) (0)	(50) 0 1 0 0 (0) (2) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)
[Body cavit	ies]				
adipose	hemorrhage	<49> 0 0 0 0 (0) (0) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)	(50) 0 1 0 0 (0) (2) (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; $*: P \le 0.05$ **: $P \le 0.01$ T	4 : Severe 'est of Chi Square			
(HPT150)					BAI

APPENDIX K 6

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

MOSUE: FEMALE: ALL ANIMALS

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

: MOUSE Crj:BDF1

ANIMAL REPORT TYPE : A1

SEX : FEMALE PAGE: 12

Organ	Findings	Group Name No. of Animals on Study Grade 1 (%)	Control 50 2 3 (%) (%)	<u>4</u> (%)	<u>1</u> (%)		3	<u>4</u> (%)	1 (%)	20000 50 2 (%)	3 (%)	<u>4</u> (%)	<u>1</u> (%)		00 ppr 50 <u>3</u> (%)		<u>4</u> %)
[Respiratory s	system]																
nasal cavit	atrophy	(0)	<50> 0 0 (0) (0)	0 (0)	0 (0) (0 0) (0 0)	0 (0) (<50) 0 0) (0	0 0)	0 (0)	0	50> 0 (0)		0 0)
	inflammation	0 (0)	0 0 (0)	0 (0)	0 (0) (0 0) (0 0)	0 (0) (1 2) (0	0 0)	0 (0)	0 (0)	0 (0)) (0 0)
	inflammatory infiltration	0 (0)	0 0	0 (0)	0 (0) (0 0) (0 0)	1 (2) (0	0	0 0)	0 (0)	0 (0)	0 (0)) (0 0)
	eosinophilic change:olfactory epith		0 0 (0)	0 (0)	1 (2) (1 2) (0 0) (0	1 (2) (0 0) (0	0	3 (6)	1 (2)	(0)		0 0)
	eosinophilic change:respiratory epi		4 0 (8) (0)	0 (0)	14 (28) (7 14) (0 0) (0 0)	14 (28) (10 20) (2 4) (0 0)	14 (28)	10 (20)	2 (4)		0 0)
	disarrangement:olfactory epithelium	(0)	0 0 (0)	0 (0)	0 (0) (0 0) (0 0)	1 (2) (0	0	0 0)	0 (0)	(0)	(0)		0 0)
	respiratory metaplasia:olfactory ep		0 0 (0)	0 (0)	0 (0) (0 0) (0 0)	0 (0) (0 (0	0	1 (2)	0 (0)	0 (0		0 0)
	respiratory metaplasia:gland	4 (8)	3 0 (6) (0)	0 (0)	6 (12) (0 0) (0 0)	2 (4) (2 4) (0	0 0)	5 (10)	4 (8)	0 (0		0 0)

Grade

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

^{1 :} Slight 2 : Moderate

^{3 :} Marked

^{4 :} Severe

⁽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)

ALL ANIMALS (0-105W)

ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1

SEX

: FEMALE

MAI E

PAGE: 13

Organ	Group Na No. of A Grade Findings	Animals on Study 50 1 2 3 4 (%) (%) (%) (%)	8000 ppm 50 1 2 3 4 (%) (%) (%) (%)	20000 ppm 50 1 2 3 4 (%) (%) (%) (%)	50000 ppm 50 1 2 3 4 (%) (%) (%) (%)
[Respiratory:	system]				
lung	congestion	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 0 1 0 0 (0) (2) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)
	hemorrhage	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (2) (0) (0) (0)	0 0 0 0 0 (0) (0)
	inflammatory infiltration	1 0 0 0 0 (2) (0) (0)	0 0 0 0 0 (0) (0)	0 1 0 0 (0) (0)	1 0 0 0 0 (2) (0) (0) (0)
	lymphocytic infiltration	0 0 0 0 0 (0) (0)	0 0 0 0 0 0 (0) (0)	1 0 0 0 0 (2) (0) (0)	1 0 0 0 0 0 (2) (0) (0)
	bronchiolar—alueolar cell hyperplasia	0 0 0 0 0 (0) (0)	1 0 0 0 0 (2) (0) (0) (0)	1 0 0 0 0 (2) (0) (0) (0)	0 0 0 0 0 (0) (0)
[Hematopoieti	c system]				
bone marrow	granulation	<50> 1 0 0 0 (2) (0) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)
spleen	atrophy	<50> 0 3 1 0 (0) (6) (2) (0)	<50> 0 0 1 0 (0) (0) (2) (0)	<50> 0 1 0 0 (0) (2) (0) (0)	<49> 0 0 2 0 0 0 0 4) (0)
Grade <a>> b (c) Significant d	1: Slight 2: Moderate 3: Marker a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 lifterence; $*:P \le 0.05$ **: $P \le 0.01$	d 4: Severe Test of Chi Square			

(HPT150)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0-105W)

ANIMAL : MOUSE Crj:BDF1 REPORT TYPE : A1

: FEMALE

Organ	Group Nam No. of An Grade Findings	e Control imals on Study 50 1 2 3 4 (%) (%) (%) (%)	8000 ppm 50 1 2 3 4 (%) (%) (%) (%)	20000 ppm 50 1 2 3 4 (%) (%) (%) (%)	50000 ppm 50 1 2 3 4 (%) (%) (%) (%)
 Hematopoie	etic system]				
spleen	deposit of melanin	<50> 1 1 0 0 (2) (2) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)
	extramedullary hematopoiesis	0 3 2 0 (0) (6) (4) (0)	3 4 4 0 (6) (8) (8) (0)	0 5 5 0 (0) (10) (10) (0)	2 5 1 0 (4) (10) (2) (0)
	follicular hyperplasia	6 1 1 0 (12) (2) (2) (0)	0 3 0 0*	2 1 2 0 (4) (2) (4) (0)	1 1 1 0 (2) (2) (0)
Circulator	ry system]				
neart	thrombus	<50> 0 1 0 0 (0) (2) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	(50) 1 0 0 0 (2) (0) (0) (0)	(50) 1 0 0 0 (2) (0) (0) (0)
	mineralization	1 0 0 0 0 (2) (3) (4)	0 0 0 0 0 0 (0) (0)	1 0 0 0 (2) (0) (0) (0)	1 0 0 0 0 (2) (0) (0) (0)
	granulation	0 0 0 0 0 0 (0) (0)	1 0 0 0 0 (2) (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0)
	arteritis	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)
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 Test of Chi Square			

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0-105W)

ANIMAL : MOUSE Crj:BDF1 REPORT TYPE : A1

SEX

: FEMALE

Groun Name Control 8000 nom 20000 nom 50000 nnm

Organ	Findings	Group Name Control	8000 ppm 50 1 2 3 4 (%) (%) (%) (%)	20000 ppm 50 1 2 3 4 (%) (%) (%) (%)	50000 ppm 50 1 2 3 4 (%) (%) (%) (%)
[Digestive :	system]				
tooth	cyst	<50> 0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	<50> 0 1 0 0 (0) (2) (0) (0)	0 0 0 0 (0) (0) (0) (0)
	inflammation	3 0 0 0 0 (6) (6) (7)	0 0 0 0 0 0 (0) (0)	1 0 0 0 0 (2) (0) (0) (0)	2 0 0 0 0 (4) (0) (0) (0)
	foreign body granuloma	0 0 0 0 0 (0) (0)	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (2) (0) (0) (0)
	dysplasia	1 0 0 0 0 (2) (0) (0)	1 1 0 0 (2) (2) (0) (0)	2 1 1 0 (4) (2) (2) (0)	1 3 2 0 (2) (6) (4) (0)
tongue	arteritis	<49> 0 0 0 0 0 0 0 0 0 0 0	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	(50) 1 0 0 0 (2) (0) (0) (0)
stomach	hyperplasia:forestomach	<pre></pre>	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 2 1 0 0 (4) (2) (0) (0)
	inflammation:forestomach	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) (2) (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 **:				

(HPT150)

BAIS3

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

ANIMAL : MOUSE Crj:BDF1 ALL ANIMAL

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

REPORT TYPE : A1

SEX : FEMALE

PAGE: 16

Organ		Group Name No. of Animals on Study Grade 1 (%)	Control 50 2 3 4 (%) (%)	8000 ppm 50 1 2 3 4 (%) (%) (%) (%)	20000 ppm 50 1 2 3 4 (%) (%) (%) (%)	50000 ppm 50 1 2 3 4 (%) (%) (%) (%)
[Digestive sy	stem]					
stomach	erosion:glandular stomach	1 (2) (<49> 0 0 0 (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 0 0 0 0 0 0 0
	hyperplasia:glandular stomach	(4) (1 0 0 (2) (0) (0)	4 0 0 0 0 (8) (0) (0) (0)	4 0 0 0 0 (8) (0) (0) (0)	1 0 0 0 0 (2) (0) (0)
small intes	ulcer	(0) ((50) 0 1 0 (0) (2) (0)	(50) 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)
liver	angiectasis	0 (0) (<50> 0 2 0 (0) (4) (0)	<50> 0 0 1 0 (0) (0) (2) (0)	<50> 0 3 0 0 (0) (6) (0) (0)	<50> 2 1 0 0 (4) (2) (0) (0)
	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 0 0 (2) (0) (0) (0)
	granulation	7 (14) (18 3 0 (36) (6) (0)	6 12 0 0 (12) (24) (0) (0)	14 5 1 0 ** (28) (10) (2) (0)	6 10 1 0 (12) (20) (2) (0)
	extramedullary hematopoiesis	1 (2) (0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
Grade < a > b (c)	1: Slight 2: Moderate 3 a: Number of animals examined at the s b: Number of animals with lesion c: b / a * 100	: Marked 4 : Severe				

(HPT150)

SEX

: MOUSE Crj:BDF1

ANIMAL REPORT TYPE : A1 : FEMALE HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)

Group Name Control 8000 ppm 20000 ppm 50000 ppm No. of Animals on Study 50 50 50 50 2 3 Findings_ (%) 0rgan (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) [Digestive system] Liver <50> <50> <50> <50> clear cell focus 1 1 0 3 1 1 0 0 3 0 1 1 10 3 1 * (2)(2)(0)(6) (2)(2)(0)(0) (0)(6)(0)(2) (2)(20)(6)(2) acidophilic cell focus 1 1 0 3 0 0 1 0 0 1 1 3 (0)(0)(2)(2) (2)(2)(0)(6) (0)(0)(2)(0) (0)(2)(2)(6) basophilic cell focus 2 4 0 0 * 1 1 0 0 0 8 4 2 ** (0) (0) (0) (0) (2)(2)(0)(0) (4)(8)(0)(0) (0)(16)(8)(4) pancreas <50> atrophy 0 0 0 0 0 0 0 0 0 0 1 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (2)(0)(0)(0) [Urinary system] kidney <50> ⟨50⟩ <50> ⟨50⟩ atrophy 0 0 0 0 0 0 1 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(2)(0) (0)(0)(0)(0) hyaline droplet 9 1 0 0 8 0 0 0 6 0 0 0 (10) (0) (0) (0) (18) (2) (0) (0) (16) (0) (0) (0) (12) (0) (0) (0) Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe a: Number of animals examined at the site (a) 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

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

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1

SEX : FEMALE

0rgan		co Name Control of Animals on Study 50 = 1 2 3 4 (%) (%) (%) (%)	8000 ppm 50 1 2 3 4 (%) (%) (%) (%)	20000 ppm 50 1 2 3 4 (%) (%) (%) (%)	50000 ppm 50 1 2 3 4 (%) (%) (%) (%)
[Urinary sys	tem]				
ridney	deposit of amyloid	<50> 0 0 0 0 (0) (0) (0) (0)	(50) 0 1 0 0 (0) (2) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)
	hyaline cast	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (2) (0) (0) (0)
	lymphocytic infiltration	1 0 0 0 0 (2) (0) (0) (0)	2 0 0 0 0 (4) (0) (0) (0)	2 0 0 0 0 (4) (0) (0) (0)	0 1 0 0 (0) (0)
	hydranephrosis	0 2 0 0 (0) (4) (0) (0)	1 1 0 0 (2) (2) (0) (0)	0 0 1 0 (0) (0) (0)	0 0 1 1 (0) (0) (2) (2)
	tubular necrosis	0 0 0 0 0 (0) (0)	0 1 0 0 (0) (2) (0) (0)	0 1 0 0 (0) (2) (0) (0)	0 0 0 0 0 0 (0) (0)
	mineralization:papilla	2 0 0 0 0 (4) (60) (60)	2 0 0 0 0 (4) (0) (0) (0)	0 0 0 0 0 (0) (0)	3 0 0 0 0 (6) (6) (0) (0)
	mineralization:pelvis	0 0 0 0 0 (0) (0)	1 1 0 0 (2) (2) (0) (0)	0 0 0 0 0 (0) (0)	0 1 0 0 (0) (2) (0) (0)
rin bladd	lymphocytic infiltration	<50> 0 0 0 0 (0) (0) (0) (0)	(50) 1 0 0 0 (2) (0) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)	(49) 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			

STUDY NO. : 0243 ANIMAL : MOUSE Crj:BDF1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0-105W)

REPORT TYPE : A1

SEX

: FEMALE

Organ	Findings	Group Name No. of Animals on Stud Grade	1	Contr 50 2 (%)	3 (%)	<u>4</u> (%)	1 (%)	8000 50 2 (%)		<u>4</u> (%)	1(%)	2000 5 2 (%)	0 ppm 0 3 (%)	<u>4</u> (%)	1 (%)	50000 i 50 2 (%)	3	<u>4</u> (%)
[Urinary syst	nem]																	
urin bladd	hyaline droplet degeneration:superfional epithelium		0	<50> 0 0) (0	0 (0)	5 (10) (<50 0 0) (0	0 (0)	12 (24) (<5 0 0	0	0 ** (0)	24 (49) (<49> 0 0) (0	0 ** 0)
(Endocrine sy	vstem]																	
pituitary	cyst	(7 14) (<50> 0 0) (0		8 (16) (<50 0 0) (0	0	8 (16) (0			6 (12) (<50> 0 0) (0	0
	hyperplasia	(1 2) (0 (0	0 (0)	1 (2)	0 (0 (0)	0 (0)	1 (2) (0 (0)	0 (0)	0 (0)	(0) (0		0 0)
	Rathke pouch	(0	0 (0	0 (0)	(0)	0 (0 (0)	0 (0)	1 (2) (0 (0)	0 (0)	0 (0)	0 (0) (0	0 (0
adrena l	hyperplasia:cortical cell	(0	<50) 0 0) (0	0 (0)	1 (2)	<50 1 2) (0		0 (0) (0		0 (0)	0 (0) (<50> 0 0) (0	0 0)
	focal fatty change:cortex	(0	0 (0	0	0 (0)	0 (0 (0)	0 (0)	1 (2) (0 (0)	0 (0)	0 (0)	0 (0) (0	0	0 0)
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 **: F																	

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

ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1

SEX

: FEMALE

Organ	Group Name No. of An Grade Findings	Control imals on Study 50	8000 ppm 50 1 2 3 4 (%) (%) (%) (%)	20000 ppm 50 $\frac{1}{(\%)}$ $\frac{2}{(\%)}$ $\frac{3}{(\%)}$ $\frac{4}{(\%)}$	50000 ppm 50 1 2 3 4
rgan	rindings	(%) (%) (%)	(%) (%) (%)	(%) (%) (%)	(%) (%) (%)
Reproducti	ive system]				
ovary	angiectasis	<50> 0 1 0 0 (0) (2) (0) (0)	(50) 0 1 0 0 (0) (2) (0) (0)	<50> 0 0 0 0 (0) (0) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)
	cyst	4 0 0 0 0 (8) (0) (0) (0)	5 0 0 0 (10) (0) (0) (0)	7 0 0 0 (14) (0) (0) (0)	4 0 0 0 0 (8) (0) (0) (0)
	mineralization	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)
ıterus	dilatation	<50> 0 1 0 0 (0) (2) (0) (0)	(50) 0 0 0 0 (0) (0) (0) (0)	(50) 0 1 0 0 (0) (2) (0) (0)	<50> 0 2 0 0 (0) (4) (0) (0)
	cystic endometrial hyperplasia	13 14 0 0 (26) (28) (0) (0)	13 11 0 0 (26) (22) (0) (0)	18 13 0 0 (36) (26) (0) (0)	12 15 0 0 (24) (30) (0) (0)
	xanthogranuloma	0 0 0 0 0 (0) (0)	0 1 0 0 (0) (2) (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 0 (0) (0)
(Nervous s	ystem]				
orain	mineralization	<50> 4 13 0 0 (8) (26) (0) (0)	<50> 8 13 0 0 (16) (26) (0) (0)	(50) 10 10 0 0 (20) (20) (0) (0)	<50> 6 14 0 0 (12) (28) (0) (0)
Grade <a> b	1: Slight 2: Moderate 3: Marked a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	4 : Severe			

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1

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

ALL ANIMALS (0-105W)

Group Name Control 8000 ppm 20000 ppm 50000 ppm

		No. of Animals on Stu	ıdy	50	1			50	0				50	ı			5	0	
		Grade	1	2	3		1	2		4	_1	<u> </u>	2	3	4	_1_	2	3	4
Organ	Findings		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%	6)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

[Special sense organs/appandage]

llarder gl degeneration

<50> ⟨50⟩ ⟨50⟩ <50> 0 0 0 0 0 0 0 0 0 1 0 0 0 (2)(0)(0)(0) (0)(0)(0)(0) (2)(0)(0)(0) (0)(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) (2)(0)(0)(0)

[Musculoskeletal system]

bone

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

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

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

b: 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

APPENDIX K 7

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

MOSUE: MALE: SACRIFICED ANIMALS

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

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

0rgan	No	oup Name . of Animals on Study ade 1 (%)	Contro 41 2 (%)	3 (%)	<u>4</u> (%)	<u>1</u> (%)		0 ppm 1 3 (%)	<u>4</u> (%)	1 (%)	800 3 2 (%)	0 ppm 7 3 (%)	<u>4</u> (%)	1(%)	2 %)		<u>4</u> (%)
[Respiratory	system]																
nasal cavit	inflammation	(2)	(41) 0 (0) (0	0 0)	0 (0)	0		0 (0)	0 (0)	<3 0 (0)	0	0 (0)	0 (0)	<422 0 0) (0	0 (0)
	eosinophilic change:olfactory epithelium		1 (2) (0	0	6 (15)	0 (0)	0 (0)	0 (0)	4 (11)	0 (0)	0 (0)	0 (0)	3 (7)	0 0) (0 0)	0 (0)
	eosinophilic change:respiratory epitheli		2 (5) (1 2) (0	4 (10)	0 (0)	0 (0)	0 (0)	1 (3)	1 (3)		0 (0)	6 (14		0 0)	0 (0)
	respiratory metaplasia:olfactory epithel		1 (2) (0 (0	7 (17)	0 (0)	0 (0)	0 (0)	1 (3)	3 (8)	0 (0)	0 (0)	10 (24)	2 5) (0 0)	0 (0)
	respiratory metaplasia:gland	7 (17)	2 (5) (0 (0	11 (27)	2 (5)	0 (0)	0 (0)	5 (14)	3 (8)	1 (3)	0 (0)	10 (24)	2 5) (1 2)	0 (0)
lung	bronchiolar—alveolar cell hyperplasia	(2)	<41> 0 (0) (0	0 0)	2 (5)	0		0 (0)	0 (0) (0	7> 0 (0)	0 (0)	0 (0)	<42: 0 0) (0	0 (0)
[Hematopoieti	c system]																
spleen	deposit of melanin	0 (0)	<41> 2 (5) (0	0 0)	2 (5)	2		0 (0)	0 (0) (0	7> 0 (0)	0 (0)	1 (2)	<422 0 0) (0	0 (0)
Grade (a) b (c)	1: Slight 2: Moderate 3: a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 lifference; $*: P \le 0.05$ **: $P \le 0$										<u></u>						

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

: MOUSE Crj:BDF1

ANIMAL REPORT TYPE : A1 SACRIFICED ANIMALS (105W)

SEX : MALE PAGE: 2 Group Name Control 3200 ppm maa 0008 20000 ppm No. of Animals on Study 41 41 37 42 Findings_ (%) (%) (%) [Hematopoietic system] spleen <41> <41> ⟨37⟩ <42> extramedullary hematopoiesis 0 0 0 0 2 0 0 0 0 0 0 1 0 0 1 (2)(0)(0)(0) (0)(5)(0)(0) (3)(0)(0)(0) (0)(2)(0)(0) follicular hyperplasia 3 1 2 0 1 0 2 0 3 3 1 0 3 2 1 0 (7)(2)(5)(0) (2)(0)(5)(0) (8)(8)(3)(0) (7) (5) (2) (0)

[Digestive system]

tooth	cyst	<pre></pre>	(41) 1 1 0 0 (2) (2) (0) (0)	<37> 0 0 0 0 0 0 0 0 0 0 0 0	(42> 0 0 0 0 (0) (0) (0) (0)
	ìnflammation	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (3) (0) (0) (0)	5 0 0 0 (12) (0) (0) (0)
	foreign body granuloma	1 0 0 0 0 (2) (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	3 1 0 0 (7) (2) (0) (0)
	dysplasia	13 2 0 0 (32) (5) (0) (0)	7 2 0 0 (17) (5) (0) (0)	4 0 2 0 * (11) (0) (5) (0)	8 4 0 0 (19) (10) (0) (0)
tongue	arteritis	<41> 0 0 0 0 0 0 0 0 0 0 0 0	(41) 0 0 0 0 (0) (0) (0) (0)	37> 1 0 0 0 (3) (0) (0) (0)	<42> 0 0 0 0 0 0 0 0 0 0 0

Grade 1: Slight

a: Number of animals examined at the site

b: Number of animals with lesion

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

(HPT150)

^{2 :} Moderate

^{3 :} Marked

^{4 :} Severe

⁽a) b

⁽c) c:b/a*100

STUDY NO. : 0243 HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL : MOUSE Crj:BDF1 SACRIFICED ANIMALS (105W)

REPORT TYPE : A1 SEX

: MALE PAGE: 3

Organ	Findings_	Group Name No. of Animals on Study Grade $\frac{1}{(\%)}$	Control 41 2 3 4 (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	8000 ppm 37 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
[Digestive s	vetem]		· .			
stomach	ulcer:forestomach	1 (2) (<41> 0 0 0 (0) (0) (0)	<41> 0 1 0 0 (0) (2) (0) (0)	<37> 0 0 0 0 0 0 0 0 0 0 0 0	<42> 0 0 0 0 0 0 0 0 0 0 0 0 0
	hyperplasia:forestomach	0 (0) (0 0 0 0 (0) (0)	1 1 0 0 (2) (2) (0) (0)	0 0 0 0 0 (0) (0) (0)	1 0 0 0 0 (2) (0) (0) (0)
	hyperplasia:glandular stomach	1 (2) (1 0 0 (2) (0) (0)	0 2 0 0 (0) (5) (0) (0)	2 1 0 0 (5) (3) (0) (0)	1 1 0 0 (2) (2) (0) (0)
iver	angiectasis	0 (0) (<41> 0 1 0 (0) (2) (0)	<41> 0 0 0 0 (0) (0) (0) (0)	<37> 0 0 0 0 0 (0) (0) (0) (0)	<42> 0 0 0 0 0 0 0 0 0 0 0
	leucocytic infiltration	0 (0) (0 0 0 0 (0) (0)	0 0 0 0 (0) (0) (0)	1 0 0 0 (3) (0) (0) (0)	0 0 0 0 0 (0) (0) (0)
	granulation	10 (24) (1 0 0 (2) (0) (0)	8 2 0 0 (20) (5) (0) (0)	7 0 0 0 (19) (0) (0) (0)	7 0 0 0 (17) (0) (0) (0)
	clear cell focus	0 (0) (1 0 0 (2) (0) (0)	0 0 0 1	0 0 1 0 (0) (0) (3) (0)	0 0 0 0 0 (0) (0) (0)
	basophilic cell focus	0 (0) (0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0) (0)	0 1 0 0

.a.> b

b: Number of animals with lesion

c:b/a*100 (c)

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

(HPT150)

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

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX

: MALE PAGE: 4

Organ	Findings	Group Name No. of Animals on Study Grade 1 (%)	Con 4 2 (%)	1 3 (%)	<u>4</u> (%)	1 (%)	3200 4: 2 (%)	3 (%)	<u>4</u> (%)	<u> </u>	<u>(</u>)	8000 37 2 (%)	3 (%)	<u>4</u> (%)	-	1 (%)	2000	0 ppm 2 3 (%)	4
[Urinary sy	stem]																		
kidney	hyperplasia:tubular epithelial cell	0 (0)	0 (0)	0 (0)	0 (0)	0 (0) (<4: 0 (0)	0	0 (0)		l 3) (<37 0 0) ("> 0 (0) (0		1 2) (0	0 (0)	0 (0)
	infarct	1 (2)	0 (0)	0 (0)	0 (0)	0 (0) (0 (0)	0 (0)	0))) (0	0 (0) (0 (0)	(0	0 0)	0 (0)	0 (0)
	hyaline droplet	(0)	0 (0)	0 (0)	0 (0)	(0) (0 (0)	0 (0)	0 (0)))) (0	0	0	(1 2) (0 0)	0 (0)	0 (0)
	basophilic change	16 (39)	0 (0)	0 (0)	0 (0)	21 (51)	0	0 (0)	0 (0)	21		0	0	0		19 45) (0 (0)	0 (0)	0 (0)
	inflammation	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)) ()	1 3)	0	0 (0)	(0	0 (0)	0 (0)	0 (0)
	lymphocytic infiltration	(0)	1 (2)	0 (0)	0 (0)	0 (0)	0	0 (0)	0 (0)	(() (0)	0	0 (0)	0	(0	0 (0)	0 (0)	0 (0)
	vacuolization of proximal tubule	21 (51)	1 (2)	0 (0)	0 (0)	13 (32)	0 (0)	0 (0)	0 (0)		0 0) (0	0 (0)	0 ** (0)	(0	0 (0)	0 (0)	0 *
	hydranephrasis	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0	0 (0)	0 (0)		3 8) (2 5)	0 (0)	0 (0)	(1 2) (0 (0)	1 (2)	0 (0)

(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)

SEX

ANIMAL : MOUSE Crj:BDF1

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

REPORT TYPE : A1

: MALE

Organ	Group Name No. of Anima Grade	Control als on Study 41 1 2 3 4 (%) (%) (%) (%)	3200 ppm 41 1 2 3 4 (%) (%) (%) (%)	8000 ppm 37 1 2 3 4 (%) (%) (%) (%)	20000 ppm 42 1 2 3 4 (%) (%) (%) (%)
[Urinary syst	tem]				
kidney	mineralization:papilla	\(\langle 41 \rangle \) \(1 0 0 0 \) \(2) \((0) (0) (0) \)	1 0 0 0 (2) (0) (0) (0)	<pre></pre>	3 0 0 0 (7) (0) (0) (0)
	mineralization:pelvis	3 0 0 0 (7) (0) (0) (0)	1 0 0 0 0 (2) (0) (0)	0 0 0 0 0 (0) (0)	4 0 0 0 (10) (0) (0) (0)
	mineralization:cortex	30 1 0 0 (73) (2) (0) (0)	29 1 0 0 (71) (2) (0) (0)	30 3 0 0 (81) (8) (0) (0)	31 0 0 0 (74) (0) (0) (0)
urin bladd	hyaline droplet degeneration:superficial cell of 1 ional epithelium	transit 0 0 0 0 0 (0) (0) (0) (0)	26 0 0 0 ** (63) (0) (0) (0)	30 4 0 0 ** (81) (11) (0) (0)	(42) 16 26 0 0 ** (38) (62) (0) (0)
[Endocrine s	ystem]				
pituitary	angiectasis	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)	(42> 0 0 0 0 (0) (0) (0) (0)
	cyst	3 2 0 0 (7) (5) (0) (0)	3 0 0 0 0 (7) (0) (0) (0)	4 0 0 0 (11) (0) (0) (0)	7 0 0 0 (17) (0) (0) (0)
Grade <a>> b (c) 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; $*: P \le 0.05$ **: $P \le 0.01$ Test	4 : Severe st of Chi Square			

(HPT150)

ANIMAL : MOUSE Crj:BDF1

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

REPORT TYPE : A1 SEX : MALE

PAGE: 6

Organ	Findings	Group Name Co No. of Animals on Study Grade 1 2 (%) (%)	ontrol 41 <u>3</u>) (%)	4 (%)		00 ppm 11 3 4 (%) (%)	1(%)	8000 37 2 (%)	3 4 (%) (%)	20000 ppm 42 1 2 3 4 (%) (%) (%) (%)
[Endocrine s	ystem]									
pituitary	hyperplasia		(41> 0) (=0) (0 0) (. 0	0 0 (0) (0)	0 (0)	<36> 0 (0) (0 0	<42> 0 0 0 0 0 0 0 0 0 0 0 0
	Rathke pouch	1 0 (2) (0)	0 (0) (0 0) (t 0 2) (0)	0 0 (0)	2 (6)	0 (0) (0 0	2 0 0 0 0 (5) (0) (0) (0)
thyroid	focal follicular cell hyperplasia		(41> 0) (0) (0 (0 0	0 0 (0) (0)	0 (0)	<37> 0 (0) (0 0 0 0) (0)	<pre></pre>
adrenal	extramedullary hematopoiesis		(41> 0) (0) (0 0) (0 (0 0 (0) (0)	0 (0)	<37> 0 (0) (42> 1 0 0 0 (2) (0) (0) (0)
	spindle-cell hyperplasia	1 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)
	hyperplasia:cortical cell	5 3 (12) (7		0 0) (1	5 3 2) (7)	0 0 (0)	6 (16)	1 (3) (0 0	7 4 0 0 (17) (10) (0) (0)
	hyperplasia:medulla	0 0	0 (0) (0 (1 0 2) (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:b/a*100

(c)

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

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1

SACRIFICED ANIMALS (105W)

SEX : MALE

Organ	Findings	Group Name Control No. of Animals on Study 41 Grade 1 2 3 4 (%) (%) (%) (%)	3200 ppm 41 1 2 3 4 (%) (%) (%) (%)	8000 ppm 37 1 2 3 4 (%) (%) (%) (%)	20000 ppm 42 1 2 3 4 (%) (%) (%) (%)
[Reproductive	system]				
testis	atrophy	<41> 0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	<37> 1 2 0 0 (3) (5) (0) (0)	<42> 1 0 0 0 (2) (0) (0) (0)
	mineralization	12 0 0 0 (29) (0) (0) (0)	6 0 0 0 (15)(0)(0)(0)	6 1 0 0 (16) (3) (0) (0)	8 0 0 0 0 (19) (0) (0) (0)
epididymis	lymphocytic infiltration	<pre></pre>	0 1 0 0 (0) (2) (0) (0)	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)
	spermatogenic granuloma	0 2 0 0 (0) (5) (0) (0)	1 0 0 0 0 (2) (0) (0)	0 2 0 0 (0) (5) (0) (0)	1 0 0 0 0 (2) (0) (0) (0)
prep/cli gl	duct ectasia	<pre></pre>	<pre></pre>	<37> 0 1 0 0 (0) (3) (0) (0)	0 2 0 0 (0) (5) (0) (0)
	inflammation	0 0 0 0 0 (0)	0 1 0 0 (0) (2) (0) (0)	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
(Nervous syste	em]				
brain	mineralization	<pre></pre>	(41) 15 21 0 0 (37) (51) (0) (0)	<pre></pre>	\$\begin{array}{cccccccccccccccccccccccccccccccccccc
<a>> b (c)	1: Slight 2: Moderate a: Number of animals examined at the b: Number of animals with lesion c: b / a * 100 ifference; *: P ≤ 0.05 **: I	3: Marked 4: Severe e site P ≤ 0.01 Test of Chi Square			

(HPT150)

BAISS

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

ANIMAL : MOUSE Crj:BDF1 REPORT TYPE : A1 SEX

: MALE

)rgan	Findings	Group Name No. of Animals on Study Grade 1 (%)		4 <u>1</u> (%)	3200 ppm 41 2 3 4 (%) (%) (%)	8000 37 1 2 (%) (%)	3 4 (%) (%)	20000 ppm 42 1 2 3 4 (%) (%) (%) (%)
[Special sens	se organs/appandage]							
farder gl	degeneration	1 (2) (<41> 0 0 0 (0) (0) (0 0	<41> 0 0 0 (0) (0) (0)	37> 0 0 (0) (0) (0 0	0 0 0 0 (0) (0) (0) (0)
	hyperplasia	(0) (0 0 0	0 0 0	0 0 0 (0) (0)	0 0 (0) (0 0 0 0) (0)	0 1 0 0 (0) (0)
Body cavitio	[se							
adipose	hemorrhage	(0) (<41> 0 0 0 (0) (0) (0 0 0	<41> 0 0 0 (0) (0) (0)	(37) 0 1 (0) (3) (0 0	<42> 0 0 0 0 0 0 0 0 0 0 0
Grade (a> b	1: Slight 2: Moderate 3 a: Number of animals examined at the s b: Number of animals with lesion c: b/a*100	: Marked 4 : Severe ite						

APPENDIX K 8

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

MOSUE: FEMALE: SACRIFICED ANIMALS

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1

: FEMALE

PAGE: 9

Organ	,	Froup Name Control Io. of Animals on Study 35 Frade 1 2 3 4 (%) (%) (%) (%)	8000 ppm 31 1 2 3 4 (%) (%) (%) (%)	20000 ppm 34 1 2 3 4 (%) (%) (%) (%)	50000 ppm 34 1 2 3 4 (%) (%) (%) (%)
[Respiratory	system]				
nasal cavit	atrophy	<35> 0 0 0 0 (0) (0) (0) (0)	(31) 0 1 0 0 (0) (3) (0) (0)	<34> 0 0 0 0 0 0 0 0 0 0 0	<34> 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)
	eosinophilic change:olfactory epitheliu	2 0 0 0 (6) (0) (0) (0)	1 1 0 0 (3) (3) (0) (0)	1 0 0 0 0 (3) (0) (0) (0)	2 1 0 0 (6) (3) (0) (0)
	eosinophilic change:respiratory epithel	8 3 0 0 (23) (9) (0) (0)	9 5 0 0 (29) (16) (0) (0)	10 8 2 0 (29) (24) (6) (0)	12 9 2 0 * (35) (26) (6) (0)
	disarrangement:olfactory epithelium	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)
	respiratory metaplasia:olfactory epithe	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:gland	4 2 0 0 (11) (6) (0) (0)	3 4 0 0 (10) (13) (0) (0)	2 2 0 0 (6) (6) (6) (0) (0)	5 2 0 0 (15) (6) (0) (0)
lung	inflammatory infiltration	<35> 1 0 0 0 (3) (0) (0) (0)	31> 0 0 0 0 (0) (0) (0) (0)	<34> 0 0 0 0 (0) (0) (0) (0)	<34> 0 0 0 0 0 0 0 0 0 0 0
Grade (a) b (c)	1: Slight 2: Moderate 3: a: Number of animals examined at the sib: Number of animals with lesion c: b / a * 100	: Marked 4 : Severe te			

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 Crj:BDF1

REPORT TYPE : A1 SEX

: FEMALE

PAGE: 10

0rgan	Findings	Group Name No. of Animals on Study Grade 1 (%)	Control 35 2 3 4 (%) (%) (%)	8000 ppm 31 1 2 3 4 (%) (%) (%) (%)	20000 ppm 34 1 2 3 4 (%) (%) (%) (%)	50000 ppm 34 1 2 3 4 (%) (%) (%) (%)
[Respiratory:	system]	,				
lung	lymphocytic infiltration	0 (0) (<35> 0 0 0 0) (0) (0)	<31> 0 0 0 0 (0) (0) (0) (0)	<34> 1 0 0 0 (3) (0) (0) (0)	34> 1 0 0 0 (3) (0) (0) (0)
	bronchiolar-alveolar cell hyperplasia		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 (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
[Hematopoieti	c system]					
bone marrow	granulation	1 (3) (<35> 0 0 0 0) (0) (0)	<pre></pre>	34> 0 0 0 0 (0) (0) (0) (0)	34> 0 0 0 0 (0) (0) (0) (0)
spleen	deposit of melanin	1 (3) (<35> 1 0 0 3) (0) (0)	31> 0 0 0 0 (0) (0) (0) (0)	<34> 0 0 0 0 0 0 0 0 0 0	<33> 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	2 1 1 0 (6) (3) (3) (0)	0 1 0 0 (0) (3) (0) (0)	2 2 0 0 (6) (6) (6) (0) (0)
	follicular hyperplasia	5 (14) (1 1 0 3) (3) (0)	0 3 0 0 (0) (10) (0) (0)	2 1 2 0 (6) (3) (6) (0)	1 1 1 0 (3) (3) (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 Hifference: *: P ≤ 0.05 **: P					

(HPT150)

ANIMAL : MOUSE Crj:BDF1

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

PAGE: 11 Group Name Control mag 0008 20000 ppm 50000 ppm No. of Animals on Study 35 31 34 34 2 3 2 3 2 3 (%) (%) (%) (%) (%) 0rgan_ Findings_ (%) (%) (%) (%) (%) [Circulatory system] heart <35> <31> <34> thrombus 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) mineralization 0 0 0 0 0 0 0 0 0 1 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (3)(0)(0)(0) [Digestive system] tooth <35> <31> <34> cyst 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) inflammation 0 0 2 0 0 0 (6)(0)(0)(0) (0)(0)(0)(0) (3)(0)(0)(0) (6)(0)(0)(0) foreign body granuloma 0 0 0 0 0 0 0 1 0 0 0 (0) (0) (0) (0) (0)(0)(0)(0) (0)(0)(0)(0) (3)(0)(0)(0) dysplasia 0 1 0 1 2 (3)(0)(0)(0) (0)(0)(0)(0) (3)(0)(3)(0) (3)(6)(6)(0) stomach ⟨31⟩ <34> <34> hyperplasia:forestomach 1 0 0 0 0 0 0 0 0 0 2 1 0 0 (0)(3)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (6)(3)(0)(0)

Grade

1: Slight

2 : Moderate

3 : Marked

4 : Severe

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

b

b: Number of animals with lesion

(c) c:b/a*100

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

(HPT150)

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

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX

: FEMALE

PAGE: 12

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

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

ANIMAL : MOUSE Crj:BDF1

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

REPORT TYPE : A1

SEX : FEMALE

Organ	Group Na No. of A Grade Findings_	me Control nimals on Study 35 1 2 3 4 (%) (%) (%) (%)	8000 ppm 31 1 2 3 4 (%) (%) (%) (%)	20000 ppm 34 1 2 3 4 (%) (%) (%) (%)	50000 ppm 34 1 2 3 4 (%) (%) (%) (%)
[Digestive s	system]				
Liver	acidophilic cell focus	355 0 0 1 1 0 0 0 0 3 (3)	31> 1 1 0 2 (3) (3) (0) (6)	34> 0 0 1 0 (0) (0) (3) (0)	(34) 0 1 1 2 (0) (3) (3) (6)
	basophilic cell focus	0 0 0 0 0 0 (0) (0)	1 1 0 0 (3) (3) (0) (0)	2 4 0 0 * (6) (12) (0) (0)	0 8 3 2 ** (0) (24) (9) (6)
pancreas	atrophy	<35> 0 0 0 0 (0) (0) (0) (0)	(31) 0 0 0 0 (0) (0) (0) (0)	(34) 0 0 0 0 (0) (0) (0) (0)	34> 1 0 0 0 (3) (0) (0) (0)
(Urinary sys	stem]				
kidney	atrophy	<35> 0 0 0 0 (0) (0) (0) (0)	(31) 0 0 0 0 (0) (0) (0) (0)	(34) 0 0 1 0 (0) (0) (3) (0)	<pre></pre>
	hyaline droplet	1 0 0 0 0 (3) (0) (0)	1 1 0 0 (3) (3) (0) (0)	1 0 0 0 0 (3) (0) (0) (0)	0 0 0 0 0 (0) (0)
	deposit of amyloid	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 (0) (0)	0 0 0 0 0 (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; *: $P \le 0.05$ **: $P \le 0.01$	d 4 : Severe Test of Chi Square			

(HPT150)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1

SEX : FEMALE

PAGE: 14

Organ	Group Name No. of Animals on S Grade Findings	Control tudy 35 1 2 3 4 (%) (%) (%) (%)	8000 ppm 31 1 2 3 4 (%) (%) (%) (%)	20000 ppm 34 $\frac{1}{(\%)}$ $(\%)$ $(\%)$ $(\%)$ $(\%)$	50000 ppm 34 1 2 3 4 (%) (%) (%) (%)
Ul gali	riiuiigs	(%) (%) (%)	(%) (%) (%)	(%) (%) (%)	(%) (%) (%)
[Urinary syst	em]				
kidney	hyaline cast	355 0 0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	<pre></pre>	34> 1 0 0 0 (3) (0) (0) (0)
	lymphocytic infiltration	1 0 0 0 0 (3) (0) (0)	2 0 0 0 0 (6) (0) (0) (0)	2 0 0 0 0 (6) (6) (0) (0)	0 1 0 0 (0) (0)
	hydronephrosis	0 2 0 0 (0) (6) (0) (0)	1 0 0 0 0 (3) (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
	mineralization:papilla	2 0 0 0 0 (6) (6) (70) (70)	2 0 0 0 0 (6) (6) (7) (7)	0 0 0 0 0 (0) (0)	2 0 0 0 0 (6) (6) (70) (70)
	mineralization:peluis	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 0 0 0 (0) (0)
urin bladd	lymphocytic infiltration	<35> 0 0 0 0 (0) (0) (0) (0)	31> 1 0 0 0 (3) (0) (0) (0)	<34> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<pre></pre>
	hyaline droplet degeneration:superficial cell of transit ional epithelium	0 0 0 0 0 0 (0) (0)	3 0 0 0 0 (10) (0) (0)	11 0 0 0 ** (32) (0) (0) (0)	20 0 0 0 ***
(Endocrine sy	stem]				
pituitary	cyst	<pre></pre>	<pre></pre>	34> 6 0 0 0 (18) (0) (0) (0)	\$\\ \ \ 5 \ \ 0 \ \ 0 \ \ (15) \ (0)

(HPT150)

(c)

c:b/a*100

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

SEX

: MOUSE Crj:BDF1

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

ANIMAL REPORT TYPE : A1

: FEMALE

Group Name Control mag 0008 20000 ppm 50000 ppm No. of Animals on Study 35 31 34 34 Grade 2 3 Findings (%) (%) (%) (%) (%) (%) (%) (%) Organ_ [Endocrine system] pituitary <35> (31) (34) <34> 0 0 0 0 0 0 hyperplasia 0 0 0 1 0 0 0 0 (3)(0)(0)(0) (3)(0)(0)(0) (3)(0)(0)(0) (0)(0)(0)(0) Rathke pouch 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (3)(0)(0)(0) (0)(0)(0)(0) adrenal <35> ⟨31⟩ <34> ⟨34⟩ hyperplasia:cortical cell 0 0 0 0 1 1 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (3)(3)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) focal fatty change:cortex 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (3)(0)(0)(0) (0)(0)(0)(0) [Reproductive system] ovary (35) ⟨31⟩ ⟨34⟩ ⟨34⟩ angiectasis 0 1 0 0 0 1 0 0 0 0 0 0 0 0 (0)(3)(0)(0) (0)(3)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) cyst 5 0 0 0 7 0 0 0 3 0 0 0 (11) (0) (0) (0) (16) (0) (0) (0) (21) (0) (0) (0) (9)(0)(0)(0) 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)

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

STUDY NO. : 0243 ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX

: FEMALE

0rgan	Findings	Group Name Control No. of Animals on Study 35 Grade 1 2 3 4 (%) (%) (%) (%)	8000 ppm 31 1 2 3 4 (%) (%) (%) (%)	20000 ppm 34 1 2 3 4 (%) (%) (%) (%)	50000 ppm 34 1 2 3 4 (%) (%) (%) (%)
[Reproductiv	e system]				
ovary	mineralization	<pre></pre>	31> 0 1 0 0 (0) (3) (0) (0)	34> 0 0 0 0 (0) (0) (0) (0)	34> 0 0 0 0 (0) (0) (0) (0)
uterus	dilatation	<35> 0 1 0 0 (0) (3) (0) (0)	31> 0 0 0 0 (0) (0) (0) (0)	34> 0 1 0 0 (0) (3) (0) (0)	34> 0 1 0 0 (0) (3) (0) (0)
	cystic endometrial hyperplasia	11 14 0 0 (31) (40) (0) (0)	12 10 0 0 (39) (32) (0) (0)	15 11 0 0 (44) (32) (0) (0)	9 15 0 0 (26) (44) (0) (0)
	xanthogranuloma	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)
[Nervous sys	rtem]				
brain	mineralization	35> 2 10 0 0 (6) (29) (0) (0)	31> 6 10 0 0 (19) (32) (0) (0)	34> 10 7 0 0 * (29) (21) (0) (0)	6 11 0 0 (18) (32) (0) (0)
[Special sen	ise organs/appandage]				
Harder gl	degeneration	(35) 1 0 0 0 (3) (0) (0) (0)	31> 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)
Grade <a>> b (c) Significant	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 ≤				

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (105W)

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1
SEX : FEMALE

Organ	Group N. No. of Grade Findings	Animals on Study 35 1 2 3 4 (%) (%) (%) (%)	8000 ppm 31 1 2 3 4 (%) (%) (%) (%)	20000 ppm 34 1 2 3 4 (%) (%) (%) (%)	50000 ppm 34 1 2 3 4 (%) (%) (%) (%)
[Special ser	nse organs/appandage]				
Harder gl	hyperplasia	<35> 0 0 0 0 (0) (0) (0) (0)	(31) 0 0 0 0 (0) (0) (0) (0)	34> 0 0 0 0 (0) (0) (0) (0)	34> 1 0 0 0 (3) (0) (0) (0)
[Musculoskel	letal system]				
bone	fracture	<35> 0 0 0 0 (0) (0) (0) (0)	(31) 0 1 0 0 (0) (3) (0) (0)	(34) 0 0 0 0 (0) (0) (0) (0)	<pre></pre>
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; *: $P \le 0.05$ **: $P \le 0.01$				
(HPT150)					BA

APPENDIX L 1

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

RAT: MALE

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

ANIMAL : RAT F344/DuCri

REPORT TYPE : A1 SEX : MALE

STUDY NO. : 0242

Time-related Items Group Name mag 0008 Control 20000 ppm 50000 ppm __Weeks_ NO. OF EXAMINED ANIMALS NO. OF ANIMALS WITH TUMORS NO. OF ANIMALS WITH SINGLE TUMORS NO. OF ANIMALS WITH MULTIPLE TUMORS NO. OF BENIGN TUMORS NO. OF MALIGNANT TUMORS NO. OF TOTAL TUMORS 53 - 78 NO. OF EXAMINED ANIMALS NO. OF ANIMALS WITH TUMORS NO. OF ANIMALS WITH SINGLE TUMORS NO. OF ANIMALS WITH MULTIPLE TUMORS NO. OF BENIGN TUMORS NO. OF MALIGNANT TUMORS NO. OF TOTAL TUMORS 79 - 104 NO. OF EXAMINED ANIMALS NO. OF ANIMALS WITH TUMORS NO. OF ANIMALS WITH SINGLE TUMORS NO. OF ANIMALS WITH MULTIPLE TUMORS NO. OF BENIGN TUMORS NO. OF MALIGNANT TUMORS NO. OF TOTAL TUMORS 105 - 105NO. OF EXAMINED ANIMALS NO. OF ANIMALS WITH TUMORS NO. OF ANIMALS WITH SINGLE TUMORS NO. OF ANIMALS WITH MULTIPLE TUMORS NO. OF BENIGN TUMORS NO. OF MALIGNANT TUMORS NO. OF TOTAL TUMORS

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

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1 SEX : MALE

PAGE: 2

Time-relatedWeeks	Items	Group Name	Control	Mdd 0008	20000 ppm	50000 ppm	
0 - 105	NO. OF EXAMINED ANIMALS		50	50	50	50	
	NO. OF ANIMALS WITH TUMORS		50	49	49	50	
	NO. OF ANIMALS WITH SINGLE TUMORS		19	10	9	9	
	NO. OF ANIMALS WITH MULTIPLE TUMORS		31	39	40	41	
	NO. OF BENIGN TUMORS		84	97	103	91	
	NO. OF MALIGNANT TUMORS		18	16	19	26	
	NO. OF TOTAL TUMORS		102	113	122	117	

(HPT070) BAIS3

APPENDIX L 2

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

RAT: FEMALE

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

STUDY NO. : 0242

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1
SEX : FEMALE

Time-related Items Group Name Control mqq 0008 20000 ppm 50000 ppm Weeks 0 - 52 NO. OF EXAMINED ANIMALS NO. OF ANIMALS WITH TUMORS NO. OF ANIMALS WITH SINGLE TUMORS NO. OF ANIMALS WITH MULTIPLE TUMORS NO. OF BENIGN TUMORS NO. OF MALIGNANT TUMORS NO. OF TOTAL TUMORS 53 - 78 NO. OF EXAMINED ANIMALS NO. OF ANIMALS WITH TUMORS NO. OF ANIMALS WITH SINGLE TUMORS NO. OF ANIMALS WITH MULTIPLE TUMORS NO. OF BENIGN TUMORS NO. OF MALIGNANT TUMORS NO. OF TOTAL TUMORS 79 - 104 NO. OF EXAMINED ANIMALS NO. OF ANIMALS WITH TUMORS NO. OF ANIMALS WITH SINGLE TUMORS NO. OF ANIMALS WITH MULTIPLE TUMORS NO. OF BENIGN TUMORS NO. OF MALIGNANT TUMORS NO. OF TOTAL TUMORS 105 - 105 NO. OF EXAMINED ANIMALS NO. OF ANIMALS WITH TUMORS NO. OF ANIMALS WITH SINGLE TUMORS NO. OF ANIMALS WITH MULTIPLE TUMORS NO. OF BENIGN TUMORS NO. OF MALIGNANT TUMORS NO. OF TOTAL TUMORS

(HPT070)

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

ANIMAL : RAT F344/DuCrj REPORT TYPE : A1

SEX : FEMALE

PAGE: 4

Time-related Weeks	Items	Group Name	Control	mag 0008	20000 ppm	50000 ppm	
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		32 22 10	33 19 14	36 17 19	37 26 11	
	NO. OF BENIGN TUMORS NO. OF MALIGNANT TUMORS NO. OF TOTAL TUMORS		35 13 48	37 12 49	51 15 66	41 15 56	
(HPT070)							RAISS

APPENDIX L 3

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

MOUSE: MALE

ANIMAL : MOUSE C-j:BDF1

REPORT TYPE : A1 SEX : MALE

ne-related _Weeks	Items	Group Name	Control	3200 ppm	mqq 0008	20000 ppm	
0 - 52	NO. OF EXAMINED ANIMALS		1	2	1	0	
	NO. OF ANIMALS WITH TUMORS		0	1	0	0	
	NO. OF ANIMALS WITH SINGLE TUMORS		0	1	0	0	
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	0	0	0	
	NO. OF BENIGN TUMORS		0	0	0	0	
	NO. OF MALIGNANT TUMORS		0	1	0	0	
	NO. OF TOTAL TUMORS		0	1	0	0	
53 - 78	NO. OF EXAMINED ANIMALS		2	0	5	1	
	NO. OF ANIMALS WITH TUMORS		1	0	3	1	
	NO. OF ANIMALS WITH SINGLE TUMORS		1	0	2	1	
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	0	1	0	
	NO. OF BENIGN TUMORS		0	0	0	0	
	NO. OF MALIGNANT TUMORS		1	0	4	1	
	NO. OF TOTAL TUMORS		1	0	4	1	
79 - 104	NO. OF EXAMINED ANIMALS		5	7	7	7	
	NO. OF ANIMALS WITH TUMORS		2	5	4	7	
	NO. OF ANIMALS WITH SINGLE TUMORS		1	4	4	7	
	NO. OF ANIMALS WITH MULTIPLE TUMORS		1	1	0	0	
	NO. OF BENIGN TUMORS		0	1	0	0	
	NO. OF MALIGNANT TUMORS NO. OF TOTAL TUMORS		3	5	4	7	
	NO. OF TOTAL TORONS		3	6	4	7	
105 - 105	NO. OF EXAMINED ANIMALS		41	41	37	42	
	NO. OF ANIMALS WITH TUMORS		17	21	13	15	
	NO. OF ANIMALS WITH SINGLE TUMORS		16	18	10	13	
	NO. OF ANIMALS WITH MULTIPLE TUMORS		1	3	3	2	
	NO. OF BENIGN TUMORS		8	12	9	9	
	NO. OF MALIGNANT TUMORS		10	12	7	8	
	NO. OF TOTAL TUMORS		18	24	16	17	

STUDY NO. : 0243 NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS - TIME RELATED

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1

SEX : MALE

Time-relatedWeeks	Items	Group Name	Control	3200 ppm	mqq 0008	20000 ppm	
0 - 105	NO. OF EXAMINED ANIMALS		49	50	50	50	
	NO. OF ANIMALS WITH TUMORS		20	27	20	23	
	NO. OF ANIMALS WITH SINGLE TUMORS		18	23	16	21	
	NO. OF ANIMALS WITH MULTIPLE TUMORS		2	4	4	2	
	NO. OF BENIGN TUMORS		8	13	9	9	
	NO. OF MALIGNANT TUMORS		14	18	15	16	
	NO. OF TOTAL TUMORS		22	31	24	25	
(UDTO70)							

PAGE: 2

(HPT070) BAIS3

APPENDIX L4

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

MOUSE: FEMALE

STUDY NO. : 0243 ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1

SEX : FEMALE

me-related Weeks	Items	Group Name	Control	mqq 0008	20000 ppm	50000 ppm	
0 - 52	NO. OF EXAMINED ANIMALS		0	0	1	0	
	NO. OF ANIMALS WITH TUMORS		0	0	1	0	
	NO. OF ANIMALS WITH SINGLE TUMORS		0	0	1	0	
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	Ō	ō	Ō	
	NO. OF BENIGN TUMORS		0	0	0	0	•
	NO. OF MALIGNANT TUMORS		0	0	1	0	
	NO. OF TOTAL TUMORS		0	0	1	0	
53 - 78	NO. OF EXAMINED ANIMALS		4	2	2	4	
	NO. OF ANIMALS WITH TUMORS		3	2	2	3	
	NO. OF ANIMALS WITH SINGLE TUMORS		2	2	2	1	
	NO. OF ANIMALS WITH MULTIPLE TUMORS		1	0	0	2	
	NO. OF BENIGN TUMORS		2	0	0	1	
	NO. OF MALIGNANT TUMORS		2	2	2	4	
	NO. OF TOTAL TUMORS		4	2	2	5	
79 - 104	NO. OF EXAMINED ANIMALS		11	17	13	12	
	NO. OF ANIMALS WITH TUMORS		9	17	13	11	
	NO. OF ANIMALS WITH SINGLE TUMORS		9	14	9	7	
	NO. OF ANIMALS WITH MULTIPLE TUMORS		0	3	4	4	
	NO. OF BENIGN TUMORS		0	3	3	2	
	NO. OF MALIGNANT TUMORS NO. OF TOTAL TUMORS		9	18	15	13	
	NO. OF IOIAL IUNORS		9	21	18	15	
105 - 105	NO. OF EXAMINED ANIMALS		35	31	34	34	
	NO. OF ANIMALS WITH TUMORS		21	21	23	25	
	NO. OF ANIMALS WITH SINGLE TUMORS		16	13	19	12	
	NO. OF ANIMALS WITH MULTIPLE TUMORS		5	8	4	13	
	NO. OF BENIGN TUMORS		10	10	14	25	
	NO. OF MALIGNANT TUMORS		18	21	13	17	
	NO. OF TOTAL TUMORS		28	31	27	42	

ANIMAL : MOUSE C-j:BDF1

REPORT TYPE : A1

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

SEX : FEMALE

PAGE: 4

Time-related Weeks	Items	Group Name	Control	8000 ppm	20000 ppm	50000 ppm	
0 - 105	NO. OF EXAMINED ANIMALS		50	50	50	50	
	NO. OF ANIMALS WITH TUMORS		33	40	39	39	
	NO. OF ANIMALS WITH SINGLE TUMORS		27	29	31	20	
	NO. OF ANIMALS WITH MULTIPLE TUMORS		6	11	8	19	
	NO. OF BENIGN TUMORS		12	13	17	28	
	NO. OF MALIGNANT TUMORS		29	41	31	34	
	NO. OF TOTAL TUMORS		41	54	48	62	
(HPT070)					····		

(HPT070)

APPENDIX M 1

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

RAT: MALE:

: RAT F344/DuCrj ANIMAL

HISTOLOGICAL FINDINGS: NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0-105W)

REPORT TYPE : A1 SEX : MALE

Group Name Control 8000 ppm 20000 ppm 50000 ppm Organ_ Findings_ No. of animals on Study 50 50 50 [Integumentary system/appandage] skin/app <50> ⟨50⟩ ⟨50⟩ ⟨50⟩ squamous cell papilloma 1 (2%) 0 (0%) 1 (2%) 1 (2%) trichoepitheliama 0 (0%) 0 (0%) 1 (2%) 0 (0%) keratoacanthoma 4 (8%) 3 (6%) 2 (4%) 4 (8%) sebaceous adenoma 0 (0%) 1 (2%) 1 (2%) 0 (0%) squamous cell carcinoma 1 (2%) 0 (0%) 0 (0%) 0 (0%) subcutis <50> <50> <50> <50> fibroma 2 (4%) 4 (8%) 1 (2%) 4 (8%) lipoma 0 (0%) 1 (2%) 0 (0%) 0 (0%) fibrosarcoma 0 (0%) 0 (0%) 1 (2%) 0 (0%) schwannoma:malignant 1 (2%) 0 (0%) 1 (2%) 0 (0%) [Respiratory system] lung <50> ⟨50⟩ ⟨50⟩ <50> bronchiolar-alveolar adenoma 0 (0%) 3 (6%) 3 (6%) 2 (4%) osteosarcoma 0 (0%) 1 (2%) 0 (0%) 0 (0%) [Hematopoietic system] bone marrow <50> <50> <50> <50> histiocytic sarcoma 0 (0%) 1 (2%) 0 (0%) 0 (0%) (a) a: Number of animals examined at the site b (c) b: Number of animals with neoplasm c : b / a * 100(HPT085)

ANIMAL : RAT F344/DuCrj REPORT TYPE : A1

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

Organ	Findings	Group Name No. of animals on Study	Control 50	8000 ppm 50	20000 ppm 50	50000 ppm 50	
[Hematopoie	tic system]						
spleen	sarcoma:NOS		<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)	<50> 0 (0%)	
	mononuclear cell leukemia		8 (16%)	1 (2%)	1 (2%)	1 (2%)	
	hemangiosarcoma		0 (0%)	1 (2%)	0 (0%)	2 (4%)	
[Digestive s	system]						
oral cavity	squamous cell papilloma		<50> 1 (2%)	<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)	
small intes	adenoma		<50> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)	
liver	hepatocellular adenoma		<50> 0 (0%)	<50> 4 (8%)	<50> 9 (18%)	<50> 9 (18%)	
	hepatocellular carcinoma		0 (0%)	0 (0%)	5 (10%)	5 (10%)	
pancreas	islet cell adenoma		<50> 3 (6%)	<50> 2 (4%)	<50> 0 (0%)	<50> 2 (4%)	
	acinar cell adenocarcinoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)	
[Urinary sys	stem]						
kidney	renal cell adenoma		<50> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)	
	liposarcoma		0 (0%)	0 (0%)	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)							BAI

BAIS3

ANIMAL : RAT F344/DuCrj

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

PAGE: 3

0rgan	Findings	Group Name No. of animals on Study	Con	trol 50	800	9 ppm 50	2000	00 ppm 50	5000	0 ppm 50
[Urinary syste	∍m]									
urin bladd	transitional cell papilloma		0	<50> (0%)	0	<50> (0%)	2	<50> (4%)	0	<50> (0%)
	mastcytoma:benign		0	(0%)	1	(2%)	0	(0%)	0	(0%)
	transitional cell carcinoma		0	(0%)	1	(2%)	4	(8%)	3	(6%)
[Endocrine sy	stem]									
pituitary	adenoma		15	<49> (31%)	10	<50> (20%)	10	<50> (20%)	10	<50> (20%)
thyroid	C-cell adenoma		3	<50> (6%)	5	<50> (10%)	5	<50> (10%)	2	<50> (4%)
	follicular adenoma		0	(0%)	0	(0%)	0	(0%)	1	(2%)
	C-cell carcinoma		0	(0%)	2	(4%)	1	(2%)	0	(0%)
	follicular adenocarcinoma		4	(8%)	3	(6%)	1	(2%)	5	(10%)
adrenal	pheochromocytoma		6	<50> (12%)	10	<50> (20%)	12	<50> (24%)	3	<50> (6%)
	gang Lioneuroma		0	(0%)	0	(0%)	0	(0%)	1	(2%)
	pheochromocytoma:malignant		2	(4%)	2	(4%)	2	(4%)	2	(4%)
[Reproductive	system]									
testis	interstitial cell tumor		43	<50> (86%)	46	<50> (92%)	47	<50> (94%)	47	<50> (94%)
(a) b (c)	a : Number of animals examined at the site b : Number of animals with neoplasm	c:b/a*100			711					

(HPT085)

ANIMAL : RAT F344/DuCrj

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

ALL ANIMALS (0-105W)

Organ	Findings	Group Name No. of animals on Study	Control 50	8000 ppm 50	20000 ppm 50	50000 ppm 50
[Reproductive	system]					
mammary gl	adenoma		<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)	<50> 1 (2%)
	fibroadenoma		2 (4%)	0 (0%)	3 (6%)	2 (4%)
prep/cligl	adenoma		<50> 4 (8%)	<50> 4 (8%)	<50> 2 (4%)	<50> 0 (0%)
	keratoacanthoma		0 (0%)	2 (4%)	0 (0%)	0 (0%)
	squamous cell carcinoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
(Nervous syst	em]					
brain	malignant reticulosis		<50> 0 (0%)	<50> 0 (0%)	<50> 0 (0%)	<50> 2 (4%)
	glioma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
[Special sens	e organs/appandage]					
Zymbal gl	adenoma		<50> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)	<50> 2 (4%)
	squamous cell carcinoma		0 (0%)	0 (0%)	0 (0%)	1 (2%)
[Musculoskele	tal system]					
bane	osteosarcoma		<50> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)	<50> 1 (2%)
(a) b (c)	a: Number of animals examined at the site b: Number of animals with neoplasm c: b/a*1	00				
(HPT085)						BA

ANIMAL : RAT F344/DuCrj

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

ALL ANIMALS (0-105W)

Croup Name Control 9000 ppg 20000 ppg 50000 ppg

Group Name 8000 ppm Control 20000 ppm 50000 ppm Organ_ Findings_ No. of animals on Study 50 50 50 [Body cavities] peritoneum ⟨50⟩ <50> ⟨50⟩ <50> mesothelioma 0 (0%) 3 (6%) 1 (2%) 2 (4%) ⟨50⟩ retroperit ⟨50⟩ <50> <50> paraganglioma:malignant 0 (0%) 1 (2%) 0 (0%) 0 (0%) (a) a: Number of animals examined at the site b (c) b: Number of animals with neoplasm c:b/a*100

(HPT085)

BAIS3

APPENDIX M 2

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

RAT: FEMALE:

SEX

(HPT085)

ANIMAL

: RAT F344/DuCrj

HISTOLOGICAL FINDINGS: NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0-105W)

REPORT TYPE : A1 : FEMALE

Group Name Control 8000 ppm 20000 ppm 50000 ppm Organ____ Findings_ No. of animals on Study 50 50 50 50 [Integumentary system/appandage] subcutis ⟨50⟩ <50> ⟨50⟩ ⟨50⟩ fibroma 1 (2%) 1 (2%) 0 (0%) 0 (0%) Lipoma 1 (2%) 0 (0%) 0 (0%) 0 (0%) schwannoma 0 (0%) 0 (0%) 0 (0%) 1 (2%) sarcoma:NOS 0 (0%) 1 (2%) 0 (0%) 0 (0%) [Respiratory system] lung <50> <50> <50> <50> bronchiolar-alveolar adenoma 1 (2%) 0 (0%) 3 (6%) 0 (0%) [Hematopoietic system] bone marrow <50> <50> <50> <50> histiocytic sarcoma 2 (4%) 0 (0%) 0 (0%) 0 (0%) thymus <50> <50> <50> <49> thymoma:benign 1 (2%) 0 (0%) 0 (0%) 0 (0%) spleen <50> <50> <50> <50> mononuclear cell leukemia 6 (12%) 7 (14%) 2 (4%) 6 (12%) [Digestive system] esophagus <50> <50> <50> <49> squamous cell papilloma 1 (2%) 0 (0%) 0 (0%) 0 (0%) large intes <50> ⟨50⟩ <50> <50> adenoma 0 (0%) 0 (0%) 0 (0%) 1 (2%) (a) a: Number of animals examined at the site b (c) b: Number of animals with neoplasm c:b/a*100

BAIS3

: UZ4Z

ANIMAL : RAT F344/DuCrj

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0-105W)

REPORT TYPE : A1 SEX : FEMALE

(HPT085)

Group Name Control 8000 ppm 20000 ppm 50000 ppm Findings_ No. of animals on Study 0rgan_ 50 50 50 50 [Digestive system] liver <50> <50> <50> <50> hepatocellular adenoma 1 (2%) 3 (6%) 3 (6%) 2 (4%) cholangiocellular adenoma 0 (0%) 0 (0%) 1 (2%) 0 (0%) hemangiosarcoma 0 (0%) 0 (0%) 0 (0%) 1 (2%) hepatocellular carcinoma 0 (0%) 0 (0%) 1 (2%) 0 (0%) <50> <50> pancreas <50> <50> islet cell adenoma 1 (2%) 0 (0%) 1 (2%) 1 (2%) [Urinary system] kidney <50> <50> <50> <50> mesenchymoma 0 (0%) 0 (0%) 1 (2%) 0 (0%) renal cell adenoma 0 (0%) 3 (6%) 6 (12%) 4 (8%) renal cell carcinoma 0 (0%) 0 (0%) 0 (0%) 1 (2%) urin bladd ⟨50⟩ <50> <50> <50> mastcytoma:benign 1 (2%) 0 (0%) 0 (0%) 0 (0%) transitional cell carcinoma 0 (0%) 2 (4%) 3 (6%) 2 (4%) [Endocrine system] pituitary ⟨50⟩ <50> <50> <50> adenoma 11 (22%) 12 (24%) 16 (32%) 11 (22%) (a) a: Number of animals examined at the site b (c) b: Number of animals with neoplasm c:b/a * 100

BAIS3

ANIMAL : RAT F344/DuCrj

ALL ANIMALS (0-105W)

REPORT TYPE : A1

SEX : FEMALE

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)

PAGE: 8

0rgan	Findings	Group Name No. of animals on Study	Control 50	8000 ppm 50	20000 ppm 50	50000 ppm 50
[Endocrine s	ystem]					
oituitary	adenocarcinoma		<50> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)
thyroid	C-cell adenoma		<50> 5 (10%)	<50> 2 (4%)	<50> 5 (10%)	<49> 1 (2%)
	follicular adenocarcinoma		2 (4%)	0 (0%)	1 (2%)	0 (0%)
adrena l	pheochromocytoma		<50> 0 (0%)	<50> 3 (6%)	<50> 2 (4%)	<50> 3 (6%)
	cortical adenoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
	pheochromocytoma:malignant		1 (2%)	0 (0%)	0 (0%)	1 (2%)
	cortical adenocarcinoma		0 (0%)	0 (0%)	1 (2%)	0 (0%)
Reproductiv	e system]					
ovary	granulosa—theca cell tumor:malignant		<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)	<50> 0 (0%)
nterus	leiomyoma		<50> 0 (0%)	<50> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)
	endometrial stromal polyp		4 (8%)	9 (18%)	8 (16%)	5 (10%)
	adenocarcinoma		0 (0%)	0 (0%)	2 (4%)	0 (0%)
	endometrial stromal sarcoma		0 (0%)	0 (0%)	0 (0%)	3 (6%)
(a) b (c)	a: Number of animals examined at the site b: Number of animals with neoplasm c:b/a*1	00				
(HPT085)						

ANIMAL : RAT F344/DuC-j

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

Organ	Findings	Group Name No. of animals on Study	Control 50	8000 ppm 50	20000 ppm 50	50000 ppm 50
[Reproductive	system]					
mammary gl	adenoma		<50> 0 (0%)	<50> 2 (4%)	<50> 0 (0%)	<50> 1 (2%)
	fibroadenoma		3 (6%)	2 (4%)	3 (6%)	9 (18%)
	adenocarcinoma		0 (0%)	0 (0%)	2 (4%)	0 (0%)
prep/cli gl	adenoma		<50> 2 (4%)	<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)
	keratoacanthoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
[Nervous syste	em]					
brain	glioma		<50> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)	<50> 1 (2%)
[Special sense	e organs/appandage]					
Zymbal gl	squamous cell carcinoma		<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)	<50> 0 (0%)
[Musculoskele	tal system]					
bone	osteosarcoma		<50> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)
[Body cavities	sl					
mediastirum	carcinoid tumor:malignant		<50> 1 (2%)	<50> 0 (0%)	<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*1	00	t atta			
(HPT085)				41		Bi

STUDY NO. : 0242 ANIMAL : RAT F344/DuCrj

HISTOLOGICAL FINDINGS: NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0-105W)

REPORT TYPE : A1

SEX : FEMALE

PAGE: 10

Organ		Group Name No. of animals on Study	Control 50	8000 ppm 50	20000 ppm 50	50000 ppm 50
[Body cavities	s]					
mediastinum	sarcoma:NOS		<50> 1 (2%)	<50> 0 (0%)	<50> 0 (0%)	<50> 0 (0%)
mesenterium	fibroma		<50> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)
adipose	lipoma		<50> 0 (0%)	<50> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)
<a>> b (c)	a: Number of animals examined at the site b: Number of animals with neoplasm c:b/a*10	0	**************************************			
(HPT085)			**			T.

(HPT085)

APPENDIX M 3

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

MOUSE: MALE

ANIMAL : MOUSE Crj:BDF1

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

REPORT TYPE : A1 SEX : MALE

PAGE: 1

Organ		Group Name No. of animals on Study	Control 49	3200 ppm 50	8000 ppm 50	20000 ppm 50
[Integumentary	v system/appandage]					
subcutis	xanthoma		<49> 1 (2%)	<50> 1 (2%)	<50> 1 (2%)	<50> 0 (0%)
	histiocytic sarcoma		1 (2%)	1 (2%)	1 (2%)	0 (0%)
[Respiratory s	system]					
nasal cavit	chondroma		<49> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)
lung	bronchiolar-alveolar adenoma		<49> 1 (2%)	<50> 3 (6%)	<50> 2 (4%)	<50> 1 (2%)
	bronchiolar—alveolar carcinoma		1 (2%)	1 (2%)	2 (4%)	0 (0%)
[Hematopoietio	c system]					
tymph node	malignant lymphoma		<49> 2 (4%)	<50> 4 (8%)	<50> 4 (8%)	<50> 3 (6%)
	mastcytoma:malignant		2 (4%)	1 (2%)	1 (2%)	2 (4%)
spleen	hemangioma		<49> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)
	malignant lymphoma		1 (2%)	2 (4%)	0 (0%)	2 (4%)
	mastcytoma:malignant		0 (0%)	0 (0%)	0 (0%)	1 (2%)
[Circulatory s	system]					
heart	hemangioma		<49> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)
<a>> b (c)	a: Number of animals examined at the site b: Number of animals with neoplasm c: b/a * 10	00				

(HPT085)

ANIMAL : MOUSE Crj:BDF1

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

REPORT TYPE : A1 : MALE

PAGE: 2

Organ	Findings	Group Name No. of animals on Study	Contral 49	3200 ppm 50	8000 ppm 50	20000 ppm 50
[Digestive sys	tem]					
salivary gl	histiocytic sarcoma		<49> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)	<50> 1 (2%)
liver	hepatocellular adenoma		<49> 4 (8%)	<50> 6 (12%)	<50> 1 (2%)	<50> 5 (10%)
	histiocytic sarcoma		2 (4%)	4 (8%)	5 (10%)	3 (6%)
	hemangiosarcoma		2 (4%)	0 (0%)	1 (2%)	0 (0%)
	hepatocellular carcinoma		1 (2%)	3 (6%)	0 (0%)	0 (0%)
[Urinary system	n]					
kidney	transitional cell carcinoma		<49> 0 (0%)	<50> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)
urin bladd	xanthoma		<49> 0 (0%)	<50> 2 (4%)	<50> 0 (0%)	<50> 0 (0%)
	histiocytic sarcoma		0 (0%)	0 (0%)	0 (0%)	2 (4%)
[Endocrine sys	tem]					
adrena l	cortical adenoma	v.	<49> 1 (2%)	<50> 0 (0%)	<50> 0 (0%)	<50> 0 (0%)
[Reproductive:	system]					
testis	interstitial cell tumor		<49> 1 (2%)	<50> 0 (0%)	<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 * 1	00				

(HPT085)

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS: NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0-105W)

: MALE PAGE : 3

Organ	Findings	Group Name No. of animals on Study	Control 49	3200 ppm 50	8000 ppm 50	20000 ppm 50	
[Reproductive	system]						
testis	histiocytic sarcoma		<49> 1 (2%)	<50> 0 (0%)	<50> 0 (0%)	<50> 0 (0%)	
epididymis	histiocytic sarcoma		<49> 1 (2%)	<50> 1 (2%)	<50> 1 (2%)	<50> 1 (2%)	
[Special sens	e organs/appandage]						
Harder gl	adenoma		<49> 0 (0%)	<50> 1 (2%)	<50> 2 (4%)	<50> 3 (6%)	
(a> b (c)	a: Number of animals examined at the site b: Number of animals with neoplasm c:b/a*	100					
(HPT085)							BAIS

APPENDIX M 4

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

MOUSE: FEMALE

ANIMAL : MOUSE Crj:BDF1

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0-105W)

REPORT TYPE : A1

(HPT085)

SEX : FEMALE

Findings	Group Name No. of animals on Study	Control 50	maga 0008 03	20000 ppm 50	50000 ppm 50
ystem/appandage]					
trichoepithelioma		<50> 1 (2%)	<50> 0 (0%)	<50> 0 (0%)	<50> 0 (0%)
xanthoma		<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)	<50> 0 (0%)
histiocytic sarcoma		0 (0%)	1 (2%)	0 (0%)	1 (2%)
hemangiosarcoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
tem]					
bronchiolar-alveolar adenoma		<50> 1 (2%)	<50> 2 (4%)	<50> 4 (8%)	<50> 0 (0%)
bronchiplar-alveplar cardinoma		2 (4%)	2 (4%)	2 (4%)	1 (2%)
ystem]					
malignant lymphoma		<50> 11 (22%)	<50> 13 (26%)	<50> 7 (14%)	<50> 7 (14%)
mastcytoma:malignant		0 (0%)	0 (0%)	1 (2%)	0 (0%)
hemangioma		<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)	<49> 0 (0%)
malignant lymphoma		4 (8%)	1 (2%)	4 (8%)	0 (0%)
m]					
squamous cell papilloma		<50> 1 (2%)	<50> 0 (0%)	<50> 0 (0%)	<50> 0 (0%)
squamous cell papili	Ls examined at the site	Ls examined at the site	Loma 1 (2%)	Loma $1 \ (2\%) \qquad 0 \ (0\%)$ Ls examined at the site	loma 1 (2%) 0 (0%) 0 (0%) Ls examined at the site

ANIMAL : MOUSE Crj:BDF1

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

REPORT TYPE : A1

SEX

(HPT085)

: FEMALE

PAGE: 5

)rgan	Findings Group Name No. of anim	Control als on Study 50	8000 ppm 50	20000 ppm 50	50000 ppm 50
Digestive sys	stem]				
salivary gl	histiocytic sarcoma	<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)	<50> 0 (0%)
stomach	mastcytoma:malignant	<49> 0 (0%)	<50> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)
arge intes	łeiomyosarcoma	<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)	<50> 0 (0%)
iver	hepatocellular adenoma	<50> 2 (4%)	<50> 3 (6%)	<50> 6 (12%)	<50> 20 (40%)
	hepatocholangiocellular adenoma	0 (0%)	0 (0%)	0 (0%)	1 (2%)
	histiocytic sarcoma	0 (0%)	3 (6%)	4 (8%)	3 (6%)
	hemangiosarcoma	3 (6%)	1 (2%)	1 (2%)	1 (2%)
	hepatocellular carcinoma	0 (0%)	2 (4%)	5 (10%)	12 (24%)
Urinary syste	em]				
rin bladd	histiocytic sarcoma	<50> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)	<49> 0 (0%)
Endocrine sys	stem]				
oituitary	adenoma	<50> 1 (2%)	<50> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)
thyroid	C-cell carcinoma	<49> 0 (0%)	<50> 1 (2%)	<50> 0 (0%)	<50> 1 (2%)

ANIMAL : MOUSE Crj:BDF1

HISTOLOGICAL FINDINGS: NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0-105W)

REPORT TYPE : A1

SEX : FEMALE

Group Name Control 8000 ppm 20000 ppm 50000 ppm 0rgan_ Findings No. of animals on Study 50 50 50 50 [Endocrine system] adrenal ⟨50⟩ <50> <50> ⟨50⟩ pheochromocytoma 0 (0%) 0 (0%) 1 (2%) 0 (0%) A-B cell tumor 0 (0%) 0 (0%) 0 (0%) 1 (2%) [Reproductive system] ovary <50> <50> ⟨50⟩ <50> cystadenoma 0 (0%) 1 (2%) 2 (4%) 0 (0%) hemangioma 2 (4%) 2 (4%) 0 (0%) 0 (0%) uterus ⟨50⟩ <50> <50> ⟨50⟩ Leiomyoma 0 (0%) 0 (0%) 1 (2%) 0 (0%) xanthoma 0 (0%) 0 (0%) 0 (0%) 1 (2%) endometrial stromal polyp 2 (4%) 1 (2%) 0 (0%) 0 (0%) leiomyosarcoma 1 (2%) 0 (0%) 0 (0%) 0 (0%) histiocytic sarcoma 6 (12%) 12 (24%) 7 (14%) 7 (14%) mammary gl <50> ⟨50⟩ (50) <50> adenocarcinoma 0 (0%) 2 (4%) 0 (0%) 0 (0%) [Special sense organs/appandage] Harder gl <50> <50> ⟨50⟩ <50> adenoma 1 (2%) 2 (4%) 3 (6%) 3 (6%)

(HPT085)

BAIS3

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

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

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

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1

SEX : FEMALE

Organ	Findings_	Group Name No. of animals on Study	Control 50	8000 ppm 50	20000 ppm 50	50000 ppm 50
[Musculoskel	etal system]					
muscle	hemangioma		<50> 0 (0%)	<50> 0 (0%)	<50> 0 (0%)	<50> 1 (2%)
bane	osteoma		<50> 1 (2%)	<50> 0 (0%)	<50> 0 (0%)	<50> 0 (0%)
	osteosarcoma		1 (2%)	0 (0%)	0 (0%)	0 (0%)
(a) b(c)	a: Number of animals examined at the site b: Number of animals with neoplasm c:b,	/ a * 100				
(HPT085)						

APPENDIX N 1

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

RAT: MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE: 1

BAIS3

ANIMAL : RAT F344/DuCrj

SEX : MALE

(HPT360A)

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

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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

		* ** ** *******************************			
Group Name	Control	8000 ppm	20000 ppm	50000 ppm	
	SITE : subcutis				
Cumor rate	TUMOR : fibroma,fibrosarcoma				
Overall rates(a)	2/50(4.0)	4/50(8.0)	2/50(4.0)	4/50(8.0)	
Adjusted rates(b)	3.03	9.30	2.33	7.32	
Terminal rates(c) Statistical analysis Peto test	1/33(3.0)	4/43(9.3)	1/43(2.3)	2/38(5.3)	
Standard method(d)	P = 0.3469				
Prevalence method(d)	P = 0.2803				
Combined analysis(d)	P = 0.2502				
Cochran-Armitage test(e)	P = 0.5514				
Fisher Exact test(e)	***	P = 0.3574	P = 0.3088	P = 0.3574	
	SITE : lung				
Tumor rate	TUMOR : bronchiolar-alveolar a	adenoma			
Overall rates(a)	0/50(0.0)	3/50(6.0)	3/50(6.0)	2/50(4.0)	
Adjusted rates(b)	0.0	6.98	6.98	5,26	
Terminal rates(c)	0/33(0.0)	3/43(7.0)	3/43(7.0)	2/38(5.3)	
Statistical analysis			, , ,	, , ,	
Peto test					
Standard method(d)	P =				
Prevalence method(d) Combined analysis(d)	P = 0.2996 P =				
Cochran-Armitage test(e)	P = 0.5948				
Fisher Exact test(e)	. 0.0010	P = 0.1325	P = 0.1325	P = 0.2574	
		CONTRACTOR			
	SITE : spleen TUMOR : mononuclear cell leuke	emia			
Tumor rate	Total Total County	Sinta			
Overall rates(a)	8/50(16.0)	1/50(2.0)	1/50(2.0)	1/50(2.0)	
Adjusted rates(b)	10.26	0.0	0.0	2.63	
Terminal rates(c)	3/33(9.1)	0/43(0.0)	0/43(0.0)	1/38(2.6)	
Statistical analysis Peto test					
Standard method(d)	P = 0.9857				
Prevalence method(d)	P = 0.8720				
Combined analysis(d)	P = 0.9924				
Cochran-Armitage test(e)	P = 0.0258*				
Fisher Exact test(e)		P = 0.0254*	P = 0.0254*	P = 0.0254*	

(HPT360A)

STUDY No. : 0242

ANIMAL : RAT F344/DuCrj

SEX : MALE

Group Name Control mag 0008 20000 ppm 50000 ppm SITE : Liver TUMOR : hepatocellular adenoma Tumor rate Overall rates(a) 0/50(0.0) 4/50(8.0) 9/50(18.0) 9/50(18.0) Adjusted rates(b) 0.0 9.30 20.93 21.05 Terminal rates(c) 0/33(0.0) 4/43(9.3) 9/43(20.9) 8/38(21.1) Statistical analysis Peto test Standard method(d) Prevalence method(d) P = 0.0032**Combined analysis(d) Cochran-Armitage test(e) P = 0.0056**Fisher Exact test(e) P = 0.0688P = 0.0029**P = 0.0029**SITE : Liver TUMOR : hepatocellular carcinoma Tumor rate Overall rates(a) 0/50(0.0) 0/50(0.0) 5/50(10.0) 5/50(10.0) Adjusted rates(b) 0.0 0.0 11.63 10.53 Terminal rates(c) 0/33(0.0) 0/43(0.0) 5/43(11.6) 4/38(10.5) Statistical analysis Peto test Standard method(d) P = 0.1138Prevalence method(d) P = 0.0158*Combined analysis(d) P = 0.0056**Cochran-Armitage test(e) P = 0.0081**Fisher Exact test(e) P = 0.5000P = 0.0360*P = 0.0360*SITE : liver TUMOR : hepatocellular adenoma, hepatocellular carcinoma Tumor rate Overall rates(a) 0/50(0.0) 4/50(8.0) 13/50(26.0) 13/50(26.0) Adjusted rates(b) 0.0 9.30 30.23 31.58 Terminal rates(c) 0/33(0.0) 4/43(9.3) 13/43(30.2) 12/38(31.6) Statistical analysis Peto test Standard method(d) P = 0.1138Prevalence method(d) P = 0.0003**Combined analysis(d) P = 0.0001**Cochran-Armitage test(e) P = 0.0002**Fisher Exact test(e) P = 0.0688P = 0.0003**P = 0.0003**(HPT360A)

BAIS3

PAGE:

3

STUDY No. : 0242 NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS ANIMAL : RAT F344/DuCrj SEX : MALE

	·····				
Group Name	Control	mqq 0008	20000 ppm	50000 ppm	
	SITE : pancreas				
	TUMOR : islet cell adenoma				
'umor rate Overall rates(a)	3/50(6.0)	2/50(4.0)	0/50(0.0)	2/50(4.0)	
Adjusted rates(b)	8.33	4.65	0.0	4.26	
Terminal rates(c)	2/33(6.1)	2/43(4.7)	0/43(0.0)	1/38(2.6)	
tatistical analysis					
Peto test	P =				
Standard method(d) Prevalence method(d)	P =				
Combined analysis(d)	P =				
Cochran-Armitage test(e)	P = 0.6779				
Fisher Exact test(e)		P = 0.4909	P = 0.1325	P = 0.4909	
		, — 41 day, — 4.			
	SITE : urinary bladder	:			
Tumor rate	TUMOR : transitional cell ca	TC1 Noma			
Overall rates(a)	0/50(0.0)	1/50(2.0)	4/50(8.0)	3/50(6.0)	
Adjusted rates(b)	0.0	2.33	8.33	7.89	
Terminal rates(c)	0/33(0.0)	1/43(2.3)	3/43(7.0)	3/38(7.9)	
Statistical analysis Peto test					
Standard method(d)	P =				
Prevalence method(d)	P = 0.0552				
Combined analysis(d)	P =				
Cochran-Armitage test(e)	P = 0.1193				
Fisher Exact test(e)		P = 0.4950	P = 0.0688	P = 0.1325	
	O.T.				
	SITE : urinary bladder	pilloma, transitional cell carcinoma			
Tumor rate	Tomon • LianSTLTUNAL COLL Pa	Freeding, Lights Freeding Cert Carcinoma			
Overall rates(a)	0/50(0.0)	1/50(2.0)	6/50(12.0)	3/50(6.0)	
Adjusted rates(b)	0.0	2.33	12.50	7.89	
Terminal rates(c)	0/33(0.0)	1/43(2.3)	4/43(9.3)	3/38(7.9)	
Statistical analysis Peto test					
Standard method(d)	P =				
Prevalence method(d)	P = 0.0689				
Combined analysis(d)	P =				
Cochran-Armitage test(e)	P = 0.1563				
Fisher Exact test(e)		P = 0.4950	P = 0.0190*	P = 0.1325	
HPT360A)					
100011)					

STUDY No. : 0242 NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

ANIMAL : RAT F344/DuCrj SEX : MALE PAGE: 5

Group Name	Control	mqq 0008	20000 ppm	50000 ppm	
	SITE : pituitary gland				
Cumor rate	TUMOR : adenoma				
Overall rates(a)	15/49(30.6)	10/50(20.0)	10/50(20.0)	10/50(20.0)	
Adjusted rates(b)	21.88	18.60	20.00	21.05	
Terminal rates(c) Statistical analysis Peto test	7/32(21.9)	8/43(18.6)	8/43(18.6)	8/38(21.1)	
Standard method(d)	P = 0.9390				
Prevalence method(d)	P = 0.5542				
Combined analysis(d)	P = 0.8294				
Cochran-Armitage test(e)	P = 0.3632	D 0.0055	D 0.000	D 0.000	
Fisher Exact test(e)		P = 0.2377	P = 0.2377	P = 0.2377	
	SITE : thyroid TUMOR : C-cell adenoma				
Tumor rate					
Overall rates(a)	3/50(6.0)	5/50(10.0)	5/50(10.0)	2/50(4.0)	
Adjusted rates(b)	7.50	11.63	11.63	5.00	
Terminal rates(c) Statistical analysis	1/33(3.0)	5/43(11.6)	5/43(11.6)	1/38(2.6)	
Peto test Standard method(d)	P =				
Prevalence method(d)	P = 0.7529				
Combined analysis(d)	P =				
Cochran-Armitage test(e)	P = 0.4581				
Fisher Exact test(e)		P = 0.3790	P = 0.3790	P = 0.4909	
	SITE : thyroid				
	TUMOR : follicular adenocarcinoma				
Tumor rate					
Overall rates(a)	4/50(8.0)	3/50(6.0)	1/50(2.0)	5/50(10.0)	
Adjusted rates(b) Terminal rates(c)	12.12 4/33(12.1)	6.98 3/43(7.0)	2.33 1/43(2.3)	13.16 5/38(13.2)	
Statistical analysis	1/00(12.1)	0/40(1.V)	1/40(2.3)	0/00(13.2)	
Peto test					
Standard method(d)	P =				
Prevalence method(d)	P = 0.2775				
Combined analysis(d)	P =				
Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.5408	P = 0.4895	P = 0.1998	P = 0.4883	
		r - V.4090	r = v.1998	P = 0.4883	

PAGE: 6

STUDY No. : 0242 NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS ANIMAL : RAT F344/DuCrj

SEX : MALE

Group Name	Control	8000 ppm	20000 ppm	50000 ppm	
	SITE : thyroid		***		
	TUMOR : C-cell adenoma, C-cell	carcinoma			
'umor rate					
Overall rates(a)	3/50(6.0)	7/50(14.0)	6/50(12.0)	2/50(4.0)	
Adjusted rates(b)	7.50	16.28	13.95	5.00	
Terminal rates(c)	1/33(3.0)	7/43(16.3)	6/43(14.0)	1/38(2.6)	
Statistical analysis					
Peto test	D.				
Standard method(d)	P =				
Prevalence method(d) Combined analysis(d)	P = 0.8244 P =				
Cochran-Armitage test(e)	P = 0.3292				
Fisher Exact test(e)	r = 0.3292	P = 0.1917	P = 0.2728	P = 0.4909	
TISHEL EXACT TEST(6)		- 0.1917	1 - 0.2720	r = 0.4909	
	SITE : thyroid				
	TUMOR : follicular adenoma, fol	licular adenocarcinoma			
Cumor rate	, ott, odta adonoma, io	ceroacai adoptodi orriona			
Overall rates(a)	4/50(8.0)	3/50(6.0)	1/50(2.0)	6/50(12.0)	
Adjusted rates(b)	12.12	6.98	2.33	14.63	
Terminal rates(c)	4/33(12.1)	3/43(7.0)	1/43(2.3)	5/38(13.2)	
Statistical analysis					
Peto test					
Standard method(d)	P =				
Prevalence method(d)	P = 0.1360				
Combined analysis(d)	P =				
Cochran-Armitage test(e)	P = 0.3002				
Fisher Exact test(e)		P = 0.4895	P = 0.1998	P = 0.3944	
	SITE : adrenal gland TUMOR : pheochromocytoma				
Tumor rate	,		•		
Overall rates(a)	6/50(12.0)	10/50(20.0)	12/50(24.0)	3/50(6.0)	
Adjusted rates(b)	16.22	23.26	26.67	7.89	
Terminal rates(c)	4/33(12.1)	10/43(23.3)	11/43(25.6)	3/38(7.9)	
Statistical analysis				•	
Peto test					
Standard method(d)	P =				
Prevalence method(d)	P = 0.9270				
Combined analysis(d)	P =				
	P = 0.1665		P = 0.1474		
Cochran-Armitage test(e) Fisher Exact test(e)		P = 0.2557		P = 0.2728	

PAGE: 7

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS STUDY No. : 0242 ANIMAL : RAT F344/DuCrj
SEX : MALE

Group Name	Control	8000 ppm	20000 ppm	50000 ppm	
	SITE : adrenal gland				
'umor rate	TUMOR : pheochromocytoma, pheoc	hromocytoma:malignant			
umor rate Overall rates(a)	6/50(12.0)	12/50(24.0)	14/50(28.0)	5/50(10.0)	
Adjusted rates(b)	16.22	25.58	28.89	13.16	
Terminal rates(c)	4/33(12.1)	11/43(25.6)	12/43(27.9)	5/38(13.2)	
tatistical analysis		,,	, (, -,	2, 33 (23.2)	
Peto test					
Standard method(d)	P = 0.5873				
Prevalence method(d)	P = 0.8030				
Combined analysis(d)	P = 0.8226				
Cochran-Armitage test(e)	P = 0.3599	D 0.14674	D 0 0010	D 0 1050	
Fisher Exact test(e)		P = 0.1474	P = 0.0810	P = 0.4872	
	SITE : testis				
	TUMOR : interstitial cell tumo	r			
umor rate					
Overall rates(a)	43/50(86.0)	46/50(92.0)	47/50(94.0)	47/50(94.0)	
Adjusted rates(b)	97.14	95.74	97.92	97.44	
Terminal rates(c) Statistical analysis	32/33(97.0)	41/43(95.3)	42/43(97.7)	37/38(97.4)	
Peto test					
Standard method(d)	P =				
Prevalence method(d)	P = 0.0876				
Combined analysis(d)	P =				
Cochran-Armitage test(e)	P = 0.2322				
Fisher Exact test(e)		P = 0.4659	P = 0.4362	P = 0.4362	
	SITE : mammary gland TUMOR : fibroadenoma				
Cumor rate	Torion • Dr Dade IDilla				
Overall rates(a)	2/50(4.0)	0/50(0.0)	3/50(6.0)	2/50(4.0)	
Adjusted rates(b)	6.06	0.0	6.98	4.35	
Terminal rates(c)	2/33(6.1)	0/43(0.0)	3/43(7.0)	1/38(2.6)	
Statistical analysis				-, (-, -,	
Peto test					
Standard method(d)	P =				
Prevalence method(d)	P = 0.3144				
Combined analysis(d)	P =				
Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.6340	D = 0 0574	D 0 4000	D 0.000	
FISHED EXACT DESILE)		P = 0.2574	P = 0.4909	P = 0.3088	

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

Group Name	Contral	8000 ppm	20000 ppm	50000 ppm
	SITE : mammary gland			
Tumor rate	TUMOR : adenoma, fibroadenoma			
Overall rates(a)	2/50(4.0)	1/50(2.0)	3/50(6.0)	0/50/ 0.0
Adjusted rates(b)	6.06	2.33	6.98	3/50(6.0) 6.52
Terminal rates(c)	2/33(6.1)	1/43(2.3)	3/43(7.0)	2/38(5.3)
Statistical analysis		-, (2.0,	0, 10(1.0)	2/00(3.3)
Peto test				
Standard method(d)	P =			
Prevalence method(d)	P = 0.2273			
Combined analysis(d)	P =			
Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.4453	D 0 4000		
TISIO EXACT TOST(6)		P = 0.4926	P = 0.4909	P = 0.4909
	SITE : preputial/clitoral gland			
_	TUMOR : adenoma			
Tumor rate	. (== (
Overall rates(a)	4/50(8.0)	4/50(8.0)	2/50(4.0)	0/50(0.0)
Adjusted rates(b) Terminal rates(c)	9.09 3/33(9.1)	9.30	4.65	0.0
Statistical analysis	3/33(9.1)	4/43(9.3)	2/43(4.7)	0/38(0.0)
Peto test				
Standard method(d)	P = 1.0000 ?			
Prevalence method(d)	P = 0.9836			
Combined analysis(d)	P = 0.9925			
Cochran-Armitage test(e)	P = 0.0356*			
Fisher Exact test(e)		P = 0.3579	P = 0.3574	P = 0.0688

(HPT360A)

BAIS3

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

ANIMAL : RAT F344/DuCrj

: MALE

PAGE:

Group Name	Control	mqq 0008	20000 ppm	50000 ppm	
	SITE : peritoneum				
	TUMOR : mesothelioma				
Tumor rate					
Overall rates(a)	0/50(0.0)	3/50(6.0)	2/50(4.0)	1/50(2.0)	
Adjusted rates(b)	0.0	4.65	4.65	2.38	
Terminal rates(c)	0/33(0.0)	2/43(4.7)	2/43(4.7)	0/38(0.0)	
Statistical analysis			, , ,	, , , , , , ,	
Peto test					
Standard method(d)	P = 0.5618				
Prevalence method(d)	P = 0.3815				
Combined analysis(d)	P = 0.4870				
Cochran-Armitage test(e)	P = 0.9478				
Fisher Exact test(e)		P = 0.1325	P = 0.2574	P = 0.4950	
(HPT360A)		- wall and			D. 100
,in 1000h)					BAIS3

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 N 2

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

RAT: FEMALE

STUDY No. : 0242 NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS ANIMAL : RAT F344/DuCrj

Group Name	Control	8000 ppm	20000 ppm	50000 ppm	
	SITE : lung				
r .	TUMOR : bronchiolar-alveola	r adenoma			
Tumor rate	1/50/ 0.0)	0/80/ 0.0	2/22/ 2 2	- 4 4	
Overall rates(a)	1/50(2.0)	0/50(0.0)	3/50(6.0)	0/50(0.0)	
Adjusted rates(b)	2.50	0.0	7.50	0.0	
Terminal rates(c)	1/40(2.5)	0/40(0.0)	3/40(7.5)	0/37(0.0)	
Statistical analysis					
Peto test	D.				
Standard method(d)	P =				
Prevalence method(d)	P = 0.6319 P =				
Combined analysis(d) Cochran-Armitage test(e)	•				
Fisher Exact test(e)	P = 0.6322	D 0. 40E0	D 0.000	D 0 4050	
FISHEL EXACT TEST(E)		P = 0.4950	P = 0.3235	P = 0.4950	
	SITE : spleen				
	TUMOR : mononuclear cell le	eukemia			
Tumor rate					
Overall rates(a)	6/50(12.0)	7/50(14.0)	2/50(4.0)	6/50(12.0)	
Adjusted rates(b)	7.50	5.00	5.00	8.11	
Terminal rates(c)	3/40(7.5)	2/40(5.0)	2/40(5.0)	3/37(8.1)	
Statistical analysis					
Peto test					
Standard method(d)	P = 0.6283				
Prevalence method(d)	P = 0.3734				
Combined analysis(d)	P = 0.5188				
Cochran-Armitage test(e)	P = 0.8698				
Fisher Exact test(e)		P = 0.4863	P = 0.1606	P = 0.3807	

SITE : Liver TUMOR : hepatocellular adenoma Tumor rate Overall rates(a) 1/50(2.0) 3/50(6.0) 3/50(6.0) 2/50(4.0) Adjusted rates(b) 2.17 7.50 7.50 5.41 Terminal rates(c) 0/40(0.0) 3/40(7.5) 3/40(7.5) 2/37(5.4) Statistical analysis Peto test Standard method(d) P = -----Prevalence method(d) P = 0.4239Combined analysis(d) P = ----Cochran-Armitage test(e) P = 0.8787Fisher Exact test(e) P = 0.3235P = 0.3235P = 0.4926

(HPT360A)

BAIS3

STUDY No. : 0242 ANIMAL : RAT F344/DuCrj SEX : FEMALE NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

Group Name	Control	8000 ppm	20000 ppm	50000 ppm
	SITE : Liver			
`umor rate	TUMOR : hepatocellular ade	noma,hepatocellular carcinoma		
Overall rates(a)	1/50(2.0)	3/50(6.0)	4/50(8.0)	2/50(4.0)
Adjusted rates(b)	2.17	7.50	10.00	5.41
Terminal rates(c)	0/40(0.0)	3/40(7.5)	4/40(10.0)	2/37(5.4)
tatistical analysis Peto test		-,,	2, 10 (2000)	2,0.(0.1)
Standard method(d)	P =			
Prevalence method(d)	P = 0.4204			
Combined analysis(d)	P =			
Cochran-Armitage test(e)	P = 0.8778			
Fisher Exact test(e)		P = 0.3235	P = 0.1998	P = 0.4926
	SITE : kidney			
	TUMOR : renal cell adenoma			
Cumor rate				
Overall rates(a)	0/50(0.0)	3/50(6.0)	6/50(12.0)	4/50(8.0)
Adjusted rates(b)	0.0	7.50	14.63	8.89
Terminal rates(c) Statistical analysis	0/40(0.0)	3/40(7.5)	5/40(12.5)	3/37(8.1)
Peto test				
Standard method(d)	P =			
Prevalence method(d)	P = 0.0937			
Combined analysis(d)	P =			
Cochran-Armitage test(e)	P = 0.1717			
Fisher Exact test(e)		P = 0.1325	P = 0.0190*	P = 0.0688
	GYER A.A.			
	SITE : kidney TUMOR : renal cell adenoma	ropal call carainams		
Cumor rate	TOTOM . I GIRAL COLL AUGI WING	or char Corr Car Cittulia		
Overall rates(a)	0/50(0.0)	3/50(6.0)	6/50(12.0)	5/50(10.0)
Adjusted rates(b)	0.0	7.50	14.63	9.09
Terminal rates(c)	0/40(0.0)	3/40(7.5)	5/40(12.5)	3/37(8.1)
Statistical analysis		· · · ·	-,,	5,0.(5.2)
Peto test				
Standard method(d)	P = 0.1225			
Prevalence method(d)	P = 0.0899			
Combined analysis(d)	P = 0.0441*			
Cochran-Armitage test(e)	P = 0.0775	D 0.400F		
Fisher Exact test(e)		P = 0.1325	P = 0.0190*	P = 0.0360*

(HPT360A)

STUDY No. : 0242 ANIMAL : RAT F344/DuCrj

SEX : FEMALE

(HPT360A)

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

BAIS3

STUDY No. : 0242 NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS ANIMAL : RAT F344/DuCrj SEX : FEMALE

Group Name	Control	8000 ppm	20000 ppm	50000 ppm	
	SITE : thyroid TUMOR : C-cell adenoma				
'umor rate	TONOR • C-Cett agencina				
Overall rates(a)	5/50(10.0)	2/50(4.0)	5/50(10.0)	1/49(2.0)	
Adjusted rates(b)	10.42	5.00	10.00	2.70	
Terminal rates(c)	4/40(10.0)	2/40(5.0)	4/40(10.0)	1/37(2.7)	
tatistical analysis Peto test					
Standard method(d)	P = 0.3825				
Prevalence method(d)	P = 0.9078				
Combined analysis(d)	P = 0.8951				
Cochran-Armitage test(e)	P = 0.1947				
Fisher Exact test(e)		P = 0.2425	P = 0.3710	P = 0.1261	
	SITE : adrenal gland				
	TUMOR: pheochromocytoma				
umor rate	priedera dinos, toma				
Overall rates(a)	0/50(0.0)	3/50(6.0)	2/50(4.0)	3/50(6.0)	
Adjusted rates(b)	0.0	7.50	4.55	8.11	
Terminal rates(c)	0/40(0.0)	3/40(7.5)	1/40(2.5)	3/37(8.1)	
Statistical analysis Peto test					
Standard method(d)	P =				
Prevalence method(d)	P = 0.1426				
Combined analysis(d)	P =				
Cochran-Armitage test(e)	P = 0.2705				
Fisher Exact test(e)		P = 0.1325	P = 0.2574	P = 0.1325	
	OTEN				
	SITE : adrenal gland TUMOR : pheochromocytoma,pheoch	oramacytoma: malianent			
umor rate	Tonon - priodor a billooy contay priodor	* Ondoy Condition (15) Raise			
Overall rates(a)	1/50(2.0)	3/50(6.0)	2/50(4.0)	4/50(8.0)	
Adjusted rates(b)	0.0	7.50	4.55	10.81	
Terminal rates(c)	0/40(0.0)	3/40(7.5)	1/40(2.5)	4/37(10.8)	
Statistical analysis					
Peto test Standard method(d)	P = 1.0000 ?				
Prevalence method(d)	P = 0.0640				
Combined analysis(d)	P = 0.1268				
Cochran-Armitage test(e)	P = 0.2385				
Fisher Exact test(e)		P = 0.3235	P = 0.4926	P = 0.1998	

STUDY No. : 0242 ANIMAL : RAT F344/DuCrj SEX : FEMALE NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

Group Name	Control	mqq 0008	20000 ppm	50000 ppm	
	SITE : uterus				
'umor rate	TUMOR : endometrial stromal po	Гур			
Overall rates(a)	4/50(8.0)	9/50(18.0)	8/50(16.0)	5/50(10.0)	
Adjusted rates(b)	9.30	20.00	17.07	13.51	
Terminal rates(c)	3/40(7.5)	8/40(20.0)	6/40(15.0)	5/37(13.5)	
tatistical analysis				, , ,	
Peto test					
Standard method(d)	P =				
Prevalence method(d)	P = 0.5848				
Combined analysis(d) Cochran-Armitage test(e)	P = P = 0.7820	•			
Fisher Exact test(e)	P = 0.7820	P = 0.1562	P = 0.2169	B 0 4000	
TISHEL EXACT TEST(A)		r - 0.136Z	r = 0.2169	P = 0.4883	
	SITE : uterus				
	TUMOR : endometrial stromal sa	CCOMA			
umor rate	Total Total Tac Ber blide Bar	Cond			
Overall rates(a)	0/50(0.0)	0/50(0.0)	0/50(0.0)	3/50(6.0)	
Adjusted rates(b)	0.0	0.0	0.0	2.63	
Terminat rates(c)	0/40(0.0)	0/40(0.0)	0/40(0.0)	0/37(0.0)	
Statistical analysis					
Peto test	D 0.0404 D				
Standard method(d) Prevalence method(d)	P = 0.0164* ? P = 0.1137				
Combined analysis(d)	P = 0.0032**?				
Cochran-Armitage test(e)	P = 0.0051**				
Fisher Exact test(e)	1 - 0.0001***	P = 0.5000	P = 0.5000	P = 0.1325	
			. 0.5000	- 0.1020	
	SITE : mammary gland				
	TUMOR : fibroadenoma				
ſumor rate					
Overall rates(a)	3/50(6.0)	2/50(4.0)	3/50(6.0)	9/50(18.0)	
Adjusted rates(b)	7.50	5.00	7.50	17.07	
Terminal rates(c)	3/40(7.5)	2/40(5.0)	3/40(7.5)	6/37(16.2)	
Statistical analysis					
Peto test Standard method(d)	P = 0.0172* ?				
Prevalence method(d)	P = 0.01/2* ? P = 0.0299*				
Combined analysis(d)	P = 0.0057**				
Cochran-Armitage test(e)	P = 0.0094**				
		D 0 4000	D 0.000		
Fisher Exact test(e)		P = 0.4909	P = 0.3392	P = 0.0899	

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

ANIMAL : RAT F344/DuCrj

SEX

: FEMALE PAGE: 15

Group Name	Control	Mad 0008	20000 ppm	50000 ppm	
	SITE : mammary gland				
F	TUMOR : adenoma, fibroadeno	ma			
Tumor rate	0.450/ 0.0)	. (50 (0 0)	2 (72 (2.2)		
Overall rates(a)	3/50(6.0)	4/50(8.0)	3/50(6.0)	10/50(20.0)	
Adjusted rates(b)	7.50	7.50	7.50	18.60	
Terminal rates(c)	3/40(7.5)	3/40(7.5)	3/40(7.5)	6/37(16.2)	
Statistical analysis					
Peto test	D 0.0000				
Standard method(d)	P = 0.0822				
Prevalence method(d)	P = 0.0221*				
Combined analysis(d) Cochran-Armitage test(e)	P = 0.0077** P = 0.0122*				
Fisher Exact test(e)	P = 0.0122*	D 0 4005			
FISHEL EXACT TEST(6)		P = 0.4895	P = 0.3392	P = 0.0604	
	SITE : mammary gland				
	TUMOR : adenoma, fibroadeno	ma.adenocarcinoma			
Tumor rate					
Overall rates(a)	3/50(6.0)	4/50(8.0)	5/50(10.0)	10/50(20.0)	
Adjusted rates(b)	7.50	7.50	10.00	18.60	
Terminal rates(c)	3/40(7.5)	3/40(7.5)	4/40(10.0)	6/37(16.2)	
Statistical analysis			, , ,	-,,	
Peto test					
Standard method(d)	P = 0.1061				
Prevalence method(d)	P = 0.0242*				
Combined analysis(d)	P = 0.0098**				
Cochran-Armitage test(e)	P = 0.0157*				

(HPT360A)

BAIS3

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 N 3

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS

MOSUE: MALE

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

EX : MALE				PAGE :	
Group Name	Control	3200 ppm	mqq 0008	20000 ppm	
	SITE : lung				
Tumor rate	TUMOR : bronchiolar-alveolar ade	noma			
Overall rates(a)	1/49(2.0)	3/50(6.0)	2/50(4.0)	1/50(2.0)	
Adjusted rates(b)	2.44	7.14	5.41	2.38	
Terminal rates(c) Statistical analysis Peto test	1/41(2.4)	2/41(4.9)	2/37(5.4)	1/42(2.4)	
Standard method(d)	P =				
Prevalence method(d)	P = 0.6489				
Combined analysis(d)	P =				
Cochran-Armitage test(e)	P = 0.6385				
Fisher Exact test(e)		P = 0.3312	P = 0.4851	P = 0.2426	
Tumor rate Ouerall rates(a)	SITE : Lung TUMOR : bronchiolar-alveolar add	enoma,bronchiolar-alveolar carcinoma	4/50(8.0)	1/50(2.0)	
Adjusted rates(b)	4.65	9.52	8.11	2.38	
Terminal rates(c)	1/41(2.4)	3/41(7.3)	3/37(8.1)	1/42(2.4)	
Statistical analysis Peto test	5			-, \ \ -,	
Standard method(d) Prevalence method(d) Combined analysis(d)	P = 0.3941 P = 0.8039 P = 0.7909				
Cochran-Armitage test(e)	P = 0.3815				
Fisher Exact test(e)		P = 0.3668	P = 0.3668	P = 0.5000	
_	SITE : Lymph nade TUMOR : malignant lymphoma				
Tumor rate	9/40/ 4 1)	4/50/ 0.0	. (7-4		
Overall rates(a) Adjusted rates(b)	2/49(4.1) 4.88	4/50(8.0)	4/50(8.0)	3/50(6.0)	
Terminal rates(c)	2/41(4.9)	4.88 2/41(4.9)	8.11 3/37(8.1)	4.76 2/42(4.8)	
Statistical analysis Peto test	M/ ** \	Δ/ 1λ (1. U/	0/0/(0.1/	2/42(4.8)	
Standard method(d)	P = 0.4018				
Prevalence method(d)	P = 0.4925				
Combined analysis(d)	P = 0.4509				
Cochran-Armitage test(e)	P = 0.9131	D 0000			
Fisher Exact test(e)		P = 0.3668	P = 0.3668	P = 0.4816	

(HPT360A)

PAGE: 2

BAIS3

STUDY No. : 0243

ANIMAL : MOUSE Crj:BDF1
SEX : MALE

Group Name	Control	3200 ppm	mqq 0008	20000 ppm	
	SITE : Liver				
Tumor rate	TUMOR : hepatocellular adenoma				
Overall rates(a)	4/49(8.2)	6/50(12.0)	1/50/ 0.0)	5/50/ 00 0	
Adjusted rates(b)	9.76	14.63	1/50(2.0) 2.70	5/50(10.0)	
Terminal rates(c)	4/41(9.8)	6/41(14.6)	1/37(2.7)	11.90 5/42(11.9)	
Statistical analysis	, , , , , , , , , , , , , , , , , , , ,	0, 11 (1110)	1/0/(2.1)	5/42(11.9)	
Peto test					
Standard method(d)	P =				
Prevalence method(d)	P = 0.4730				
Combined analysis(d)	P =				
Cochran-Armitage test(e)	P = 0.9515				
Fisher Exact test(e)		P = 0.4066	P = 0.1936	P = 0.4763	
	CITT				
	SITE : Liver				
Tumor rate	TUMOR : histiocytic sarcoma				
Overall rates(a)	2/49(4.1)	4/50(8.0)	E/E0/ 10 0)		
Adjusted rates(b)	0.0	2.44	5/50(10.0)	3/50(6.0)	
Terminal rates(c)	0/41(0.0)	1/41(2.4)	0.0 0/37(0.0)	0.0	
Statistical analysis	, , , , , , , , , , , , , , , , , , , ,	1, 11 (2.1)	0/3/(0.0)	0/42(0.0)	
Peto test					
Standard method(d)	P = 0.4006				
Prevalence method(d)	P = 0.5459				
Combined analysis(d)	P = 0.4660		••		
Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.9113				
TISHEL EXACT TEST(E)		P = 0.3668	P = 0.2510	P = 0.4816	
	SITE : liver				
Tumor rate	TUMOR : hepatocellular carcinoma				
Overall rates(a)	1/49(2.0)	3/50(6.0)	0/50(0.0)	a facilities and	
Adjusted rates(b)	2.44	3/50(6.0) 4.88	0/50(0.0)	0/50(0.0)	
Terminal rates(c)	1/41(2.4)	2/41(4.9)	0.0 0/37(0.0)	0.0	
Statistical analysis	•	-/ *** ****/	0/5/\ 0.0/	0/42(0.0)	
Peto test					
Standard method(d)	P = 0.5565				
Prevalence method(d)	P = 0.9107				
Combined analysis(d)	P = 0.9354				
Cochran-Armitage test(e)	P = 0.1480				
Fisher Exact test(e)		P = 0.3312	P = 0.5000	P = 0.5000	

STUDY No. : 0243 ANIMAL : MOUSE Crj:BDF1

SEX : MALE

er adenoma,hepatocellular carcinoma 9/50(18.0) 19.51 8/41(19.5) P = 0.2494	1/50(2.0) 2.70 1/37(2.7) P = 0.1163	5/50(10.0) 11.90 5/42(11.9) P = 0.3592	
9/50(18.0) 19.51 8/41(19.5)	2.70 1/37(2.7)	11.90 5/42(11.9)	
19.51 8/41(19.5)	2.70 1/37(2.7)	11.90 5/42(11.9)	
19.51 8/41(19.5)	2.70 1/37(2.7)	11.90 5/42(11.9)	
8/41(19.5)	2.70 1/37(2.7)	11.90 5/42(11.9)	
	1/37(2.7)	5/42(11.9)	
P = 0.2494	P = 0.1163	P = 0.3592	
P = 0.2494	P = 0.1163	P = 0.3592	
P = 0.2494	P = 0.1163	P = 0.3592	
P = 0.2494	P = 0.1163	P = 0.3592	
P = 0.2494	P = 0.1163	P = 0.3592	
P = 0.2494	P = 0.1163	P = 0.3592	
P = 0.2494	P = 0.1163	P = 0.3592	
and			
ıı u			
1/50(2.0)	0/50/ 4.0	-11	
	2/50(4.0)	3/50(6.0)	
1/41(2.4)	2/37(5.4)	3/42(7.1)	
P = 0.4900	P = 0.2626	P = 0.1364	
	2.44 1/41(2.4) P = 0.4900	2.44 1/41(2.4) 5.41 2/37(5.4)	2.44 5.41 7.14 1/41(2.4) 2/37(5.4) 3/42(7.1)

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

Standard method : Death analysis

Prevalence method: Incidental tumor test

Combined analysis: Death analysis + Incidental tumor test

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

PAGE: 3

BAIS3

⁽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.

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

ANIMAL : MOUSE Cri:BDF1

SEX : MALE

Group Name Control 3200 ppm mag 0008 20000 ppm SITE : ALL SITE TUMOR : histiocytic sarcoma Tumor rate Overall rates(a) 5/49(10.2) 7/50(14.0) 7/50(14.0) 7/50(14.0) Adjusted rates(b) 7.32 9.76 2.70 4.76 Terminal rates(c) 3/41(7.3) 4/41(9.8) 1/37(2.7) 2/42(4.8) Statistical analysis Peto test Standard method(d) P = 0.1637Prevalence method(d) P = 0.7660Combined analysis(d) P = 0.3667Cochran-Armitage test(e) P = 0.6864Fisher Exact test(e) P = 0.4195P = 0.4195P = 0.4195SITE : ALL SITE TUMOR : malignant Lymphoma Tumor rate Overall rates(a) 3/49(6.1) 6/50(12.0) 4/50(8.0) 5/50(10.0) Adjusted rates(b) 7.32 9.76 8.11 9,52 Terminal rates(c) 3/41(7.3) 4/41(9.8) 3/37(8.1) 4/42(9.5) Statistical analysis Peta test Standard method(d) P = 0.4018Prevalence method(d) P = 0.3970Combined analysis(d) P = 0.3735Cochran-Armitage test(e) P = 0.7426Fisher Exact test(e) P = 0.2829P = 0.4788P = 0.3899(HPT360A)

Standard method : Death analysis

Prevalence method: Incidental tumor test

Combined analysis: Death analysis + Incidental tumor test

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

PAGE: 1

BAIS3

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

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

⁽c): Observed tumor incidence at terminal kill.

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

⁽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 N 4 NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANIMALS MOSUE :FEMALE

STUDY No. : 0243 ANIMAL : MOUSE Crj:BDF1 SEX : FEMALE PAGE: 4

`umor rate Overall rates(a) Adjusted rates(b) Terminal rates(c)	TUMOR : bronchiolar-alveolar 1/50(2.0)				
umor rate Overall rates(a) Adjusted rates(b) Terminal rates(c)	1/50(2.0)				
Overall rates(a) Adjusted rates(b) Terminal rates(c)					
Adjusted rates(b) Terminal rates(c)		9/50(4.0)	4/50/ 0.0	0/50/ 0 0)	
Terminal rates(c)	2.00			0/50(0.0) 0.0	
				0/34(0.0)	
Jansical adalysis	1700(2.07	1/01(0.2)	0,04(0.0)	0,04(0.0)	
	P =				
Prevalence method(d)	P = 0.7895				
Combined analysis(d)	P =				
Cochran-Armitage test(e)	P = 0.4120				
SITE Lung Lung	P = 0.4950				
Overall rates(a) Adjusted rates(b) Terminal rates(c) Statistical analysis Peto test Standard method(d)	8.57 3/35(8.6) P = 0.2547	9.38	15.79	1/50(2.0) 0.0 0/34(0.0)	
	P = 0.3002	D = 0 4905	D 0. 9790	P = 0.3235	
Trailer Exact test(e)		1 - 0.4055	r - 0.2720	r = 0.3233	
	SITE : Lymph node				
ſumor rate					
Overall rates(a)		, , ,		7/50(14.0)	
Adjusted rates(b)				5.88	
• •	7/35(20.0)	5/31(16.1)	3/34(8.8)	2/34(5.9)	
	P - 0 5909		•		
Combined analysis(d)	P = 0.9127				
Cochran-Armitage test(e)	P = 0.1630				
Fisher Exact test(e)		P = 0.4450	P = 0.2711	P = 0.2711	

STUDY No. : 0243 NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS ANIMAL : MOUSE Crj:BDF1

Group Name	Control	8000 ppm	20000 ppm	50000 ppm
	SITE : spleen			
`umor rate	TUMOR : malignant lymphoma			
Overall rates(a)	4/50(8.0)	1/50(2.0)	4/50(8.0)	0/40/ 0 0)
Adjusted rates(b)	11.43	3.23	8.82	0/49(0.0) 0.0
Terminal rates(c)	4/35(11.4)	1/31(3.2)	3/34(8.8)	0/33(0.0)
tatistical analysis				,,,,,,
Peto test	D 0.000			
Standard method(d) Prevalence method(d)	P = 0.3828 P = 0.9606			
Combined analysis(d)	P = 0.9471			
Cochran-Armitage test(e)	P = 0.1204			
Fisher Exact test(e)		P = 0.1998	P = 0.3579	P = 0.0715
	SITE : Liver			
	TUMOR : hepatocellular adenoma			
umor rate				
Overall rates(a)	2/50(4.0)	3/50(6.0)	6/50(12.0)	20/50(40.0)
Adjusted rates(b) Terminal rates(c)	5.71 2/35(5.7)	9.68 3/31(9.7)	15.79	58.82
Statistical analysis	2/30(5.1)	3/31(9.7)	5/34(14.7)	20/34(58.8)
Peto test				
Standard method(d)	P =			
Prevalence method(d)	P < 0.0001**			
Combined analysis(d)	P =			
Cochran-Armitage test(e) Fisher Exact test(e)	P < 0.0001**	P = 0.4000	5 0 1000	
Trision Exact test(e)		P = 0.4909	P = 0.1606	P = 0.0003**
	SITE : liver			
	TUMOR : histiocytic sarcoma			
'umor rate				
Ouerall rates(a)	0/50(0.0)	3/50(6.0)	4/50(8.0)	3/50(6.0)
Adjusted rates(b) Terminal rates(c)	0.0	0.0	2.56	0.0
Terminal rates(c) Statistical analysis	0/35(0.0)	0/31(0.0)	0/34(0.0)	0/34(0.0)
Peto test				
Standard method(d)	P = 0.1645			
Prevalence method(d)	P = 0.4029			
Combined analysis(d)	P = 0.1764			
Cochran-Armitage test(e)	P = 0.3135			
Fisher Exact test(e)		P = 0.1325	P = 0.0688	P = 0.1325

(HPT360A)

: FEMALE

SEX

STUDY No. : 0243 NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS ANIMAL : MOUSE C-j:BDF1
SEX : FEMALE

Group Name	Control	8000 ppm	20000 ppm	maq 00005	
	SITE : Liver				
'umor rate	TUMOR : hemangiosarcoma				
Overall rates(a)	3/50(6.0)	1/50(2.0)	1/50(2.0)	1/50/ 0.0)	
Adjusted rates(b)	5.71	3.23	0.0	1/50(2.0) 2.94	
Terminal rates(c)	2/35(5.7)	1/31(3.2)	0/34(0.0)	1/34(2.9)	
Statistical analysis			., ,	1,01(5.0)	
Peto test	B =				
Standard method(d)	P = 0.7236				
Prevalence method(d) Combined analysis(d)	P = 0.6784 P = 0.7963				
Cochran-Armitage test(e)	P = 0.3947				
Fisher Exact test(e)	1 0.0041	P = 0.3235	P = 0.3235	P = 0.3235	
				1 = 0.3233	
	SITE : Liver				
	TUMOR : hepatocellular carcinom	a			
umor rate					
Overall rates(a)	0/50(0.0)	2/50(4.0)	5/50(10.0)	12/50(24.0)	
Adjusted rates(b)	0.0	6.45	8.82	29.41	
Terminal rates(c) Hatistical analysis	0/35(0.0)	2/31(6.5)	3/34(8.8)	10/34(29.4)	
Peto test					
Standard method(d)	P = 0.1852				
Prevalence method(d)	P < 0.0001**				
Combined analysis(d)	P < 0.0001**				
Cochran-Armitage test(e)	P < 0.0001**				
Fisher Exact test(e)		P = 0.2574	P = 0.0360*	P = 0.0005**	
	SITE : Liver				
	TUMOR : hepatocellular adenoma,	hopotocollulor coroinene			
umor rate	Totton Thepatocettotal adelibilia,	Liebarncerrafai cai C.H.Inilia			
Overall rates(a)	2/50(4.0)	5/50(10.0)	11/50(22.0)	26/50(52.0)	
Adjusted rates(b)	5.71	16.13	25.00	70.59	
Terminal rates(c)	2/35(5.7)	5/31(16.1)	8/34(23.5)	24/34(70.6)	
tatistical analysis				,	
Peto test Standard method(d)	D = 0 1959				
Prevalence method(d)	P = 0.1852 P < 0.0001**?				
Combined analysis(d)	P < 0.0001**? P < 0.0001**?				
Cochran-Armitage test(e)	P < 0.0001**				
Fisher Exact test(e)		P = 0.2425	P = 0.0170*	P < 0.0001**	
			,	1 / 0.0001***	

BAIS3

STUDY No. : 0243

ANIMAL : MOUSE Crj:BDF1

SEX : FEMALE

Group Name	Control	mqq 0008	20000 ppm	50000 ppm
	SITE : uterus			
Tumor rate	TUMOR : histiocytic sarcoma			
Overall rates(a)	6/50(12.0)	12/50(24.0)	E/E0/ 14 0)	7/7-/ >
Adjusted rates(b)	2.86	12/50(24.0)	7/50(14.0) 5.88	7/50(14.0)
Terminal rates(c)	1/35(2.9)	6/31(19.4)	2/34(5.9)	11.63
Statistical analysis	-, (-, -,	0,01(10.4)	2/04(3.8)	3/34(8.8)
Peto test				
Standard method(d)	P = 0.8854			
Prevalence method(d)	P = 0.2838			
Combined analysis(d) Cochran-Armitage test(e)	P = 0.6873 P = 0.6996			
Fisher Exact test(e)	r = 0.0990	P = 0.1474	P = 0.4863	B 0 1000
			1 - 0.4000	P = 0.4863
	SITE : Harderian gland TUMOR : adenoma			
Tumor rate	230103110			
Overall rates(a)	1/50(2.0)	2/50(4.0)	3/50(6.0)	3/50(6.0)
Adjusted rates(b)	2.86	5.13	7.32	8.33
Terminal rates(c)	1/35(2.9)	1/31(3.2)	2/34(5.9)	2/34(5.9)
Statistical analysis Peto test				
1910 (62)				
Standard method(d)	P =			
Standard method(d) Prevalence method(d)	P = P = 0.1766			
Standard method(d) Prevalence method(d) Combined analysis(d)	P = P = 0.1766 P =			
Prevalence method(d)	P = 0.1766			

(HPT360A)

BAIS3

PAGE: 7

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.

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

ANIMAL : MOUSE Crj:BDF1 SEX : FEMALE

Group Name	Control	8000 ppm	20000 ppm	50000 ppm	
	SITE : ALL SITE				
r .	TUMOR : histiocytic sarcoma				
Tumor rate	0/50/ +0.0				
Overall rates(a)	6/50(12.0)	18/50(36.0)	11/50(22.0)	11/50(22.0)	
Adjusted rates(b)	2.86	25.81	7.69	14.63	
Terminal rates(c)	1/35(2.9)	8/31(25.8)	2/34(5.9)	4/34(11.8)	
Statistical analysis					
Peto test	P - 0 0000				
Standard method(d) Prevalence method(d)	P = 0.6823 P = 0.2553				
Combined analysis(d)	P = 0.2553 P = 0.4854				
Cochran-Armitage test(e)	P = 0.8805				
Fisher Exact test(e)	1 - 0.0000	P = 0.0222*	D 0 10FF		
Train into cose(o)		1 - 0.0222+	P = 0.1955	P = 0.1955	
	SITE : ALL SITE				
	TUMOR : malignant lymphoma				
Tumor rate					
Overall rates(a)	15/50(30.0)	14/50(28.0)	11/50(22.0)	7/50(14.0)	
Adjusted rates(b)	31.43	19.35	17.65	5.88	
Terminal rates(c)	11/35(31.4)	6/31(19.4)	6/34(17.6)	2/34(5.9)	
Statistical analysis					
Peto test	D 0 5500				
Standard method(d)	P = 0.5762				
Prevalence method(d) Combined analysis(d)	P = 0.9965				
Cochran-Armitage test(e)	P = 0.9770 P = 0.0395*				
Fisher Exact test(e)	r - v.vava*	D 0 4010			
Ligher Exact feat(6)		P = 0.4810	P = 0.3167	P = 0.0941	
IPT360A)					
,					

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

Standard method : Death analysis

Prevalence method: Incidental tumor test

Combined analysis: Death analysis + Incidental tumor test

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

PAGE: 2

BAIS3

⁽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 O 1

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

RAT: MALE: ALL ANIMALS

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1

SEX : MALE

HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR (SUMMARY)

ALL ANIMALS (0-105W)

· ·		Group Name Control No. of Animals on Study 50	8000 ppm 50	20000 ppm 50	50000 ppm 50
rgan	Findings				
[Respiratory :	system]				
nasal cavit	leukemic cell infiltration	<50> 1	<50> 0	<50> 0	<50> 0
	metastasis:pancreas tumor	0	0	0	1
lung	leukemic cell infiltration	<50> 4	<50> 1	<50> 1	<50> 0
	metastasis:thyroid tumor	1	1	0	0
	metastasis:pancreas tumor	0	0	0	1
	metastasis:bone tumor	0	0	1	1
	metastasis:preputial/clitoral gland tumo	or 1	0	0	0
[Hematopoieti	c system]				
bone marrow	leukemic cell infiltration	<50> 4	<50> 1	<50> 1	<50> 1
Lymph node	leukemic cell infiltration	<50> 3	<50> 0	<50> 0	<50> 0
(Circulatory	system]				
heart	leukemic cell infiltration	<50> 1	<50> 0	<50> 0	<50>
	metastasis:thyroid tumor	1	0	0	0
[Digestive sy	stem]				
salivary gl	leukemic cell infiltration	<50> 1	<50> 0	<50> 0	<50> 0
< a > b	a: Number of animals examined at the s b: Number of animals with lesion	ite			

HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR (SUMMARY)

ALL ANIMALS (0-105W)

ANIMAL : RAT F344/DuCrj REPORT TYPE : A1

SEX : MALE

rgan		Group Name Control No. of Animals on Study 50 —	8000 pm 50	20000 ppm 50	50000 ppm 50
oigestive sy	rsteml				
tomach		⟨50⟩	<50>	<50>	(F0)
ORGOT	leukemic cell infiltration	1	0	0	<50> 0
all intes		<50>	<50>	<50>	<50>
	leukemic cell infiltration	1	0	0	0
rge intes	leukemic cell infiltration	<50> 1	<50> 0	<50> 0	<50> 0
ver		<50>	<50>	< 50>	<50>
	leukemic cell infiltration	5	1	1	1
ncreas		<50>	<50>	<50>	< 50>
	leukemic cell infiltration	2	0	0	0
rinary syst	tem]				
dney		<50>	<50>	<50>	<50>
	leukemic cell infiltration	3	1	1	0
	metastasis:pancreas tumor	0	0	0	1
in bladd	leukemic cell infiltration	<50> 1	<50> 0	<50>	<50>
	code in the actor	1	U	0	0
ndocrine sy	vstem]				
tuitary		<49>	<50>	<50>	<50>
	leukemic cell infiltration	1	0	0	0
	metastasis:pancreas tumor	0	0	0	1
yroid	leukemic cell infiltration	<50>	<50>	<50>	<50>
		1	0	0	0
a> b	a : Number of animals examined at the sib : Number of animals with lesion	te			
PT150)					

⁽JPT150)

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1 SEX : MALE HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR (SUMMARY) ALL ANIMALS (0-105W)

gan		Group Name No. of Animals on Study	Control 50	8000 pm 50	20000 ppm 50	50000 ppm 50
Endocrine s	vstem]					
adrena l	leukemic cell infiltration		<50> 2	<50> 1	<50> 1	<50>
	metastasis:pancreas tumor		0	0	0	1
Reproductive	e system]			,		
prostate	leukemic cell infiltration		<50> 1	<50> 0	<50> 0	<50> 0
(Nervous sys	cem]					
orain	leukemic cell infiltration		<50> 2	<50> 1	<50> 1	<50> 0
(Musculaskele	etal system]					
muscle	leukemic cell infiltration		<50> 0	<50> 1	<50> 0	<50> 0
	metastasis:pancreas tumor		0	0	0	1
[Body cavitie	es]					
oleura	metastasis:bone tumor		<50> 0	<50> 0	<50> 0	<50> 1
retroperit	metastasis:preputial/clitoral gland tumo	-	<50> 1	<50> 0	<50> 0	<50> 0
a> b	a: Number of animals examined at the si b: Number of animals with lesion	te				

APPENDIX O 2

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

RAT: FEMALE: ALL ANIMALS

ANIMAL : RAT F344/DuCrj

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

ALL ANIMALS (0-105W)

0rgan		Group Name No. of Animals on Study	Control 50	8000 ppm 50	20000 ppm 50	50000 ppm 50
[Respiratory	system]					
nasal cavit	leukemic cell infiltration		<50> 0	<50> 0	<50> 0	<50> 1
lung	leukemic cell infiltration		<50> 4	<50> 6	<50> 1	<50> 4
	metastasis:bone tumor		0	0	1	0
	metastasis:mammary gland tumor		0	0	1	0
	metastasis:mediastinum tumor		1	0	0	0
(Hematopoieti	c system]					
bone marrow	leukemic cell infiltration		<50> 0	<50> 3	<50> 0	<50> 3
tymph nade	leukemic cell infiltration		<50> 3	<50> 0	<50> 0	<50> 3
	metastasis:uterus tumor		0	0	0	1
[Circulatory	system]					
heart	leukemic cell infiltration		<50> 0	<50> 1	<50> 0	<50> 1
	metastasis:mediastinum tumor		1	0	0	0
[Digestive sy	vstem]					
tongue	metastasis:subcutis tumor		<50> 0	<50> 1	<50> 0	<50> 0
<a>>	a: Number of animals examined at the s b: Number of animals with lesion	te		***************************************		
(IDT150)						

ANIMAL : RAT F344/DuC-j

REPORT TYPE : A1 SEX : FEMALE

(JPT150)

HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR (SUMMARY)

ALL ANIMALS (0-105W)

PAGE: 2 Group Name Control 8000 ppm 20000 ppm 50000 ppm No. of Animals on Study 50 50 50 50 0rgan_ Findings_ [Digestive system] salivary gl <50> <50> <50> <50> leukemic cell infiltration 0 0 stomach <50> <50> <50> <50> leukemic cell infiltration 1 0 metastasis:uterus tumor 0 0 1 small intes <50> ⟨50⟩ <50> <50> leukemic cell infiltration 1 0 0 0 large intes <50> <50> <50> <50> leukemic cell infiltration 1 0 liver <50> <50> (50) <50> leukemic cell infiltration 5 metastasis:uterus tumor 0 0 1 1 pancreas ⟨50⟩ <50> <50> ⟨50⟩ leukemic cell infiltration 0 1 [Urinary system] kidney <50> <50> <50> <50> leukemic cell infiltration 1 3 2 3 metastasis:mediastinum tumor 1 0 0 [Endocrine system] pituitary <50> ⟨50⟩ <50> <50> leukemic cell infiltration 1 0 1 <a>> a: Number of animals examined at the site b b: Number of animals with lesion

BAIS3

STUDY NO. : 0242 ANIMAL : RAT F344/DuCrj HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR (SUMMARY) ALL ANIMALS (0-105W)

REPORT TYPE : A1 : FEMALE

rgan	Findings	Group Name Com No. of Animals on Study	ntrol 50	8000 ppm 50	20000 ppm 50	50000 ppm 50
				, , , , , , , , , , , , , , , , , , , ,		
Endocrine sys	tem]					
drenat	leukemic cell infiltration		<50> 3	<50> 3	<50>	<50> 3
			·	v		3
Reproductive	system]					
ovary	leukemic cell infiltration		<50> 0	<50> 2	<50> 0	<50> 0
				_	-	, and the second
Nervous syste	em]		•			
orain	leukemic cell infiltration		<50>	<50> 3	<50> 0	<50> 2
	metastasis:pituitary tumor		0	0	I	0
pinal cord			<50>	<50>	<50>	<50>
	leukemic cell infiltration		0	3	0	1
Musculoskelet	tal system]					
nuscle			<50>	<50>	<50>	<50>
	leukemic cell infiltration		1	0	0	1
Body cavities	5]					
oleura	motoptopia modications to accomp		<50>	<50>	<50>	<50>
	metastasis:mediastinum tumor		1	0	0	0
eritoneum	metastasis:uterus tumor		<50> 0	<50> 0	<50> 0	<50> 1
etroperit	metastasis:uterus tumor		<50> 0	<50> 0	<50> 1	<50> 0

APPENDIX O 3

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

RAT: MALE: SACRIFICED ANIMALS

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

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1
SEX : FEMALE

in roth back i

		Group Name Control	8000 ppm	20000 ppm	50000 ppm
gan	Findings	No. of Animals on Study 40	40	40	37
espiratory :	system]				
ng	leukemic cell infiltration	<40> 2	<40> 1	<40> 1	<37> 2
ematopoieti	c system]				
one marrow	leukemic cell infiltration	<40> 0	<40> 0	<40> 0	<37> 1
mph nade	leukemic cell infiltration	<40> 1	<40> 0	<40> 0	<37> 1
igestive sy	stem]				
alivary gl	leukemic cell infiltration	<40> 1	<40> 0	<40> 0	<37> 0
tomach	leukemic cell infiltration	<40>	<40> 0	<40> 0	<37> 0
nall intes	leukemic cell infiltration	<40>	<40> 0	<40> 0	<37> 0
arge intes	leukemic cell infiltration	<40> 1	<40> 0	<40> 0	<37> 0
iver	leukemic cell infiltration	<40>	<40>	<40>	<37> 3
ncreas	leukemic cell infiltration	<40>	<40> 0	<40> 0	<37> 0
Jrinary syst	em]				
idney	leukemic cell infiltration	<40> 0	<40> 0	<40> 2	<37>

(JPT150)

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR (SUMMARY)

SACRIFICED ANIMALS (105W)

Organ		oup Name . of Animals on Study	Control 40	8000 ppm 40	20000 ppm 40	50000 ppm 37
Endocrine s	system]					
pituitary	leukemic cell infiltration		<40> 1	<40> 0	<40> 0	<37> 0
adrena l	leukemic cell infiltration		<40> 1	<40> 0	<40> 1	<37> 1
Nervous sys	rtem]					
rain	leukemic cell infiltration		<40>	<40> 0	<40> 0	<37> 0
a >	a: Number of animals examined at the site b: Number of animals with lesion					
(JPT150)						

APPENDIX O 4

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

RAT: FEMALE: SACRIFICED ANIMALS

HISTOLOGICAL FIND

ANIMAL : RAT F344/DuCrj REPORT TYPE : A1

SEX : MALE

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

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

ANIMAL : RAT F344/DuCrj

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

SACRIFICED ANIMALS (105W)

PAGE: 2

Organ		iroup Name io. of Animals on Study	Control 33	8000 ppm 43	20000 ppm 43	50000 ppm 38

(Endocrine	system]					
adrenal	leukemic cell infiltration		<33> 0	<43> 0	<43> · · 0	<38> 1
	metastasis:pancreas tumor		0	0	0	1
(Musculoske	eletal system]					
muscle	metastasis:pancreas tumor		<33> 0	<43> 0	<43> 0	<38> 1
<a>> b	a: Number of animals examined at the sit b: Number of animals with lesion	Ce				
(JPT150)						

BAIS3

APPENDIX O 5

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

MOUSE: MALE: ALL ANIMALS

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : AI SEX : MALE

HISTOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)

ALL ANIMALS (0-105W)

PAGE: 1 Group Name Control 3200 ppm mag 0008 20000 ppm No. of Animals on Study 50 50 50 Organ__ Findings_ [Respiratory system] nasal cavit <49> <50> ⟨50⟩ ⟨50⟩ metastasis: liver tumor metastasis:subcutis tumor metastasis:spleen tumor metastasis:urinary bladder tumor 0 0 1 lung <49> <50> <50> <50> leukemic cell infiltration 1 1 metastasis:liver tumor metastasis:spleen tumor metastasis:urinary bladder tumor [Hematopoietic system] bone marrow <49> <50> <50> ⟨50⟩ leukemic cell infiltration 0 metastasis:subcutis tumor 1 0 lymph nade <49> <50> <50> <50> metastasis:liver tumor 0 0 1 metastasis:subcutis tumor 0 0 spleen ⟨49⟩ <50> <50> <50> leukemic cell infiltration 3 2 metastasis:liver tumor 0 0 1 (a) a: Number of animals examined at the site b: Number of animals with lesion b

(JPT150)

ANIMAL : MOUSE Crj:BDF1

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

ALL ANIMALS (0-105W)

Group Name Control 3200 ppm Mqq 0008 20000 ppm No. of Animals on Study 49 50 50 50 Organ_ Findings [Hematopoietic system] spleen <49> <50> <50> <50> metastasis:lympho node tumor 0 0 [Circulatory system] heart <49> <50> <50> <50> leukemic cell infiltration 0 1 metastasis:liver tumor 0 2 0 [Digestive system] tongue **<49>** ⟨50⟩ <50> ⟨50⟩ leukemic cell infiltration 0 1 0 0 salivary gl <49> ⟨50⟩ <50> <50> leukemic cell infiltration 0 metastasis:liver tumor 0 1 metastasis:subcutis tumor 0 0 0 stomach <49> ⟨50⟩ <50> ⟨50⟩ leukemic cell infiltration 0 1 metastasis:liver tumor 1 1 metastasis:lympho node tumor 1 0 0 small intes **<49>** <50> <50> <50> metastasis:liver tumor 1 0 0 metastasis:epididymis tumor 0 0 0 1 < a > a: Number of animals examined at the site b b: Number of animals with lesion (JPT150)

BAIS3

ANIMAL : MOUSE Crj:BDF1

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

ALL ANIMALS (0-105W)

Organ		Group Name Contro No. of Animals on Study 49	L 3200 ppm 50	8000 ppm 50	20000 ppm 50
Digestive sys	steml				
	, com	440			
large intes	metastasis:epididymis tumor	<49> 0	<50> 0	<50> 0	<50> 1
iver	leukemic cell infiltration	<49>	<50> I	<50> 2	<50> 1
	metastasis:subcutis tumor	0	0	1	0
	metastasis:spleen tumor	0	0	0	1
	metastasis:urinary bladder tumor	0	0	0	1
	metastasis:epididymis tumor	0	0	0	1
	metastasis:lympho node tumor	1	0	0	1
vancreas	leukemic cell infiltration	<49>	<50> 2	<50> 0	<50> 0
	metastasis:liver tumor	1	0	0	0
	metastasis:urinary bladder tumor	0	0	0	1
Urinary syste	em]				
cidney	leukemic cell infiltration	<49>	<50> 1	<50> 2	<50> 1
	metastasis:liver tumor	1	1	1	2
	metastasis:spleen tumor	0	0	0	1
	metastasis:salivary gland tumor	0	0	0	I
	metastasis:lympho node tumor	1	0	0	0
(a)	a: Number of animals examined at the si b: Number of animals with lesion	te			

ANIMAL : MOUSE Crj:BDF1

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

REPORT TYPE : A1 SEX : MALE

Organ		Group Name No. of Animals on Study	Control 49	3200 ррт 50	8000 ppm 50	20000 ppm 50
[Urinary syst	em]					
urin bladd			<49>	<50>	< 50>	<50>
	leukemic cell infiltration		1	0	0	0
	metastasis:epididymis tumor		1	0	0	0
Endocrine sy	stem]					
panc islet			<49>	< 50>	< 50>	< 50>
	metastasis:lympho node tumor		1	0	0	0
adrena l	metastasis:spleen tumor		<49>	<50> 0	<50> 0	<50>
	ne tastasts spreet tunu		V	V	U	1
[Reproductive	system]					
testis	metastasis:liver tumor		<49>	<50> 1	<50> 0	<50>
	metastasis:subcutis tumor					0
			0	0	1	0
	metastasis:epididymis tumor		0	0	0	1
	metastasis:salivary gland tumor		0	1	0	0
epididymis	laukania aali infilississ		<49>	<50>	<50>	<50>
	leukemic cell infiltration		1	0	1	0
	metastasis:subcutis tumor		0	0	1	0
semin ves	leukemic cell infiltration		<49>	<50>	<50>	<50>
			0	1	1	0
	metastasis:liver tumor		1	0	0	0
(a) b	a : Number of animals examined at the si b : Number of animals with lesion	te				

ANIMAL : MOUSE Crj:BDF1

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

REPORT TYPE : A1

SEX : MALE

Organ		Group Name No. of Animals on Study	Contral 49	3200 ppm 50	8000 ppm 50	20000 ppm 50
[Reproductive	evetam					
	373 (611)					
prostate	leukemic cell infiltration		<49>	<50> 0	<50>	<50> 0
	tourouro obte mired delai		V	V	1	V
[Musculoskele	tal system]					
muscle			<49>	<50>	<50>	<50>
	metastasis:liver tumor		0	0	0	1
[Body cavitie	s]					
mediastinum			<49>	<50>	<50>	<50>
	metastasis:liver tumor		0	0	1	0
•	metastasis:lung tumor		0	0	1	0
peritoneum			<49>	<50>	<50>	<50>
	metastasis:liver tumor		0	0	1	0
⟨a⟩ b	a : Number of animals examined at the si b : Number of animals with lesion	te				
(JPT150)						

APPENDIX O 6

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

MOUSE: FEMALE: ALL ANIMALS

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

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1

(JPT150)

SEX : FEMALE

0rgan	Findings	Group Name No. of Animals on Study	Control 50	8000 ppm 50	2000 ppm 50	50000 ppm 50
[Integumentar	ry system/appandage]					
skin/app	leukemic cell infiltration		<50> 0	<50> 0	<50> 0	<50> 3
[Respiratory	system]					
nasal cauit	leukemic cell infiltration		<50> 0	<50> 1	<50> 1	<50> 0
	metastasis:liver tumor		0	1	0	0
	metastasis:uterus tumor		0	1	1	0
larynx	metastasis:thyroid tumor		<50> 0	<50> 1	<50> 0	<50> 0
lung	leukemic cell infiltration		<50> 4	<50> 11	<50> 7	<50> 5
	metastasis:liver tumor		0	1	4	2
	metastasis:uterus tumor		3	2	2	0
	metastasis:subcutis tumor		0	1	0	0
	metastasis:bone tumor		1	0	0	0
[Hematopoieti	c system]					
bone marrow	leukemic cell infiltration		<50> 0	<50> 3	<50> 2	<50> 0
	metastasis:liver tumor		0	0	0	1
	metastasis:uterus tumor		1	0	0	0

SEX

ANIMAL : MOUSE Crj:BDF1 REPORT TYPE : A1 : FEMALE

HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR (SUMMARY)

ALL ANIMALS (0-105W)

_		Group Name No. of Animals on Study	Control 50	8000 ppm 50	20000 ppm 50	50000 ppm 50
rgan	Findings					
[Hematopoieti	c system]					
bone marrow	metastasis:lympho node tumor		<50> 0	<50> 0	<50> 1	<50> 0
lymph nade	metastasis:liver tumor		<50> 0	<50> 0	<50> 1	<50> 0
spleen	leukemic cell infiltration		<50> 6	<50> 9	<50> 5	<50> 7
	metastasis:liver tumor		0	0	1	2
	metastasis:lympho node tumor		0	0	1	0
[Circulatory	system]					
neart	leukemic cell infiltration		<50> 0	<50> 3	<50> 2	<50> 3
	metastasis:liver tumor		0	1	0	0
[Digestive sy	stem]					
tongue	leukemic cell infiltration		<50> 0	<50> 1	<50> 0	<50> 0
salivary gl	leukemic cell infiltration		<50> 2	<50> 5	<50> 3	<50> 2
stomach	leukemic cell infiltration		<50> 2	<50> 3	<50> 2	<50> 1
	metastasis:liver tumor		0	1	0	0
	metastasis:uterus tumor		1	2	2	0
(a >	a: Number of animals examined at the s b: Number of animals with lesion	ite				

ANIMAL : MOUSE Crj:BDF1

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

REPORT TYPE : A1

SEX : FEMALE

rgan		Group Name Control No. of Animals on Study 50	8000 ppm 50	20000 ppm 50	50000 ppm 50
Digestive sy	vstem]				
mall intes	leukemic cell infiltration	<50> 0	<50> 0	<50> 1	<50>
	metastasis:uterus tumor	0	1	0	0
arge intes	leukemic cell infiltration	<50> 0	<50> 0	<50> 1	<50> 0
liver	leukemic cell infiltration	<50> 8	<50> 10	<50> 6	<50> 5
	metastasis:uterus tumor	6	6	5	2
	metastasis:subcutis tumor	0	1	0	0
	metastasis:bone tumor	1	0	0	0
	metastasis:lympho node tumor	0	0	1	0
ancreas	leukemic cell infiltration	<50> 0	<50> 2	<50> 2	<50> 0
	metastasis:uterus tumor	1	0	1	0
Urinary sys	tem)				
idney	leukemic cell infiltration	<50> 4	<50> 8	<50> 6	<50> 3
	metastasis:liver tumor	0	0	1	1
	metastasis:uterus tumor	1	1	2	0
	metastasis:subcutis tumor	0	1	0	0
(a)	a: Number of animals examined at the si b: Number of animals with lesion	te			

ANIMAL : MOUSE Crj:BDF1

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

REPORT TYPE : A1

SEX

: FEMALE

0rgan		Group Name No. of Animals on Study	Control 50	Maa 0008 50	20000 ppm 50	50000 ppm 50
Urinary syst	em]					
kidney	metastasis:stomach tumor		<50> 0	<50> 0	<50> 0	<50> 1
	metastasis:urinary bladder tumor		0	1	0	0
	metastasis:lympho node tumor		0	0	1	0
rin bladd	leukemic cell infiltration		<50> 3	<50> 7	<50> 4	<50> 1
	metastasis:liver tumor		0	1	0	0
	metastasis:subcutis tumor		0	1	0	0
Endocrine sy	stem]					
thyroid	leukemic cell infiltration		<50> 0	<50> 0	<50> 0	<50> 1
adrenal	leukemic cell infiltration		<50> 1	<50> 3	<50> 1	<50> 1
Reproductive	system]					
Duary	leukemic cell infiltration		<50> 4	<50> 10	<50> 2	<50> 4
	metastasis:liver tumor		0	1	1	0
	metastasis:uterus tumor		3	3	5	2
	metastasis:subcutis tumor		0	1	0	0
rterus	leukemic cell infiltration		<50> 1	<50> 5	<50> 2	<50> 0
(a) b	a: Number of animals examined at the si b: Number of animals with lesion	te				

ANIMAL

: MOUSE Crj:BDF1

HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR (SUMMARY)

ALL ANIMALS (0-105W)

REPORT TYPE : A1 SEX : FEMALE

Group Name Control 8000 ppm 20000 ppm 50000 ppm No. of Animals on Study 50 50 50 50 Findings_ [Reproductive system] vagina <50> <50> <50> <50> leukemic cell infiltration 0 0 metastasis:subcutis tumor 0 [Nervous system] brain <50> <50> <50> ⟨50⟩ leukemic cell infiltration 0 0 metastasis:liver tumor 0 0 0 periph nerv <50> <50> ⟨50⟩ <50> metastasis:liver tumor 0 [Special sense organs/appandage] өуе (50) <50> ⟨50⟩ <50> leukemic cell infiltration Harder gl <50> <50> <50> <50> leukemic cell infiltration 0 [Musculoskeletal system] muscle ⟨50⟩ ⟨50⟩ <50> ⟨50⟩ leukemic cell infiltration 2 [Body cavities] mediastinum <50> <50> <50> <50> metastasis:bone tumor 1 0 (a) a: Number of animals examined at the site b b: Number of animals with lesion (JPT150)

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1

SEX : FEMALE HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR (SUMMARY)

ALL ANIMALS (0-105W)

Organ		Group Name No. of Animals on Study	Control 50	MQQ 0008 50	20000 ppm 50	50000 ppm 50
Body cavities	s]					
mediastinum	metastasis:lympho node tumor		<50> 0	<50> 0	<50> 1	<50> 0
eritoneum	leukemic cell infiltration		<50> 4	<50> 5	<50> 1	<50> 2
	metastasis:liver tumor		0	0	1	0
a > b	a: Number of animals examined at the si b: Number of animals with lesion	te				
(JPT150)		'n'interior				

BAIS3

APPENDIX O 7

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

MOUSE: MALE: SACRIFICED ANIMALS

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : AI SEX : MALE

HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR (SUMMARY)

SACRIFICED ANIMALS (105W)

PAGE: 1 Group Name Control 3200 ppm 8000 ppm 20000 ppm No. of Animals on Study 41 41 37 42 Organ_ Findings_ [Respiratory system] nasal cavit (41) (41) ⟨37⟩ <42> metastasis:spleen tumor 0 1 lung <41> (41) <37> <42> leukemic cell infiltration 1 1 metastasis:spleen tumor 0 [Hematopoietic system] bone marrow <41> <41> ⟨37⟩ **〈42〉** leukemic cell infiltration 0 lymph node <41> <41> ⟨37⟩ <42> metastasis:subcutis tumor 0 0 spleen <41> <41> ⟨37⟩ <42> leukemic cell infiltration 2 2 2 metastasis:lympho node tumor 1 0 0 [Circulatory system] heart <41> (41) ⟨37⟩ <42> leukemic cell infiltration 1 0 metastasis:liver tumor 0 [Digestive system] tongue **<41>** <41> <37> <42> leukemic cell infiltration 0 1 0 0 (a) a: Number of animals examined at the site b b: Number of animals with lesion

(JPT150)

ANIMAL. : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : MALE

(JPT150)

HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR (SUMMARY)

SACRIFICED ANIMALS (105W)

PAGE: 2 Group Name Control 3200 ppm mqq 0008 20000 ppm No. of Animals on Study 41 41 37 42 0rgan_ Findings_ [Digestive system] salivary gl <41> <41> ⟨37⟩ <42> leukemic cell infiltration 0 1 0 metastasis:subcutis tumor 0 0 0 stomach <41> <41> ⟨37⟩ (42> leukemic cell infiltration 0 1 metastasis:lympho node tumor 1 0 0 Liver <41> <41> ⟨37⟩ <42> leukemic cell infiltration 1 metastasis:spleen tumor 0 1 metastasis:lympho node tumor 1 0 0 pancreas <41> (41) ⟨37⟩ <42> leukemic cell infiltration 1 0 0 [Urinary system] kidney <41> (41) (37) ⟨42⟩ leukemic cell infiltration 1 0 metastasis:spleen tumor 0 metastasis:salivary gland tumor 0 0 1 metastasis:lympho node tumor 1 0 urin bladd <41> <41> ⟨37⟩ <42> leukemic cell infiltration 1 metastasis:epididymis tumor 1 0 0 (a) a: Number of animals examined at the site b b: Number of animals with lesion

ANIMAL : MOUSE Crj:BDF1

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

REPORT TYPE : A1 SEX : MALE

PAGE: 3

0rgan		Group Name No. of Animals on Study	Control 41	3200 ppm 41	8000 ppm 37	20000 ppm 42
(Endocrine sys	stem]					
panc islet	metastasis:lympho node tumor		<41> 1	<41> 0	<37> 0	<42> 0
drenal	metastasis:spleen tumor		<41> 0	<41> 0	<37> 0	<42> 1
Reproductive	system]					
estis	metastasis:salivary gland tumor		<41> 0	<41>	<37> 0	<42> 0
pididymis	leukemic cell infiltration		<41>	<41> 0	<37> 1	<42> 0
semin ves	leukemic cell infiltration		<41> 0	<41> 1	<37> 1	<42> 0
prostate	leukemic cell infiltration		<41> 0	<41> 0	<37> 1	<42> 0
a> b	a: Number of animals examined at the si b: Number of animals with lesion	te				

BAIS3

APPENDIX O 8

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

MOUSE: FEMALE: SACRIFICED ANIMALS

HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR (SUMMARY)

PAGE: 4

ANIMAL : MOUSE Crj:BDF1

SACRIFICED ANIMALS (105W)

REPORT TYPE : A1

SEX : FEMALE

brann		Group Name No. of Animals on Study	Control 35	8000 ppm 31	20000 ppm 34	50000 ppm 34
)rgan	riidii 95					
[Respiratory s	system]					
nasal cavit	metastasis:uterus tumor		<35> 0	<31> 1	<34> 0	<34> 0
lung	leukemic cell infiltration		<35> 1	<31> 6	<34> 3	<34> 0
	metastasis:liver tumor		0	0	1	0
[Hematopoietio	c system]					
bone marrow	leukemic cell infiltration		<35> 0	<31> 2	<34> 0	<34> 0
	metastasis:lympho node tumor		0	0	1	0
spleen	leukemic cell infiltration		<35> 4	<31> 5	<34> 3	<34> 2
	metastasis:lympho node tumor		0	0	1	0
(Circulatory	system]					
heart	leukemic cell infiltration		<35> 0	<31> 1	<34> 1	<34> 0
(Digestive sy	stem]					
salivary gl	leukemic cell infiltration		<35> 1	<31> 2	<34> 2	<34> 0
stomach	leukemic cell infiltration		<35> 0	<31> 1	<34> 1	<34> 0
⟨a⟩ b	a: Number of animals examined at the s b: Number of animals with lesion	te				

ANIMAL : MOUSE Crj:BDF1

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

REPORT TYPE : A1

SEX : FEMALE

0rgan	Findings	Group Name No. of Animals on Study	Control 35	8000 ppm 31	20000 ppm 34	50000 ppm 34
Discotive						
[Digestive sy	S (OIII)					
stomach	metastasis:uterus tumor		<35> 1	<31> 0	<34> 0	<34> 0
liver	leukemic cell infiltration		<35> 5	<31> 5	<34> 3	<34>
	metastasis:uterus tumor		1	2	0	0
	metastasis:lympho node tumor		0	0	1	0
pancreas	leukemic cell infiltration		<35> 0	<31> 1	<34> 1	<34> 0
	metastasis:uterus tumor		1	0	0	0
[Urinary syst	tem]					
kidney	leukemic cell infiltration		<35> 3	<31> 5	<34> 3	<34> 1
	metastasis:uterus tumor		0	1	0	0
	metastasis:urinary bladder tumor		0	1	0	0
	metastasis:lympho node tumor		0	0	1	0
urin bladd	leukemic cell infiltration		<35> 2	<31> 4	<34> 3	<34> 0
(Endocrine sy	ystem]					
adrenal	leukemic cell infiltration		<35> 0	<31>	<34> 1	<34> 0
(a)	a: Number of animals examined at the b: Number of animals with lesion	site				
(JPT150)						D

ANIMAL : MOUSE Crj:BDF1

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

SACRIFICED ANIMALS (105W)

PAGE: 6 Croup Name Control 8000 ppm 20000 ppm 50000 ppm No. of Animals on Study 35 31 34 34 Findings [Reproductive system] ovary ⟨35⟩ <31> <34> ⟨34⟩ leukemic cell infiltration 2 metastasis:uterus tumor 1 1 0 uterus ⟨35⟩ <31> <34> ⟨34⟩ leukemic cell infiltration 1 0 vagina <35> <31> ⟨34⟩ ⟨34⟩ leukemic cell infiltration 0 2 0 metastasis:subcutis tumor 0 0 0 [Nervous system] brain <35> <31> <34> (34) leukemic cell infiltration [Musculoskeletal system] muscle <35> ⟨31⟩ <34> <34> leukemic cell infiltration [Body cavities] mediastinum <35> ⟨31⟩ <34> (34) metastasis:lympho node tumor per i toneum <35> <31> <34> ⟨34⟩ leukemic cell infiltration 1 1 0 (a) a: Number of animals examined at the site b b: Number of animals with lesion

(JPT150)

BAIS3

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

A.Lot No.507E4208

1. Identity(Spectral data)

(1) Mass Spectrometry

Instrument

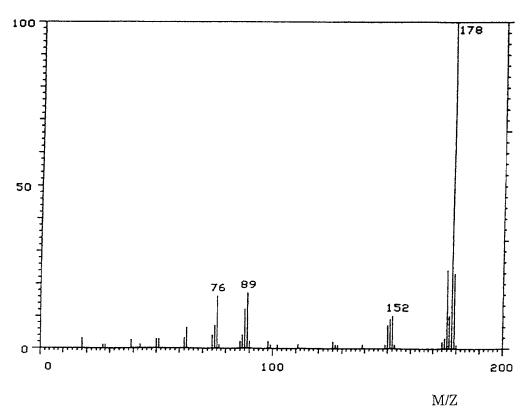
; Hitachi M-80B Mass Spectrometer

Ionization

; EI(Electron Ionization)

Ionization Voltage

; 70eV



Mass Spectrum of Test Substance

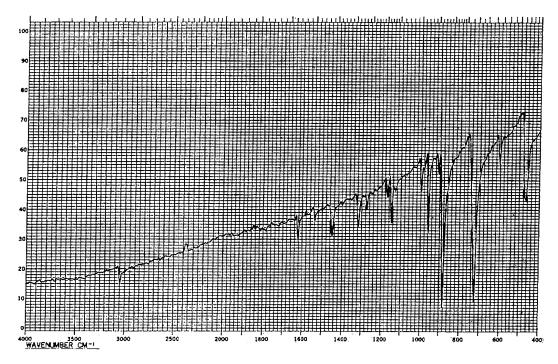
Results; The mass spectrum was consistent with literature spectrum.

Determined	Literature Value"
Molecular and Fragment Peak(M/Z)	Molecular and Fragment Peak(M/Z)
178[M] ⁺	178[M] ⁺
152	152
89	89
76	76
	(* EPA/NIH Mass Spectral Data Base(1978) Vol.1, p. 882.)

(2) Infrared Spectrometry

Instrument ; Hitachi 270-30 Infrared Spectrometer

Cell ; KBr Slit ; Medium



Infrared Spectrum of Test Substance

Results; The infrared spectrum was consistent with literature spectrum.

Determines	Literature Values*
Wave Number(cm ⁻¹)	Wave Number(cm ⁻¹)
460~ 490	460~ 490
700~ 750	700~ 750
860~ 900	860~ 900
940~ 970	940~ 970
990~1010	990~1010
1130~1160	1130~1160
1300~1330	1300~1330
1440~1470	1440~1470
	1530~1550
1610~1640	1610~1640
3030~3080	3010~3050
	(Sadtler Handbook

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

2. Impurity(Gas Chromatography)

Instrument

; Hewlett Packard 5890A Gas Chromatograph

Column

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

Column Temperature

; 170°C

Flow Rate

; 1 ml/min

Detector

; FID(Flame Ionization Detector)

Injection Volume

; 1 μ l

Results; Gas chromatography indicated one major peak(peak No.1) and two

impurities. It was identified only by comparing its gas chromatograph with that of the Carbazole(peak No.3) in the

Anthracene, the amount in the test substance was 0.0857% by standard

sample(Carbazole).

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

3. Conclusions; The result of the mass spectrum and the infrared spectrum agreed with the literature values. Consequently, the test substance was identified as Anthracene.

Gas chromatography indicated one major peak and two impurities, it was identified only by comparing its gas chromatograph with that of the Carbazole, the amount in the test substance was 0.0857%.

- Identity(Spectral data)
- (1) Mass Spectrometry

Instrument

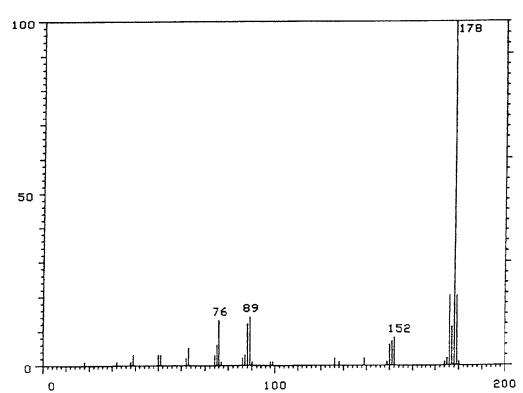
; Hitachi M-80B Mass Spectrometer

Ionization

; EI(Electron Ionization)

; 70eV

Ionization Voltage



Mass Spectrum of Test Substance

Results; The mass spectrum was consistent with literature spectrum.

Determined	<u>Literature Value*</u>
Molecular and Fragment Peak(M/Z)	Molecular and Fragment Peak(M/Z)
178[M] ⁺	178[M] ⁺
152	152
89	89
76	76 (* EPA/NIH Mass Spectral Data Base(1978) Vol.1, p. 882.)

(2) Infrared Spectrometry

Instrument

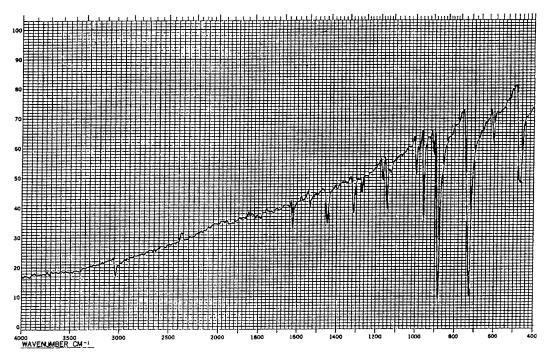
; Hitachi 270-30 Infrared Spectrometer

Cell

; KBr

Slit

; Medium



Infrared Spectrum of Test Substance

Results; The infrared spectrum was consistent with literature spectrum.

Determines	Literature Values*
Wave Number(cm ⁻¹)	Wave Number(cm ⁻¹)
460~ 490	460~ 490
700~ 750	700~ 750
860~ 900	860~ 900
940~ 970	940~ 970
990~1010	990~1010
1130~1160	1130~1160
1300~1330	1300~1330
1440~1470	1440~1470
	1530~1550
1610~1640	1610~1640
3030~3080	3010~3050
	(Sadtler Handbook
	by Sadtler Research
	Laboratories, Inc.
	(1978) p. 78.)

2. Impurity(Gas Chromatography)

Instrument

; Hewlett Packard 5890A Gas Chromatograph

Column

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

Column Temperature

; 170°C

Flow Rate

; 1 ml/min

Detector

)

; FID(Flame Ionization Detector)

Injection Volume

; 1 μ 1

Results; Gas chromatography indicated one major peak(peak No.1) and two

impurities. It was identified only by comparing its gas chromatograph with that of the Carbazole(peak No.3) in the

Anthracene, the amount in the test substance was 0.0841% by standard $\,$

sample(Carbazole).

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

3. Conclusions; The result of the mass spectrum and the infrared spectrum agreed with the literature values. Consequently, the test substance was identified as Anthracene.

Gas chromatography indicated one major peak and two impurities, it was identified only by comparing its gas chromatograph with that of the Carbazole, the amount in the test substance was 0.0841%.

- 1. Identity(Spectral data)
- (1) Mass Spectrometry

Instrument

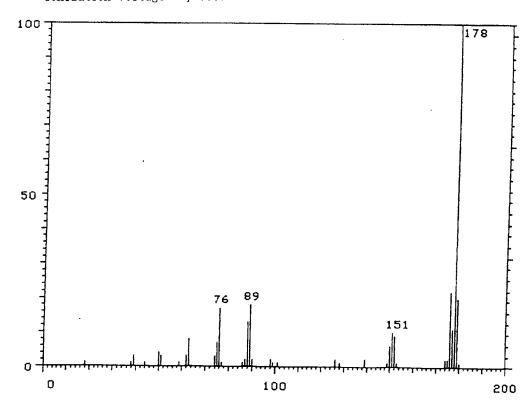
; Hitachi M-80B Mass Spectrometer

Ionization

; EI(Electron Ionization)

Ionization Voltage

; 70eV



Mass Spectrum of Test Substance

Results; The mass spectrum was consistent with literature spectrum.

Determined	Literature Value*
Molecular and Fragment Peak(M/Z)	Molecular and Fragment Peak(M/Z)
178[M] ⁺	178[M] ⁺
152	152
89	89
76	76
	(* EPA/NIH Mass Spectral
	Data Base(1978) Vol.1,
	p. 882.)

(2) Infrared Spectrometry

Instrument

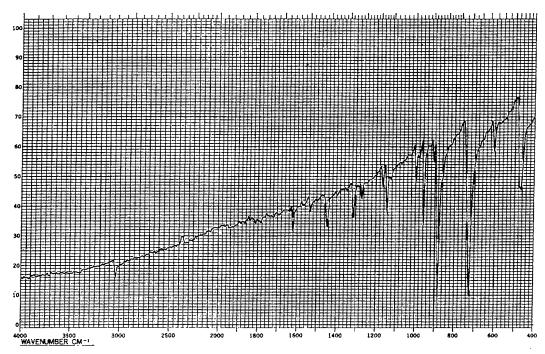
; Hitachi 270-30 Infrared Spectrometer

Cell

; KBr

Slit

; Medium



Infrared Spectrum of Test Substance

Results; The infrared spectrum was consistent with literature spectrum.

Determines	Literature Values*
Wave Number(cm ⁻¹)	Wave Number(cm ⁻¹)
460~ 490	460~ 490
700~ 750	700~ 750
860~ 900	860~ 900
940~ 970	940~ 970
990~1010	990~1010
1130~1160	1130~1160
1300~1330	1300~1330
1440~1470	1440~1470
	1530~1550
1610~1640	1610~1640
3030~3080	3010~3050
	(Sadtler Handbook
	by Sadtler Research
	Laboratories, Inc.
	(1978) p. 78.)

2. Impurity(Gas Chromatography)

Instrument ; He

; Hewlett Packard 5890A Gas Chromatograph

Column

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

Column Temperature

; 170°C

Flow Rate

; 1 ml/min

Detector

)

)

; FID(Flame Ionization Detector)

Injection Volume

; 1 μ l

Results; Gas chromatography indicated one major peak(peak No.1) and two

impurities. It was identified only by comparing its gas chromatograph with that of the Carbazole(peak No.3) in the

Anthracene, the amount in the test substance was 0.0594% by standard

sample(Carbazole).

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

3. Conclusions; The result of the mass spectrum and the infrared spectrum agreed with the literature values. Consequently, the test substance was identified as Anthracene.

Gas chromatography indicated one major peak and two impurities, it was identified only by comparing its gas chromatograph with that of the Carbazole, the amount in the test substance was 0.0594%.

${\bf APPENDIX\ P\ 2}$ STABILITY OF ANTHRACENE IN THE 2-YEAR FEED STUDIES

Stability of Anthracene in the 2-Year Feed Studies

A.Lot No.507E4208

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

2. Infrared Spectrometry

Instrument

; Hitachi 270-30 Infrared Spectrometer

Cell

; KBr

Slit

; Medium

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

1993.08.04.	1994.06.23.
Wave Number(cm ⁻¹)	Wave Number(cm ⁻¹)
460~ 490	460~ 490
700~ 750	700~ 750
860~ 900	860~ 900
940~ 970	940~ 970
990~1010	990~1010
1130~1160	1130~1160
1300~1330	1300~1330
1440~1470	1440~1470
1610~1640	1610~1640
3030~3080	3030~3080

3. Gas Chromatography

Instrument

; Hewlett Packard 5890A Gas Chromatograph

Column

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

Column Temperature ; 170°C

Flow Rate

)

; 1 ml/min

Detector

; FID(Flame Ionization Detector)

Injection Volume

; 1 μ l

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

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

^{4.} Conclusions; The results indicated that the test substance did not change when stored in the dark at room temperature during this period(for about 11 months).

)

B.Lot No.507E4209

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

Instrument

; Hitachi 270-30 Infrared Spectrometer

Cell

; KBr

Slit

; Medium

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

1995.06.08.
Wave Number(cm ⁻¹)
460~ 490
700~ 750
860~ 900
940~ 970
990~1010
1130~1160
1300~1330
1440~1470
1610~1640
3030~3080

3. Gas Chromatography

Instrument

; Hewlett Packard 5890A Gas Chromatograph

Column

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

Column Temperature ; 170°C

Flow Rate

; 1 ml/min

Detector

)

; FID(Flame Ionization Detector)

Injection Volume

; 1 μ l

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

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

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

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

Instrument

; Hitachi 270-30 Infrared Spectrometer

Cell

; KBr

Slit

; Medium

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

1993.08.04.	1995.10.12.
Wave Number(cm ⁻¹)	Wave Number(cm ⁻¹)
460~ 490	460~ 490
700~ 750	700~ 750
860~ 900	860~ 900
940~ 970	940~ 970
990~1010	990~1010
1130~1160	1130~1160
1300~1330	1300~1330
1440~1470	1440~1470
1610~1640	1610~1640
3030~3080	3030~3080

3. Gas Chromatography

Instrument

; Hewlett Packard 5890A Gas Chromatograph

Column

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

Column Temperature ;

; 170°C

Flow Rate

; 1 ml/min

Detector

)

; FID(Flame Ionization Detector)

Injection Volume

; 1 μ 1

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

Date	Peak No.	Retention Time(min)	(percent of total peak)
993.08.04	1	16.458	99.8018
date analyzed)	2	16.882	0.1388
	3	17.842	0.0595
995.10.12	1	16.457	99.8043
date analyzed)	2	16.875	0.1397
	3	17.833	0.0560

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

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

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

^{(*) %} of target concentration

Analytical method: The sample were analyzed by the GC.

Instrument

: Hewlett Packard 5890A

Flow Rate

: 1ml/min

Column

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

Detector

: FID(Flame Ionization Detector)

Column Temperature: 260°C

: He

Injection Volume

 $: 1\mu l$

Carrier

APPENDIX P $_4$ CONCENTRATION OF ANTHRACENE IN FORMULATED DIETS IN MICE IN THE 2-YEAR FEED STUDY

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

(Male)

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

^{(*) %} of target concentration

Analytical method: The sample were analyzed by the GC.

Instrument : Hewlett Packard 5890A

· : METHYL SILICONE(0.2mm $\phi \times 30$ m)

Flow Rate : 1ml/min

Detector : FID(Flame Ionization Detector)

Column Temperature: 260°C Carrier

Column

: He

Injection Volume $: 1\mu l$

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

(Female)

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

^{(*) %} of target concentration

Analytical method: The sample were analyzed by the GC.

Instrument : Hewlett Packard 5890A

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

Flow Rate : 1ml/min

Detector : FID(Flame Ionization Detector)

Column Temperature: 260°C

: He

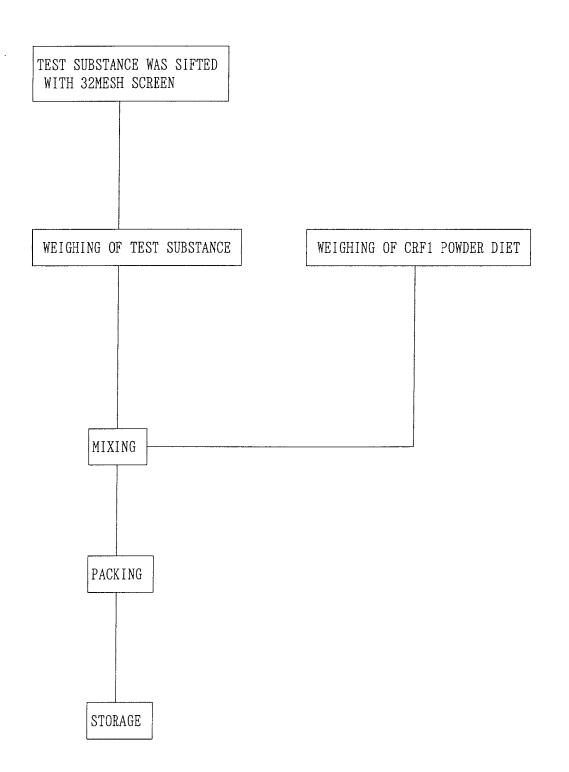
Injection Volume : 1µ1

Carrier

Column

APPENDIX P 5 STABILITY OF ANTHRACENE IN FORMULATED DIETS IN THE 2-YEAR FEED STUDY

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



APPENDIX Q 1

DOSE FORMULATIONS OF ANTHRACENE IN THE 2-YEAR FEED STUDIES (PREPARED IN JAPAN BIOASSAY RESEARCH CENTER)

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

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

a; Date of preparation

Analytical method; The samples were analyzed by the GC.

Instrument

: Hewlett Packard 5890A

Flow Rate

: 1ml/min

 $: 1\mu l$

Column

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

Detector

Column Temperature: 260°C

Injection Volume

: FID(Flame Ionization Detector)

Carrier

: He

b; The stability of Anthracene in formulated diets were established for 15 days when stored at animal room($24\pm2^{\circ}$ C).

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

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

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

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

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

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

a; Date of preparation

Analytical method; The samples were analyzed by the GC.

Instrument Column

: Hewlett Packard 5890A

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

Flow Rate

: 1ml/min

: FID(Flame Ionization Detector)

Column Temperature: 260°C

Detector Injection Volume

 $: 1\mu 1$

Carrier

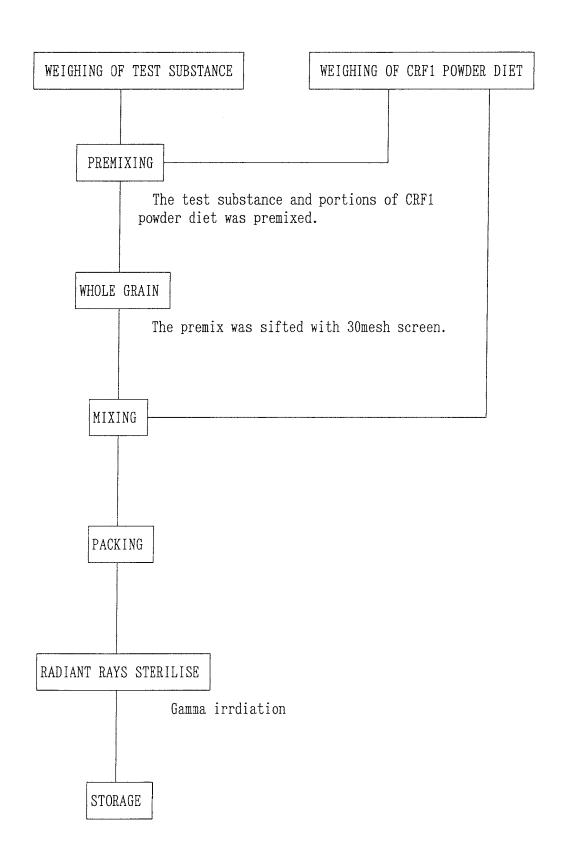
: He

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

APPENDIX Q 2

DOSE FORMULATIONS OF ANTHRACENE IN THE 2-YEAR FEED STUDIES (PREPARED BY ORIENTAL YEAST CO.,LTD.)

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



${\bf APPENDIX~R~1}$ ${\bf METHODS~FOR~HEMATOLOGY, BIOCHEMISTRY~AND~URINALYSIS}$

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS

Item	Method	Unit
Hematology Red blood cell (RBC) Hemoglobin (Hgb) Hematocrit (Hct) Mean corpuscular volume (MCV) Mean corpuscular hemoglobin (MCH) Mean corpuscular hemoglobin concentration (MCHC) Platelet White blood cell (WBC) Differential WBC Reticulocyte Prothrombin time Activated partial thromboplastin time (APTT)	Light scattering method 1) Cyanmethemoglobin method 1) Calculated as RBC×MCV/10 1) Light scattering method 1) Calculated as Hgb/RBC×10 1) Calculated as Hgb/Hct×100 1) Light scattering method 1) Light scattering method 1) Light scattering method 1) Pattern recognition method 2) (May-Grunwald-Giemsa staining) Pattern recognition method 2) (New methyleneblue staining) Quick one stage method 3) Ellagic acid activated method 3)	×10 ⁶ /μl g/dl % fl pg g/dl ×10 ³ /μl ×10 ³ /μl % sec sec
Biochemistry Total protein (TP) Albumin (Alb) A/G ratio T-bilirubin Glucose T-cholesterol Triglyceride Phospholipid Glutamic oxaloacetic transaminase (GOT) Glutamic pyruvic transaminase (GPT) Lactate dehydrogenase (LDH) Alkaline phosphatase (ALP) y-Glutamyl transpeptidase (G-GTP) Creatine phosphokinase (CPK) Urea nitrogen Creatinine Sodium Potassium Chloride Calcium	Biuret method 4) BCG method 4) Calculated as Alb/(TP-Alb) 4) Michaelson method 4) Enzymatic method (HK·G-6-PDH) 4) Enzymatic method (CEH·COD·POD) 4) Enzymatic method (GK·GPO·POD) 4) Enzymatic method (PLD·COD·POD) 4) Karmen method 4) Karmen method 4) Wroblewski-LaDue method 4) GSCC method 4) L- \gamma-Glutamyl-p-nitroanilide	g/dl g/dl mg/dl mg/dl mg/dl IU/l iu
Inorganic phosphorus Urinalysis PH, Protein, Glucose, Ketone body, Bilirubin, Occult blood, Urobilinogen	Enzymatic method (SPL·PGM·G-6-PDH) 4) Urinalysis reagent paper method 6)	mg/dl

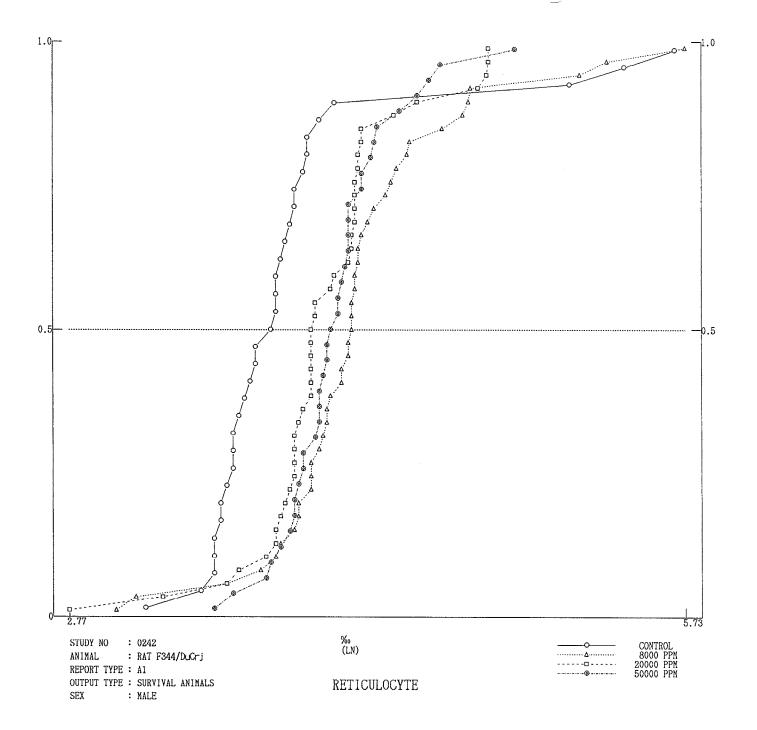
- 1) Automatic blood cell analyzer (Technicon H·1: Technicon Instruments Corporation, USA)
- 2) Automatic blood cell differential analyzer (Hitachi 8200 : Hitachi, Ltd., Japan)
- 3) Automatic coagulometer (Amelung KC-10: Heinrich Amelung GmbH, Germany)
- 4) Automatic analyzer (Hitachi 705 : Hitachi, Ltd., Japan)
- 5) Flame photometer (Hitachi 750 : Hitachi, Ltd., Japan)
- 6) Ames reagent strips for urinalysis (Multistix, Uro-Labstix: Miles Sankyo Co., Ltd., Japan)

${\bf APPENDIX~R~2}$ UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

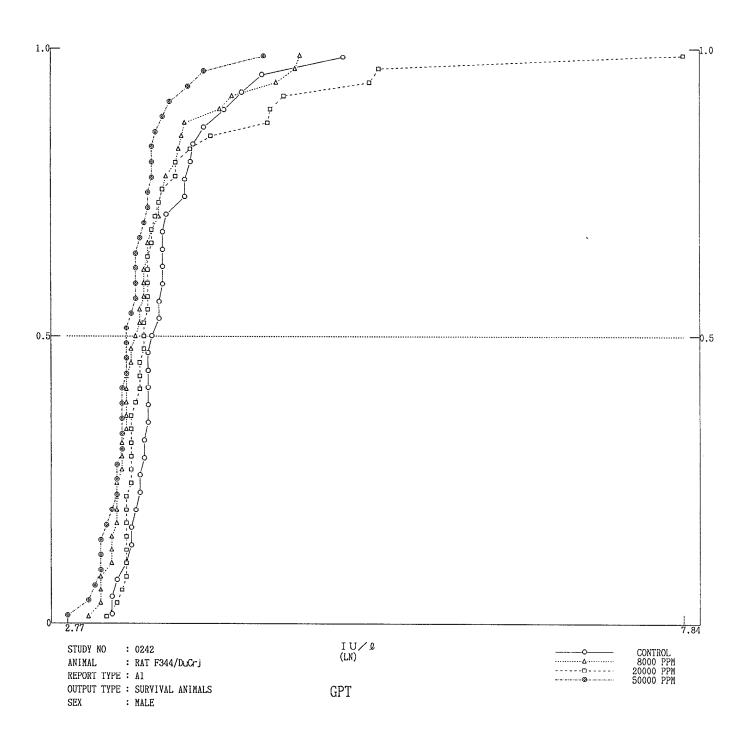
	TEST ITEM	DECIMAL PLACE	UNIT
HEMATOLOGY	Red blood cell	2	10 ⁶ /μ
	Hemoglobin	1	g/dl
	Hematocrit	1	%
	MCV	1	fl
	MCH	1	pg
	MCHC	1	g/dl
	Platelet	0	$\times 10^{3}/\mu 1$
	Prothrombin time	1	sec.
	APTT	1	sec.
	White blood cell	2	×10³/μΙ
	Differential WBC	0	%
	Reticulocyte	1	%
BIOCHEMISTRY	Total protein	1	~/4!
	Albumin	1	g/dl
	A/G ratio	1	g/dl
	T-bilirubin	2	
	Glucose	0	mg/dl
	T-cholesterol	. 0	mg/dl
	Triglyceride	0	mg/dl
	Phospholipid	0	mg/dl
	GOT	0	mg/dl IU/I
	GPT	0	10/1
	LDH	0	10/1
	ALP	0	10/1
	γ-GTP	0	10/1
	CPK	0	10/1
	Urea nitrogen	1	mg/dl
	Creatinine	1	mg/dl
	Sodium	0	mEq/l
	Potassium	1	mEq/I
	Chloride	0	mEq/l
	Calcium	1	mg/dl
	Inorganic phosphorus	1	mg/dl
L	morganic phospholus		mg/dl

APPENDIX S 1 Q PLOT GRAPH FOR RETICULOCYTE OF MALE RATS IN THE 2-YEAR FEED STUDY OF ANTHRACENE



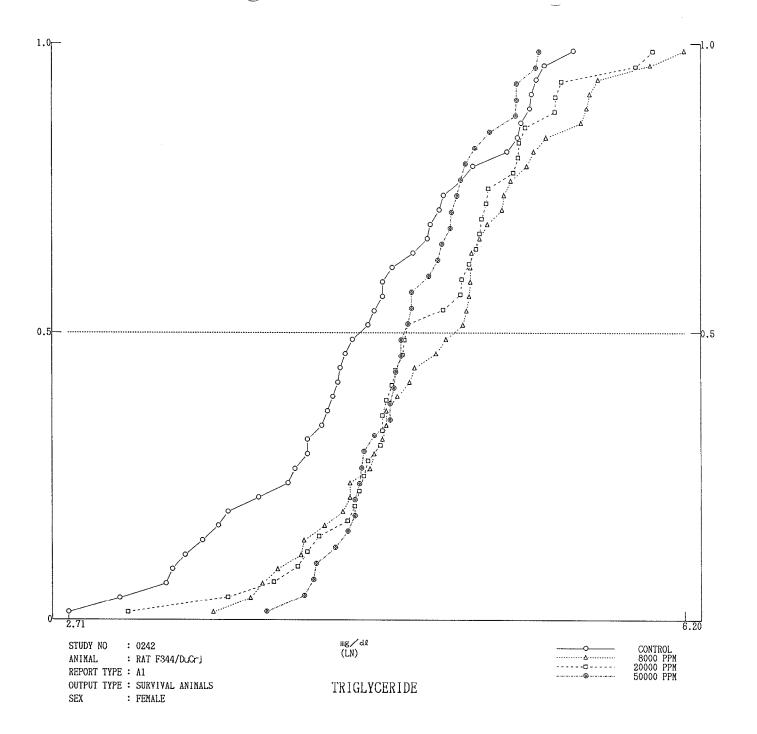
APPENDIX S 2

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



APPENDIX S 3 $\begin{tabular}{llll} Q PLOT GRAPH FOR TRIGLYCERIDE OF FEMALE RATS IN THE \\ \end{tabular}$

2-YEAR FEED STUDY OF ANTHRACENE



.

APPENDIX S 4 Q PLOT GRAPH FOR A/G RATIO OF MALE MICE IN THE 2-YEAR FEED STUDY OF ANTHRACENE

