Summary of Inhalation Carcinogenicity Study of 1-Bromobutane in B6D2F1 Mice

March 2008

Japan Bioassay Research Center

Japan Industrial Safety and Health Association

PREFACE

The tests were contracted and supported by the Ministry of Health, Labour and Welfare of Japan. The tests were conducted by Japan Bioassay Research Center (JBRC) and the report was prepared by JBRC and peer reviewed by outside expert pathologist. Complete report was submitted to Ministry of Health, Labour and Welfare of Japan on March 31, 2008.

This English Summary was translated by JBRC from Japanese complete report.

Summary of Inhalation Carcinogenicity Study of 1-Bromobutane in B6D2F1 Mice

Purpose, materials and methods

1-Bromobutane (CAS No. 109-65-9) is a colorless liquid with a boiling point of 101.3°C. It is soluble in alcohol and ether and insoluble in water.

The carcinogenicity and chronic toxicity of 1-bromobutane (greater than 99.7% pure) were examined by inhalation exposure using groups of B6D2F1/Crlj mice. Each group of test animals consisted of either 50 male or 50 female mice. Test animals were exposed to 1-bromobutane vapor at a target concentration of 0 (clean air), 20, 50 or 125 ppm (v/v) for 6 hours/day, 5 days/week for 2 years (104 weeks). Both sexes were exposed to each concentration of 1bromobutane vapor. The highest dose level was chosen so as not to exceed the maximum tolerated dose (MTD), based on both growth rate and toxicity in the previous 13-week toxicity study. The identity of the 1-Bromobutane used in these experiments was confirmed by both infrared spectrometry and mass spectrometry, and it was analyzed by gas chromatography before and after its use to affirm its stability. Stainless-steel inhalation exposure chambers (volume: 3900 L) were used throughout the 2-year exposure period. 1-Bromobutane vapor-air mixtures were generated by bubbling clean air through 1-bromobutane liquid and the mixtures supplied to the inhalation exposure chambers. Air concentrations of 1-bromobutane vapor in the inhalation exposure chambers were monitored at 15 min intervals by gas chromatography. The animals were observed daily for clinical signs and mortality. Body weight and food consumption were measured once a week for the first 14 weeks and every 4 weeks thereafter. All animals, including those found dead or in a moribund state as well as those surviving to the end of the 2-year exposure period, underwent complete necropsy. Urinalysis was performed near the end of the exposure period. For hematology and blood biochemistry at the terminal necropsy, surviving animals were fasted overnight and bled under deep ether anesthesia. Organs and tissues were removed, weighed and examined for macroscopic lesions at necropsy. The organs and tissues were then fixed and embedded in paraffin. Five µm thick tissue sections were prepared and stained with hematoxylin and eosin and examined microscopically. Incidences of neoplastic lesions were statistically analyzed by Fisher's exact test. Any positive dose-response trends of 1-Bromobutane induction of neoplastic lesions were analyzed by Peto's test. Incidences of non-neoplastic lesions and urinalysis were analyzed by the Chi-square test. Changes in body weight, food consumption, hematological and blood biochemical parameters, and organ weights were analyzed by Dunnett's test. The present studies were conducted in accordance with the Organisation for Economic Co-operation and Development (OECD) Good

Laboratory Practice and with reference to the OECD Guideline for Testing of Chemicals 451 "Carcinogenicity Studies".

Results

No significant difference in survival rate, clinical symptoms, body weight or food consumption was found between any 1-bromobutane-exposed group of either sex and their respective controls.

The incidence of bronchiolar-alveolar carcinomas in the lung was increased in males exposed to 50 ppm and 125 ppm 1-bromobutane. No significant increases in the incidence of neoplastic lesions was found in any of the 1-bromobutane-exposed female groups. There was, however, an increase in the incidence of eosinophilic change in the olfactory epithelium of females exposed to 125 ppm 1-bromobutane.

Conclusions

There was clear evidence of carcinogenic activity of 1-bromobutane in male mice. There was no evidence of carcinogenic activity of 1-bromobutane in females.

SELECTED TABLES

TABLE A	CONCENTRATIONS OF 1 - BROMOBUTANE IN THE
	INHALATION CHAMBER OF THE 2-YEAR INHALATION STUDY
TABLE D1	BODY WEIGHT CHANGES AND SURVIVAL ANIMAL NUMBERS :
	MALE
TABLE D2	BODY WEIGHT CHANGES AND SURVIVAL ANIMAL NUMBERS :
	FEMALE
TABLE D3	BODY WEIGHT CHANGES: MALE
TABLE D4	BODY WEIGHT CHANGES: FEMALE
TABLE E1	FOOD CONSUMPTION CHANGES AND SURVIVAL ANIMAL
	NUMBERS: MALE
TABLE E2	FOOD CONSUMPTION CHANGES AND SURVIVAL ANIMAL
	NUMBERS: FEMALE
TABLE E3	FOOD CONSUMPTION CHANGES: MALE
TABLE E4	FOOD CONSUMPTION CHANGES: FEMALE
TABLE F1	HEMATOLOGY: MALE
TABLE F2	HEMATOLOGY: FEMALE
TABLE G1	BIOCHEMISTRY: MALE
TABLE G2	BIOCHEMISTRY: FEMALE
TABLE H1	URINALYSIS: MALE
TABLE H2	URINALYSIS: FEMALE

TABLE J1	ORGAN WEIGHT, ABSOLUTE: MALE
TABLE J2	ORGAN WEIGHT, ABSOLUTE: FEMALE
TABLE K1	ORGAN WEIGHT, RELATIVE: MALE
TABLE K2	ORGAN WEIGHT, RELATIVE: FEMALE
TABLE L1	HISTOPATHOLOGICAL FINDINGS: NON-NEOPLASTIC
	LESIONS : MALE: ALL ANIMALS
TABLE L4	HISTOPATHOLOGICAL FINDINGS: NON-NEOPLASTIC
	LESIONS: FEMALE: ALL ANIMALS
TABLE O1	NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL
	ANALYSIS: MALE
TABLE O2	NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL
	ANALYSIS: FEMALE
TABLE Q	HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC
	LESIONS IN JAPAN BIOASSAY RESEARCH CENTER:
	B6D2F1 /Crlj MALE MICE
TABLE R	CAUSE OF DEATH OF MICE IN THE 2-YEAR INHALATION
	STUDY OF 1 - BROMOBUTANE

TABLE A

CONCENTRATIONS OF 1 - BROMOBUTANE IN THE INHALATION CHAMBER OF THE 2-YEAR INHALATION STUDY

CONCENTRATIONS OF 1-BROMOBUTANE IN THE INHALATION CHAMBER OF THE 2-YEAR INHALATION STUDY

Group Name	Concentration(ppm) $Mean \pm S.D.$
Control	0.0 ± 0.0
$20~\mathrm{ppm}$	20.1 ± 0.2
50 ppm	50.1 ± 0.4
125 ppm	125.2 ± 0.7

TABLE D1

BODY WEIGHT CHANGES AND SURVIVAL ANIMAL

NUMBERS: MALE

Av. Wt. : g

 $\langle \ \rangle : No. \ of \ effective animals, ():No. \ of \ measured animals$

(BI0040)

MEAN BODY WEIGHTS AND SURVIVAL

PAGE: 1

STUDY NO. : 0561

ANIMAL : MOUSE B6D2F1/Cr1;[Crj:BDF1]
UNIT : g

REPORT TYPE : A1 104

SEX : MALE

	1			mdd nz			ndd Oc	md		125 ppm	III'
	Av. Wt.	No. of	Av. Wt.	% of	No. of	Av. Wt.	% of	No. of	Av. Wt.	% of	No. of
week−Day on Study	. 2	Surviv.		cont.	Surviv.		cont.	Surviv.		cont.	Surviv.
or or or or		200		(ne)			<90			<20>	
0-0	23.6 (50)	20/20	23.6 (50)	100	50/50	9	100	50/50	23.6 (50)	100	50/50
1-7		20/20		101	20/20	_	100	50/50	_	100	50/50
2-7		20/20		100	20/20	6	100	20/20	_	66	50/50
3-7		20/20		100	20/20	7	100	50/50	_	97	50/50
4-7		20/20		66	50/50	4	100	20/20	26. 5 (50)	26	50/50
2-2	-	20/20		66	20/20	0	100	50/50	_	96	50/20
2-9	-	20/20	28.0 (50)	86	20/20	9	100	50/50	_	96	50/50
2-2	29.1 (50)	20/20		86	20/20	0	100	50/50	_	96	50/20
2-8		20/20	29.0 (50)	26	20/20	9	66	50/50	_	96	50/50
2-6		20/20		26	20/20	2	66	50/50		96	50/50
10-7	^1	20/20		86	20/20	0	66	50/50	29.7 (50)	95	50/50
11-7	7	20/20		26	20/20	4	66	50/50		94	50/50
12-7		20/20		64	20/20	23	86	20/20		92	50/50
13-7	33.5 (50)	20/20	32.5 (50)	26	20/20	33.1 (50)	66	50/50	31.9 (50)	95	50/50
14-7		20/20		26	20/20	00	66	50/50		96	50/50
18-7		20/20		66	50/50	6	100	50/50	35.4 (50)	86	50/50
22-7		20/20	37.6 (50)	86	20/20	7	86	20/20		26	50/50
26-7		20/20		66	20/20	0	66	20/20		86	20/20
30-7		20/20		66	20/20	4	86	20/20		26	50/50
34-7	43.8 (50)	20/20		86	20/20	2	26	20/20		96	50/50
38-7		20/20	_	86	20/20	2	96	20/20		96	50/50
42-7	46.7 (50)	20/20		86	20/20	6	96	20/20		92	50/50
46-7		20/20		66	20/20	2	26	50/50		96	50/50
50-7		20/20		66	20/20	_	86	20/20	46.5 (50)	96	50/50
54-7		20/20		86	20/20	7	26	20/20		96	50/50
58-7	49.7 (50)	20/20		26	20/20	4	26	20/20		95	50/50
62-7		49/20		86	20/20	00	26	20/20		96	49/50
2-99		49/20	49.4 (50)	26	20/20	2	26	20/20	_	95	47/50
7-07		49/20		96	20/20	00	26	20/20	_	92	47/50
74-7		49/20	_	96	48/50	2	96	20/20	_	92	47/50
78-7	53.2 (49)	49/20	51.0 (48)	96	48/50	6	96	20/20	_	92	47/50
82-7		48/50	-	96	46/50	0	96	47/50	50.8 (46)	96	46/50
2-98	52.6 (48)	48/50	50.2 (46)	92	46/50	9	96	45/50	50.7 (45)	96	45/50
2-06		48/20		96	43/50	4	26	43/50	51.8 (44)	86	44/50
94-7		45/50	-	100	37/50	9	66	39/20	_	86	43/50
2-86	51.4 (42)	42/20	-	102	34/50	6	66	37/50	-	86	40/50
102-7	_	40/50	-	103	33/50	6	100	25/50	48 6 (30)	0.7	20 / 50
						,	201	00/00	_	-	29/20

TABLE D2

BODY WEIGHT CHANGES AND SURVIVAL ANIMAL

NUMBERS: FEMALE

STUDY NO.	• •	0561
ANIMAL	٠.	MOUSE B6D2F1/Cr1j[Crj:BDF1]
UNIT	••	
REPORT TYPE : A1 104	• •	A1 104
SEX	٠.	FEMALE

	-	10171100		ındd oo	III		mdd oc	E		mdd czi	E	
Week-Day on Study	Av. Wt.	No. of Surviv. <50>	Av. Wt.	% of cont. <50>	No. of Surviv.	Av. Wt.	% of cont. <50>	No. of Surviv.	Av. Wt.	% of cont. <50>	No. of Surviv.	
0-0	1 -			100	50/50		100	50/50	19 3 (50)	100	E0 /E0	
1-7	_			101	50/50		101	50/50		3 8	50/50	
2-7	20.8 (50)	20/20	20.8 (50)	100	50/50	20.8 (50)	100	50/50	20. 7 (50)	100	50/50	
3-7	_			66	20/20		100	50/50	_	86	50/50	
4-7	_			100	50/50		100	50/50	_	8 8	50/50	
2-2	22.5 (50)			66	20/20		66	50/50	_	86	50/50	
2-9	_			86	20/20		86	50/50	_	26	50/50	
2-7	_			86	20/20		86	50/50	_	26	50/50	
2-8	_			100	20/20		66	50/50	23.1 (50)	26	50/50	
2-6	_			100	20/20	2	86	50/50	_	26	50/50	
10-7	_			100	20/20	0	86	50/50	23. 6 (50)	96	50/50	
11-7	24.4 (50)		24.3 (50)	100	50/50	24.3 (50)	100	50/50		26	50/50	
12-7	24.7 (50)			100	50/50	2	86	50/50	_	26	50/50	
13-7	_			100	20/20	~	66	50/50		86	50/50	
14-7	_			100	50/50	က	100	50/50		86	50/50	
18-7				102	50/50		66	20/20	25.8 (50)	66	50/50	
227	27.2 (50)		27.5 (50)	101	20/20	26.8 (50)	66	20/20	26.0 (50)	96	20/20	
26-7				100	20/20		100	50/50	27.5 (50)	26	20/20	
30-7				101	20/20		66	20/20		26	49/50	
34-7			30.4 (50)	100	20/20	29.7 (50)	86	20/20		96	49/50	
38-7				100	20/20		26	20/20		96	49/50	
42-7	31.7 (50)			101	20/20	2	86	20/20	30.4 (49)	96	49/50	
46-7				66	20/20	9	26	20/20		92	49/50	
)-0c	_			66	20/20		100	20/20	_	26	49/50	
54-7				88	20/20		26	20/20		96	49/50	
28-7	33.7 (50)			66	20/20	33.7 (49)	100	49/20	_	26	48/50	
17.9	_			101	20/20		100	48/50	_	26	44/50	
2-99	_		34.3 (50)	100	20/20	34.3 (48)	100	48/50	32.8 (44)	96	44/50	
20-7	_			101	47/50		66	47/50		26	44/50	
74-7	35.0 (48)			100	46/50		66	44/50	_	26	44/50	
7-87	_			101	46/50		66	43/50	34.7 (43)	26	43/50	
822	35.8 (43)	43/50	_	101	46/50		66	40/20	34.8 (41)	26	41/50	
2-98	_		_	101	44/50		86	38/20	34.7 (41)	96	41/50	
206	_			103	41/50	36.4 (35)	100	35/50	36.1 (37)	66	37/50	
94-7	35.1 (29)		37.2 (37)	106	37/50	36.6 (30)	104	30/20	_	100	34/50	
2-86	_	26/20	36.6 (34)	104	34/50		103	28/20	_	101	31/50	
102-7	34.4 (20)		36.5 (32)	106	32/50	36.7 (25)	107	25/50	_	100	26/50	
04-7	34.9 (18)	18/50	37 6 (31)	110	21/50	36 6 (94)	107	04/60	`	,	0L/ 00	

(BI0040)

TABLE D3

BODY WEIGHT CHANGES: MALE

STUDY NO. : 0561 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SFX : MAIR	[Cr.j:BDF1]		BODY WEIGHT CHANGES ALL ANIMALS	(SUMMARY)			
Group Name	Administration week-day	л жеек-дау			The state of the s	THE THE PROPERTY OF THE PROPER	PAGE: 1
	0-0	1-7	2-7	3–7	4-7	2-2	L-9
Control	23.6± 0.9	25.0± 1.0	26.0± 1.2	26.8± 1.3	27.4± 1.4	27.9± 1.5	28.6± 1.6
20 ppm	23.6± 0.9	25.2 ± 1.1	25.9 ± 1.2	26.7± 1.4	27.1± 1.3	27.6± 1.5	28.0± 1.5
50 ppm	23.6± 0.9	25.1 ± 1.0	25.9 ± 1.1	26.7 ± 1.3	27.4 ± 1.4	28.0± 1.5	28.6± 1.6
125 ppm	23.6± 0.9	25.0± 1.0	25.7± 1.2	26.1± 1.4*	26.5± 1.6**	26.9± 1.7**	27.5± 1.9**

Significant difference ;	*: P ≤ 0.05	* : P ≤ 0.01		Test of Dunnett			

(HAN260)

STUDY NO. : 0561 ANTMAL : MOUSE B6D2F1/Orlj[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : MALE	[[Crj:BDF1]		BODY WEIGHT CHANGES ALL ANIMALS	(SUMMARY)			PAGE :
Group Name	Administration week-day_7-7	n week-day 8-7	L-6	7-01	11-7	12-7	13-7
Control	29.1± 1.7	29.8± 2.0	30.5± 2.2	31.2± 2.3	31.7 ± 2.5	32.8± 2.6	33.5± 2.6
20 ppm	28.5± 1.5	29.0 ± 1.7	29.6 ± 1.9	30.5± 1.9	30.7 ± 2.2	31.9± 2.4	32.5± 2.4
50 ppm	29.0± 1.9	29.6± 2.0	30.2± 2.0	31.0 ± 2.1	31.4± 2.3	32.2 ± 2.4	33.1± 2.5
125 ppm	27.9± 2.1**	28.5± 2.2**	29.2 ± 2.3**	29.7± 2.5**	29.8± 2.5**	31.0± 2.6**	31.9± 2.6**
Significant difference;	* : P ≤ 0.05	‡ : P ≤ 0.01		Test of Dunnett			

(HAN260)

SIDDI NO USB1 ANIMAL : MOUSE B6D2F1/Crjj[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : MALE	j[Cr.j:BDF1]		BODY WEIGHT CHANGES ALL ANIMALS	(SUMMARY)			PAGE: 3
Group Name	Administration week-day_ 14-7	on week-day	22-7	26-7	30-7	34-7	
				- Walter and			
Control	34.2 ± 2.8	36.0 ± 3.1	38.3± 3.4	40.5 ± 3.9	42.1± 4.3	43.8± 4.4	45.5± 4.6
. 20 ppm	33.1 ± 2.4	35.5± 2.7	37.6± 2.9	39.9± 3.3	41.6± 3.5	42.8± 4.1	44.7± 4.1
50 ppm	33.8± 2.5	35.9± 2.8	37.7 ± 3.3	40.0± 3.9	41.4± 4.2	42.7± 4.2	43.7± 4.6
125 ppm	32.7± 2.7**	35.4 ± 3.0	37.2± 3.5	39.6± 3.8	40.8± 4.2	42.2± 4.2	43.5± 4.5
Significant difference ;	*:P≤0.05	** : P ≤ 0.01		Test of Dunnett	7007040000	TO CONCRETE VALLEY OF THE PARTY	
(HAN260)		and the state of t			MACCO	- PERSONAL PARTY NAME OF THE P	BAIS 4

STUDY NO. : 0561 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : MALE	[Cr.j:BDF1]		BODY WEIGHT CHANGES ALL ANIMALS	(SUMMARY)				-
Group Name	Administration week-day	n week-day	CREATE TO THE PARTY OF THE PART			- privately	rage .	4
	42-7	46-7	2-0-2	54-7	58-7	62-7	L-99	
				THE PROPERTY OF THE PROPERTY O	- Attion	The state of the s		
Control	46.7± 4.7	47.6± 4.6	48.2± 5.2	49.1 ± 5.3	49.7 ± 5.2	50.1 ± 5.1	51.0± 5.6	
20 ppm	45.7± 4.0	47.0± 3.8	47.8± 3.9	48.2± 4.1	48.2± 4.2	48.9± 4.0	49.4± 4.4	
90 ppm	44.9± 4.4	46.2± 4.5	47.1± 4.5	47.7± 4.6	48.4± 4.8	48.8± 5.1	49.5± 5.3	
125 ppm	44.5± 4.7	45.8± 4.8	46.5± 4.8	47.0± 5.0	47.4± 5.2	48.2± 5.4	48.6± 5.5	
Significant difference;	* : P ≤ 0.05	**: P ≤ 0.01		Test of Dunnett				1

(HAN260)

STUDY NO. : 0561 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : g REPORT TYPE : A1 104	[Crj:BDF1]		BODY WEIGHT CHANGES ALL ANIMALS	(SUMMARY)			
SEA : MALE		-	THE STATE OF THE S			***************************************	PAGE: 5
vroup Name	Administration week-day_74-	n week-day	7-87	82–7	2–98	2-06	94-7
			1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 -	THE WAY AND A STATE OF THE STAT	(The Application of the Applicat		THE PROPERTY OF THE PROPERTY O
Control	51.5 ± 6.1	52.2± 6.5	53.2 ± 6.9	52.9± 6.3	52.6± 6.8	52.9± 7.5	52.3± 8.2
20 ppm	49.2	50.2 ± 5.9	51.0± 6.7	50.9± 6.8	50.2± 7.6	50.6± 8.9	52.1± 8.1
50 ppm	49.8± 5.8	50.2± 6.2	50.9± 7.7	51.0± 7.0	50.6土 6.9	51.4± 7.4	51.6± 7.2
125 ppm	48.9± 6.2	49.5± 6.5	50.6 ± 7.3	50.8± 6.2	50.7 ± 7.0	51.8± 6.6	51.1± 7.3
Significant difference ;	*: P ≤ 0.05	** : P ≤ 0.01	The second secon	Test of Dunnett			

SEX : MALE					PAGE: 6
Group Name	Administration week-day	week-day_			11000000
	J-86	102-7	104-7		expension of the second of the
Control	51.4 ± 8.3	50.0 ± 8.5	49.8± 8.6		
20 ppm	52.3± 7.4	51.6± 7.8	51.9± 7.6		
50 ppm	50.9± 7.6	49.9± 7.3	49.7± 7.4		
125 ppm	50.3± 7.4	48.6士 8.5	48.5± 8.5		
Significant difference ;	* : P ≤ 0.05	★ : P ≤ 0.01		Test of Dunnett	700000000000000000000000000000000000000

TABLE D4

BODY WEIGHT CHANGES: FEMALE

STUDY NO. : 0561 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : FEMALE	[Cr.j:BDF1]		BODY WEIGHT CHANGES ALL ANIMALS	(SUMMARY)			PAGE: 7
Group Name	Administration week-day_0-0	week-day	2-7	3-7	4-7	5-7	<i>L</i> -9
Control	19.3± 0.8	20.0± 0.8	20.8± 0.7	21.6± 0.8	21.9± 0.7	22.5± 0.8	23.0± 0.8
20 ppm	19.3± 0.8	20.1± 0.8	20.8± 0.9	21.3± 0.8	21.9± 0.8	22.2 ± 1.0	22.5± 1.0*
50 ppm	19.3± 0.8	20.1± 1.0	20.8± 1.0	21.5± 1.1	21.8 ± 1.0	22.2± 1.0	22.6± 1.1
125 ppm	19.3± 0.8	19.8± 0.9	20.7± 0.9	21.1± 0.9**	21.5± 0.9	22.0± 0.9	22.3± 1.0**
Significant difference ;	* : P ≤ 0.05	**: P ≤ 0.01		Test of Dunnett			
(HAN260)	TOTAL PROPERTY AND THE	T TOWNS WAS	- Account of the contract of t	The second secon			BAIS 4

ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : FEMALE	[[Cr.j:80FI]		ALL ANIMALS	(SURMAINT)			PAGE :
Group Name	Administration week-day	n week-day	- Company		THE PROPERTY AND THE PR	**************************************	The state of the s
Village of the second of the s	2-2	2–8	2-6	10-7	11-7	12-7	13-7
				TO THE PARTY OF TH		- Contribution	- Anna Anna Anna Anna Anna Anna Anna Ann
Control	23.5 ± 0.9	23.7 ± 0.8	24.1 ± 0.9	24.5 ± 1.0	24.4± 0.9	24.7± 1.2	24.9± 1.2
20 ppm	23.0 ± 1.1	23.6± 1.1	24.1± 1.4	24.4± 1.4	24.3± 1.3	24.7 ± 1.5	24.9± 1.7
50 ppm	23.1 ± 1.2	23.4± 1.2	23.7 ± 1.3	24.0 ± 1.3	24.3± 1.3	24.2± 1.8	24.7± 1.5
125 ppm	22.7± 1.2**	23.1± 1.2**	23.3± 1.3**	23.6± 1.5**	23.7± 1.5**	24.0 ± 1.4**	24.4± 1.5
Significant difference ;	*: P ≤ 0.05	* : P ≤ 0.01		Test of Dunnett			
(HAN260)	NA MANAGARA	- ON THE PROPERTY OF THE PROPE	The state of the s	T P O BEACH			BAIS 4

STUDY NO. : 0561 ANIMAL : MOUSE BEDZF1/Cr1j[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : FEMALE][Cr.j:BDF1]		BODY WEIGHT CHANGES ALL ANIMALS	(SUMMARY)			. SOA G	
Group Name	Administration week-day	n week-day	Market and the second	10.002.011	Pri	The second secon	raue .	S
	14-7	18-7	22–7	26-7	30–7	34-7	38-7	
						174411111	1,000,000,000,000	
Control	25.4 ± 1.3	26.1 ± 1.6	27.2± 1.8	28.3 ± 2.1	29.2 ± 2.2	30.3 ± 2.6	31.3 ± 3.0	
20 ppm	25.3 ± 1.8	26.5± 2.0	27.5± 2.5	28.2± 3.0	29.4± 3.3	30.4± 3.8	31.4± 3.8	
i								
50 ppm	25.3 ± 1.4	25.8± 1.5	26.8± 1.6	28.4 ± 2.6	28.8± 2.7	29.7 ± 2.8	30.5± 3.3	
125 ppm	24.8± 1.7	25.8+ 1.8	26 O+ 2 1**	27 5+ 2 6	+6 00			
!					60.3 - 6.3	. 5 ± 0. 5 ± 0. 6 ± 0. 6 ± 0.	29.9∓ 3.3	
The state of the s	A A Marine Street Control	000000000000000000000000000000000000000						
Significant difference;	*: P ≤ 0.05	**: P ≤ 0.01		Test of Dunnett	Addition of the Addition of th	Advisor a sea	A Constant of the Constant of	

(HAN260)

STUDY NO. : 0561 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : FEMALE Group Name Admi	[Crj:BDF1] Administration week-day_	n week-day	BODY WEIGHT CHANGES ALL ANIMALS	(SUMMARY)				PAGE: 10
	42-7	46-7	20-7	54-7	28-7	62–7	L-99	
	31.7 ± 3.0	32.6± 3.7	32.7 ± 3.4	33.5± 3.6	33.7± 3.3	33.6± 3.6	34.2± 3.5	
	31.9± 4.2	32.4± 4.5	32.5± 4.9	32.9 ± 4.3	33.4± 4.6	34.1± 5.0	34.3± 5.5	
	31.2± 3.3	31.6± 3.4	32.7± 3.5	32.6± 3.5	33.7± 3.7	33.7 ± 4.2	34.3± 3.8	
	30.4± 3.4	31.1± 4.1	31.6± 3.8	32.3 ± 4.1	32.6± 3.7	32.5± 3.5	32.8± 3.3	
*	* : P ≤ 0.05	** : P ≤ 0.01	A. A	Test of Dunnett	7 0000000		The second secon	
		- 04/4/4 (0) to					- Province and the control	BAIS 4

Group Name Administration week-day_ 78-7 82-7 86-7 90-7 94-7 Control 34,7± 4.0 35.0± 4.8 35.8± 3.8 35.8± 3.7 36.2± 3.6 4.4 4.9 36.1± 4.9 36.4± 4.8 37.2± 4.4 20 ppm 35.0± 4.6 35.0± 4.8 36.2± 4.9 36.6± 4.5 37.4± 4.8 37.2± 4.4 50 ppm 34.4± 3.5 3.4 4.0 36.3± 3.9 36.4± 3.9<	ANJAMAL : MOUSE BODZFL/CFIJICFJ:BDFLJ UNIT : g REPORT TYPE : AI 104 SEX : FEMALE	.131cF3 : BBF1.J		ALL ANIWALS				PAGE: 11
Control 34.7 \pm 4.0 35.0 \pm 3.4 35.8 \pm 3.8 35.8 \pm 3.7 36.2 \pm 3.6 36.4 \pm 4.3 35.1 \pm 5.9 20 ppm 35.0 \pm 4.6 35.0 \pm 4.8 36.2 \pm 4.9 36.1 \pm 4.9 36.6 \pm 4.5 37.4 \pm 4.8 37.2 \pm 4.4 50 ppm 34.4 \pm 3.5 34.6 \pm 3.6 35.3 \pm 3.9 35.3 \pm 4.1 35.6 \pm 3.9 36.4 \pm	roup Name	Administration 70-7	жееk-day 74-7	7-87	82-7	L-98	<i>L</i> -06	<i>L</i> -76
20 ppm 35.0 ± 4.6 35.0 ± 4.8 36.2 ± 4.9 36.1 ± 4.9 36.6 ± 4.5 37.4 ± 4.8 37.4 ± 4.8 37.2 ± 4.4 50 ppm 34.4 ± 3.5 34.6 ± 3.6 35.3 ± 3.9 34.7 ± 4.0 35.6 ± 3.9 34.7 ± 4.0 36.1 ± 6.9 36.1	Control		35.0± 3.4		35.8± 3.7			35.1± 5.9
50 ppm 34.4 ± 3.5 34.6 ± 3.6 35.3 ± 3.9 35.3 ± 4.1 35.6 ± 3.3 36.4 ± 3.2 36.4 ± 3.2 36.6 ± 3.7 125 ppm 33.5 ± 3.4 33.9 ± 3.8 34.7 ± 4.0 34.8 ± 3.9 34.7 ± 4.0 36.1 ± 6.9 35.1 ± 3.8 ifficant difference; $*:P \le 0.05$ $**:P \le 0.01$ Test of Dunnett	20 ppm							
125 ppm $33.5\pm\ 3.4$ $33.9\pm\ 3.8$ $34.7\pm\ 4.0$ $34.8\pm\ 3.9$ $34.7\pm\ 4.0$ $36.1\pm\ 6.9$ $35.1\pm\ 3.8$ ificant difference; $*:P\le0.05$ **: $P\le0.01$ Test of Dunnett								
ificant difference ; *: P \leq 0.05 **: P \leq 0.01	125 ppm	33.5± 3.4	33.9± 3.8					
ificant difference ; * : P \leq 0.05 ** : P \leq 0.01 Test of Dunnett	MATERIAL MAT	- Control of the Cont						
	Significant difference;	* : P ≤ 0.05	** : P ≤ 0.01		Test of Dunnett		To 100 (100 (100 (100 (100 (100 (100 (100	*
	JAN260)						NAME OF THE PROPERTY OF THE PR	BAIS 4

ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : FEMALE	[[Cr]:BDF1]		BODY WEIGHT CHANGES ALL ANIMALS	(SUMMARY) PAGE: 12
Group Name	Administration week-day	n week-day	PARAMETER PARAME	
	L-86	102-7	104-7	
		TO THE PROPERTY OF THE PROPERT		
Control	35.2± 5.0	34.4 ± 5.0	34.2± 5.5	
20 ppm	36.6 ± 5.2	36.5 ± 5.2	37.6 ± 4.4	
50 ppm	36.4± 3.9	36.7± 3.9	36.6± 3.6	
125 ppm	35.6± 4.1	34.5± 4.2	35.6± 5.3	
		1 doc.		
Significant difference;	*: P ≤ 0.05	* *: P ≤ 0.01		Test of Dunnett
(HAN260)				BAIS 4

TABLE E1

FOOD CONSUMPTION CHANGES AND SURVIVAL ANIMAL

NUMBERS: MALE

(BI0040)

MEAN FOOD CONSUMPTION (FC) AND SURVIVAL

STUDY NO. : 0561
ANIMAL : MOUSE BEDZF1/Crlj[Crj:BDF1]
UNIT : g
REPORT TYPE : Al 104
SEX : MALE

		TO 11 1100		udd 07	E		mad oc	s		125 ppm		
Week-Day on Study	Av. FC.	No. of Surviv. <50>	Av. FC.	% of cont. <50>	No. of Surviv.	Av. FC.	% of cont. <50>	No. of Surviv.	Av. FC.	% of cont. <50>	No. of Surviv.	
1-7	3.9 (50)	50/50	4.0 (50)	103	50/50	3.9 (50)	100	50/50	3 8 (50)	07	50/50	
2-7	3.9 (50)	20/20	3.8 (50)	97	50/50	3.8 (50)	97	50/50	3.9 (50)	1001	50/50	
3-7	4.1 (50)	20/20	4.1 (50)	100	20/20	4.0 (50)	86	50/50	4.0 (50)	86	50/50	
4-7	4.1 (50)	_	4.0 (50)	86	50/50	4.0 (50)	86	50/50	4.0 (50)	86	50/50	
2-2	4.1 (50)	_	4.1 (50)	100	20/20	4.0 (50)	86	50/50	4.0 (50)	86	50/50	
2-9	4.2 (50)		4.1 (50)	86	20/20	4.0 (50)	92	50/50	4.1 (50)	86	50/50	
2-2	4.1 (50)		4.1 (50)	100	20/20	4.0 (50)	86	50/50	4.1 (50)	100	50/50	
28	_		4.1 (50)	86	20/20	4.1 (50)	86	50/50	4.1 (50)	86	50/50	
2-6	4.3 (50)		4.2 (50)	86	20/20	4.1 (50)	95	50/50	4.2 (50)	86	50/50	
10-7	_		4.3 (50)	100	20/20	4.1 (50)	95	20/20	4.2 (50)	86	50/50	
11-7	4.2 (50)		4.2 (50)	100	20/20	4.1 (50)	86	50/50	4.0 (50)	92	50/50	
12-7	_	20/20	4.4 (50)	100	20/20	4.2 (50)	95	50/50	4.3 (50)	86	50/50	
13-7			4.2 (50)	86	20/20	4.1 (50)	92	20/20	4.2 (50)	86	50/50	
14-7				100	20/20	4.3 (50)	100	20/20	4.3 (50)	100	50/50	
18-7				100	20/20	4.5 (50)	86	50/50	4.6 (50)	100	50/50	
22-7			4.7 (50)	86	20/20	4.7 (50)	86	50/50	9	96	50/50	
26-7				100	20/20	4.6 (50)	100	20/20	4.5 (50)	86	50/50	
30-7	4.7 (50)		4.6 (50)	86	20/20		86	50/50	4.6 (50)	86	50/50	
34-7			4.9 (50)	100	50/50	4.8 (50)	86	20/20	4.7 (50)	96	50/50	
38-7	0		5.0 (50)	100	20/20	∞	96	20/20	4.8 (50)	96	50/50	
42-7	0		5.0 (50)	100	20/20	5.0 (50)	100	20/20	4.8 (50)	96	50/50	
46-7	0		0	100	20/20	4.9 (50)	86	50/50	4.8 (50)	96	50/50	
20-7	0		5.0 (50)	100	20/20	4.9 (50)	86	20/20	4.9 (50)	86	50/50	
54-7	0			100	20/20	4.9 (50)	86	50/50	4.7 (50)	94	50/50	
28-7	5.0 (50)		4.9 (50)	86	20/20	4.9 (50)	86	20/20	4.7 (50)	94	50/50	
62-7	5.2 (49)		5.1 (50)	86	20/20	4.9 (50)	94	20/20	4.9 (49)	94	49/50	
2-99	_	49/50	5.0 (50)	86	20/20	_	100	50/50	4.9 (47)	96	47/50	
2-07	5.1 (49)	49/50	5.0 (50)	86	20/20	5.0 (50)	86	50/50	4.8 (47)	94	47/50	
74-7	~	49/50	5.2 (48)	100	48/50	0	96	50/50	4.9 (47)	94	47/50	
2-87	~	49/50	5.1 (48)	86	48/50	0	96	20/20	4.9 (47)	94	47/50	
82-7	۵,	48/50		100	46/50	5.0 (47)	96	47/50	4.9 (46)	94	46/50	
2-98	~	48/50	5.0 (46)	96	46/50	4.8 (45)	62	45/50	4.9 (45)	94	45/50	
2-06	2	48/50	5.3 (43)	96	43/50	5.2 (43)	95	43/50	5.1 (44)	93	44/50	
94-7	5.4 (45)	45/50	5.2 (37)	96	37/50	5.2 (39)	96	39/20	0	93	43/50	
2-86	5.3 (42)	42/50	5.3 (32)	100	34/50	4.9 (37)	65	37/50	4.9 (40)	85	40/50	
102-7	4.8 (40)	40/20	5.2 (33)	108	33/50	4.7 (35)	86	35/20	4.8 (39)	100	39/20	
104-7	4.8 (39)	39/20	5.2 (32)	108	32/50	4.9 (32)	102	32/50	4.8 (39)	100	39/50	

TABLE E2

FOOD CONSUMPTION CHANGES AND SURVIVAL ANIMAL

NUMBERS: FEMALE

(BI0040)

MEAN FOOD CONSUMPTION (FC) AND SURVIVAL

STUDY NO. : 0561

ANIMAL : MOUSE B6DZF1/Cr1;[Cr;:BDF1]
UNIT : g

REPORT TYPE : A1 104
SEX : FEMALE

		TOTALION		mdd nz	a .		mdd oc	ē		125 ppm	S	
Week-Day on Study	Av. FC.	No. of Surviv. <50>	Av. FC.	% of cont. <50>	No. of Surviv.	Av. FC.	% of cont. <50>	No. of Surviv.	Av. FC.	% of cont. <50>	No. of Surviv.	
1-7	3.3 (50)	_	3.3 (50)	100	50/50	1 -	97	50/50	3.2 (50)	97	50/50	
2-7	3.4 (50)) 20/20	33	26	20/20	3.3 (50)	97	50/50	n (۲)	97	50/20	
3-7	3.7 (50)	_	3.6 (50)	97	20/20	_	95	50/50	3.5 (50)	95	50/50	
4-7	3.7 (50)		9	97	20/20		95	50/50		97	50/50	
22	3.8 (50)		3.7 (50)	97	50/50	3.6 (50)	95	50/50	3, 7 (50)	97	50/50	
29	3.9 (50)		3.7 (50)	92	20/20	3.7 (50)	95	50/50	~	95	50/50	
2-7	4.0 (50)) 20/20	3.9 (50)	86	50/50	3.8 (50)	92	50/50	m	95	50/50	
2-8	3.9 (50)		6	100	20/20	3.9 (50)	100	20/20	3.8 (50)	26	50/50	
2-6	4.1 (50)		4.0 (50)	86	20/20	3.9 (50)	92	20/20	_	95	50/50	
10-7			4.0 (50)	100	20/20	3.9 (50)	86	20/20	6	86	50/50	
117	-		3.8 (50)	100	20/20	3.9 (50)	103	50/50	_	103	50/50	
12-7			4.0 (50)	100	20/20	3.9 (50)	86	50/50	3.9 (50)	86	50/50	
137			3.8 (50)	26	20/20	3.9 (50)	100	50/50	3.9 (50)	100	50/50	
14-7	_		4.0 (50)	100	20/20	4.1 (50)	103	20/20	4.0 (50)	100	20/20	
18-7	4.3 (50)		4.4 (50)	102	50/50	4.3 (50)	100	50/50	4.3 (50)	100	20/20	
22-7			4.4 (50)	100	50/50		100	50/50	_	86	50/50	
29-2			4.3 (50)	86	20/20		100	50/50	4.3 (50)	86	50/50	
30-7) 20/20	4.4 (50)	100	50/50	4.4 (50)	100	50/50	_	100	49/50	
34-7	9		4.6 (50)	100	20/20		86	20/20	4.4 (49)	96	49/50	
38-7	∞		4.6 (50)	96	20/20	4.5 (50)	94	20/20	4.6 (49)	96	49/50	
42-7	4.7 (50)		4.6 (50)	86	20/20		86	20/20	4.6 (49)	86	49/50	
467	4.8 (50)		4.7 (50)	86	20/20		96	20/20	4.5 (49)	94	49/50	
20-2	4.6 (50)		4.6 (50)	100	20/20	4.5 (50)	86	20/20	4.5 (49)	86	49/50	
54-7	4.7 (50)		4.5 (50)	96	20/20	4.5 (50)	96	20/20	4.5 (49)	96	49/50	
287	4.6 (50)			100	20/20	4.7 (49)	102	49/50	4.6 (48)	100	48/50	
2-29				102	20/20		100	48/50	4.6 (44)	86	44/50	
2-99	4.6 (49)			86	20/20	_	100	48/50	4.5 (44)	86	44/50	
7-07	4.7 (49)		4.8 (47)	102	47/50		86	47/50	4.7 (44)	100	44/50	
74-7	4.7 (48)		4.7 (46)	100	46/50	4.6 (44)	86	44/50	4.7 (44)	100	44/50	
78-7	4.7 (45)) 45/50	4.7 (46)	100	46/50	4.7 (43)	100	43/50	4.7 (43)	100	43/50	
228	4.7 (43)		4.9 (46)	104	46/50	4.7 (40)	100	40/50	4.6 (41)	86	41/50	
2-98	4.7 (38)		4.6 (44)	86	44/50	4.5 (38)	96	38/20	4.4 (41)	94	41/50	
2-06	4.9 (36)		0	102	41/50	4.9 (35)	100	35/50	4.8 (37)	86	37/50	
94-7	o,		5.1 (37)	104	37/20	5.0 (30)	102	30/20	4.8 (34)	86	34/50	
2-86	5.0 (26)		4.9 (34)	86	34/50	4.9 (28)	86	28/50	4.7 (31)	94	31/50	
102-7	4.7 (20)	_	4.8 (32)	102	32/50	4.8 (25)	102	25/50	4.5 (26)	96	26/50	
104-7	4.6 (18)	() 18/20	4.9 (31)	107	31/50	4.8 (24)	104	24/50	4.5 (26)	86	26/50	

TABLE E3

FOOD CONSUMPTION CHANGES: MALE

REPORT TYPE : A1 104 SEX : MALE							PAGE :
Group Name	Administration 1-7(6)	Administration week-day(effective)	3-7(7)	4-7 (7)	5-7(7)	(2) 2-9	(1) 1-1
Control	3.9± 0.3	3.9± 0.3	4.1± 0.3	4.1± 0.3	4.1± 0.3	4.2± 0.3	4.1 ± 0.3
20 ррт	4.0± 0.3	3.8± 0.3	4.1 ± 0.3	4.0 ± 0.3	4.1 ± 0.3	4.1± 0.3	4.1 ± 0.3
50 ppm	3.9± 0.3	3.8± 0.3	4.0 ± 0.3*	4.0± 0.3	4.0± 0.3	4.0± 0.3**	4.0 ± 0.3
125 ppm	3.8± 0.2	3.9± 0.3	4.0 ± 0.3	4.0± 0.2	4.0± 0.3	4.1± 0.3	4.1 ± 0.3
Significant difference :	W G G G G G G G G G G G G G G G G G G G	10 U V d **		- + 0 C			

SEX : MALE							PAGE :
Group Name	Administration 8-7(7)	Administration week-day(effective)8-7(7)	10-7(7)	11-7(7)	12-7 (7)	13-7 (7)	14-7(7)
Control	4.2± 0.3	4.3 + 0.3	4.3± 0.3	4.2± 0.3	4.4± 0.3	4.3 ± 0.2	4. 3± 0.3
20 ppm	4.1± 0.3	4.2± 0.3	4. 3± 0.3	4.2± 0.4	4.4± 0.3	4.2± 0.3	4.3± 0.3
50 ррт	4.1± 0.4	4.1± 0.3*	4. 1± 0.3	4.1± 0.3*	4.2± 0.3*	4.1± 0.3*	4.3 ± 0.2
125 ppm	4.1 ± 0.3	4.2± 0.3	4.2 ± 0.4	4.0± 0.3*	4.3± 0.3	4.2± 0.3	4.3± 0.3
	TO COMPANY OF THE PROPERTY OF	Production in the second secon	TOTAL PARTY OF THE	To control of the con			
Significant difference;	* : P ≤ 0.05	** : P ≤ 0.01		Test of Dunnett			

Group Name Administration week-day(effective) $25-7(7)$ $25-7(7)$ $39-7(7)$ $39-7(7)$ $39-7(7)$ $39-7(7)$ $42-7(7)$ Control 4.6± 0.3 4.6± 0.3 4.6± 0.3 4.6± 0.3 4.6± 0.3 5.0± 0.3 5.0± 0.3 5.0± 0.3 20 ppm 4.6± 0.3 4.6± 0.3 4.6± 0.3 4.6± 0.3 4.6± 0.3 5.0± 0.3 5.0± 0.3 5.0± 0.3 50 ppm 4.6± 0.3 4.6± 0.3 4.6± 0.3 4.6± 0.3 4.8± 0.3 4.8± 0.3 5.0± 0.3 125 ppm 4.6± 0.3 4.6± 0.3 4.6± 0.3 4.6± 0.3 4.8± 0.3 4.8± 0.4 4.8± 0.4	NITT : E REPORT TYPE : AI 104 SEX : MALE		•	CONTRACTOR				PAGE :
4.6±0.34.8±0.34.6±0.34.7±0.34.9±0.25.0±0.35.0±4.6±0.34.6±0.34.6±0.34.6±0.34.6±0.34.8±0.34.8±0.35.0±4.5±0.24.6±0.34.6±0.34.6±0.34.8±0.34.8±0.35.0±4.6±0.34.6±0.3*4.6±0.3*4.6±0.3*4.8±0.44.8±*: P ≤ 0.05**: P ≤ 0.01Test of Dunnett	Group Name	Administration 18-7(7)	week-day(effective)		30-7(7)	34-7 (7)	38-7(7)	42-7(7)
$4.6\pm$ 0.3 $4.6\pm$ 0.3 $4.6\pm$ 0.3 $4.6\pm$ 0.3 $4.9\pm$ 0.4 $5.0\pm$ 0.3 $5.0\pm$ 0.3 $4.5\pm$ 0.2 $4.7\pm$ 0.3 $4.8\pm$ 0.3 $4.8\pm$ 0.3 $4.8\pm$ 0.3 $4.8\pm$ 0.3 $5.0\pm$ 0.3 $4.6\pm$ 0.3 $4.6\pm$ 0.3 $4.6\pm$ 0.3 $4.7\pm$ 0.3* $4.8\pm$ 0.4 $4.8\pm$ 0.4	Control	4.6 ± 0.3						
$4.5\pm$ 0.2 $4.7\pm$ 0.3 $4.6\pm$ 0.3 $4.6\pm$ 0.3 $4.8\pm$ 0.3 $4.8\pm$ 0.3 $4.8\pm$ 0.3 $5.0\pm$ 0.0 $4.6\pm$ 0.3 $4.6\pm$ 0.3 $4.7\pm$ 0.3* $4.8\pm$ 0.4 $4.8\pm$ 0.4 $4.8\pm$ 0.4	20 ppm							
4.6 \pm 0.3 4.6 \pm 0.3 4.7 \pm 0.3* 4.7 \pm 0.3* 4.8 \pm 0.4 4.8 \pm * : P \leq 0.05 ** : P \leq 0.01 Test of Dunnett	50 ppm							
*: P ≤ 0.05 **: P ≤ 0.01	125 ppm	4.6± 0.3	4.6± 0.3*					
*: P ≤ 0.05 **: P ≤ 0.01	de de la constantina	WWW.	d many					
	Significant difference;		*: P ≤ 0.01		Test of Dunnett			

SEX : MALE	***************************************			THE PARTY OF THE P	The state of the s		PAGE :
Group Name	Administration 46-7(7)	Administration week-day(effective)	54-7(7)	58-7(7)	62-7(7)	(2) 2–99	70-7 (7)
Control	5.0 + 0.3	5.0± 0.4	5.0± 0.3	5.0± 0.3	5.2± 0.3	5.1± 0.3	5,1± 0.3
20 ppm	5.0± 0.3	5.0± 0.3	5.0士 0.4	4.9 ± 0.3*	5.1 ± 0.3	5.0± 0.4	5.0± 0.5
50 ppm	4.9± 0.3	4.9± 0.3	4.9± 0.3	4.9± 0.3*	4.9± 0.4**	5.1 ± 0.3	5.0 ± 0.4
125 ppm	4.8± 0.3**	4.9± 0.3	4.7± 0.4**	4.7± 0.4**	4. 9± 0.4**	4.9± 0.4**	4.8 ± 0.8**
Significant difference;	*: P ≤ 0.05	** : P ≤ 0.01		Test of Dunnett			

AEFOKI 11FE - AI 104 SEX : MALE							PAGE :
Group Name	Administration 74-7(7)	Administration week-day(effective)	82-7 (7)	(2) 2-98	(2) 2-06	94-7(7)	(2) 2–86
Control	5.2± 0.3	5.2± 0.7	5.2± 0.4	5.2± 0.4	5.5± 0.5	5.4生 0.8	5.3± 0.7
20 ppm	5.2	5.1± 0.4	5.2± 0.4	5.0± 0.6	5.3± 0.9	5.2± 0.8	5.3± 0.5
50 ppm	5.0± 0.4	5.0± 0.6	5.0± 0.6*	4.8± 0.6**	5.2± 0.7	5.2± 0.6	4.9± 0.7*
125 ppm	4.9± 0.4**	4.9± 0.6*	4.9± 0.6**	4.9± 0.6*	5.1± 0.5**	5.0± 0.7	4.9± 0.5*
							TO CONTRACT OF THE PARTY OF THE
Significant difference;	*:P≤0.05 *	* : P ≤ 0.01		Test of Dunnett			

Control 4.8± 20 ppm 5.2±	uistration week-	-day(effective)	PAGE:
50 ppm 4.7±	0.7	4.9± 0.5 4.8± 0.7	
Significant difference; *:P≦0.05		* : P ≤ 0.01	Test of Dunnett

TABLE E4

FOOD CONSUMPTION CHANGES: FEMALE

STUDY NO. : 0561 ANIMAL : MOUSE B6DZF1/Crij[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : FEMALE	[Crj:BDF1]	FO	FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS	SS (SUMMARY)			PAGE - 7
Сгоир Ламе	Administration 1-7(6)	Administration week-day(effective)	3-7(7)	4-7(7)	(2) 2-9	(1) 1-9	
Control	3.3 ± 0.2	3.4± 0.2	3.7 ± 0.2	3.7± 0.2	3.8± 0.2	3.9± 0.2	4.0± 0.3
20 ppm	3.3± 0.2	3.3± 0.2	3.6± 0.2*	3.6 ± 0.2	3.7± 0.2**	3.7± 0.2**	3.9± 0.3
20 ррш	3.2± 0.2	3.3± 0.2	3.5± 0.2**	3.5± 0.2**	3.6± 0.2**	3.7± 0.2**	3.8± 0.3≠
125 ppm	3.2 ± 0.3**	3.3± 0.2	3.5± 0.2**	3.6± 0.2*	3.7± 0.2**	3.7± 0.2**	3.8± 0.3
Significant difference;	* · · P · · · · · · · · · · · · · · · ·	** : P \square 0.01		Test of Dunnett			

STUDY NO. : 0561 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : g REPORT TYPE : A1 104	[Cr.j:BDF1]	FOO	FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS	ES (SUMMARY)				
SEX : FEMALE		The second secon	T T T T T T T T T T T T T T T T T T T				PAGE:	30
Group Name	Administration 8-7(7)	Administration week-day(effective)8-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)	14-7 (7)	
				The second secon	Vindo)	THE STATE OF THE S	The second secon	1
Control	3.9 ± 0.2	4.1± 0.3	4.0 ± 0.2	3.8 ± 0.2	4.0± 0.2	3.9 ± 0.3	4.0± 0.3	
20 ppm	3.9± 0.3	4.0± 0.3	4.0± 0.3	3.8± 0.3	4.0± 0.3	3.8 ± 0.3	4.0 ± 0.3	
	3.9± 0.3	3.9± 0.2*	3.9± 0.3	3.9 ± 0.3	3.9 ± 0.4	3.9 ± 0.3	4.1± 0.3	
125 ppm	3.8± 0.2	3.9± 0.2	3.9± 0.3	3.9± 0.3	3.9± 0.2	$3.9\pm$ 0.3	4.0± 0.3	
		TOTAL CONTRACTOR CONTR	The second secon	er gordon en				
Significant difference ;	*: P ≤ 0.05	** : P ≤ 0.01		Test of Dunnett				

STUDY NO. : 0561 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : FEMALE	[Crj:BDF1]		FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS	GES (SUMMARY)			PAGE :	•
Group Name	Administration	Administration wook-day(offective)	THE PROPERTY OF THE PROPERTY O	mind below.			TOU 1	
	18–7(7)	22-7 (7)	26-7(7)	30-7 (7)	34-7(7)	38-7(7)	42-7(7)	
						7.	TO THE REAL PROPERTY OF THE PR	
Control	4.3 ± 0.3	4.4 ± 0.4	4.4 ± 0.4	4.4 ± 0.4	4.6± 0.4	4.8 ± 0.5	4.7± 0.3	
20 ppm	4.4 ± 0.3	4.4± 0.4	4.3± 0.5	4.4± 0.5	4.6± 0.5	4.6 + 0.4	4.6± 0.5	
50 ppm	4.3 ± 0.3	4.4± 0.3	4.4± 0.4	4.4± 0.5	4.5± 0.4	4.5± 0.5	4.6± 0.5	
125 ppm	4.3± 0.3	4.3± 0.4	4.3 ± 0.4	4.4± 0.3	4.4 + 0.4*	4.6± 0.5	4.6± 0.5	
Significant difference ;	*: P ≤ 0.05	★ : P ≤ 0.01	THE THE PROPERTY OF THE PROPER	Test of Dunnett	Prinder,		TOWARD AND AND AND AND AND AND AND AND AND AN	

ABFORT TIFE . AL 104 SEX : FEMALE							. godi
Group Name	Administration 46-7(7)	Administration week-day(effective)46-7(7) 50-7(7)	54-7(7)	58-7(7)	(2) (2)	(1) 1-99	70-1(7)
Control	4.8 ± 0.5	4.6+ 0.4	4.7± 0.5	4.6± 0.5	4.7± 0.4	4.6± 0.4	4.7± 0.6
20 ppm	4.7± 0.4	4.6± 0.6	4.5± 0.5	4.6± 0.5	4.8 ± 0.5	4.5± 0.8	4.8± 0.5
50 ந்தவ	4.6± 0.4	4.5± 0.5	4.5± 0.5	4.7 ± 0.5	4.7 ± 0.5	4.6 ± 0.5	4.6± 0.6
125 ppm	4.5± 0.6*	4.5± 0.5	4.5± 0.6	4.6± 0.4	4.6± 0.5	4.5 ± 0.6	4.7± 0.9
The control of the co	10.00 (A)	- Total Marketing and the second and	The state of the s				
Significant difference;	*: P ≤ 0.05	** : P ≤ 0.01		Test of Dunnett			

PAGE: 11 5.0 ± 1.0 4.9 ± 0.9 4.7 ± 0.6 4.9 ± 0.7 (2) 2-86 0.7 0.8 4.9 ± 1.2 4.8 ± 0.6 94-7(7) 5.1± 5.0± 0.9 9.0 0.7 4.9 ± 0.7 90-7(7)5.0± $4.9\pm$ 4.8± Test of Dunnett 0.6 4.5 ± 0.6 4.4 ± 0.6 4.7 ± 0.7 (2) 2-98 4.6± FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS 0.6 0.5 0.5 4.7 ± 0.6 82-7(7) $4.9 \pm$ 4.7± 4.6± Administration week-day(effective)_74-7(7) 0.5 0.5 0.7 4.7 ± 0.7 ***** : P ≤ 0.01 4.7± 4.7± 4.7± 4.7 ± 0.5 4.7 ± 0.5 4.6 ± 0.6 4.7 ± 0.5 *: P ≤ 0.05 STUDY NO.: 0561

ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]
UNIT : g

REPORT TYPE : A1 104
SEX : FEMALE Significant difference; 20 ppm 50 ppm 125 ppm Control Group Name

PAGE: 12								BAIS 4
FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS	effective) -7(7)	0.8	. 0.7	: 1.1	. 0.6		0.01 Test of Dunnett	
	Administration week-day(effective)	0.7 4.6±	0.6 4.9±	0.7 4.8±	0.5 4.5±	or a land	.05 ★ : P ≤ 0.01	
STUDY NO. : 0561 ANIMAL : MOUSE BGD2F1/Cr1j[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : FEMALE	Admini 102-7(4.7± 0.7	4.8+	4.8+	4.5± 0.5	Anna Control	lifference ; * : P ≤ 0.05	
STUDY NO. : 0561 ANIMAL : MOUSE BGI UNIT : g REPORT TYPE : A1 104 SEX : FEMALE	Group Name	Control	20 ppm	50 ppm	125 ppm		Significant difference;	(HAN260)

TABLE F1

HEMATOLOGY: MALE

STUDY NO. : 0561 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1] MEASURE. TIME : 1 SFX : MAIF	B6D2F1/Cr1	F1/Cr1j[Crj:BDF1] pHDAPT TVDE · 41		HEM	HEMATOLOGY (SUMMARY) ALL ANIMALS (105W)	MMARY) OSW)									
7777	MCI ON I	IIFE · AI												PAGE :	
Group Name	NO. of Animals	RED BLOOD CELL 1 Φ⁄μℓ	JL HEMOGLOBIN g/dl	IN	HEMATOCRIT	RIT	MCV f &		MCH p g		MCHC g / dl		PLATELET 1 03/µl	rr ne	
				TOTAL PROPERTY AND THE		THE PERSON NAMED IN COLUMN TO SERVICE OF SER			-	TOTAL DESCRIPTION AND ADDRESS OF THE PARTY O		- Vinit Title Orlandoss	77777000000		
Control	39	9.25± 1.94	13.4±	2.6	40.3±	7.4	43.7±	2.0	14.5	9.0	33.2±	1.4	1538±	431	
20 ppm	32	9.41± 1.16	13.5±	1.7	40.9±	4.5	43.7±	2. 2	14.4±	0.6	33.0±	1.1	1649±	333	
mdd 09	31	9.49± 0.65	13.6±	0.9	$41.0\pm$	2. 4	43.2±	1.7	14.3±	0.5	33.1±	6.0	$1646\pm$	295	
125 ppm	38	9.82± 1.28	14.0±	1.8	42.4 ±	5.3	43.2±	2.7	14.2±	1.0	32.9±	1.0	1545±	511	
Significant d	ifference ;	Significant difference; *: P ≤ 0.05	** : P ≤ 0.01		*		Test of Dunnett	nett							

(HCL070)

	PAGE :							BAIS 4
ALL ANIMALS (105W)							Test of Dunnett	Parameter (Control of Control of
ALL							* : P ≤ 0.01	Terminological Administration (Assessment Control of Co
: BDF1	: A1	RETICULOCYTE %	3.5 + 4.1	2.9± 1.8	2.7 ± 1.2	2.8± 1.4	*:P ≤ 0.05	
B6D2F1/Cr1j[Cr.	REPORT TYPE : A1	NO. of Animals	39	32	31	38	fference; *	######################################
ANTMAL : MOUSE BODZF1/Crlj[Crj:BDF1] MEASURE. TIME : 1	SEX : MALE	Group Name	Control	20 ppm	50 ppm	125 ppm	Significant difference;	(HCL070)

			2	က	8	2	
	PAGE:	OTHER	2+	! !	1+	+1	***************************************
			13	12	12	13	
		LYMPHO	÷29	64±	∓99	十29	
			2	2	73	63	nada and succession a
		MONO	+1	1 €	2+	4 ±	
			0	0	0	0	
		BASO	#10	+0	†1	+10	
				1	1	63	
(,,		EOSINO	2±	5 †	7	2+	
HEMATOLOGY (SUAMARY) ALL ANIMALS (105W)		13	12	11	12		
	WBC (%) N-SEG	29±	27±	76±	28 +	AMANA, A LOTTO VOTO VOTO VOTO VOTO VOTO VOTO VOT	
	Differential)	1	1	-	63		
	Dif N-BAND	5 +	5+1	1	5±		
		2	3.47	2. 72	2. 02	2.38	
j[Crj:BDF1]	REPORT TYPE : A1	ΨBC 1 0³ ∕ μβ	4.83±	4.70±	4.17±	4.99+	
B6D2F1/Crl	REPORT	NO. of Animals	39	32	31	38	
STUDY NO. : 0561 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] MEASURE. TIME : 1	SEX : MALE	Group Name	Control	20 ppm	50 ppm	125 ppm	

Test of Dunnett

**: P ≤ 0.01

Significant difference ; * : P \leq 0.05

(HCL070)

TABLE F2

HEMATOLOGY: FEMALE

	4							
	PAGE:	T &		234	323	305	332	
		PLATELET 1 0³ ∕ µℓ	A North Print a common of the	1002±	±010∓	1025±	848±	
		100000000000000000000000000000000000000	- Contain the	8.0	1.6	2.4	2.3	
		MCHC g / d2		33.5±	33.0±	32.8±	32.7±	
		79000		0.5	1.5	6.0	0.6	
		MCH p.g		14.7±	15.1±	14.7±	14.9±	
				1.8	9.2	6.1	5.5	nett
		MCV f 2		44.0±	45.9 ±	45.1 ±	46.0±	Test of Dunnett
MMARY) 05W)		RIT		2.4	4.4	6.6	8.1	
HEMATOLOGY (SUMMARY) ALL ANIMALS (105W)		HEMATOCRIT		42.3±	40.8±	41.9±	40.0±	
1		BIN		0.9	1.9	2.5	3.0	1
		HEMOGLOBIN g / dl		14.1±	13.5±	13.8±	13.2±	** : P ≤ 0.01
	** O TO MARKET	RED BLOOD CELL 1 O ⁶ / m ⁶		0.80	1.66	1.86	2.08	. 05
[Crj:BDF1]	REPORT TYPE : A1	RED BLOOD 1 O ⁶ / μθ		9.62+	9.11‡	9. 49±	8. 92±	» . P ≤ 0
B6D2		NO. of Animals		18	25	22	26	ifference ;
STUDY NO. : 0561 ANIMAL : MOUSE MEASURE. TIME : 1	SEX : FEMALE	Group Name		Control	20 ppm	50 ppm	125 ppm	Significant difference; * : P ≤ 0.05

(HCL070)

Mainals Methori Type : Al Methoric Methoric Methoric Monant Methodic Monant Methoric Monant	ANTMAL : MOUSE MEASURE TIME : 1	B6D2F1/Cr1j	Crj:BDF1]	FIEWALOLOGI (SOUMAKE) ALL ANIMALS (105W)	
NO. of Animals RETICULOCYTE Animals % trol 18 2.6± 1.1 ppm 25 4.6± 6.8 ppm 22 3.6± 6.0 ppm 26 5.3± 8.2 cant difference; *: P ≤ 0.05 ***: P ≤ 0.01	SEX : FEMALE	REPORT 1	YPE : A1		PAGE : 5
1 8 0 ** : P ≤ 0.01	Group Name	NO. of Animals	RETICULOCYTE %		
8 0 2 ** : P ≤ 0.01	Control	18			
0 2 ** : P ≤ 0.01	20 ppm	25			
2 ** : P ≤ 0.01	50 ppm	22			
** : P ≤ 0.01	125 ppm	26			
	Significant di	fference ;			

	9			2	4	17	20**	
	PAGE :	OTHER	Andreas	<u>1</u> +	2±	+1	11 ±	
		The proposed of the control of the c		20	15	19	21	
		ГУМРНО	may provide the second sections.	∓99	+ 63	+ 29	22 	
		**************************************	#MANAGAMENT III	73	67	63	က	
		MONO		4+	4+	1 4	4 7	
				0	0	0	0	
		BASO		+ 0	+10	+10	+10	
				7	23	-	2	
(XX)		EOSINO		2+	5+	2+	1+	
HEMATOLOGY (SUMMARY) ALL ANIMALS (105W)	(%)		18	11	13	18		
	l WBC (%)		25 +	27±	24+	26±		
	Differential WBC		23	2	73	က		
	Did N-BAND		2+	2+	5 +	5+		
1.3	ر	c /ue		3.15 ± 2.01	1.87	12.35	10.67± 17.82	
j[Crj:BDF	REPORT TYPE : A1	WBC 1 O³∕μβ		3.15±	3.70±	6. 19±	10.67±	
; B6D2F1/Cr1	REPORT	NO. of Animals		18	25	22	56	
STUDY NO. : 0561 ANTMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] MEASURE. TIME : 1	SEX : FEMALE	Group Name		Control	20 ppm	50 ppm	125 ppm	

Test of Dunnett

** : P ≤ 0.01

Significant difference ; * : $P \le 0.05$

(HCL070)

TABLE G1

BIOCHEMISTRY: MALE

STUDY NO. : 0561 ANIMAL : MOUSE BGD2F1/Cr1j[Crj:BDF1] MEASURE. TIME : 1	B6D2F1/Crlj	[Crj:BDF1]			BIC	BIOCHEMISTRY (SUMMARY) ALL ANIMALS (105W)	SUMMARY) 05W)								
SEX : MALE	REPORT	REPORT TYPE : A1													PAGE:
Group Name	NO. of Animals	TOTAL P g /dl	TOTAL PROTEIN g/dl	ALBUMIN g/dl	77747000000	A/G RATIO	01	T-BILIRUBIN mg/d2	UBIN	GLUCOSE mg/dl		T-CHOLESTEROL mg/dl	TEROL	TRIGLYCERIDE mg/dl	RIDE
					77.00	177707						* ************************************	TO POST OFFICE AND ADDRESS OF THE POST OF		
Control	36	5.1±	0.7	2.5+	0.4	1.0±	0.2	0.13±	0.03	161±	52	126±	111	46±	28
20 ppm	32	5.3+	9.0	2.7±	0.4	1.1+	0.1	0.13±	0.02	181	32	120±	46	49 +	25
mdd 09	32	5.3+	0.6	2.7±	0.4	1.0+	0.2	0.14±	0.03	182±	32	119±	38	20∓	23
125 ppm	38	5.7±	0.9**	2.9+	0. 4**	1.0±	0.2	0.14±	0.05	174±	32	131±	59	47±	32
Significant difference; * : P ≤ 0.05	ifference ;) ≥! 4 : *		* : P ≤ 0.01	1			Test of Dunnett	nett						

52

STUDY NO. : 0561 ANIMAL : WOUSE B6D2F1/Crlj[Crj:BDF1] MEASURE. TIME : 1 SEX : MALE REPORT TYPE : A1	B6D2F1/Cr1j	F1/Cr1j[Crj:BDF1] REPORT TYPE : A1			BI	BIOCHEMISTRY (SUMMARY) ALL ANIMALS (105W)	(SUMMARY) [05W)								. 17.VQ
Group Name	NO. of Animals	PHOSPHOLIPID mg/dl	LIPID	AST I U / g	8	ALT I U / g	8	LDH I U / g	R	ALP I U / g	8	G-GTP I U / g		CK IU/2	1 1
Control	39	206±	137	142±	205	₩	139	∓299	1548	∓806	4820	#	-	248±	1065
20 ppm	32	215±	75	94±	62	199	65	373±	270	139±	69	#	1	799	36
50 ppm	32	709∓	22	213±	729	103±	322	549±	1368	121±	31	#	1	+ 02	24
125 ppm	38	234±	88 **	175 ±	276	114	144	7902	488	159±	26	1+	1	121±	327
Significant difference; *: P ≤ 0.05	ifference ;	0 VII *		** : P ≤ 0.01	21	To the state of th		Test of Dunnett	mett						

53

	PAGE : 3	sn						
		INORGANIC PHOSPHORUS		1.0	1.0	0.9	6.0	
		INORGANI mg/d2		6.5±	6.3±	6.2	6.3+	
				0.5	1.0	0.4	0.6*	
		CALCIUM mg/d2		8.8	9.1+	8.8 +1	9.2+	
		m		က	က	ю	က	lett
		CHLORIDE m Eq / 2	William Table	122±	122±	123±	121 ±	Test of Dunnett
(SUMMARY) (05W)		UM E		0.5	0.5	0.5	0.4	
BIOCHEMISTRY (SUMMARY) ALL ANIMALS (105\P)		POTASSIUM m.Eq./2		4. 3±	4.4 ±	4.3+	4.4 ±	
H A		6		က	2	8	2	
		SODIUM m.Eq./ 2		155±	154±	154±	153±	# : P ≤ 0.01
		UREA NITROGEN mg/dl		15.3	11.5	4.9	7.0	0.05
j[Crj:BDF1]	REPORT TYPE : A1	UREA N		28.1±	24.6±	22.9±	23.2±	VII d. *
B6D2F1/Cr1	REPORT	NO. of Animals		39	32	32	38	ifference;
STUDY NO. : 0561 ANIMAL : MOUSE BEDZFL/Crlj[Crj:BDFl] MEASURE. TIME : 1	SEX : MALE	Group Name		Control	20 ppm	50 ppm	125 ppm	Significant difference ; * : P ≤ 0.05

TABLE G2

BIOCHEMISTRY: FEMALE

PAGE: 4	TRIGLYCERIDE mg/dl	31 34± 17	18 45± 48	40 42± 21	22 41± 23	***************************************
	T-CHOLESTEROL mg/d2	84+	+108	+08	70±	
	GLUCOSE mg/dl	113± 49	129± 35	133 ± 23	122± 35	
	T-BILIRUBIN mg/d2	0.17± 0.08	0.14± 0.07	0.15± 0.05	0.16± 0.08	
BIOCHEMISTRY (SUMMARY) ALL ANIMALS (105W)	A/G RATIO	1.1	1.0± 0.3	1.1± 0.2	1.2± 0.3	
B	ALBUMIN g / d2	2.5± 0.2	2.5± 0.4	2.7± 0.2*	2.6± 0.3	
F1/Cr1j[Crj:BDF1] REPORT TYPE : A1	TOTAL PROTEIN g / dl	5.0± 0.4	5.0± 0.8	5.1± 0.5	4.9± 0.9	
STUDY NO. : 0561 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] MEASURE. TIME : 1 SEX : FEMALE REPORT TYPE : A1	Group Name NO. of Animals	Control 18	20 ppm 26	50 ppm 22	125 ppm 26	

NO. of PHOSPHOLIPID AST ALT LDH ALP G-GTP CK IU/P IU/P	No. of PHOSPHOLIPID AST ALT LDH ALP IU/P IU/	No. of PHOSPHOLIPID AST ALT LDH ALP G-GTP CK TU/\ell TU/	STUDY NO. : 0561 ANIMAL : MOUSE I MEASURE. TIME : 1 SEX : FEMALE	B6D2	<pre>2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1</pre>			BI	BIOCHEMISTRY (SUMMARY) ALL ANIMALS (105W)	(SUMMARY)								. 5040
18 137± 33 133± 90 61± 61 61± 61 390± 415 179± 54 1± 3 128± 1 26 144± 39 135± 112 48± 35 1146± 3031 143± 55 1± 1 104± 1 22 150± 72 166± 177 82± 110 788± 1280 185± 92 1± 2 81± 26 131± 39 174± 161 64+ 58 1962+ 5365 185+ 191 1+ 0 965+	18 137± 33 133± 90 61± 61 390± 415 179± 54 1± 3 128± 1 26 144± 39 135± 112 48± 35 1146± 3031 143± 55 1± 1 104± 1 22 150± 72 166± 177 82± 110 788± 1280 185± 92 1± 2 81± 26 131± 39 174± 161 64± 58 1962± 5395 188± 121 1± 0 265± 6	3 133± 90 61± 61 390± 415 179± 54 1± 3 128± 1 2 166± 177 82± 110 788± 1280 185± 92 1± 2 81± 9 174± 161 64± 58 1962± 5395 188± 121 1± 0 265± 6		NO. of Animals	PHOSPHO mg/d/	LIPID	AST I U	6	ALT I U	6	T I I	8	ALP I U / ,	g .	g-GTP I U A		CK I U	
26 144± 39 135± 112 48± 35 1146± 3031 143± 55 1± 1 104± 1 22 150± 72 166± 177 82± 110 788± 1280 185± 92 1± 2 81± 26 131± 39 174± 161 64+ 58 1962+ 5305 186+ 191 1+ 0 005± 64	26 144± 39 135± 112 48± 35 1146± 3031 143± 55 1± 1 104± 1 22 150± 72 166± 177 82± 110 788± 1280 185± 92 1± 2 81± 26 131± 39 174± 161 64± 58 1962± 5395 188± 121 1± 0 265± 6	9 135± 112 48± 35 1146± 3031 143± 55 1± 1 104± 1 2 166± 177 82± 110 788± 1280 185± 92 1± 2 81± 9 174± 161 64± 58 1962± 5395 188± 121 1± 0 265± 6	trol	18	137±	33	133±	06	÷19	19	390±	415	179	24	1 1	က	128±	131
22 150± 72 166± 177 82± 110 788± 1280 185± 92 1± 2 81± 26 131± 39 174± 161 64+ 58 1962+ 5305 188+ 191 1+ 0 005±	$ 22 150 \pm 72 166 \pm 177 82 \pm 110 788 \pm 1280 185 \pm 92 1 \pm 2 81 \pm \\ 26 131 \pm 39 174 \pm 161 64 \pm 58 1962 \pm 5395 188 \pm 121 1 \pm 0 265 \pm 6 $	2 166± 177 82± 110 788± 1280 185± 92 1± 2 81± 9 174± 161 64± 58 1962± 5395 188± 121 1± 0 265± 6	mdd	26	144#	39	135±	112	48±	35	1146土	3031	143±	55	1+		104 =	116
26 131± 39 174± 161 64+ 58 1962+ 5305 188+ 191 1+ 0 0.05±	26 $131\pm$ 39 $174\pm$ 161 $64\pm$ 58 $1962\pm$ 5395 $188\pm$ 121 $1\pm$ 0 $265\pm$	9 174± 161 64± 58 1962± 5395 188± 121 1± 0 265±	mđđ	22	150±	72	166±	177	82±	110	788±	1280	185±	85	1+	2	81+	56
			wdd	56	131±	36	174±	191	64±	28	1962±	5395	188±	121	1+	0	792∓	634

	PAGE: 6					
	INORCANIC PHOSPHORUS mg/d2	6.7± 2.0	6.4± 0.9	6.5± 1.4	6.6± 1.2	
	CALCIUM mg/d2	8.9± 0.2	9.0土 0.5	9.0 ∓0.6	8.9± 0.4	
	CHLORIDE m Eq / 2	121 ± 3	123± 3	122 ± 3	124± 5*	Test of Dunnett
BIOCHEMISTRY (SUMMARY) ALL ANIMALS (105W)	POTASSIUM m.Eq./ &	4.0+	4.1± 0.6	4.0± 0.7	4.2± 0.7	T
BIOC	SODIUM m Eq / &	152± 3	153± 2	152± 2	153± 4	** : P ≤ 0.01
F1/Crlj[Crj:BDF1] RRPORT TVPR : A1	UREA NITROGEN	21.8± 15.3	17.6± 7.8	15.6± 3.2	20.8± 14.6	
1561 10USE B6D2 ?:1	NO. Ani	Control 18	20 ppm 26	50 ppm 22	125 ppm 26	Significant difference; * : P ≤ 0.05
STUDY NO. : C ANIMAL : M MEASURE. TIME SEX : FEMALE.	Group Name					Sign

TABLE H1

URINALYSIS : MALE

Group Name NO. of pH. Protein. Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI $-\pm+$				
	2+ 3+ 4+ CHI	Glucose — + 2+3+4+ CHI	Ketone body $-\pm+2+3+4+$ CHI	Occult blood - ± + 2+ 3+ CHI
Control 40 0 5 10 6 17 2 0 0 1 1.	0 1 14 23 1 1 4	40 0 0 0 0 0	8 32 0 0 0 0	37 0 1 0 2
20 ppm 32 0 2 4 11 12 3 0 0 0 1:	0 13 19 0 0	32 0 0 0 0 0	8 24 0 0 0 0	30 0 0 0 2
50 ppm 33 0 4 9 4 8 8 0 0 0.1;	0 13 19 1 0 3	33 0 0 0 0 0	6 26 1 0 0 0	31 0 0 0 2
125 ppm 39 0 2 2 11 12 12 0 *** 0 1 10	1 10 25 3 0 3	39 0 0 0 0 0	631 2 0 0 0	35 0 2 0 2

MEASURE. TIME: 1 SEX: MALE REPORT TYPE: A1 Group Name NO. of Urobilinogen Animals ± + 2+ 3+ 4+	+ CHI
40 0 0	
32 0 0 0 33 0 0 0	
39 0 0 0	0
*: P ≤ 0.05	5 *# : P ≤ 0.01 Test of CHI SQUARE

TABLE H2

URINALYSIS : FEMALE

Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI - + + 2+ 3+ 4+			7
	3+ 4+ CHI - ± + 2+ 3+ 4+ CHI	Metone body II $-\pm + 2 + 3 + 4 + \text{CHI}$	Occult blood - ± + 2+ 3+ CHI
			1.0000000000000000000000000000000000000
Control 18 0 0 1 3 4 9 1 0 2 9 6	1 0 18 0 0 0 0	10 7 0 1 0 0	13 0 0 0 5
20 ppm 31 0 0 4 5 4 18 0 0 3 20 8	0 0 0 31 0 0 0 0	10 19 2 0 0 0	29 1 0 1 0 *
$50 \ \mathrm{ppm} \qquad 24 \qquad \qquad 0 \qquad 1 1 3 7 12 0 \qquad \qquad 0 3 9 \ 11$	1 0 24 0 0 0 0	6 14 4 0 0 0	22 0 0 0 2
125 ppm 26 0 0 4 4 5 13 0 0 11111 3 0	3 0 26 0 0 0 0 0	1 18 5 2 0 0 **	19 1 2 2 2

SEX : FEMALE REPORT TYPE : A1	REPORT TYPE : A1	YPE : A1			PAGE: 4
Group Name	NO. of Animals	Urobilinogen ± + 2+ 3+ 4+ CHI	IK		
Control	18	18 0 0 0 0			
20 ppm	31	31 0 0 0 0			
50 ppm	24	24 0 0 0 0			
125 ppm	26	26 0 0 0 0			
ignificant di	fference ;	Significant difference ; *: P ≤ 0.05	** : P ≤ 0.01	Test of CHI SQUARE	

TABLE J1

ORGAN WEIGHT, ABSOLUTE: MALE

(A)		
ORGAN WEIGHT: ABSOLUTE (SUMMAR	SURVIVAL ANIMALS (105W)	
STUDY NO. : 0561	ANTMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]	REPORT TYPE : A1

	SEX : MALE UNIT: g													PA
	Group Name	NO. of Animals	Body Weight	ADRENALS	NALS	TESTES	S	HEART		TUNGS		KIDNEYS	EYS	
	Control	36	45.6± 8.8	0.011±	0.002	0.228±	0.032	0.228±	0.028	0. 228 ±	0.119	1.178±	3. 250	
	20 mag	32	47.9± 7.9	0.011±	0.002	0.223±	0. 033	0.228±	0.022	0.220±	0.099	0.650±	0.052	
66	50 ppm	32	45.7± 7.4	0.011±	0.002	0.225±	0.031	0. 228±	0.020	0.229+	0.092	0.661±	0.061	
	125 ppm	39	44. 3± 8.5	0.011±	0.002	0.219±	0.030	0.226±	0.022	0.254±	0.125	0.711±	0.446	
	Significant difference;	ifference ;	* : P ≤ 0.05	** : P ≤ 0.01			Test	Test of Dunnett						

(HCL040)

ORCAN WEIGHT: ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (105W) PAGE : 2	LIVER BRAIN	$1.809\pm \ 0.606$ $0.450\pm \ 0.013$	1.898 ± 0.581 0.447 ± 0.011	1.684 ± 0.327 0.451 ± 0.011	2.161 ± 1.067 0.449 ± 0.012	** : P ≤ 0.01 Test of Dunnett
STUDY NO. : 0561 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 SEX : MALE UNIT: g	SPLEEN	0.187± 0.345	0.178± 0.427	0.115± 0.108	0.111± 0.104	*: P \le 0.05 **:
	Group Name NO. of Animals	Control 39	20 ppm 32	50 ppm 32	125 ppm 39	Significant difference ;
1-02	'			67		. '

TABLE J2

ORGAN WEIGHT, ABSOLUTE: FEMALE

	KIDNEYS	:± 0.044	∓ 0.088	:± 0.062	1 0.050
ORGAN WEIGHT:ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (105W)	, X	0.445±	0.474±	0.472±	0.464±
	TUNGS	0.014	0.020	0.031	0. 112
		$0.191\pm$	0. 195±	0. 202 ±	0. 225±
	HEART	0.021	0.026	0.025	0.023
		$0.179 \pm$	$0.179\pm$	0.188±	0.181±
	ADRENALS OVARIES	0.030	0.184	0.306	0.023
		0.041±	$0.091\pm$	0.122±	0.042±
		0.002	0.002	0.004	0.002
		0.014±	0.014土	0.016±	0.014±
	Body Weight	5.3	4.5	4.2	5.4
ij [Cr.j:BDF1]	Body	30.3±	33.5±	32.3	31.6± 5.4
se bedzf1/cr1	NO. of Animals	18	31	24	26
STUDY NO. : 0561 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REFORT TYPE : A1 SEX : FEMALE UNIT: g	Group Name	Control	20 ppm	50 ppm	125 ppm
				0.7	

PAGE: 3

BAIS 4

Test of Dunnett

★: P ≤ 0.01

Significant difference ; * : P \leq 0.05

(HCL040)

ORGAN WEIGHT:ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (105W) 0.016 0.018 0.067 0.020BRAIN 0. $493 \pm$ $0.478\pm$ 0.474 \pm $0.473\pm$ 0.284 1.218 1.340 0.500 LIVER 1.396 \pm 1. $790\pm$ $1.676\pm$ 1.933 \pm 0.174 0.376 0.339 0.235 SPLEEN 0.150± $0.250\pm$ $0.311\pm$ $0.232 \pm$ STUDY NO. : 0561
ANIMAL : MOUSE BEDZF1/Cr1;[Cr;:BDF1]
REPORT TYPE : A1
SEX : FEMALE
UNIT: g NO. of Animals 18 31 24 26 125 ppm 20 ррт 20 ppm Control Group Name

PAGE: 4

BAIS 4

Test of Dunnett

 $\star\star$: P \leq 0.01

*: P ≤ 0.05

Significant difference;

(HCL040)

TABLE K1

ORGAN WEIGHT, RELATIVE : MALE

%	SEX : MALE UNIT: %							PAGE: 1
Group Name NO. of Animals	ν .	Body Weight (g)	ADRENALS	TESTES	HEART	LUNGS	KIDNEYS	
Control 39	45.6±	8.8	$0.026\pm\ 0.007$	0.519 ± 0.128	0.517 ± 0.124	0.545± 0.453	2.480± 6.170	
20 ppm 32	47.9±	9± 7.9	0.023± 0.006	$0.478\pm\ 0.099$	$0.487\pm\ 0.074$	0.476 ± 0.268	1.388± 0.222	
50 ppm 32	45.7±	7± 7.4	0.025± 0.005	0.501 ± 0.085	0.511 ± 0.077	0.520 ± 0.250	$1.476\pm\ 0.212$	
125 ppm 39	44.3±	3+ 8.5	0.026± 0.007	0.512 ± 0.115	0.528± 0.110	$0.620\pm\ 0.437$	1.718± 1.525	
Significant difference ;	ence ; *: P ≤ 0.05		* : P ≤ 0.01	Test	Test of Dunnett	The second secon		

Group Name NO. of Animals SPLEEN LIVER BRAIN Control 39 0.414± 0.719 4.149± 1.958 1.030± 0.234 20 ppm 32 0.424± 1.170 4.065± 1.545 0.960± 0.169 50 ppm 32 0.264± 0.254 3.770± 0.992 1.015± 0.178 125 ppm 39 0.266± 0.280 5.067± 2.630 1.056± 0.233 Significant difference : * : P ≤ 0.05 ** : P ≤ 0.01 Test of Dumett	SEEE	STUDY NO. : 0561 ANIMAL : MOUSE BGDZFL/Crlj[Crj:BDF1] REPORT TYPE : A1 SEX : MALE TATT: 0	B6D2F1/Cr1j[7: j:BDF1]	ORGAN 'SURVIV,	ORGAN WEIGHT:RELATIVE (SUMMARY) SURVIVAL ANIMALS (105W)	
Control 39 0.414 ± 0.719 4.149 ± 1.958 1.030 ± 0.234 20 ppm 32 0.424 ± 1.170 4.065 ± 1.545 0.960 ± 0.169 0.060 ± 0.169 0.060 ± 0.169 0.060 ± 0.169 0.060 ± 0.169 0.060 ± 0.169 0.060 ± 0.169 0.060 ± 0.169 0.060 ± 0.269 0.060 ± 0.169 0.060 ± 0.069 0.060 ± 0.169	5 15	oup Name	NO. of Animals	1	LIVER	BRAIN	PAGE: 2
20 ppm 32 0.424 ± 1.170 4.065 ± 1.545 0.960 ± 0.169 50 ppm 32 0.264 ± 0.254 3.770 ± 0.992 1.015 ± 0.178 125 ppm 39 0.266 ± 0.280 5.057 ± 2.630 1.056 ± 0.233 ifficant difference; $*:P\le0.05$ $**:P\le0.01$		Control	39	0.414± 0.719	4.149± 1.958	$1.030\pm\ 0.234$	
50 ppm 32 0.264 ± 0.254 3.770 ± 0.992 1.015 ± 0.178 125 ppm 39 0.266 ± 0.280 5.057 ± 2.630 1.056 ± 0.233 ifficant difference; $*:P\leq0.05$ **: $P\leq0.01$		20 ppm	32	0.424± 1.170	4.065± 1.545	$0.960\pm\ 0.169$	
125 ppm 39 0.266 ± 0.280 5.057 ± 2.630 1.056 ± 0.233 ificant difference; $*:P\leq0.05$		50 ppm	32	0.264 ± 0.254	3.770 ± 0.992	1.015± 0.178	
ificant difference ; * : P \leq 0.05 ** : P \leq 0.01		125 ppm	39	0.266± 0.280	$5.057\pm\ 2.630$	$1.056\pm\ 0.233$	
	i	Significant di	ifference ;		*: P ≤ 0.01	Test of Dunnett	
(HCL042)	10	ICL042)	**************************************				BAIS 4

TABLE K2

ORGAN WEIGHT, RELATIVE : FEMALE

PAG	Hermited the Control					
	KIDNEYS	1.505± 0.281	$1.425\pm\ 0.245$	1.469± 0.157	1.500 ± 0.238	
	LUNGS	0.649± 0.127	0.589 ± 0.074	0.633 ± 0.115	0.743± 0.493	
(A)	HEART	0.610± 0.136	0.540 ± 0.090	$0.585\pm\ 0.074$	0.588± 0.112	Test of Dunnett
ORCAN WEIGHT:RELATIVE (SUMMARY) SURVIVAL ANIMALS (105W)	OVARIES	0.137± 0.096	0.273 ± 0.530	0.365± 0.918	0.136± 0.084	Tes
ORGAN SURVIN	ADRENALS	0.049± 0.012	$0.043\pm\ 0.007$	$0.049\pm\ 0.013$	0.045± 0.010	** : P ≤ 0.01
[Crj:BDF1]	Body Weight (g)	30.3± 5.3	33.5士 4.5	32.3± 4.2	31.6 ± 5.4	* : P ≤ 0.05
B6D2F1/Cr1j	NO. of Animals	18	31	24	26	ifference ;
STUDY NO. : 0561 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1] REPORT TYPE : A1 SEX : FEMALE UNIT: %	Group Name	Control	20 ppm		125 ppm	Significant difference : (HCL042)

BAIS 4

Croup Name NO. of Animals SPLEBN LIVBR BRAIN PAGE: 4 Croup Name Animals 1.700 ± 0.702 ± 0.7		STUDY NO. : 0561 ANIMAL : WOUSE B6D2F1/Crlj[Crj:BDF1] REPORT TYPE : A1 SEX : FEMALE INST: 94	E B6D2F1/Crlj[Cr.j:BDF1]	ORGAN WI SURVIVAI	ORGAN WEIGHT:RELATIVE (SUMMARY) SURVIVAL ANIMALS (105W)	
Control 18 0.479± 0.508 4.627± 0.660 1.692± 0.484 20 ppm 31 0.702± 0.732 5.269± 2.975 1.435± 0.176 50 ppm 24 0.800± 1.300 5.179± 1.379 1.500± 0.189 125 ppm 26 0.959± 1.004 5.942± 3.042 1.542± 0.285 Significant difference; *: $P \le 0.05$ #*: $P \le 0.01$		Group Name	NO. of Animals	SPLEEN	LIVER	BRAIN	PAGE: 4
20 ppm 31 0.702 \pm 0.732 5.269 \pm 2.975 1.435 \pm 0.176 50 ppm 24 0.800 \pm 1.300 5.179 \pm 1.379 1.500 \pm 0.189 1.25 ppm 26 0.959 \pm 1.004 5.942 \pm 3.042 1.542 \pm 0.285 Significant difference; *: P \leq 0.05 \Longrightarrow 5.001		Control		0.479 ± 0.508	4.627± 0.660	1.692士 0.484	
50 ppm 24 0.800 \pm 1.300 5.179 \pm 1.379 1.500 \pm 0.189 1.25 ppm 26 0.959 \pm 1.004 5.942 \pm 3.042 1.542 \pm 0.285 Significant difference; *: P \leq 0.05 **: P \leq 0.01		20 ppm		0.702± 0.732	5.269士 2.975	$1.435\pm\ 0.176$	
0.959± 1.004 5.942± 3.042 1.542± 0.285 $*: P ≤ 0.05 **: P ≤ 0.01$	76	50 ppm		$0.800\pm\ 1.300$	5.179 ± 1.379	$1.500\pm\ 0.189$	
*: P ≤ 0.05		125 ppm		$0.959\pm\ 1.004$	$5.942\pm\ 3.042$	1. $542\pm$ 0. 285	
		Significant c	difference ;		P ≤ 0.01	Test of Dunett	

TABLE L1

HISTOPATHOLOGICAL FINDINGS:

NON-NEOPLASTIC LESIONS : MALE

ALL ANIMALS

BAIS4

Test of Chi Square

** : $P \le 0.01$

Significant difference ; $*:P \le 0.05$

(HPT150)

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

STUDY NO. : 0561 ANIMAL : MOUSE B6D2F1/Cr1;[Crj:BDF1]

PAGE: 1 4 8 06 00 o 6 06 00 00 00) 00 125 ppm 0 1 0 0 0) (2) (0) (00 o 6 o 6 m 38 00 00 o 6 0 1 0) (2) (2 4 .) 00 - -- 6 20 2 8 00 00 06 0 0 00) 00 . 00) 00 - S 00 4 8 o 6 00 00 00 00 00 00 50 ppm 0 0) 00 0 (0) (0) (0) J $\overline{}$ 0 0 0 e 8€ 00 0 2 0 0) (4) (0) 00 7 1 0 (2) (2 (2)) 00 0 0 0 2 S 20 0 0) 00) 00 00 -18 3 4 00 00 00 00 00 00 00 o 6 20 ppm 1 0 2) (0) (-) (0) (0 $\overline{}$ $\overline{}$ $\overline{}$ 1 0 (2) (0 0 0 00 1 $\overline{}$ \smile $\overline{}$ N SE 20 00 00 2 4 00 2) - -- 6 0 0) 00 000 \smile o 6 00 - 8 00 4 8 06 00 00 00 00 00) 00 Control $\overline{}$ 2 3 (%) (%) 0 0 0 0 $\overline{}$ $\overline{}$ J 00 00 00 00 00 1 5 - -- 6 00 。 。 0 (0 20 $\overline{}$ 1 2 06 0 0) 00 2 () 1 2) (2 ()) 00 $\overline{}$ 4 : Severe o 6 No. of Animals on Study Group Name 3 : Marked 1: Slight 2: Moderate 3: Manber of animals examined at the site b: Number of animals with lesion c: b/a*100 squamous cell hyperplasia (Integumentary system/appandage) kanthogranuloma epidermal cyst inflammation Findings_ erosion ulcer scab cyst REPORT TYPE : A1 SEX : MALE skin/app subcutis Grade (a) b Organ_

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

STUDY NO. : ANIMAL : REPORT TYPE : SEX :	: 0561 : MOUSE B6D2F1/Cr1j[Crj:BDF1] : A1 : MALE	4	HISTOPATHOLOGICAL FINDINGS ALL ANIMALS (0-105W)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)		PAGE:	2
Organ	Findings	Group Name No. of Animals on Study Grade	Control 50 1 2 3 4 (%) (%) (%) (%)	20 ppm 50 1 2 3 4 (%) (%) (%)	50 ppm 50 4 (%) (%) (%) (%)	125 ppm 50 1 2 3 4 (%) (%) (%) (%)	
{Respiratory system}	system)						
nasal cavit	eosinophilic change:olfactory epithelium	elium	<50> 24 0 0 0 (48) (0) (0) (0)	<50> 32 0 0 0 (64) (0) (0) (0)	<50> 24 2 0 0 (48) (4) (0) (0)	<50> 19 2 0 0 (38) (4) (0) (0)	
	eosinophilic change:respiratory epithelium	thelium	18 0 0 0 (36) (36) (0) (0)	15 0 0 0 0 (30) (30) (30) (30) (30) (30) (17 0 0 0 (34) (34) (0) (0) (0)	20 0 0 0 (40) (40) (0) (0)	
	respiratory metaplasia:olfactory epithelium	ithelium	12 0 0 0 (24) (0) (0) (0)	13 0 0 0 (26) (26) (0) (0) (0)	9 0 0 0 (0) (18) (18) (19) (19)	10 0 0 0 (20) (20) (0) (0)	
	respiratory metaplasia:gland		21 1 0 0 (42) (2) (0) (0)	23 2 0 0 (46) (46) (4) (0) (0)	25 2 0 0 (50) (4) (0) (0)	22 0 0 0 (44) (44) (6) (6) (6)	
	atrophy:olfactory epithelium		2 0 0 0 (4) (4) (6) (6)	4 0 0 0 0 (8) (8) (0) (0)	1 0 0 0 (2) (2) (3) (4) (4)	2 0 0 0 (4) (5) (6) (6)	
lung	hemorrhage		(0)(0)(0)(0) 0 0 0 0 0 0 0 0	<50> 2 0 0 0 (4) (0) (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)	<50> 2 0 0 0 (4) (0) (0) (0)	
	едета		3 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	1 0 0 0 (2) (3) (3) (4)	2 1 0 0 (4) (2) (0) (0)		
	inflammatory infiltration		1 0 0 0 (2) (2) (3) (3)			1 0 0 0 (2) (2) (0) (0)	
Grade 1 : Slight <a> a : Number b b : Number (c) c : b / a * Significant difference;	1: Slight 2: Moderate 3: 1 a : Number of animals examined at the site b : Number of animals with lesion c: b / a * 100 ifference; $*: P \le 0.05$ **: $P \le 0.05$	3 : Marked 4 : 9 site 5 0.01 Test of Chi	: Severe hi Square				1

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

PAGE: 3 STUDY NO. : 0561

ANIMAL : MOUSE BEDZF1/Crlj[Crj:BDF1]

REPORT TYPE : A1

SEX : MALE

	oroup name No. of Animals on Grade	Study 50	20 ppm 50 2 3	50 ppm 50 2 3	125 ppm 50 2 3
Organ	Findings	(%) (%)	(%) (%) (%) (%)	(%) (%) (%)	(%) (%) (%)
(Respiratory system)	system)				
lung	lymphocytic infiltration	<50> 1 0 0 0 (2) (0) (0) (0)	(0) (0) (0) (0) 0 0 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)
	bronchiolar-alveolar cell hyperplasia	1 0 0 0 (2) (2) (3) (4) (4)	3 1 0 0 (6) (2) (0) (0)	0 2 0 0 (0) (4) (0) (0)	
	uremic pneumonitis				2 0 0 0 (4) (4) (5) (6) (6) (7)
natopoiet	(Hematopoietic system)				
bone marrow	thrombus	<pre></pre>	<pre></pre>	(0) (0) (0) (0) (0) (0)	(0) (0) (0) (0) (0) (0) (0) (0) (0) (0)
	atrophy:focal		0 1 0 0 (0) (0) (0)		
	granulation	1 0 0 0 (2) (2) (3) (4) (4)			
	granulopoiesis:increased		2 0 0 0 (4) (4) (6) (6) (6)		
Grade (a > b b (c c)	Grade 1: Slight 2: Moderate 3: Marked <a> a: Number of animals examined at the site b: Number of animals with lesion (c) c: b/a*100	4 : Severe			

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105%)

STUDY NO. : 0561

ANIMAL : MOUSE BEDZF1/Cr1j[Crj:BDF1]

REPORT TYPE : A1

SEX : MALE

PAGE: 4

	Group Name No. of Animals on Study	Control 50	20 ppm 50	50 ppm	125 ppm 50
Organ	Findings	(%) (%) (%) (%)	(%) (%) (%) (%)	(%) (%) (%) (%)	(%) (%) (%) (%)
(Hematopoietic system)	ic system)				
lymph node	lymphadenitis	(0)(0)(0)(0) 0 0 0 0 0 0 0 0	<50> 0 2 0 0 (0) (4) (0) (0)	(50) 1 0 0 0 (2) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0)
spleen	angiectasis	<50> 0 1 0 0 (0) (2) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 <005>	(0)(0)(0)(0) 0 0 0 0 0 0 0 0	(0) (0) (0) (0) 0 0 0 0 0 0 0 0
	increased extramedullary hematopoiesis	4 7 1 0 (8)(14)(2)(0)	7 8 1 0 (14) (16) (2) (0)	6 6 0 0 (12) (12) (0) (0)	6 8 1 0 (12) (16) (2) (0)
	follicular hyperplasia	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	3 0 1 0 (6)(0)(2)(0)	2 1 1 0 (4) (2) (2) (0)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
{Circulatory system}	system)				
heart	mineralization	(0) (0) (0) (0) 0 0 0 0 0 0 0 0	(0)(0)(0)(0)	(5) (0) (0) (0)	<pre></pre>
	myocardial fibrosis	1 0 0 0 (2) (2) (3) (4)		$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	
Grade	Grade 1: Slight 2: Moderate 3: Marked (a > a : Number of animals examined at the site b : Number of animals with lesion (c) c: b / a * 100 C of Control of	4 : Severe			

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

PAGE: 5 STUDY NO. : 0561
ANIMAL : MOUSE BGDZF1/Cr1j[Crj:BDF1]
REPORT TYPE : A1
SEX : MALE

Organ	Findings	No. of Animals on Study 50 Grade (%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)	50 1 2 3 4 (%) (%) (%) (%)	50 1 2 3 (%) (%) (%)	(%)
{Circulatory system}	system)					
heart	arteritis	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	(20) (0) (0) (0) (0) (0) (0)	$\langle 50 \rangle$ 0 1 0 0 (0) (2) (0) (0)	<pre></pre>	0 0 0
{Digestive system}	ystem}					
tongue	arteritis	<50> 0 0 0 0 (0) (0) (0)	<50> 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 0 0 0	• ô
stomach	hyperplasia:forestomach	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	(50) 1 0 0 0 (2) (0) (0) (0)	(0) (0) (0) (0) (0) (0) (0)	<50> 2 0 0 (4) (0) (0)	0 (0)
	erosion:glandular stomach	4 0 0 0 (8) (0) (0) (0)	4 0 0 0 (8) (8) (9) (9)		1 0 0 (2) (2) (3) (4)	0 0
	hyperplasia:glandular stomach	11 15 0 0 (22) (30) (0) (0)	16 10 0 0 (32) (20) (0) (0)	17 9 0 0 (34) (18) (0) (0)	15 11 0 (30) (22) (0)	0 0
small intes	inflammation	<50> 0 0 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)	<50> 0 0 0 (0) (0) (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	arked 4 : Severe				

BAIS4

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

STUDY NO. ANTMAL REPORT TYPE SEX	: 0561 : MOUSE B6D2F1/Cr1j[Crj:BDF1] : A1 : MALE		HISTOPATHOLOGICAL FINDINGS :1 ALL ANIMALS (0-105#)	STOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) L ANIMALS (0-105%)		PAGE: 6
Organ	Findings	Group Name No. of Animals on Study Grade	on Study 50 Control 1 2 3 4 (%) (%) (%) (%)	20 ppm 50 1 2 3 4 (%) (%) (%) (%)	50 ppm 50 4 (%) (%) (%) (%)	125 ppm 50 1 2 3 4 (%) (%) (%) (%)
{Digestive system}	system}					
liver	angiectasis		<50> 1 0 1 0 (2) (0) (2) (0)	(0) (0) (0) (0) 0 0 0 0 0 0 0 0 0	<50> 3 1 0 0 (6) (2) (0) (0)	<50> 1 1 0 0 (2) (2) (0) (0)
	hemorrhage			0 0 1 0 (0) (0) (0) (0)		1 0 0 0 (2) (3) (4) (5)
	necrosis:central		0 1 0 0 (0) (0) (0) (0)			0 1 0 0 (0) (0) (0)
	necrosis:focal		2 0 2 0 (4) (0) (4) (0)	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$		1 0 0 0 (2) (3) (4) (5)
	collapse				0 1 0 0 (0) (0) (0) (0)	
	degeneration:central		1 0 0 0 (2) (2) (3) (4)			
	granulation		11 0 0 0 (22) (22) (3) (3) (3)	13 0 0 0 (26) (26) (0) (0) (0)	15 0 0 0 0 (30) (30)	15 1 0 0 (30) (30) (2) (0) (0)
	scar			0 1 0 0 (0) (0) (0)		
Grade (a) b (c) Significant	Grade 1: Slight 2: Moderate 3: N < 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.	farked 01	4 : Severe Test of Chi Square			

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105%)

STUDY NO. : ANIMAL : REPORT TYPE : SEX :	: 0561 : MOUSE B6D2F1/Cr1j[Crj:BDF1] : A1 : MALE	HJ AT	ISTOPATHOLOGICAL FINDINC LL ANIMALS (0-105#)	ISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) L ANIMALS (0-105%)	MARY)	PAGE : 7
Organ	Findings	Group Name No. of Animals on Study Grade	Control tudy 50 4 (%) (%) (%) (%)	20 ppm 50 1 2 3 4 (%) (%) (%) (%)	50 ppm 50 ppm (%) (%) (%) (%) (%)	125 ppm 50 1 2 3 4 (%) (%) (%)
(Digestive system)	stem)					
liver	clear cell focus		<50> 2 1 1 0 (4) (2) (2) (0)	<50> 2 1 1 0 (4) (2) (2) (0)	<50> 1 0 0 0 (2) (0) (0) (0)	<50> 3 3 1 0 (6) (6) (2) (0)
	acidophilic cell focus		0 2 1 0 (0) (4) (2) (0)	1 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 2 0 0 (0) (10) (10) (10)	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
	basophilic cell focus		2 1 0 0 (4) (2) (0) (0)	1 1 0 0 (2) (3) (0) (0)	0 2 0 0 (0) (0) (0) (0)	1 2 0 0 (2) (4) (0) (0)
	bile duct hyperplasia				0 1 0 0 (0) (0) (0) (0)	
	biliary cyst				2 0 0 0 0 (4) (4) (6) (6) (6)	
gall bladd	hyperplasia:epithelium		<50> 1 0 0 0 (2) (0) (0) (0)	(50) (0) (0) (0) (0) (0) (0) (0)	<50> (0) (0) (0) (0) (0) (0)	(0·) (0) (0) (0) 0 0 0 0 <09>
(Urinary system)	en)					
kidney	cyst		<50> 1 0 0 0 (2) (0) (0) (0)	<pre></pre>	<50> 1 0 0 0 0 (2) (0) (0) (0)	(50) 1 0 0 0 (2) (0) (0) (0)
Grade 1: Slight <a> a: Number b b: Number (c) c: b/a* Significant difference;	1: Slight 2: Moderate 3: Na Number of animals examined at the site b: Number of animals with lesion $c:b/a*100$ ifference; $*:P \le 0.05$ **: $P \le 0.05$	3 : Marked 4 : S ne site P ≤ 0.01 Test of Chi	Severe ii Square			

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105%)

STUDY NO. : ANIMAL : REPORT TYPE : SEX :	: 0561 : MOUSE B6D2F1/Cr1j[Crj:BDF1] : A1 : MALE	HI VI	HISTOPATHOLOGICAL FINDINGS ALL ANIMALS (0-105W)	STOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)		PAGE :	∞
Organ	Findings	Group Name No. of Animals on Study Grade	tudy 50 Control (%) (%) (%) (%)	20 ppm 50 1 2 3 4 (%) (%) (%) (%)	50 ppm 1 2 3 4 (%) (%) (%) (%)	125 ppm 50 1 2 3 4 (%) (%) (%) (%)	
{Urinary system} Kidney	.em) hyaline droplet		450> 3 0 0 0 6 (0) (0) (0)	(0) (0) (0) 0 0 0 0 0 0 0 0	<50> 1 1 0 0 (2) (2) (0) (0)	\$50\$ 2 0 0 0 (4) (0) (0) (0)	
	deposit of amyloid		0 0 1 0) (0) (2) (
	inflammatory infiltration				1 0 0 0 (2) (2) (3) (4)	1 0 0 0 (2) (2) (3) (4) (4)	
	lymphocytic infiltration		1 0 0 0 (0) (0)		1 0 0 0 (2) (3) (4) (4)	(0)(0)(0)(0)(0)	
	scar		1 0 0 0 (2) (2) (3) (4)	2 0 0 0 (4) (4) (6) (6)	2 0 0 0 (4) (4) (0) (0)	3 0 0 0 0 (0) (0) (0)	
	inflammatory polyp		0 0 2 0 (0) (0) (4) (0)	0 1 0 0 (0) (0) (0) (0)		0 1 1 0 (0) (2) (2) (0)	
	hydronephrosis		(0)(2)(2)(0)	0 0 2 0 (0) (0) (4) (0)	2 0 1 0 (4)(0)(2)(0)	0 0 3 1	
	mineralization:cortex		1 0 0 0 (2) (2) (3) (4)	1 0 0 0 (2) (3) (4) (4)	1 0 0 0 (2) (2) (3) (4) (5)		
Grade < a > b	1: Slight 2: Moderate 3: Na 3: Number of animals examined at the site b: Number of animals with lesion	3 : Marked 4 : ne site	Severe				
(c) c:b/a* Significant difference;	c : b / a * 100 lifference ; * : P ≤ 0.05 ** : P	P ≤ 0.01 Test of Chi	i Square				1

BAIS4

(HPT150)

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105%)

STUDY NO. : 0561
ANIMAL : MOUSE B6DZF1/Cr1j[Crj:BDF1]
REPORT TYPE : A1
SEX : MALE

Organ	Group Name No. of Animals on Study Grade 1	Control s on Study 50 4 (%) (%) (%) (%)	20 ppm 50 1 2 3 4 (%) (%) (%) (%)	50 ppm 50 1 2 3 4 (%) (%) (%) (%)	125 ppm 50 12 2 3 4 (%) (%) (%) (%) (%) (%) (%)
(Urinary system)	ten)				
kidney	regeneration:proximal tubule	<50> 1 0 0 0 (2) (0) (0) (0)	(0)(0)(0)(0)	<00 (0) (0) (0) (0) (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)
	hemorrhage:papilla			(2) (0) (0) (0)	
urin bladd	dilatation	(0)(9)(0)(0) 0 0 3 0 0 0 3 0	<pre></pre>	<50> 2 0 4 0 (4) (0) (8) (0)	<50> (0) (10) (0) (0) (0)
	ulcer		0 1 0 0 (0) (0) (0) (0)		
	simple hyperplasia:transitional epithelium				1 0 0 0 (2) (2) (3) (4) (4)
	xanthogranuloma	(0)(0)(0)(0)(0)		0 1 0 0 (0) (0) (0) (0)	
(Endocrine system) pituitary hy	ystem) hyperplasia	(0) (0) (0) (0) 0 0 0 0 <05>	<50> 1 0 0 0 (2) (0) (0) (0)	<00	<50> 0 0 0 0 0 (0) (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	4 : Severe			

00

) 00

。 。

27 ((54) (

00

o 6

0 (0

0 (0

29 (

00

) 0 0

24 0 ((48) (0) ((

spindle-cell hyperplasia

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105%)

STUDY NO. : 0561
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]
REPORT TYPE : A1
SEX : MALE

PAGE: 10

	The second secon				
		Name Control Animals on Study 50	20 ppm 50	50 ppm 50	125 ppm 50
Organ	Findings	Grade 1 2 3 4 (%) (%) (%) (%)	(%) (%) (%) (%)	(%) (%) (%) (%)	(%) (%) (%) (%)
(Endocrine system)	stem)				
pi tui tary	Rathke pouch	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	<pre></pre>	<pre></pre>	<50> 7 0 0 0 (14) (0) (0) (0)
thyroid	cyst	<50> 4 0 0 0 (8) (0) (0) (0)	<50> 3 1 0 0 (6) (2) (0) (0)	<50> 4 0 0 (8) (0) (0) (0)	<pre></pre>
	C-cell hyperplasia	21 0 0 0 (42) (42) (0) (0)	22 0 0 0 (44) (44) (6) (6) (6)	23 0 0 0 (46) (46) (0) (0) (0)	22 0 0 0 (44) (44) (6) (6) (6)
parathyroid	cyst	<50> 0 0 0 0 (0) (0) (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)	<pre></pre>	(0) (0) (0) (0) 0 0 0 0 0 0 0 0
adrenal	deposit of amyloid	<50> 1 0 0 0 (2) (0) (0) (0)	<pre></pre>	<00 (0) (0) (0) (0) (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	hyperplasia:cortical cell		C	8 3 0 0 16) (6) (0) (0)	2 (4) (0 0 0	* 00	1 0 (2) (0)	0 0) # (i)	4 (8) (0)	(0) (0	0 0
Grade <a>b (c) Significa	Grade 1: Slight 2: Moderate 3: Marked $\langle a \rangle$ a : Number of animals examined at the site b b Number of animals with lesion c : b \rangle a * 100 c : b \rangle a * 100 Significant difference ; * : P \leq 0.05 ** : P \leq 0.01	1: Slight 2: Moderate 3: № b : Number of animals examined at the site b: Number of animals with lesion c: b a * 100 . Eference; * : P ≤ 0.05 ** : P ≤ 0.	1: Slight 2: Moderate 3: Marked a: Number of animals examined at the site b: Number of animals with lesion c: b 100 a * 100 tference; * : P ≤ 0.05 ***: P ≤ 0.01	4 : So Test of Chi	evere									

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

STUDY NO. SAVIMAL SEPORT TYPE SEX	: 0561 : MOUSE B6D2F1/Cr1j[Crj:BDF1] : A1 : MALE	HISTOPATHOLOGICAL FINDINGS :N ALL ANIMALS (0-105W)	STOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) L ANIMALS (0-105W)		PAGE: 11
Organ	Findings	Group Name Control No. of Animals on Study 50 Grade (%) (%) (%) (%) (%)	20 ppm 50 1 2 3 4 (%) (%) (%) (%)	50 ppm 50 (%) (%) (%) (%)	125 ppm 50 1 2 3 4 (%) (%) (%)
{Reproductive system}	e system)				
testis	atrophy	<50> 6 5 0 0 (12) (10) (0) (0)	(50) 5 2 0 0 (10) (4) (0) (0)	<50> (10) (4) (0) (0)	<50> 5 3 0 0 (10) (6) (0) (0)
	mineralization	23 0 0 0 (46) (46) (9) (9) (9)	18 0 0 0 (36) (36) (36) (36) (36) (36) (36) (36)	29 0 0 0 0 (58) (58) (6) (7) (7)	25 0 0 0 (50) (50) (0) (0)
epididymis	spermatogenic granuloma	(9) (0) (0) (0) 3 0 0 0 (9) (0) (0)	<50> 3 3 0 0 (6) (6) (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)	\(\sqrt{50}\) \(1 1 0 (2) \(2) \(2) \(0) \(0) (0) \q
prostate	inflammation	(0) (0) (0) (0) 0 0 0 0 0 0 00	<50> 0 1 1 0 (0) (2) (2) (0)	(0) (0) (0) (0) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 0 0 0 0
prep/cli gl	duct ectasia	<pre></pre>	<50> 1 1 0 0 (2) (2) (0) (0)	<50> 0 2 0 (0) (4) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 000
	inflammation				$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
(Nervous system)	tem)				
brain	mineralization	<50> 22 0 0 0 (44) (0) (0) (0)	<50> 21 0 0 0 (42) (0) (0) (0)	<50> 29 0 0 0 (58) (0) (0) (0)	<50> 20 0 0 (40) (0) (0) (0)
Grade < a > b (c) Significant	Grade 1: Slight 2: Moderate 3:) < 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.	$3:$ Marked $4:$ Severe le site $P \leq 0.01$ Test of Chi Square			

BAIS4

(HPT150)

STUDY NO. ANIMAL REPORT TYPE SEX	: 0561 : MOUSE BGD2F1/Cr1j[Crj:BDF1] : A1 : MALE	HISTOPATHOLOGI ALL ANIMALS (0	ICAL FINDINGS :NOI D-105W)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)		PA	PAGE: 12
Organ	Findings	Group Name No. of Animals on Study 5 Grade 1 2 (%) (%)	Control 50 3 4 (%) (%)	20 ppm 50 1 2 3 4 (%) (%) (%) (%)	50 ppm 50 1 2 3 4 (%) (%) (%)	125 ppm 50 (%) (%) (%)	(%)
(Special sen	(Special sense organs/appendage)						
eye	keratitis	(0)(0) 00 9	<50> (0) (0) (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)	<00> (0) (0) (0) (0) (0) (0) (0) (0) (0) (0)	0 6
	mineralization:cornea	0 0	(0) (0)	1 0 0 0 (2) (3) (4)		1 0 0 (2) (0) (0) (0 (0
Harder gl	lymphocytic infiltration	9> 0 0 (0)(0)	<50> 0 0 0 0 (0) (0) (0)	<pre></pre>	<50> (0) (0) (0) (0) (0)) (0) (0) (0) 0 0 0 0 <0\$>	0 0
	hyperplasia	1 0 (2) (0)	(0) (0)		2 0 0 0 (4) (4) (0) (0) (0)	1 0 0 (2) (3) (4) (5) (5) (5) (6)	0 (0
(Musculoskel	(Musculoskeletal system) nuscle mineralization		0	<50> 0	0 <0	<50>	0
		(0) (0)	(0) (0) (0	(0)(0)(0)(0)	(2) (0) (0) (0)	(4)(0)(0)((0
(Body cavilles) adipose	les) granulation	(0) (0) 0 0	<50> (0) (0) (0 (0)	(50) 0 1 0 0 (0) (2) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 0 0 0	<00	0 (0
Grade < a > b (c) Significant	Grade 1: Slight 2: Moderate 3:) (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.	3 : Marked 4 : Severe ne site P ≤ 0.01 Test of Chi Square					

TABLE L4

HISTOPATHOLOGICAL FINDINGS:

NON-NEOPLASTIC LESIONS : FEMALE

ALL ANIMALS

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

STUDY NO. : ANTIMAL : REPORT TYPE : . SEX	: 0561 : MOUSE B6D2F1/Crlj[Crj:BDF1] : A1 : FEMALE	HISTO	HISTOPATHOLOGICAL FIND: ALL ANIMALS (0-105W)	INGS : NON-	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)		PAGE : 13
Organ	Findings	Group Name No. of Animals on Study Grade	Control 50 1 2 3 K) (%) (%)	4 (%)	20 ppm 50 1 2 3 4 (%) (%) (%)	50 ppm 50 1 2 3 4 (%) (%) (%)	125 ppm 50 1 2 3 4 (%) (%) (%)
(Integumentary	[Integumentary system/appandage]						
skin/app	squamous cell hyperplasia		<00 (0) (0) (0) (0) (0) (0) (0) (0) (0) (0 (0	<50> (0) (0) (0) (0) (0)	(50) 1 0 0 0 (2) (0) (0) (0)	<pre></pre>
	scab	<u> </u>	1 0 0 2	0 (0			1 0 0 0 (2) (2) (0) (0) (0)
[Respiratory system]	(meass)						
nasal cavit	mineralization		<50> 1 0 0 2) (0) (0) (0 (0	<pre></pre>	(0)(0)(0)(0) 0 0 0 0 0 0 0	<pre></pre>
	eosinophilic change:olfactory epithelium		22 1 0 (44) (2) (0) (0 0	26 0 0 0 (52) (0) (0) (0)	27 2 0 0 (54) (4) (0) (0)	34 1 0 0 * (68) (2) (0) (0)
	eosinophilic change:respiratory epithelium		36 6 0 72) (12) (0) (0 (0	35 4 1 0 (70) (8) (2) (0)	39 8 0 0 (18) (78) (16) (0) (0)	34 12 0 0 (68) (24) (0) (0)
	inflammation:foreign body	C	0 0 0	0 (0		1 0 0 0 0 (2) (2) (3) (3)	1 0 0 0 (2) (2) (3) (4)
	respiratory metaplasia:olfactory epithelium		9 0 0 (18) (18) (18) (18)	0 0	7 0 0 0 (14) (14) (14) (15) (15)	1 0 0 0 * (2) (0) (0) (0)	6 0 0 0 (12) (12) (0) (0) (0)
Grade 1 : Slight <a> a : Number b b : Number (c) c : b / a * Significant difference;	2 : Moderate of animals examined at the of animals with lesion 100 *: P ≤ 0.05 **: P	3 : Marked 4 : 5 site ≦ 0.01 Test of Chi	Severe				

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

STUDY NO. : ANIMAL : REPORT TYPE : SEX :	: 0561 : MOUSE B6D2F1/Cr1j[Crj:BDF1] : A1 : FEMALE	HISTOI ALL AI	HISTOPATHOLOGICAL FINDIN ALL ANIMALS (0-105#)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)	NS (SUMMARY)		ā.	PAGE: 14
Organ	Findings	Group Name No. of Animals on Study Grade (9	Control y 50 1 2 3 4 (%) (%) (%) (%)	1 2 (%) (%)	20 ppm 3 4 (%) (%)	50 ppm 50 3 4 (%) (%) (%) (%)	125 ppm 50 (%) (%) (%) (%) (%)	m (%)
(Respiratory system)	system)							
nasal cavit	respiratory metaplasia:gland	28 (56)	(0) (0) (0) (9 0 0 0 8 <20>	(50) 39 1 0 (78) (2) (0)	* (0) (<50> 41 0 0 0 ** (82) (0) (0) (0)	33 0 0 (0) (6) (6) (6) (7) (6) (7) (7) (7)	0 (0
	hyperplasia:transitional epithelium			1 0 0	0 0		1 0 0 (2) (3) (4) (5) (5) (6) (6)	0 0
	atrophy:olfactory epithelium	`Ü	4 0 0 0 8) (0) (0) (0)	1 0 0	0 0	2 0 0 0 (4) (4) (6) (6)	2 0 0 (4) (7) (7) (7)	0 0
trachea	eosinophilic change	Ü	<50> 1 0 0 0 2) (0) (0) (0)	<50> (0) (0) (0) (0)	0) (<pre></pre>	<05> <50> (0) (0) (0) (0) (0) (0) (0) (0) (0) (0)	0 (0
lung	hemorrhage		<00> (0) (0) (0 (0) (0 (0) (0 (0) (0) (0)	(50) (0) (0) (0) (0)	0 (0) (<50> (0) (0) (0) (0) (0)	<50> 1 0 0 (2) (0) (0) (0 (0
	lymphocytic infiltration	Ü	$\begin{matrix} 1 & 0 & 0 & 0 \\ 2) & (0) & (0) & (0) \end{matrix}$	1 0 0 (2) (3) (4) (5)	(0) (2 0 0 0 (4) (4) (6) (6)		0 (0
	bronchiolar-alveolar cell hyperplasia	Č	2 0 0 0 4) (0) (0) (0)	1 2 0	(0)	0 3 0 0 (0) (0)	2 1 0 (4) (2) (0) (0 (6
Grade 1 : Slight <a>> a : Number b b : Number (c) c : b / a * Significant difference :	2 : Moderate of animals examined at the of animals with lesion 100 x: P ≤ 0.05 **: P	3 : Marked 4 : 5 site ≤ 0.01 Test of Chi	Severe Square					

00

0 1 0 0 (0) (2) (0) (0)

(0) (0) (0) (0

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

dilatation

Test of Chi Square

**: P ≤ 0.01

Grade 1: Slight 2: Moderate 3: Mk < 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 0.0

(HPT150)

4 : Severe

3 : Marked

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

STUDY NO. : 0561
ANIMAL : MOUSE BGD2F1/Cr1j[Crj:BDF1]
REPORT TYPE : A1
SEX : FEMALE

PAGE: 15

			THE RESPONSITION OF THE PARAMETER AND THE PARAME	a to a series of the series of	
	Group Name No. of Anii	Control als on Study 50	20 ppm 50	50 ppm	125 ppm 50
0rgan	Grade Findings.	(%) (%) (%) (%)	(%) (%) (%) (%)	(%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)
(Respiratory system)	ystem)				
lung	uremic pneumonitis	<50> 1 0 0 0 (2) (0) (0) (0)	<00> 0 0 0 0 0 0 0 0 0 0 0 0	(0)(0)(0)(0) 0 0 0 0 0 0 0 0 0 0 0 0	(0)(0)(0)(0) 0 0 0 0 0 0 0 0
(Hematopoietic system)	: system)				
bone marrow	granulation	<50> 1 0 0 0 (2) (0) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 <05>	<pre></pre>	<pre></pre>
lymph node	lymphadenitis	<50> 0 1 0 0 (0) (2) (0) (0)	<50> 2 0 0 0 (4) (0) (0) (0)	(50) 0 1 0 0 (0) (2) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 0 000
spleen	increased extramedullary hematopoiesis	<50> 3 10 1 0 (6) (20) (2) (0)	<50> 5 11 0 0 (10) (22) (0) (0)	<50> 6 10 0 0 (12) (20) (0) (0)	<pre></pre>
	follicular hyperplasia	3 0 0 0 0 (0) (0)	0 2 0 0 (0) (1) (1) (1) (1)	0 2 0 0 (0) (4) (0) (0)	4 2 0 0 (8)(4)(0)(0)
{Circulatory system}	system)				
heart	:	\$ \$20\$ \$	(20)	<20>	<50>

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105%)

STUDY NO. : ANIMAL : REPORT TYPE : SEX :	: 0561 : MOUSE B6D2F1/Cr1j[Crj:BDF1] : A1 : FBMALE	HISTOPATHOLOGICAL FINDINGS :NA ALL ANIMALS (0-105W)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)		PAGE : 16
Organ	Findings	Group Name No. of Animals on Study Grade 1 2 3 4 (%) (%) (%) (%)	20 ppm 50 1 2 3 4 (%) (%) (%) (%)	50 ppm 50 1 2 3 4 (%) (%) (%) (%)	125 ppm 50 1 2 3 4 (%) (%) (%) (%)
{Circulatory system}	system)				
heart	thrombus	<50> 1 0 0 0 (2) (0) (0) (0)	<00 (0) (0) (0) (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)	<50> (0) (0) (0) (0)
	mineralization		(0)(0)(0)(0)(0)		1 0 0 0 0 (2) (2) (3) (4) (4)
	lymphocytic infiltration	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$			(0)(0)(0)(0)(0)
	arteritis		1 0 0 0 (2) (3) (4)		0 1 0 0 (0) (0) (0) (0)
(Digestive system)	stem)	Control	(G)	33	Č
9 3 3 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	arteritis		2 0 0 0 (4) (0) (0) (0)		
stomach	hyperplasia:forestomach	(0)(0)(0)(0) 0 0 0 0 0 0 0 0	<00	<50> 0 1 0 0 (0) (2) (0) (0)	<50> 0 1 0 0 (0) (2) (0) (0)
Grade 1 : Slight <a> a : Number b b : Number (c) c c b / a . Significant difference ;	1 : Slight 2 : Moderate 3 : } a : Number of animals examined at the site b : Number of animals with lesion c : b / a * 100 ifference ; * : P \leq 0.05 ** : P \leq 0.	3 : Marked 4 : Severe e site P ≤ 0.01 Test of Chi Square			

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS $(0{\text{--}}105\%)$

STUDY NO. : ANIMAL : REPORT TYPE : SEX :	: 0561 : MOUSE B6D2F1/Cr1j[Crj:BDF1] : A1 : FBMALE	HISTOPA ALL ANI	HISTOPATHOLOGICAL FINDINGS :NC ALL ANIMALS (0-105W)	STOPATHOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)		PAGE: 17
Огдал	Findings_	Group Name No. of Animals on Study Grade	Control 50 3 4 (%) (%) (%)	20 ppm 50 1 2 3 4 (%) (%) (%)	50 ppm 50 (%) (%) (%) (%) (%)	125 ppm 50 1 2 3 4 (%) (%) (%)
{Digestive system}	stem)					
stomach	erosion:glandular stomach	2 (4)	<50> 0 0 0 (0) (0) (0)	(50) 1 0 0 0 (2) (0) (0) (0)	<pre></pre>	<50> 1 0 0 0 (2) (0) (0) (0)
	hyperplasia.glandular stomach	4 (8)	1 0 0 (2) (3) (4) (4)	8 1 0 0 (16) (16) (2) (0) (0)	6 1 0 0 (12) (2) (0) (0)	3 2 0 0 (6) (7) (7)
liver	anglectasis	(O)	<50> 2 0 0 (4) (0) (0)	<pre></pre>	<pre></pre>	<pre></pre>
	necrosis:central	(0)	(0)(0)(0)	1 0 0 0 (2) (2) (3) (4) (4)	0 1 0 0 (0) (0) (0) (0)	(0)(0)(0)(0)(0)
	necrosis:focal	(0)	(0)(0)(0)		1 0 0 0 (2) (2) (0) (0) (0)	1 0 0 0 (2) (2) (3) (4) (4)
	degeneration:central	(O)	(0)(0)(0)		0 1 0 0 (0) (0) (0) (0)	
	lymphocytic infiltration	(O)	(0)(0)(0)(0)	1 0 0 0 (2) (2) (3) (4) (4)	(0)(0)(0)(0)(0)	
	granulation	14 (28)	(0)(0)(0)(0)	20 1 0 0 (40) (2) (0) (0)	17 0 0 0 (34) (34) (0) (0) (0)	18 0 0 0 0 (36) (36) (36) (36)
Grade 1 : Slight <a> a : Number b b : Number (c) c : b / a * Significant difference ;	1: Slight 2: Moderate 3: Na a: Number of animals examined at the site b: Number of animals with lesion $c:b/a*100$ iifference; $*:P\le 0.05$ **: $P\le 0.05$	3: Marked 4: Severe le site P ≤ 0.01 Test of Chi Square	are			

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105%)

STUDY NO. : 0561

ANIMAL : MOUSE BEDZF1/Cr1j[Crj:BDF1]

REPORT TYPE : A1

SEX : FEMALE

Organ Findings	Group Name No. of Animals on Study Grade (9	Control 50 1 2 3 4 (%) (%) (%) (%)	20 ppm 50 1 2 3 4 (%) (%) (%)	50 ppm 50 1 2 3 4 (%) (%) (%)	125 ppm 50 1 2 3 4 (%) (%) (%)
(Digestive system)					
liver inflammatory cell nest		<50> 1 0 0 0 (2) (0) (0) (0)	<50> (0) (0) (0) (0) (0)	<00 (0) (0) (0) (0) (0)	<0) (0) (0) (0) (0) (0) (0) (0) (0) (0) (
scar				(0)(0)(0)(0)(0)	1 0 0 0 (2) (3) (3) (4)
extramedullary hematopoiesis	esis				2 0 0 0 (4) (4) (6) (6)
clear cell focus		$\begin{pmatrix} 1 & 1 & 0 & 0 \\ (2) & (2) & (0) & (0) \end{pmatrix}$	(2) (2) (0) (0)	2 4 0 0 (4)(8)(0)(0)	(2) (2) (2) (0)
acidophilic cell focus		3 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	(2) (2) (0) (0)	(0)(0)(0)(0)	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
bile duct hyperplasia		2 0 0 0 (4) (4) (6) (6)			
biliary cyst		$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	(0)(0)(0)(0)(0)		
xanthogranuloma			(0)(2)(0)		
Grade 1: Slight 2: Moderate 3: }	3 : Marked the site	4 : Severe			

BAIS4

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105%)

STUDY NO. : 0561 ANIMAL : MOUSE BGDZF REPORT TYPE : A1 SEX : FEMALE	: 0561 : MOUSE B6D2F1/Cr1j[Crj:BDF1] : A1 : FEMALE	HIST ALL	OPATHOLOGICAL FI ANIMALS (0-105W)	GICAL 1 (0-105)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)	: NON-NEO	PLASTI	c LESI	ONS (SUR	MARY)								PAGE :	: 19
OrganFindings_		Group Name No. of Animals on Study Grade	y 1 2 (%) (%)	Control 50 3	tro1 4 (%)		1 (%)	50 2 (%) (9)	20 ppm 3 4 (%) (%)		1 (%)	2 2 (%)	50 ppm 50 3 (%) (# 4 (%)	1 88	2 8	125 ppm 50 3 (%) (ppm 4 (%)	
(Urinary system) kidney cyst			0) (0	<50> 0 0 0) (0)	0)	C	0 0	(20) ((20) ((20)	(0) (0 0 0		0 0	(5) (0)	<50> (50> (0) (0)	0 0	1 (2)	[™] 0 60 ∪	(50) (0) (0)	0 0	
hyaline droplet	iroplet	Ü	14 0 28) (0)	0 0 0	0 0	1 (2	111 (222) (000	(O) (O O O		12 (24)	0 0	0 0	0 (0	11 (22)	0 0	0 (0)	0 0	
deposit o	deposit of amyloid	Ü	(0) (0 0 0	0 0 (0	0 ()	J	0 (0	0 (0	(O) (O O 0		0 (0)	0 0	0 0)	0 (0)	0)	0 0	1 (2)	0 (0)	
hyaline cast	ast	Ü	3 1 6) (2)	0 0 (0	0)	J	8) ((0 (0	(0) (0		, 2 4)	0 0)	0 (0)	0 (0)	3 (9)	0 0	0 6	0 (0)	
lymphocyt	lymphocytic infiltration	Ü	5 0	0 0 0	0 0	. (1	8 ;	3 (9	0 0		2 (4)	0 0	0 0	0 (0)	7 (14)	1 (2)	0 0	0 0	
scar		C	2 0 4) (0)	0 0	0)	. ~	1 (2) ((00	0 0		1 (2)	0 6	0 0	0 0)	0 0	0 0	0 0	0 0	
inflammat	inflammatory polyp	C	0 1 0) (2)	0 0 0	0 0	J	00	0 0	0 0		1 (2)	o 6	0 0	0 0	1 (2)	(2)	0 0	0 0	
hydronephrosis	irosis	Ü	(0) (0 0 0	3 (6)	0 (0)	J	0 6	0 6	(0) (0		0 ô	o ô	1 (2)	0 (0)	0)	1 (2)	(2)	0 0	
Grade 1 : Slight <a>> a : Number of an b : Number of an c : b / a * 100 Significant difference ; *	Slight 2: Moderate 3: B. Number of animals examined at the site: Number of animals with lesion b / a * 100 erence; * : P ≤ 0.05 **: P ≤ 0.	farked 4:	Severe																

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

PAGE: 20

STUDY NO. : 0561
ANIMAL : MOUSE BEDZF1/Crlj[Crj:BDF1]
REPORT TYPE : A1
SEX : FEMALE

Organ	Findings	Group Name Control No. of Animals on Study 50 Grade 1 2 3 (%) (%) (%) (%) (20 ppm 50	50 ppm 50 (%) (%) (%) (%)	125 ppm 50 (%) (%) (%) (%)
{Urinary system}	em)				
ki dney	papillary necrosis	<pre> (0) (0) (0) 0</pre>	(0) (0) (0) (0) (0 0 0 0 0 0 0 0 0 0	<pre></pre>	(50) 1 0 0 0 (2) (0) (0) (0)
urin bladd	dilatation	(20) (0) (0) (0) (0) (0) (0)	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	<00 (0) (0) (0) (0) (0)	<50> 0 0 1 0 (0) (0) (2) (0)
(Endocrine system)	stem)				
pituitary	angiectasis	<020> 6 0 0 (12) (0) (17)	(49) 0 1 1 0 0 0) (2) (2) (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)
	hyperplasia	2) (4) (0 7 2 1 0 0 0 (14) (4) (2) (0)	4 2 1 0 (8)(4)(2)(0)	8 4 0 0 (16) (8) (0) (0)
	Rathke pouch	1 0 0 (2) (0) (0) (0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	1 0 0 0 (2) (2) (3) (4)	3 0 0 0 (0) (0) (0)
thyroid	cyst	3 0 0 (0) (0) (9) (0) (0) (0) (0) (0) (0) (0) (0) (0) (0	<pre></pre>	<50> 2 0 0 0 (4) (0) (0) (0)	<50> 4 2 0 0 (8) (4) (0) (0)
Grade 1 : Slight <a> a : Number b b : Number (c) c : b / a * Significant difference :	2: Moderate of animals examined at the of animals with lesion :100 *:P ≤ 0.05 **:P	3: Marked 4: Severe site ≤ 0.01 Test of Chi Square			

BAIS4

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS $(0{\text{--}}105\%)$

STUDY NO. : ANIMAL : REPORT TYPE : SEX :	: 0561 : MOUSE BGDZF1/Crlj[Crj:BDF1] : Al : FEMALE		HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)	INGS :NON-NEOPLASTIC L	JESIONS (SUMMARY)		PAGE : 21
Organ	Findings	Group Name No. of Animals on Study Grade	Control 50 (%) (%)	(%) (%) (%)	20 ppm 50 3 4 (%) (%)	50 ppm 50 1 2 3 4 (%) (%) (%) (%)	125 ppm 50 1 2 3 4 (%) (%) (%)
(Endocrine system)	rstem)						
thyroid	C-cell hyperplasia		<50> 23 0 0 (46) (0) (0) (0 30 0 0 (60) (0)	<50> 0 0 0 0 0 0 0 0	<50> 26 0 0 (52) (0) (0) (0)	<50> 26 0 0 0 (52) (0) (0) (0)
adrenal	thrombus		<50> 0 1 0 (0) (2) (0) ((50) (0) (0) (0)	(0)(0)(0)(0) 0 0 0 0 0 0 0 0	(0) (0) (0) (0) 0 0 0 0 0 0 0 0
	extramedullary hematopoiesis		0 0 0	0 0 0	(0) (0)		1 0 0 0 (2) (2) (3) (4) (4)
	spindle-cell hyperplasia		17 25 0 (34) (50) (0) (0 22 26 0) (44) (52)	(0) (0)	19 26 1 0 (38) (52) (2) (0)	24 19 0 0 (48) (38) (0) (0)
	focal fatty change:cortex		1 0 0 (2) (3) (4) (5) (5)	0 0 0	(0) (0)	(2) (0) (0) (0)	5 0 0 0 0 (10) (10) (10) (10)
	focal hyperplasia		0 0 0	(0)(0)(0	(0) (0)		1 0 0 0 (2) (2) (3) (4)
(Reproductive system)	e system)						
ovary	thrombus) (0) (0) (0) 0 0 0 (20)	(50) (0) (0) (0 (0 (0 (0 (0 (0 (0 (0 (0 (0 (0 (0 (0	<50> (0) (0) (0) (0)	(50) 0 1 0 (0) (2) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 0 0 0
Grade 1 : Slight <a> a : Number b b : Number (c) c : b / a * Significant difference ;	2 : Moderate of animals examined of animals with lesi r 100 r : P ≤ 0.05	3: Marked at the site on *** : P ≤ 0.01 Test of	4 : Severe Test of Chi Square				

(HPT150)

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

PAGE: 22

STUDY NO. : 0561
ANIMAL : MOUSE B6D2F1/Cr1;[Crj:BDF1]
REPORT TYPE : A1
SEX : FEMALE

Organ	Group No. of Grade	Group Name Control No. of Animals on Study 50 Grade (%) (%) (%) (%)	20 ppm 50 1 2 3 4 (%) (%) (%) (%)	50 ppm 50 (%) (%) (%) (%)	125 ppm 50 1 2 3 4 (%) (%) (%)
(Reproduct)	(Reproductive system)				
ovary	cyst	<50> 6 0 0 (12) (0) (0) (0)	<50> 7 0 0 0 (14) (0) (0) (0)	(50) 4 1 0 0 (8) (2) (0) (0)	<50> 7 0 0 0 (14) (0) (0) (0)
uterus	cystic endometrial hyperplasia	<50> 16 5 0 0 (32) (10) (0) (0)	<pre></pre>	<50> 14 9 0 0 (28) (18) (0) (0)	<50> 14 6 0 0 (28) (12) (0) (0)
{Nervous system}	/stem)				
brain	hemorrhage	<50> 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 <05>	<50> (0) (0) (0) (0) (0) (0)
	vacuolic change			$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	
	mineralization	12 0 0 0 (24) (24) (0) (0) (0)	13 0 0 0 (26) (26) (30) (30)	14 0 0 0 (28) (0) (0) (0)	9 0 0 0 (18) (18) (18) (19)
(Special se	(Special sense organs/appendage)				
eye	keratitis	<50> 1 0 0 0 (2) (0) (0) (0)	(0)(0)(0)(0)	(0) (0) (0) (0) 0 0 0 0 0 (0) (0) (0)	<50> 1 0 0 (2) (0) (0) (0)
Grade 1: Slight	1 : Slight 2 : Moderate 3 : Marked a : Number of animals examined at the site b : Number of animals with lesion c : b / a * 100	rked 4 : Severe			

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

STUDY NO. ANIMAL REPORT TYPE SEX	: 0561 : MOUSE B6D2F1/Cr1j[Crj:BDF1] : A1 : FEMALE	HISTOPATHOLOGICAL FINDINGS :N ALL ANIMALS (0-105W)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)	- (PAGE : 23
Organ	Findings	Group Name Control No. of Animals on Study 50 Grade 1 2 3 4 (%) (%) (%) (%)	20 ppm 50 1 2 3 4 (%) (%) (%) (%)	50 ppm 50 4 (%) (%) (%) (%)	125 ppm 50 1 2 3 4 (%) (%) (%)
(Special sene	(Special sense organs/appendage) eye phthisis bulbi	<00 (0) (0) (0) (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)	(0)(0)(0)(0) 0 0 0 0 <20>	(0) (0) (0) (0) 0 0 0 0 0 0 0 0 0
	mineralization:cornea	8 0 0 0 0 (16) (16) (16) (16) (17)	2 0 0 0 (4) (4) (6) (6) (6)	1 0 0 0 *	3 0 0 0 0 0 (9)
Harder gl	inflammation	<50> 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 0 0 0	<50> (0) (0) (0) (0)
	lymphocytic infiltration		1 0 0 0 (2) (2) (3) (4) (4)		2 0 0 0 (4) (4) (6) (6) (6)
	hyperplasia	1 0 0 0 (2) (2) (0) (0) (0)	2 0 0 0 (4) (4) (6) (6) (6)	0 1 0 0 (0) (0) (0) (0)	2 0 0 0 (4) (4) (6) (6)
(Musculoskeletal system) muscle minerali	etal system} mineralization	<50> 1 0 0 0 (2) (0) (0) (0)	(0)(0)(0)(0) 0 0 0 0 0 0 0 0	<50> 1 0 0 0 (2) (0) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 0 0 0
Grade <a>b b (c) Significant of	Grade 1: Slight 2: Moderate <a> a: Number of animals examined at the b: Number of animals with lesion c: b / a * 100 Significant difference; *: P ≤ 0.05 **: P	3 : Marked 4 : Severe e site P ≤ 0.01 Test of Chi Square			

BAIS4

TABLE 01

NEOPLASTIC LESIONS-INCIDENCE

AND STATISTICAL ANALYSIS: MALE

P = 0.0004**

P = 0.0099**

P = 0.2977

(HPT360A)

BAIS4

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE:

MOUSE B6D2F1/Cr1j[Crj:BDF1] : 0561 STUDY No. ANIMAL SEX

mdd 8/50(16.0) 18.18 7/39(17.9) 125) P = 0.3871ppi 17.14 5/32(15.6) 6/50(12.0) 20 P = 0.620220 ppm 10.53 4/50(8.0) 1/32(3.1) P = 0.3703SITE : lung TUMOR : bronchiolar—alveolar adenoma Control 6/50(12. 0) 15. 38 6/39(15. 4) P = 0.1641 P = -----P = 0.3359Cochran-Armitage test(e) Prevalence method(d) Combined analysis(d) Fisher Exact test(e) Group Name Statistical analysis Peto test Standard method(d) Adjusted rates(b) Terminal rates(c) Overall rates(a) Tumor rate

28. 13 9/32 (28. 1) 13/50(26.0) P = 0.0019**7/50 (14. 0) 12. 50 4/32 (12. 5) P = 0.0798SITE : lung TUMOR : bronchiolar—alveolar carcinoma 2/50(4.0) 5.13 2/39(5.1) P = 0.0001** P = 0.0005**P = 0.0004**P = 0.5009Cochran-Armitage test(e) Prevalence method(d) Combined analysis(d) Fisher Exact test(e) Statistical analysis Standard method(d) Adjusted rates(b) Terminal rates(c) Overall rates(a) Numor rate Peto test

16/50(32.0) 38.46 15/39(38.5)

SITE : lung TUMOR : bronchiolar-alveolar adenoma,bronchiolar-alveolar carcinoma

Numor rate

10/50(20.0) 18.92 4/32(12.5) 7/50(14. 0) 17. 95 7/39(17. 9) P = 0.0001** P = 0.0002** P = 0.0002** P = 0.5009Cochran-Armitage test(e) Fisher Exact test(e) Prevalence method(d) Combined analysis(d) Statistical analysis Standard method(d) Adjusted rates(b) Terminal rates(c) Overall rates(a) Peto test

53.85 21/39(53.8) 23/50 (46.0)

18/50 (36. 0) 41. 67 13/32 (40. 6)

P = 0.0002**

103

Group Name	Control	20 ppm	50 ppm	125 ppm	
	SITE : lymph node TUMOR : malignant lymphoma				
Tumor rate Overall rates(a)	14/50(28.0)	5/50(10.0)	4/50(8.0)	7/50(14-0)	
Adjusted rates(b)	17.95	12. 50		12.82	
Terminal rates(c) Statistical analysis	7/39(17.9)	4/32 (12.5)	2/32(6.3)	5/39(12.8)	
Peto test Standard method(d)	P = 0 9044				
Prevalence method(d)	P = 0.6819				
Combined analysis(d)	P = 0.8883				
Cochran Annitage lest(e) Fisher Exact test(e)	r = 0.2305	P = 0.0198*	P = 0.0087**	P = 0,0698	
	SITE : spleen				
Tumor rate					
Overall rates(a)	1/50(2.0)	2/50(4.0)	4/50(8.0)	0/20(0 0)	
Adjusted rates(b)	2.56		11.76	(0:0) (0:0) (0:0) (0:0)	
Terminal rates(c)	1/39(2.6)	1/32(3.1)	3/32(9.4)	0/39(0.0)	
Peto test					
Standard method(d)	11				
Prevalence method(d)	P = 0.7910				
Cochran-Armitage +art(a)	7 ==				
Fisher Exact test(e)	1 - 0.1160	P = 0.5000	P = 0.1811	P = 0.5000	
					Manada Ada Andreas and the state of the stat
	SITE : spleen TUMOR : hemangioma,hemangiosarcoma	Ba			
Tumor rate					
Overall rates(a)	2/50(4.0)	2/50(4.0)	4/50(8.0)	0/50(0.0)	
Aujusteu Tates(b) Terminal rates(c)	5,13 2/39(5 1)	5.41	11.76	0.0	
			3/32(9.4)	0/39(0.0)	
Peto test Standard mothod(d)	- a				
Dreyalence method(d)	P = 0 8767				
Combined analysis(d)	p = d.				
Cochran-Armitage test(e)	P = 0.2543				
Fisher Exact test(e)		D = 0 6013	0000 0 - 0	1000	

SEX MALE BODZII/CrijlCrj:BDFil	rij(crj.burij			
Group Name	Control	20 ppm	eo ppm	125 ppm
	SITE : liver TUMOR : hepatocellular adenoma			
lumor rate Overall rates(a) Adjusted rates(b) Terminal rates(c) Statistical analysis	12/50(24. 0) 28. 21 11/39(28. 2)	13/50(26.0) 34.29 10/32(31.3)	11/50 (22. 0) 27. 78 8/32 (25. 0)	20/50 (40. 0) 51. 28 20/39 (51. 3)
Peto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e)	P = P = 0.0308* P = P = 0.0544	P = 0.5000	P = 0.5000	P = 0, 0664
÷	SITE : liver TUMOR : hemangiosarcoma			
immor race Overall rates(a) Adjusted rates(b)	2/50(4.0) 5.13	5/50 (10. 0) 7. 14	5/50(10.0)	1/50(2.0)
Terminal rates(c) Statistical analysis	2/39(5.1)	1/32(3.1)	2/32(6.3)	1/39(2.6)
Peto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e)	P = 0. 6694 P = 0. 7593 P = 0. 8095 P = 0. 3376	P = 0.2180	P = 0.2180	P = 0.5000
,	SITE : liver TUMOR : hepatocellular carcinoma			
lumor rate Overall rates(a)	7/50(14.0)	10/50(20.0)	3/50(6.0)	9/50 (18.0)
Adjusted rates(b) Terminal rates(c) Statistical analysis	16. 67 5/39(12. 8)	21.88 7/32(21.9)	6.25 2/32(6.3)	21. 43 8/39(20. 5)
Peto test Standard method(d) Prevalence method(d) Combined analysis(d)	P = 0.7106 P = 0.3286 P = 0.4204			
Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.7956	P = 0.2977	P = 0.1589	P = 0.3929
(HPT360A)				

BAIS4

က

PAGE:

P = 0.0779

P = 0.3329

P = 0.4176

(HPT360A)

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

: MOUSE B6D2F1/Cr1j[Crj:BDF1] : MALE

: 0561

STUDY No.

ANIMAL SEX

4

PAGE:

ppou 3/50(6.0) 7.69 3/39(7.7) 25/50(50.0) 61.54 24/39(61.5) 61.54 24/39 (61.5) 25/50(50.0) 125 P = 0.0779P = 0.6611mdd 33. 33 10/32 (31. 3) 33. 33 10/32(31.3) 9.38 6/50(12.0) 3/32(9.4) 14/50(28.0) 14/50 (28.0) 20 P = 0.2435P = 0.3329SITE : liver TUMOR : hepatocellular adenoma, hepatocellular carcinoma, hepatoblastoma 20 ppm SITE : liver TUMOR : hepatocellular adenoma,hepatocellular carcinoma 19/50 (38. 0) 42. 86 13/32 (40. 6) 19/50 (38.0) 42.86 13/32 (40.6) 7/50(14.0) 2/32(6.3) P = 0.4176P = 0.1589SITE : liver TUMOR : hemangioma, hemangiosarcoma Control 7.14 5.1) 38. 10 14/39(35.9) 17/50 (34.0) 38.10 14/39 (35.9) 3/50(6.0) 17/50(34.0) P = 0. 0342* P = 0. 0552 P = 0. 0914 P = 0.0286* P = 0.0587 P = 0.0914 P = 0.5924 P = 0.6800 P = 0.5721P = 0.7106P = 0.6694P = 0.79062/39(Cochran-Armitage test(e) Cochran-Armitage test(e) Cochran-Armitage test(e) Fisher Exact test(e) Prevalence method(d) Prevalence method(d) Combined analysis(d) Prevalence method(d) Combined analysis(d) Fisher Exact test(e) Fisher Exact test(e) Combined analysis(d) Group Name Statistical analysis Standard method(d) Statistical analysis Standard method(d) Statistical analysis Standard method(d) Adjusted rates(b) Terminal rates(c) Adjusted rates(b) Terminal rates(c) Overall rates(a) Adjusted rates(b) Terminal rates(c) Overall rates(a) Overall rates(a) Tumor rate Peto test umor rate Peto test Numor rate Peto test

STATISTICAL
₽
LESIONS-INCIDENCE
NEOPLASTIC

: 0561 : MOUSE BGDZF1/Cr1j[Crj:BDF1] : MALE

STUDY No. ANIMAL SEX

ANALYSIS

ß

PAGE:

Group Name	Control	20 ppm	edd 09	125 ppm
	SITE : gall bladder			
Tumor rate	tomon : papitialy adelloma			
Overall rates(a)	3/50(6.0)	1/50(2.0)	0/50(0.0)	1/50(2.0)
Adjusted rates(b) Terminal rates(c)	7. 69	3.13	0.0	2.56
Statistical analysis	0/39(1:1)	1/32(-3.1)	0/32(0.0)	1/39(2.6)
Peto test				
Standard method(d)	P =			
Prevalence method(d)	P = 0.8259			
Combined analysis(d)	P =			
Cochran-Armitage test(e)	P = 0.3462			
Fisher Exact test(e)		P = 0.3087	P = 0.1212	P = 0.3087
	The state of the s			
	SITE : Harderian gland			
·	TUMOR : adenoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	1/50(2.0)	4/50(8.0)	0/20(0'0)
Adjusted rates(b)	10. 26	3.13		
Terminal rates(c)	4/39(10.3)	1/32(3.1)	2/32(6.3)	0/39(0.0)
Statistical analysis Peto test				
Standard method(d)	P =			
Prevalence method(d)	P = 0.9446			
Combined analysis(d)	P =			
Cochran-Armitage test(e)	P = 0.1161			
Fisher Exact test(e)		P = 0.1811	P = 0.6425	P = 0.0587
(HPT360A)				DATE

BAIS4

N.C.:Statistical value cannot be calculated and was not significant. **: P ≤ 0.01

⁽a): Number of tumor-bearing animals/number of animals examined at the site.
(b): Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.
(c): Observed tumor incidence at terminal kill.
(d): Beneath the control incidence are the P-values associated with the trend test.

Standard method : Death analysis

Prevalence method: Incidental tumor test
Combined analysis: Death analysis + Incidental tumor test
(e): The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.
?: The conditional probabilities of the largest and smallest possible out comes can not estimated or this P-value is beyond the estimated P-value.

⁻⁻⁻⁻⁻ There is no data which should be statistical analysis. Significant difference ; * : P \le 0.05 ** : P \le 0.01

	BAI
P = 0, 0448*	
P = 0.0047**	

SITE : ALL TUMOR : hem TUMOR : hem TUMOR : hem Overall rates(a) 3/50(6. 4 Adjusted rates(b) 4. 4 Adjusted rates(c) 1/39(2. 5 Adjusted rates(c) 1/39(2. 5 Adjusted rates(c) 1/39(2. 5 Peto test Standard method(d) P = 1.0000 Prevalence method(d) P = 0.4691 Combined analysis(d) P = 0.5681 Cochran-Armitage test(e) P = 0.7847 Fisher Exact test(e)	TE : ALL SITE MACR : hemangioma 3/50(6.0) 4.76 1/39(2.6) P = 1.0000 ? P = 0.4691 P = 0.5681	5/50(10.0) 12.50 3/32(9.4)	(4.17.707.6	MODIFICATION OF THE PROPERTY O	
11) 11) 12) 13)	/50(6,0) 4.76 /39(2,6) 1.0000? 0.4691 0.5681	5/50 (10. 0) 12. 50 3/32 (9. 4)	70 77 70 76		
(a) (b) (c) (c)	4.76 /39(2.6) 1.0000 ? 0.4691 0.5681	12.50 3/32(9.4) 0 - 0.9575	(/ 20 (14. 0)	3/50(6.0)	
4) 1) st(e) e)	1. 0000 ? 0. 4691 0. 5681	0 - 0 - 0 - 0	16. 67 4/32 (12.5)	7.14	
U				(1.0.10./2	
0					
2413	0. 7847		P = 0. 1589	P = 0.6611	
	: ALL SITE : histiocytic sarcoma				
lumor rate Overall rates(a) 1/	1/50(2.0)	2/50(4.0)	5/50(10.0)	5/50(10.0)	
İs	0/39(0.0)	0.0	3.13 1/32(3.1)	7. 69 3/39(7. 7)	
<pre>Peto test Standard method(d) P = Prevalence method(d) P =</pre>	P = 0.3425 P = 0.0146*				
3	P = 0.0597				
	0. 0093	P = 0.5000	P = 0.1022	P = 0.1022	
SITE : TUMOR :	: ALL SITE : malignant lymphoma				
Tumor rate Overall rates(a) 15/	15/50(30.0)	7/50(14.0)	4/50(8 0)	7/50(14.0)	
	20.51	18.18	6.25	12.82	
lerminal rates(c) 8/ Statistical analysis Peto test	8/39(20.5)	5/32(15.6)	2/32(6.3)	5/39(12.8)	
	P = 0.9044 P = 0.8344 P = 0.9449				
Cochran-Armitage test(e) $Y = F$ isher Exact test(e)	r = 0.1142	P = 0.0448*	P = 0.0047**	P = 0, 0448*	

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

: 0561 : MOUSE B6D2F1/Cr1j[Crj:BDF1] : MALE

STUDY No. ANIMAL SEX

ANALYSIS
STATISTICAL
W
CESIONS-INCIDENCE
NEOPLASTIC

: 0561 : MOUSE B6D2F1/Cr1;[Cr;:BDF1] : MALE

STUDY No. ANIMAL SEX

PAGE : 2	125 ppm	2/50(4.0) 5.13 2/39(5.1) P = 0.6913	RATS4
	50 ppm	5/50(10. 0) 6. 25 2/32(6. 3) P = 0. 2180	
	20 ppm	6/50(12.0) 7.14 $1/32(3.1)$ $P = 0.1343$	
THE STATE OF THE S	Control	SITE : ALL SITE TUMOR : hemangiosarcoma 2/50(4.0) 5.13 2/39(5.1) P = 0.7419 P = 0.7419 P = 0.5484 P = 0.7074 P = 0.5294	
P. SPACE STATE STA	Group Name	Tumor rate Overall rates(a) Adjusted rates(b) Terminal rates(c) Statistical analysis Peto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e)	(111 10001)

BAIS4

(a): Number of tumor-bearing animals/number of animals examined at the site.
(b): Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.
(c): Observed tumor incidence at terminal kill.
(d): Beneath the control incidence are the P-values associated with the trend test.

Standard method : Death analysis Prevalence method : Incidental tumor test

Combined analysis: Death analysis + Incidental tumor test

(e): The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.
? : The conditional probabilities of the largest and smallest possible out comes can not estimated or this P-value is beyond the estimated P-value.

-----: There is no data which should be statistical analysis. Significant difference ; *: P \leq 0.05 ***: P \leq 0.01 N.C.:Statistical value cannot be calculated and was not significant.

TABLE 02

NEOPLASTIC LESIONS-INCIDENCE

AND STATISTICAL ANALYSIS: FEMALE

ANALYSIS
STATISTICAL
WD
LESIONS-INCIDENCE
NEOPLASTIC

SITE TUMOR Tumor rate Overall rates(a) Adjusted rates(b) Terminal rates(c) Statistical analysis Peto test Standard method(d) Provalence method(d) P = -	Control	20 ppm	50 ppm	125 ppm	
e. e	: lung : bronchiolar-alveolar adenoma				
d. a	4/50(8.0)	5/50(10.0)	6/50(12.0)	3/50(6 0)	
G 0	11.54	16.13	17.14	60.6	
method(d) P		0/ 51 (10. 1)	2/24(8.3)	2/26(7.7)	
Д					
. Δ	= 0.7112 =				
(e)	P = 0.5938				
Fisher Exact test(e)		P = 0.5000	P = 0.3703	P = 0.5000	
SITE	: lung : bronchiolar—alveolar adenoma bronchiolar—alveolar carcinema	pronchiolar—alveolar carcinoma			
	5/50(10.0)	5/50(10.0)	6/50(12.0)	5/50(10.0)	
	11. 54	16.13	17.14	15.38	
ares(c) analysis	2/18(1L. 1)	5/31(16.1)	2/24(8.3)	4/26(15.4)	
Standard method(d) $P = I$. Prevalence method(d) $P = 0$	P = 1.0000 ? P = 0.4259				
Ъ	= 0.5233				
ge test(e) P	= 0.9952				
Fisher Exact test(e)		P = 0.6297	P = 0.5000	P = 0.6297	
SITE	: lvmnh node		MANAGAMATAN AND AND AND AND AND AND AND AND AND A		
TUMOR	malignant lymphoma				
ıtes(a)	15/50(30.0)	11/50 (22.0)	12/50(24.0)	15/50/ 30 0)	
~	19.05	16.13	20.83	19.23	
ates(c)	3/18(16.7)	5/31(16.1)	5/24(20.8)	5/26(19.2)	
Statistical analysis Peto test					
method(d)	P = 0.4074				
	P = 0.4160				
۱۱ کبر د	P = 0.3819				
II	0. (0/4	P = 0.2472	P = 0 3264	D - 0 5023	

L ANALYSIS
STATISTICAL
AND
LESIONS-INCIDENCE
NEOPLASTIC

Charles Man-					
oroup name	Control	20 ppm	50 ppm	125 ppm	
	SITE : spleen TIMOR : malionant lumnhoma				WANTED THE PROPERTY OF THE PRO
Tumor rate					
Overall rates(a)	3/50(6.0)	3/50(6 0)	3/50(6.0)	(0 0) (1) 4	
Adjusted rates(b)	0.0			4/50(8.0)	
	0/18(0.0)	3/31(9.7)	4. 17 1/24(4. 2)	11. 54 3/26(11. 5)	
Statistical analysis					
reto test Standard mothod(4)	- a				
Prevalence method(d)	$\Gamma = 0.0945$ D = 0.1695				
Combined analysis(d)	P = 0,3493				
Cochran-Armitage test(e)	P = 0.6451				
Fisher Exact test(e)		P = 0.6611	P = 0.6611	P = 0.5000	
	SITE : liver				
£					
Tumor rate					
Overall rates(a)	3/50(6.0)	4/50(8.0)	2/50(4.0)	6/50(12.0)	
Adjusted rates(b)	11.11	9.68	5.71	12. 20	
Statistical analysis	2/10(11:1)	3/31(9.7)	1/24(4.2)	2/26(7.7)	
Peto test					
Standard method(d)	P = 0.4719				
Prevalence method(d)	P = 0.1039				
Combined analysis(d)	P = 0.1319				
Cochran-Armitage test(e)	P = 0.2611				
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0, 2435	
	SITE : liver				
Tumor rate	romon . Heparocerrurar adelionia				
Overall rates(a)	4/50(8.0)	3/50(6.0)	1/50(2.0)	2/50 (4.0)	
Adjusted rates(b)	16.67				
	3/18(16.7)	2/31(6.5)	1/24(4.2)	2/26(7.7)	
Statistical analysis					
Peto test	ſ				
Standard method(d)	F = 4				
Frevalence method (d)	P = 0.8209				
Cohmined analysis (d)	P = 0.3032				
Fisher Exact test(e)	1 - 0:303	D = 0 5000	0 - 0 1011		
				V = 0.3389	

ANALYSIS
E AND STATISTICAL
AND AND
NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

Group Name	Control	20 ppm	50 ppm	125 ppm	
	SITE : liver TUMOR : hemangioma, hemangiosarcoma	rcoma			
lumor rate Overall rates(a)	3/50(6 0)	4 /En (0 b)			
Adjusted rates(b)	3/30(0.0)		2/50(4.0)	7/50(14.0)	
Terminal rates(c)	2/18(11.1)	3/31(9.7)	1/24(4.2)	12.50 2/26(7.7)	
recipitat analysis Peto test					
Standard method(d)	P = 0.2185				
Prevalence method(d)	P = 0.0967 P = 0.0660				
Cochran-Armitage test(e)	P = 0.0300				
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.1589	
Dinor yato	SITE : liver TUMOR : hepatocellular adenom	liver hepatocellular adenoma, hepatocellular carcinoma			
Overall rates(a)	4/50(8 0)	4 (50 / 00 0)			
Adjusted rates(b)	16.67	4/50(8.0)	2/50(4.0)	3/50(6.0)	
Terminal rates(c)	3/18(16.7)	3/31(9.7)	8.33	10.34	
Statistical analysis					
Standard method(d)	р =				
Prevalence method(d)	P = 0.6845				
Combined analysis(d)	P =				
Cochran-Armitage test(e)	P = 0.6343				
Fisher Exact test(e)		P = 0.6425	P = 0.3389	P = 0.5000	
	SITE : pituitary gland				
lumor rate Overall rates(a)	7/50/ 0 0)	(0 01 /07/)			
Adjusted rates(h)	4/ 50 (5: 0) 10 53	0/49(12.2)	(/50(14.0)	3/50(6.0)	
Terminal rates(c)	1/18(5.6)	19. 53 6/31 (19. 4)	25.00	11.54 $3/96(11.5)$	
Statistical analysis					
Standard method(d)	P = 1.0000?				
	P = 0.7083				
Combined analysis(d)	P = 0.7866				
Cocnran—Armitage test(e) Fisher Exact test(e)	r = 0.5100	P = 0.3574	D = 0 9693	0000	
			l		

ANALYSI
STATISTICAL
AND
NEOPLASTIC LESIONS-INCIDENCE

: 0561 : MOUSE B6D2F1/Cr1j[Crj:BDF1] : FEMALE

STUDY No. ANIMAL SEX

PAGE: 9	md		
	125 ppm	3/50(6.0) 11.54 3/26(11.5)	7
	50 ppm	7/50(14.0) 25.00 6/24(25.0)	
	20 ppm	6/49(12. 2) 19. 35 6/31(19. 4) P = 0. 4856	
THE COLUMN TWO COLUMNS TO THE COLUMN TWO COL	Control	SITE : pituitary gland TUMOR : adenoma, adenocarcinoma 5/50(10.0) 15.79 2/18(11.1) P = 1.0000 ? P = 0.7901 P = 0.8518 P = 0.3778	
SEA : FEMALE	Group Name	Tumor rate Overall rates(a) Adjusted rates(b) Terminal rates(c) Statistical analysis Peto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e)	

	15/50 (30. 0) 24. 14 6/26 (23. 1)		P = 0.1779
	8/50(16.0) 4.17 1/24(4.2)		P = 0.3976
	14/50(28. 0) 22. 58 7/31(22. 6)		P = 0, 2415
SITE : uterus TUMOR : histiocytic sarcoma	10/50(20. 0) 5. 56 1/18(5. 6)	P = 0, 4312 P = 0, 1139 P = 0, 2036	
Tumor rate	Overall rates(a) Adjusted rates(b) Terminal rates(c)	Statistical analysis Peto test Standard method(d) Prevalence method(d) Combined analysis(d)	Cochran-Armitage test(e) Fisher Exact test(e)

(HPT360A)

BAIS4

⁽a): Number of tumor-bearing animals/number of animals examined at the site.
(b): Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.
(c): Observed tumor incidence at terminal kill.
(d): Beneath the control incidence are the P-values associated with the trend test.

Standard method : Death analysis Prevalence method : Incidental tumor test

Combined analysis : Death analysis + Incidental tumor test

⁽e): The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.
?: The conditional probabilities of the largest and smallest possible out comes can not estimated or this P-value is beyond the estimated P-value.
= ... There is no data which should be statistical analysis.
Significant difference; *: P ≤ 0.05 **: P ≤ 0.01
N.C.:Statistical value cannot be calculated and was not significant.

Group Name	Control	20 ppm	50 ppm	125 ppm	
	SITE : ALL SITE TUMOR : hemangioma		,		
lumor rate Overall rates(a) Adjusted rates(b) Terminal rates(c) Statistical analysis	3/50(6.0) 11.11 2/18(11.1)	8/50(16.0) 16.13 5/31(16.1)	4/50(8.0) 12.50 3/24(12.5)	9/50(18. 0) 21. 21 4/26(15. 4)	
reto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e)	P = 0, 6883 P = 0, 0348* P = 0, 0888 P = 0, 1489				
Fisher Exact test(e)		P = 0.0999	P = 0.5000	P = 0.0606	
limor rate	SITE : ALL SITE TUMOR : histiocytic sarcoma				The state of the s
Overall rates(a) Adjusted rates(b)	12/50(24. 0) 5. 56	15/50 (30. 0) 22 58	9/50(18.0)	15/50(30.0)	
Terminal rates(c) Statistical analysis Peto test	1/18(5.6)	7/31(22. 6)	1/24(4.2)	6/26(23. 1)	
Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e)	P = 0, 6166 P = 0, 1183 P = 0, 3421 P = 0, 6355				
Fisher Exact test(e)		P = 0.3264	P = 0.3121	P = 0.3264	

ANALYSIS
STATISTICAL
AND N
S-INCIDENCE
LESIONS
NEOPLASTIC

: 0561 : MOUSE BGDZF1/Crlj[Crj:BDF1] : FEMALE

STUDY No. ANIMAL SEX

4

PAGE: 4				RAISA
The state of the s	125 ppm	19/50 (38. 0) 30. 77 8/26 (30. 8)	P = 0.5000	
THE PARTY OF THE P	wdd 09	15/50 (30. 0) 25. 00 6/24 (25. 0)	P = 0.3355	
	20 ppm	14/50 (28. 0) 25. 81 8/31 (25. 8)	P = 0.2603	
The second secon	Control	SITE : ALL SITE TUMOR : malignant lymphoma 18/50(36.0) 19.05 3/18(16.7) P = 0.5007 P = 0.2008 P = 0.3265 P = 0.5526		
	Group Name	Tumor rate Overall rates(a) Adjusted rates(b) Terminal rates(c) Statistical amalysis Peto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e)	Fisher Exact test(e)	(HPT360A)

BAIS4

(a): Number of tumor-bearing animals/number of animals examined at the site.
(b): Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.
(c): Observed tumor incidence at terminal kill.
(d): Beneath the control incidence are the P-values associated with the trend test.

Standard method : Death analysis Prevalence method : Incidental tumor test Combined analysis : Death analysis + Incidental tumor test

(e): The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.
? The conditional probabilities of the largest and smallest possible out comes can not estimated or this P-value is beyond the estimated P-value.

Significant difference : * : P \leq 0.05 ** : P \leq 0.01 N.C.:Statistical value cannot be calculated and was not significant.

TABLE Q

HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER : $B6D2F1/Crlj\ MALE\ MICE$

TABLE Q HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER: B6D2F1/Crlj MALE MICE

Organs Tumors	No. of animals examined	No. of animals bearing tumor	Incidence (%)	Min Max. (%)
Lung Bronchiolar-alveolar adenoma 1) Bronchiolar-alveolar carcinoma 2) 1) + 2)	1895	165 196 361	8.7 10.3 19.1	2 - 18 0 - 24 2 - 34
Liver Hepatocellular adenoma 1) Hepatocellular carcinoma 2) 1) + 2)	1896	376 352 657	19.8 18.6 34.7	4 - 38 2 - 42 8 - 68
All organ histiocytic sarcoma	1896	178	9.4	0 - 22

Thirty eight carcinogenicity studies examined in Japan Bioassay Research Center were used. Study No.: 0044, 0060, 0062, 0064, 0066, 0068, 0096, 0105, 0116, 0140, 0159, 0163, 0190,

0206, 0211, 0225, 0243, 0268, 0270, 0279, 0285, 0297, 0319, 0329, 0343, 0348,

 $0366,\,0372,\,0402,\,0406,\,0418,\,0422,\,0438,\,0449,\,0458,\,0462,\,0498,\,0515$

TABLE R

CAUSE OF DEATH OF MICE IN THE 2-YEAR INHALATION STUDY OF 1 - BROMOBUTANE

TABLE R CAUSE OF DEATH OF MICE IN THE 2-YEAR INHALATION STUDY OF 1-BROMOBUTANE

	Male				Female			
Group name	Control	20 ppm	50 ppm	125 ppm	Control	20 ppm	50 ppm	125 ppm
Number of dead or moribund animals	11	18	18	11	32	19	26	24
Hepatic lesions	0	1	1	0	0	0	0	0
Urinary system lesions	0	1	0	0	0	0	0	0
Renal lesions	0	0	1	0	0	0	0	0
Urinary retention	1	1	3	2	0	1	0	0
Cardiovascular lesions	0	0	0	0	0	0	1	0
Arteritis	0	0	0	0	0	0	0	1
Hydronephrosis	0	2	1	3	1	0	1	1
Tumor death: leukemia	7	1	2	2	14	6	9	11
subcutis	1	1	0	1	2	1	1	0
lung	0	3	2	1	1	0	0	0
heart	0	0	0	0	0	0	1	0
bone marrow	0	1	0	0	0	0	0	0
liver	1	6	6	0	2	2	1	2
urinary bladder	0	0	0	0	0	1	0	0
pituitary gland	0	0	0	1	1	0	0	0
testis	1	0	0	0	-	-	-	-
epididymis	0	0	0	1	-	-	-	-
ovary	-	-	-	-	0	1	1	0
uterus	-	-	-	-	8	7	9	8
mammary gland	0	0	0	0	1	0	1	0
peripheral nerve	0	0	1	0	0	0	0	0
muscle	0	1	0	0 .	0	0	0	0
mediastinum	0	0	1	0	0	0	0	0
peritoneum	0	0	0	0	0	0	0	1
retroperitoneum	0	0	0	0	1	0	0	0
No microscopical confirmation	0	0	0	0	1	0	1	0

FIGURES

FIGURE 1	1 - BROMOBUTANE VAPOR GENERATION SYSTEM AND INHALATION SYSTEM
FIGURE 2	SURVIVAL ANIMAL RATE OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1 - BROMOBUTANE
FIGURE 3	SURVIVAL ANIMAL RATE OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 1 - BROMOBUTANE
FIGURE 4	BODY WEIGHT CHANGES OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1 - BROMOBUTANE
FIGURE 5	BODY WEIGHT CHANGES OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 1 - BROMOBUTANE
FIGURE 6	FOOD CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1 - BROMOBUTANE
FIGURE 7	FOOD CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 1 - BROMOBUTANE

FIGURE 1 1-BROMOBUTANE VAPOR GENERATION SYSTEM AND INHALATION SYSTEM

COMPRESSED CLEAN AIR

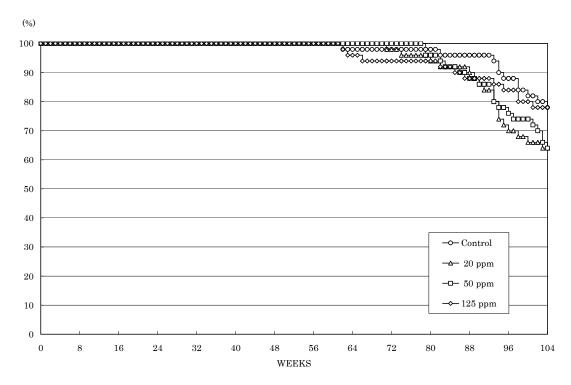


FIGURE 2 SURVIVAL ANIMAL RATE OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1-BROMOBUTANE

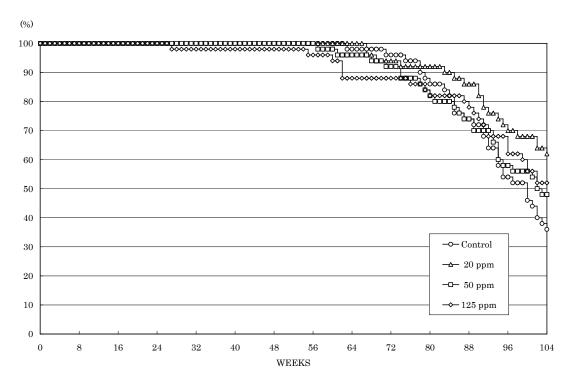


FIGURE 3 SURVIVAL ANIMAL RATE OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 1-BROMOBUTANE

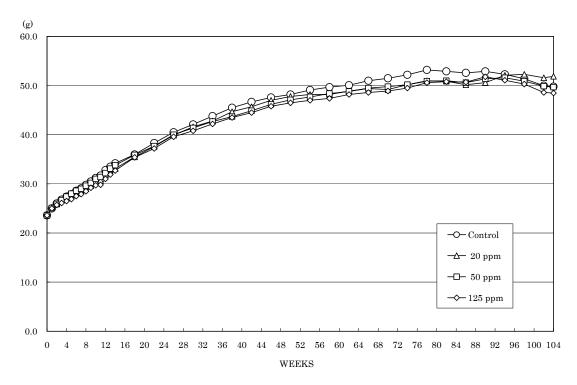


FIGURE 4 BODY WEIGHT CHANGES OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1-BROMOBUTANE

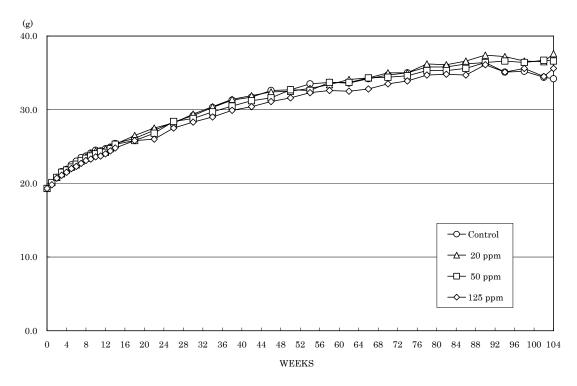


FIGURE 5 BODY WEIGHT CHANGES OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 1-BROMOBUTANE

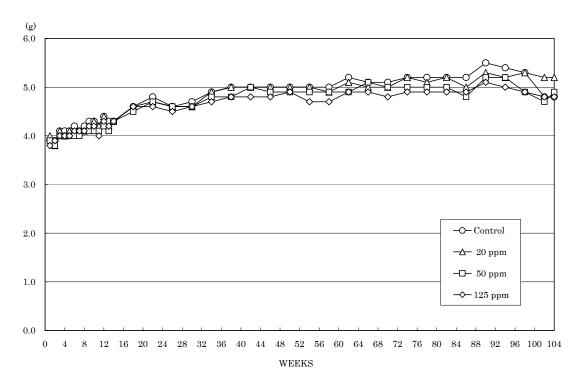


FIGURE 6 FOOD CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1-BROMOBUTANE

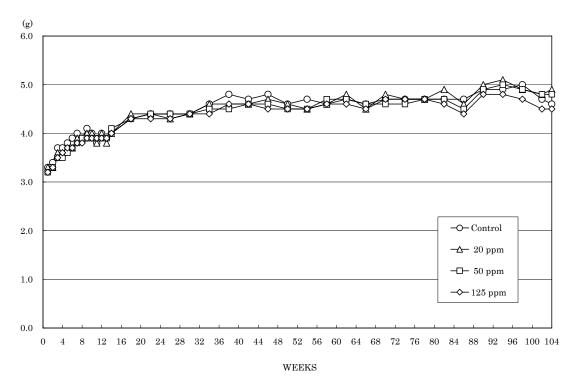
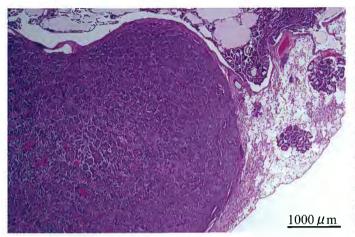
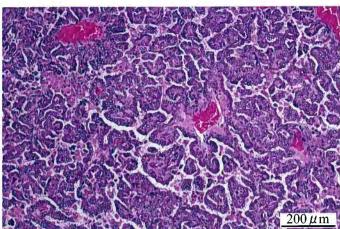


FIGURE 7 FOOD CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 1-BROMOBUTANE



Photograph 1 Lung: Bronchiolar-alveolar carcinoma Mouse, Male, 125 ppm, Animal No. 0561-1347 (H&E)



Photograph 2 Lung: Bronchiolar-alveolar carcinoma Higher magnification of photograph 1