Summary of Inhalation Carcinogenicity Study of 2,4-Pentanedione in B6D2F1 Mice

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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 26, 2010.

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

Summary of Inhalation Carcinogenicity Study of 2,4-Pentanedione in B6D2F1 Mice

Purpose, materials and methods

2,4-Pentanedione (CAS No. 123-54-6) is a colorless liquid with a boiling point of 139°C (746 mmHg). It is soluble in ethanol, acetone, and water.

The carcinogenicity and chronic toxicity of 2,4-pentanedione (greater than 99.9% pure) were examined by inhalation exposure using B6D2F1/Crlj mice. Groups of test animals were exposed to 2,4-pentanedione vapors at target concentrations of 0 (clean air), 100, 200 or 400 ppm (v/v) for 6 hours/day, 5 days/week for 2 years (104 weeks). Each group of test animals consisted of either 50 male or 50 female rats. Both sexes were exposed to each concentration of 2,4pentanedione 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 a previous 13-week toxicity study. The identity of the 2,4-pentanedione used in these experiments was confirmed by both infrared spectrometry and mass spectrometry. It was analyzed by gas chromatography before and after its use to affirm its stability. Stainless-steel inhalation exposure chambers (volume: 3.7m³) were used throughout the 2-year exposure period. 2,4-Pentanedione vapor-air mixtures were generated by bubbling clean air through 2,4-pentanedione liquid and the mixtures delivered to the inhalation exposure chambers. Air concentrations of the 2,4-pentanedione 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. Hematology and blood biochemistry analysis were performed 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 2,4-pentanedione 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 differences in survival rates and clinical signs were found between any of the groups exposed to 2,4-pentanedione and their respective controls. The body weights of the males exposed to 400 ppm 2,4-pentanedione were suppressed during the first half of the exposure period; thereafter the body weights became similar to the controls: the terminal body weights of the 400 ppm-exposed males was 97% of the controls. The body weights of all other 2,4-pentanedione exposed groups, both male and female, were similar to their respective controls throughout the exposure period. Food consumption by the males exposed to 400 ppm 2,4-pentanedione decreased after 30 weeks. Food consumptions of all other 2,4-pentanedione exposed groups, both male and female, were similar to their respective controls throughout the exposure period. There were no 2,4-pentanedione related changes in the hematology parameters or organ weights. Plasma albumin globulin ratios (A/G ratio) and plasma levels of glucose were increased in males exposed to 200 and 400 ppm 2,4-pentanedione and aspartate aminotransferase, alanine aminotransferase, creatine kinase, urea nitrogen and inorganic phosphorus were significantly decreased in males exposed to 400 ppm 2,4-pentanedione. Urinalysis showed an increase in protein and ketone bodies in females exposed to 400 ppm 2,4pentanedione. Pituitary nodules and enlargement were noted in females exposed to 200 and 400 ppm 2,4-pentanedione.

No significant increases in the incidence of neoplastic lesions was found in any of the 2,4-pentanedione-exposed group of either sex compared with their respective controls. Non-neoplastic lesions in the nasal cavity were noted in both sexes: squamous metaplasia (males and females), eosinophilic change (males), ulcer (males and females), necrosis (females) and transitional cell hyperplasia (males) in the respiratory epithelium and atrophy (males and females), respiratory metaplasia (males and females), eosinophilic change (females), necrosis (females) in the olfactory epithelium were observed. Respiratory metaplasia in the submucosal gland was observed in both sexes. The exudate and atrophy in the olfactory epithelium occurred in both males and females exposed to 100 ppm 2,4-pentanedione (the lowest dose tested) and above. Using nasal lesions as endpoint markers, the lowest-observed-adverse-effect-level (LOAEL) of 2,4-pentanedione, exposure by inhalation, was 100 ppm for both male and female mice.

Conclusions

There was no evidence for carcinogenicity of 2,4-pentanedione in male or female mice.

Incidences of selected neoplastic lesions of male mice in the 2-year inhalation carcinogenicity study of 2,4-pentanedione

	Dose (ppm)	0	100	200	400	Peto test	Cochran- Armitage test
1	Number of examined animals	50	50	49	50		
benign tumo	r						
lung	bronchiolar-alveolar adenoma	4	4	3	5		
liver	hepatocellular adenoma	6	8	18 *	10		
Harderian gland	adenoma	2	4	4	4		
malignant tu	mor						
lung	bronchiolar-alveolar carcinoma	2	3	2	3		
lymph node	malignant lymphoma	9	6	6	13		
liver	hepatocellular carcinoma	5	8	4	2		
	hemangiosarcoma	6	3	3	3		
all organs	histiocytic sarcoma	3	2	2	4	$\uparrow \uparrow ^{a)}$	

Incidences of selected neoplastic lesions of female mice in the 2-year inhalation carcinogenicity study of 2,4-pentanedione

	Dose (ppm)	0	100	200	400	Peto test	Cochran- Armitage test
	Number of examined animals	50	49	50	50		
benign tumo	r						
liver	hepatocellular adenoma	1	5	3	3		
pituitary	adenoma	10	11 b)	13	12		
ovary	adenoma	1	0	0	3		
Harderian gland	adenoma	1	0	3	2		
malignant tu	mor						
lymph node	malignant lymphoma	15 9	14 7	15 14	13 8		
uterus	histiocytic sarcoma	9	/	14	8		

^{a)}: Significant in plevalence method only.

Significant difference

 $\uparrow: p \leq 0.05 \quad \text{increase} \qquad \qquad \uparrow \uparrow: p \leq 0.01 \quad \text{increase} \qquad \qquad \text{(Peto, Cochran-Armitage test)} \\ \downarrow: p \leq 0.05 \quad \text{decrease} \qquad \qquad \downarrow \downarrow: p \leq 0.01 \quad \text{decrease} \qquad \qquad \text{(Cochran-Armitage test)}$

b): Numer of examined animal of pituitary is 48.

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TABLE A

CONCENTRATIONS OF 2,4-PENTANEDIONE IN THE INHALATION CHAMBER OF THE 2-YEAR INHALATION STUDY

CONCENTRATIONS OF 2,4-PENTANEDIONE IN THE INHALATION CHAMBER OF THE 2-YEAR INHALATION STUDY

Group Name	Concentration(ppm) $Mean \pm S.D.$
Control	0.0 ± 0.0
100 ppm	100.9 ± 0.9
200 ppm	200.9 ± 1.4
400 ppm	401.0 ± 1.8

TABLE D1

BODY WEIGHT CHANGES AND SURVIVAL ANIMAL NUMBERS : MALE

(BI0040)

MEAN BODY WEIGHTS AND SURVIVAL

STUDY NO. : 0676
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

								•				
Week on Study	Av. Wt.	No. of Surviv. <50>	Av. Wt.	% of cont. <50>	No. of Surviv.	Av. Wt.	% of cont. <49>	No. of Surviv.	Av. Wt.	% of cont. <50>	No. of Surviv.	
0		(50) 50/50	23. 5	100	50/50	23.5 (49)	100	49/49	23. 5 (50)	100	50/50	
1	24.6 (_		66	20/20	24.9 (49)	101	49/49	· ~	66	50/50	
2	_	_	25.1	86	20/20	25.6 (49)	100	49/49	_	26	50/50	
က	_	_	25.3	96	20/20		66	49/49	_	26	50/50	
4	_	_	25.5	92	20/20		100	49/49	_	26	50/50	
· 22	_	(50) 50/50	26.3	96	49/50	27.5 (49)	100	49/49	26.5 (49)	96	49/50	
9 1	_	_		96	49/20		66	49/49	_	96	49/50	
	_	_	27.6	96	49/20		66	49/49	_	92	49/50	
∞ «			28.7	26	48/50	29.3 (49)	66	49/49		94	49/50	
ဘ	_		29. 2	96	48/20		86	49/49		94	49/50	
10	30.9		29. 5	92	48/20		86	49/49	29.1 (49)	94	49/50	
11		_	30.1	96	48/50		66	49/49	29.9 (49)	92	49/50	
12		_	31.2	96	48/50		86	49/49		94	49/50	
13	_		31.8	96	48/50		86	49/49		94	49/50	
14			31.9	96	48/50		66	49/49		95	49/50	
18	36.1 ((20) 20/20	35.0 (48)	26	48/50	35.8 (49)	66	49/49		95	49/50	
22			38.0	66	48/50		66	49/49		92	49/50	
56		(20) 20/20	39.3	66	48/50		100	49/49	38.3 (49)	96	49/50	
30			41.5	100	48/20		100	49/49		26	49/50	
34			43.6	100	48/20		100	49/49	_	26	49/50	
38			45.1	101	48/20		101	49/49		26	49/50	
42			46.0	101	48/20		100	49/49	44.2 (49)	26	49/50	
46		_	46.6	101	48/50		101	49/49		96	49/50	
20			47.3	100	48/50		101	48/49	_	92	49/50	
54		(20) 20/20	48.3	100	46/50		66	48/49		92	48/50	
23	48.9 (48.7	100	45/50		100	48/49	46.6 (48)	92	48/50	
29		_	49. 1	66	44/50		66	48/49	47.2 (48)	92	48/50	
99	50.2 (49.5	66	44/50		86	47/49	47.9 (48)	95	48/50	
20		_	50.1	86	44/50		86	47/49	48.6 (48)	92	48/50	
74	52.0 (86	44/50		26	47/49	49.0 (47)	94	47/50	
78	_	_	50.6	86	42/50		86	47/49	49.7 (47)	96	47/50	
82	_	(47) $47/50$	51.9	100	40/20		66	47/49	49.9 (46)	26	46/50	
98			51.0	100	40/20		100	43/49	49.8 (45)	86	45/50	
90	51.5	(40) $40/50$	51.2	66	37/20		86	41/49	49.6 (44)	96	44/50	
94	_	_	50.7	66	35/20		66	38/49	49.3 (44)	96	44/50	
86	_	_	49.7	66	33/20		101	37/49	49.0 (41)	86	41/50	
[02	49.1 ((36) 36/50		101	31/50		102	36/49	47.8 (40)	26	40/50	
	0 00											

TABLE D2

BODY WEIGHT CHANGES AND SURVIVAL ANIMAL NUMBERS : FEMALE

(BI0040)

PAGE: 2

STUDY NO. : 0676

ANIMAL : MOUSE B6D2F1/Cr1;[Cr.j:BDF1]
UNIT : g

REPORT TYPE : A1 104

SEX : FEMALE

1	No. of	Surviv.		50/50	50/50	50/50	20/20	50/50	20/20	20/20	50/50	20/20	20/20	49/50	49/50	49/50	49/50	49/50	49/50	49/50	49/50	49/50	49/50	49/50	49/50	49/50	48/50	47/50	47/50	47/50	47/50	40/30	46/50	45/50	43/50	42/50	39/20	37/50	36/50	34/50
2	% of	cont.	<20>	100	66	86	66	100	100	100	100	66	101	101	102	66	100	102	102	100	102	103	102	101	101	103	102	86	100	001	001	99	66	101	101	101	102	101	102	101
	Av. Wt.			19. 5 (50)	_	20.3 (50)	_	_	21.9 (50)	_	_	_	23.7 (50)	-	_	24.7 (49)	24.7 (49)	_	26.6 (49)	-	28.0 (49)	_	_	-		_	32.1 (48)	_	_		33. 1 (47)	_	_	_	_	35.2 (42)	35.6 (39)	34.3 (37)	_	33.9 (34)
	No. of	Surviv.		50/50	20/20	50/50	20/20	50/50	50/50	50/50	50/50	20/20	50/50	20/20	50/50	50/50	20/20	20/20	20/20	20/20	20/20	20/20	49/50	49/50	49/20	49/50	49/20	49/50	48/50	48/50	47/50	47/50	46/50	43/50	39/20	38/20	32/50	29/20	26/20	26/50
	% of	cont.	<20>	100	100	66	66	100	101	101	100	101	102	102	102	100	101	103	103	102	104	105	106	106	106	107	107	106	107	109	109	108	106	108	109	108	106	111	109	110
	Av. Wt.			19.5 (50)	_	_	20.9 (50)	_	22.3 (50)	22.7 (50)	22.9 (50)	23.8 (50)	23.9 (50)	24.2 (50)	24.4 (50)	25.0 (50)	25.0 (50)	25.3 (50)			28.5 (50)	30.0 (50)			_		_		34.9 (48)		36. 0 (47)		_	_		37.6 (38)	_	_	36.7 (26)	37.0 (26)
	No. of	Surviv.		49/49	49/49	49/49	49/49	49/49	49/49	49/49	49/49	49/49	49/49	49/49	49/49	49/49	49/49	49/49	49/49	49/49	48/49	48/49	48/49	48/49	48/49	48/49	48/49	47/49	47/49	47/49	41/49	40/49	44/49	43/49	42/49	38/49	36/49	34/49	29/49	27/49
	% of	cont.	<49>	100	66	86	86	66	86	100	66	66	66	66	100	86	66	101	101	101	102	102	102	102	101	103	103	104	105	104	100	105	105	106	106	107	107	111	111	111
110000	Av. Wt.			19.5 (49)	19.7 (49)	_	_	_	_	_	22.8 (49)	_	_	23.5 (49)	6	_	24.5 (49)	_	26.5 (49)	_	_	29.1 (48)	-	_	31.2 (48)		32. 6 (48)		34. 1 (47)			36. 1 (44)	-	37.0 (43)	_	37.1 (38)	_	_	37.6 (29)	37.3 (27)
	No. of	urviv.	6	50/50	20/20	20/20	20/20	20/20	49/50	49/50	49/.50	49/50	49/50	49/50	49/20	49/50	49/50	49/20	49/50	49/50	49/50	49/50	49/50	49/50	49/20	49/20	48/50	48/50	47/50	47/50	45/50	45/50	45/50	44/50	44/50	42/50	41/50	37/20	32/20	31/20
	Av. Wt.	Ñ	<20>	19.5 (50)	_	20.8 (50)	_	_	22.0 (49)	_	_	23.5 (49)	4	_	0	6	_	-	-	27.1 (49)		28.5 (49)			30.9 (49)	_	31.6 (48)	_	32.5 (47)	32. b (47)		_	_	_	_	34.8 (42)	35.0 (41)	_	_	33.7 (31)
		Week	on Study	0	-	2	က	4	വ	9	7	&	6	10	11	12	13	14	18	22	56	30	34	38	42	46	20	¥ :	× 50	29 29	8 8	74	78	82	98	06	94	86	102	104

TABLE D3

BODY WEIGHT CHANGES: MALE

ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : MALE	[Crj:BDF1]		ALL ANIMALS				PAGE :
Group Name	Administration week 0	n week 1	2	8	4	വ	9
Control	23.5士 0.9	24.6± 1.1	25.7± 1.2	26.3± 1.4	26.8± 1.5	27.5± 1.6	28.1± 1.9
100 ppm	23.5± 0.9	24.4 ± 1.1	25.1± 1.1*	25.3± 1.4*	25.5± 1.8**	26.3± 1.8**	26.9± 1.9**
200 ppm	23.5士 0.8	24.9 ± 1.0	25.6 ± 1.3	26.1 ± 1.4	26.7± 1.6	27.5± 1.6	27.9± 1.8
400 ppm	23.5士 0.9	24.3± 1.6	24.9± 1.1**	25.6± 1.1*	26.1 ± 1.3	26.5± 1.4*	27.0± 1.5**
Significant difference ;	* : P ≤ 0.05	**: P ≤ 0.01		Test of Dunnett			

ANIMAL : MOUSE B6DZF1/Cr1;[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : MALE	[¢r.j:80F1.]		ALL ANIMALS				PAGI	PAGE: 2
Group Name	Administration week 7	on week	6	10	11	12	13	
Control	28.9± 1.9	29.7± 2.0	30.3± 2.2	30.9± 2.5	31.5± 2.6	32.5± 2.6	33.0± 2.8	
100 ррш	27.6± 2.0**	28.7± 1.9*	29.2± 1.9*	29.5± 2.0₩	30,1± 2,2**	31.2± 2.2*	31.8± 2.3	
200 ppm	28.5± 1.8	$29.3\pm\ 2.0$	29.7± 2.2	30.4 ± 2.4	31.2± 2.4	31.9± 2.6	32.5 ± 2.6	
400 ppm	27.5± 1.7**	28.0± 1.9**	28.5± 2.0**	29.1± 2.1**	29.9± 2.4**	30.6± 2.4**	31.1± 2.6**	
		The second secon						
Significant difference;	*: P ≤ 0.05	**: P ≤ 0.01		Test of Dunnett				
(HAN260)	The second secon							BAIS 4

ANIMAL . MOUSE BODZFI/CEIJICEJ:EDFIJ UNIT : g REPORT TYPE : AI 104 SEX : MALE	(Cr.): BBFLJ		ALL ANJMALS				PAGE :
Group Name	Administration week	on week					
	14	18	22	26	30	34	38
Control	33.3± 3.0	36.1± 3.2	38.4 ± 3.8	39.8± 4.2	41.6± 4.4	43.7± 4.4	44.8± 4.6
100 ppm	31.9± 2.4*	$35.0\pm\ 2.7$	38.0± 3.2	39.3 ± 3.7	41.5 ± 3.9	43.6 ± 4.2	45.1± 4.2
200 ppm	33.0± 2.9	35.8± 3.1	38.1± 3.6	39.8 ± 4.1	41.8± 4.5	43.9 ± 4.5	45.1± 4.7
400 ppm	31.5± 2.6**	34.3± 3.1**	36.6± 3.5	38.3± 3.6	40.2± 3.8	42.5 ± 4.0	43.4± 4.2
Significant difference ;	* : P ≤ 0.05	** : P ≤ 0.01		Test of Dunnett			
(1000)	THE PROPERTY AND ADDRESS OF THE PERSON OF TH						

Administration week 42	KEPOKI 1YPE : AI 104 SEX : MALE							1d	PAGE:
45.7± 4.6 46.3± 4.5 47.3± 4.8 48.2± 4.6 48.9± 4.7 49.5± 4.4 50.2± 46.0± 4.3 4.6 4.5 47.3± 4.5 48.3± 4.1 48.7± 4.2 49.1± 4.0 49.5± 45.8± 4.7 46.8± 4.8 4.7 4.8 4.9 49.0± 5.1 49.3± 44.2± 4.1 44.6± 4.1 45.1± 4.1* 46.6± 4.4* 46.6± 4.4* 47.2± 4.7 47.9±	Jp Name	Administration 42		50	. 54	58	62	99	
46.0± 4.3 46.6± 4.2 47.3± 4.5 48.3± 4.1 48.7± 4.2 49.1± 4.0 49.5± 45.8± 4.7 46.8± 4.8 47.6± 5.0 47.8± 4.9 48.8± 4.9 49.0± 5.1 49.3± 44.2± 4.1 44.6± 4.1 45.1± 4.1* 46.0± 4.4* 46.6± 4.4* 47.2± 4.4 47.2± 4.4 47.9±	Control	45.7± 4.6				48.9± 4.7	49.5± 4.4	50.2± 4.5	
45.8± 4.7 46.8± 4.8 47.6± 5.0 47.8± 4.9 48.8± 4.9 49.0± 5.1 49.3± 44.2± 4.1 44.6± 4.1* 46.0± 4.4* 46.6± 4.4* 47.2± 4.4 47.9±	100 ppm	46.0± 4.3						49.5± 4.0	
44.2± 4.1 44.6± 4.1 45.1± 4.1* 46.0± 4.4* 46.6± 4.4* 47.2± 4.4 47.9±	200 ррт	45.8土 4.7						49.3± 5.4	
	400 ppm	44.2± 4.1						47.9土 4.3	
* . P < 0.05	Significant difference :	. * 	10 c V a		Took of Dunnett				

REPORT TYPE : AI 104 SEX : MALE							PA	PAGE: 5
Group Name	Administration week 70	л week 74	78	83	98	06	94	
Control	51.0± 4.4	52.0± 4.9	51.7 ± 6.0	51.7± 6.3	50.9± 6.0	51.5± 6.4	51.2± 6.2	
100 ррш	50.1± 4.5	50.9士 4.8	50.6± 5.6	51.9± 5.7	51.0 ± 6.2	51.2± 6.3	50.7± 6.7	
200 ppm	50.1± 5.5	50.4 ± 6.1	50.9士 6.2	51.2± 6.5	50.8± 6.4	50.4± 7.4	50.6± 6.9	
400 ppm	48.6± 4.6	49.0± 4.9	49.7 ± 5.1	49.9± 6.3	49.8± 5.2	49.6 ± 5.2	49.3 ± 5.0	
Significant difference ;	*: P ≤ 0.05	‡ : P ≤ 0.01		Test of Dunnett				

Group Name Administration week 102 104 Control \$0.1± \$0.1± \$1 \$49.8± 7.7 100 ppm \$9.5± 7.8 \$49.6± 8.2 \$48.6± 8.7 200 ppm \$9.5± 7.0 \$49.9± 7.4 \$50.4± 7.0 400 ppm \$49.0± 5.3 \$47.8± 6.5 \$48.3± 5.5 Significant difference: *:P ≤ 0.05 **:P ≤ 0.01 *** P ≤ 0.01 *	ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : MALE	j[Cr.j:BDF1.]		ALL ANIMALS	PAGE:
1trol 50.1± 6.9 49.1 ± 8.1 49.8 ± 7.7 104 105 104 105 104 105 104 105	Group Name	Administrati	on week		
Control 60.1 ± 6.9 49.1 ± 8.1 49.8 ± 7.7 100 ppm 49.7 ± 7.8 49.6 ± 8.2 48.6 ± 8.7 100 ppm 49.0 ± 5.3 47.8 ± 6.5 48.3 ± 5.5 110 ppm 49.0 ± 5.3 47.8 ± 6.5 48.3 ± 5.5 110 Test of Dunnett		86	1	104	
100 ppm 49.7 ± 7.8 49.6 ± 8.2 48.6 ± 8.7 20.0 ppm 50.5 ± 7.0 49.9 ± 7.4 50.4 ± 7.0 49.9 ± 7.4 50.4 ± 7.0 49.9 ± 7.4 50.4 ± 7.0 49.0 ± 5.3 47.8 ± 6.5 48.3 ± 5.5 ifficant difference; $*:P \le 0.05$ **: $P \le 0.01$ Test of Dunnett	Control	50.1± 6.9	49.1± 8.1	49.8+ 7.7	
100 ppm 49.7 ± 7.8 49.6 ± 8.2 48.6 ± 8.7 49.0 ± 7.4 50.4 ± 7.0 49.0 ppm 49.0 ± 5.3 47.8 ± 6.5 48.3 ± 5.5 48.3 ± 5.5 48.3 ± 5.5 Test of Dunnett			:		
200 ppm 50.5± 7.0 49.9± 7.4 50.4± 7.0 40.9± 7.4 50.4± 7.0 40.0pm 49.0± 5.3 47.8± 6.5 48.3± 5.5 48.3± 5.5 ificant difference; *:P ≤ 0.05 **:P ≤ 0.01 Test of Dunnett	100 ppm	49.7± 7.8			
400 ppm 49.0 ± 5.3 47.8 ± 6.5 48.3 ± 5.5 48.3 ± 5.5 if icant difference; *: P \leq 0.05 **: P \leq 0.01 Test of Dunnett	200 ppm	50.5± 7.0		50.4± 7.0	
ificant difference ; *:P ≤ 0.05 **:P ≤ 0.01 Test of Dunnett	400 ppm	49.0± 5.3			
ificant difference; *:P≤0.05 **:P≤0.01 Test of Dunnett					
	Significant difference ;		★ : P ≤ 0.01		Test of Dunnett
	(HAN260)				BA1S4

TABLE D4

BODY WEIGHT CHANGES: FEMALE

STUDY NO. : 0676 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1] UNIT : g REPORT TYPE : A1 104	[Cr.j:BDF1]		BODY WEIGHT CHANGES ALL ANDMALS	(SUMMARY)			
SEX : FEMALE							PAGE: 7
Group Name	Administration week 0	on week	2		4	2	ω
	1	1		and the state of t			
Control	19.5 ± 0.8	20.0 ± 0.9	20.8 ± 1.0	21.1 ± 1.0	21.6 ± 0.9	22.0土 1.1	22.4 ± 1.1
100 ppm	19.5± 0.8	19.7± 0.9	20.3 ± 1.1	20.7 ± 0.9	21.3± 1.0	21.6± 1.1	22.3± 0.9
200 ррт	19.5± 0.8	19.9± 0.8	20.5± 1.0	20.9± 0.8	21.5 ± 1.0	22.3± 1.0	22.7 ± 1.0
400 ррш	19.5± 0.8	19.8± 0.8	20.3± 0.9	20.9± 0.8	21.5 ± 0.9	21.9 ± 1.0	22.4 ± 1.1
			•				
Significant difference;	*: P ≤ 0.05	★ : P ≤ 0.01	The state of the s	Test of Dunnett			

SIDY NO. : UG/O ANUMAL : MOUSE BEDZF1/Cr1j[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : FEMALE	[Cr.j:BDF1]		BODY WEIGHT CHANGES ALL ANIMALS	(SUMMARY)			PAGE: 8
Group Name	Administration week	on week 8	o.	10	11	12	13
Control	23.0± 1.1	23.5± 1.3	23.4± 1.2	23.7± 1.1	24.0± 1.0	24.9± 1.4	24.7± 1.4
100 mag	22.8± 1.2	23.2± 1.3	23.1 ± 1.2	23.5 ± 1.2	23.9 ± 1.3	24.5 ± 1.5	24.5± 1.5
	22.9 ± 1.1	23.8± 1.3	23.9 ± 1.1	24.2± 1.3	24.4± 1.3	25.0 ± 1.3	25.0± 1.5
400 ppm	23.0± 1.0	23.3 ± 1.3	23.7 ± 1.4	24.0 ± 1.4	24.4 ± 1.5	24.7 ± 1.6	24.7± 1.6
Significant difference;	* · · P · 0.05	* : P IS 0.01		Test of Dunnett			

ANIMAL : MOUSE BODZFI/CrijiCri;BDF1JUNIT : g UNIT : g REPORT TYPE : AI 104 SEX : FEMALE][Cr.j:BDf1]						PAGE :
Group Name	Administration week 14	л week	22	56	30	. 34	38
Control	24.6± 1.4	26.2± 1.6	. 27.1± 1.7	27.5± 2.1	28.5± 2.4	29.9± 2.8	30.2± 2.6
100 ppm	24.9± 1.5	26.5± 1.6	27.4± 2.3	28.0 ± 2.4	29.1 ± 2.5	30.5± 2.8	30.9± 3.1
200 ppm	25.3± 1.6	27.0± 1.8	27.7± 2.0	28.5± 2.5	30.0 ± 3.5	31.8± 3.4**	32.0 ± 4.0
400 ppm	25.1 ± 1.5	26.6± 1.8	27.2± 1.8	28.0± 2.2	29.4± 3.1	30.4± 3.0	30.5± 3.0
Significant difference ;	* : P ≤ 0.05	* : P ≤ 0.01		Test of Dunnett			

STUDY NO. : 0676 ANIMAL : MOUSE BEDZF1/Cr1j[Crj:BDF1] UNIT : g REPORT TYPE : A1 104	[Cr.j:BDF1]		BODY WEIGHT CHANGES ALL ANIMALS	(SUMMARY)			
SEX : FEMALE Group Name	Administration week	n week					PAGE: 10
	42	46	50	54	58	62	99
Control	30.9± 2.9	31.1± 3.2	31.6± 3.3	32.4± 3.3	32.5± 3.6	32.6± 3.9	33.1± 4.2
100 ррш	31.2± 3.1	31.9± 3.3	32.6± 3.7	33.6± 3.6	34.1± 3.9	33.9± 4.0	35.2± 4.2*
200 ppm	32.6± 4.0*	33.3± 4.0**	33.8± 4.2*	34.5	34.9± 4.6**	35.4± 4.8**	36.0± 4.6**
400 ppm	31.3 ± 3.0	32.1 ± 3.6	32.1 ± 3.3	31.9 ± 3.6	32.6± 3.5	32.7 ± 3.6	33.1± 3.7
Significant difference;	*: P ≤ 0.05	* : P ≤ 0.01		Test of Dunnett			

STODI NO. : UGTO ANTMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : FEMALE	[Cr.j:BDF1]		BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS	(SUMMARY)			PAGE: 11
Group Name	Administration week 70	п жеек 74	78	82	86	06	94
Control	33.8± 4.4	34.5± 4.5	34.9± 5.3	34.9± 4.2	34.4± 4.1	34.8± 4.6	35.0± 5.0
100 ррш	35.6± 4.9	36.1 ± 4.9	36.6± 4.8	37.0± 4.5	36.6± 4.6	37.1± 4.9*	$37.3\pm$ 4.8
200 ppm	36.9± 5.0**	37.1± 5.0*	37.0± 5.4	37.7± 4.5*	37.5± 4.7**	37.6± 6.6*	37.1 ± 4.9
400 ppm	33.9± 3.8	34.3± 3.8	34.6 ± 3.8	35.1 ± 4.0	34.6± 4.0	35.2 ± 3.9	35.6± 5.3
Significant difference ;	*: P ≤ 0.05	‡ : P ≤ 0.01		Test of Dunnett			

PAGE: 12							LACORATION AND ADDRESS OF THE PARTY OF THE P	BAIS 4
PAG								
		- - - - -						
							ŧ	
(TATANA)							Test of Dunnett	
							Test	
		3.9	4.1*	6.3*	 4.			
ALL ANIMALS	104	33.7±	37.3±	37.0±	33.9±			
ALI		3.2	4.5**	4.7*	თ			
	102	33.8± 3.	37.6± 4.	36.7± 4.	34.4± 5.9		‡ : P ≤ 0.01	
	Administration week 98			.,	.,		<u>∵</u> ‡	
	inistrati	4.3	4.9**	37.5± 4.6**	34.3 ± 3.5		≤ 0.05	
Crj:BDF1]	Admi 98	33.9±	37.6±	37.5=	34. 3		*:P≤0.05	
2F1/Cr1j[1	rence ;	
ANIMAL : MOUSE BGD2F1/Cr1j[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : FEMALE		o.	w ďc	wďc	කුරු		ınt diffe	
TE TE	Group Name	Control	100 ppm	200 ppm	400 ppm		Significant difference ;	(HAN260)
ANIMAL UNIT REPORT T SEX : FE	Grou							(HAN

TABLE E1

FOOD CONSUMPTION CHANGES AND SURVIVAL ANIMAL NUMBERS : MALE

Av. FC. : g

< >:No. of effective animals, ():No. of measured animals

(BI0040)

MEAN FOOD CONSUMPTION (FC) AND SURVIVAL

STUDY NO. : 0676
ANIMAL : MOUSE BGDZF1/Cr1j[Crj:BDF1]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

	•	Control		100 ррш	Щ		200 ррп	E		400 ppm	E	
Week on Study	Av. FC.	No. of Surviv. <50>	Av. FC.	% of cont. <50>	No. of Surviv.	Av. FC.	% of cont. <49>	No. of Surviv.	Av. FC.	% of cont. <50>	No. of Surviv.	
1	3.8 (50)	50/50	3.7 (50)	26	50/50	3.8 (49)	100	49/49	3.7 (50)	76	50/50	
2	8	_	3.7 (50)	26	20/20	3.8 (49)	100	49/49	3.6 (50)	92	50/50	
က	3.8 (50)	_	3.7 (50)	≥ 97	20/20	3.9 (49)	103	49/49	8	100	50/50	
4	3.9 (50)	_	3.8 (50)	26	20/20	3.9 (49)	100	49/49	3.8 (50)	26	50/50	
2	3.9 (50)	_	3.9 (49)	100	49/50	4.0 (49)	103	49/49	6	100	49/50	
9	4.0 (50)		4.0 (49)	100	49/50	4.0 (49)	100	49/49	6	86	49/50	
2	4.1 (50)	_	4.0 (49)	86	49/50	4.1 (49)	100	49/49	_	86	49/50	
8	4.1 (50)		4.1 (48)	100	48/50	4.1 (49)	100	49/49	_	86	49/50	
6	4.2 (50)		4.2 (48)	100	48/50	4.2 (49)	100	49/49	4.1 (49)	86	49/50	
10	4.1 (50)		4.1 (48)	100	48/50	4.2 (49)	102	49/49	4.1 (49)	100	49/50	
11	4.1 (50)	_	4.0 (48)	86	48/50	4.1 (49)	100	49/49	4.0 (49)	86	49/50	
12	4.4 (50)	_	4.4 (48)	100	48/50	4.3 (49)	86	49/49	4.2 (49)	95	49/50	
13	_	_	2	100	48/20	4.3 (49)	102	49/49	_	102	49/50	
14				86	48/20		100	49/49	4.2 (49)	86	49/50	
18			വ	100	48/50		102	49/49	4.6 (49)	102	49/50	
22				100	48/20		100	49/49	4	86	49/50	
26	4.6 (50)		9	100	48/20	4.7 (49)	102	49/49	2	86	49/50	
30			∞	100	48/20		100	49/49	9	96	49/50	
34			6	100	48/20		100	49/49	4.7 (49)	96	49/20	
္တ	_	_	4.8 (48)	100	48/20		102	49/49	4.6 (49)	96	49/20	
42	4.8 (50)	_		86	48/50		100	49/49	_	96	49/50	
46	4.7 (50)	_	4.6 (48)	86	48/20	4.7 (49)	100	49/49	4.5 (49)	96	49/20	
20	_	_	2	86	48/20	4.7 (48)	86	48/49	_	96	49/20	
54	_			100	46/20		86	48/49	_	94	48/50	
28	8		4.7 (45)	86	45/20	4.9 (48)	102	48/49	4.5 (48)	94	48/50	
62	6			86	44/50		96	48/49	4.5 (48)	85	48/50	
99	0	_		86	44/50		86	47/49	4.7 (48)	94	48/50	
70	5.0 (50)	_		86	44/50	4.9 (47)	86	47/49	4.7 (48)	94	48/50	
74	0	_	6	86	44/50	5.1 (46)	102	47/49	4.8 (47)	96	47/50	
82	2	_	0	96	42/50	5.2 (46)	100	47/49	4.9 (47)	95	47/50	
82	_	_	~	86	40/20	5.2 (47)	86	47/49	5.0 (46)	25	46/50	
98	0	_	4.9 (40)	86	40/20		102	43/49	_	94	45/50	
06	ಣ	_	_	96	37/20	5.2 (41)	86	41/49	_	92	44/50	
24	0	_	6	86	35/20	5.2 (38)	104	38/49	~	96	44/50	
86	0	37/20	4.9 (33)	86	33/20	5.3 (37)	106	37/49	~	86	41/50	
102	4.9 (36)	_	_	102	31/50	_	104	36/49	4.7 (40)	96	40/20	
104	5.1 (30)	_	5.0 (31)	86	31/20	5.2 (34)	102	34/49	5.1 (39)	100	39/20	

TABLE E2

FOOD CONSUMPTION CHANGES AND SURVIVAL ANIMAL NUMBERS : FEMALE

(BI0040)

MEAN FOOD CONSUMPTION (FC) AND SURVIVAL

STUDY NO. : 0676
ANIMAL : MOUSE B6DZF1/Crlj[Crj:BDF1]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

	ĺ							i		inda oot		
W1-	Av. FC.	No. of	Av. FC.	% of	No. of	Av. FC.	% of	No. of	Av. FC.	% of	No. of	
meek on Study	∵ ♥	Surviv. (50)		cont. <49>	Surviv.		cont. <50>	Surviv.		cont. <50>	Surviv.	
1	3.2 (50)	50/50	3.1 (49)	26	49/49	3.1 (50)	97	50/50	3.2 (50)	100	50/50	
2	_	20/20	3.2 (49)	100	49/49	3.2 (50)	100	50/50	3. 2 (50)	100	50/50	
က	_	20/20	3.4 (49)	100	49/49	3.4 (50)	100	50/50	3.4 (50)	100	50/20	
4	_	20/20	3.5 (49)	100	49/49	3.6 (50)	103	20/20	3.5 (50)	100	50/20	
2	3.6 (49)	49/50	3.6 (49)	100	49/49	3.8 (50)	106	50/50	3.6 (50)	100	50/50	
9	_	49/20	3.8 (49)	103	49/49	3.8 (50)	103	50/50	3.7 (50)	100	50/50	
2	_	49/20	3.8 (49)	26	49/49	3.9 (50)	100	20/20	3.9 (50)	100	50/50	
&	_	49/20	3.8 (49)	26	49/49	3.9 (50)	100	50/50	3.8 (50)	26	50/50	
6	_	49/20	3.9 (49)	100	49/49	3.9 (50)	100	50/50	4.0 (50)	103	50/50	
0.	_	49/20	3.8 (49)	26	49/49	3.9 (50)	100	50/50	4.0 (49)	103	49/50	
1	3.8 (49)	49/20	3.7 (49)	26	49/49		100	50/50	3.6 (49)	92	49/50	
[2	_	49/50	4.0 (49)	86	49/49	4.0 (50)	86	50/50	4.0 (49)	86	49/50	
13	_	49/50	3.9 (49)	86	49/49	4.0 (50)	100	50/50	4.0 (49)	100	49/50	
4	_	49/20	3.9 (49)	100	49/49	4.1 (50)	105	50/50	4.1 (49)	105	49/50	
18	_	49/20	4.2 (49)	102	49/49	4.3 (50)	105	50/50	4.3 (49)	105	49/50	
~ ~	_	49/20	4.0 (49)	86	49/49	Ē	102	20/20	4.2 (49)	102	49/50	
	-	49/20	~	86	48/49	ত	100	20/20	4.3 (49)	100	49/50	
o .	-	49/20	4.4 (48)	100	48/49	4.5 (50)	102	20/20	4.4 (49)	100	49/50	
	_	49/50	4.7 (48)	100	48/49		100	49/50	4.6 (49)	86	49/50	
~	_	49/20	4.4 (48)	86	48/49		102	49/50	4.3 (49)	96	49/50	
	_	49/50	4.2 (48)	86 .	48/49		105	49/50	4.2 (49)	86	49/50	
	4.2 (49)	49/20	4.2 (48)	100	48/49	4	102	49/50	4.2 (49)	100	49/50	
_	_	48/20	4.2 (48)	92	48/49		102	49/50	4.3 (48)	86	48/50	
	_	48/20	4.4 (47)	86	47/49	4.5 (49)	100	49/50	4.1 (47)	91	47/50	
~	4.2 (47)	. 47/50	4.4 (47)	105	47/49		107	48/50	4.2 (47)	100	47/50	
01	4.1 (47)	47/50	4.0 (47)	86	47/49	4.2 (48)	102	48/50	4.0 (47)	86	47/50	
,		45/20	4.5 (47)	102	47/49		102	47/50	4.2 (47)	92	47/50	
_	_	45/50	4.4 (46)	86	46/49		102	47/50	4.4 (46)	86	46/50	
€#1	4.5 (45)	45/50	4.5 (44)	100	44/49		102	47/50	4.4 (46)	86	46/50	
80	4.6 (45)	45/20	4.6 (44)	100	44/49	4.5 (46)	86	46/50	4.5 (46)	86	46/50	
~1	4.6 (44)	44/50	4.7 (43)	102	43/49		100	43/50	4.6 (45)	100	45/50	
9	4.4 (44)	44/50	4.5 (42)	102	42/49	4.6 (39)	105	39/20	4.5 (43)	102	43/50	
0	4.6 (42)	42/50	4.8 (38)	104	38/49	4.7 (38)	102	38/20	4.7 (42)	102	42/50	
94	4.5 (41)	41/50	4.7 (36)	104	36/49	9	102	32/50	4.5 (39)	100	39/50	
86	4.5 (37)	37/20	4.8 (34)	107	34/49	5.0 (29)	111	29/20	4.6 (37)	102	37/50	
83	_	32/20	4.6 (29)	105	29/49	4.8 (26)	109	26/50	4.4 (36)	100	36/50	
104	4.5 (31)	31/50	4 6 (97)	109	97/40		107	96/50	(VC) (VV)	101	24/50	

TABLE E3

FOOD CONSUMPTION CHANGES: MALE

UNIT : g REPORT TYPE : A1 104 SEX : MALE							PAG	PAGE:
Group Name	Administration week	on week		The second secon	The second secon			
	1	2	e	4	5	9	7	
Control	3.8± 0.2	3.8 ± 0.2	3.8± 0.3	3.9± 0.3	3.9± 0.3	4.0± 0.2	4.1± 0.3	
100 ppm	3.7 ± 0.3	3.7± 0.3*	3.7 ± 0.4	3.8± 0.5	3.9± 0.3	4.0 + 0.4	4.0 ± 0.4	
200 ррт	3.8± 0.2	3.8± 0.3	3.9 ± 0.3	3.9 ± 0.4	4.0 ± 0.3	4.0 ± 0.3	4.1± 0.3	
400 ppm	3.7± 0.4	3.6± 0.3**	3.8± 0.3	3.8± 0.3**	3.9 ± 0.3	3.9± 0.3	4.0± 0.3	
Significant difference ;	*: P ≤ 0.05	**: P ≤ 0.01		Test of Dunnett				
(HAN260)								BAIS 4

							rage
Group Name	Administration week 8	week 9	10	11	12	13	14
Control	4.1 ± 0.3	4.2± 0.2	4.1 ± 0.3	4.1± 0.3	4.4± 0.3	4.2± 0.2	4.3± 0.2
100 ррш	4.1 ± 0.3	4.2± 0.3	4.1 ± 0.3	4.0± 0.3	4.4± 0.3	4.2± 0.3	4.2± 0.3
200 ppm	4.1± 0.3	4.2± 0.3	4.2± 0.4	4.1± 0.3	4.3± 0.3	4.3 ± 0.3	4.3± 0.3
400 ppm	4.0 ± 0.3	4.1± 0.3	4. 1 ± 0.3	4.0± 0.3*	4.2 ± 0.3	4.3± 0.3	4.2± 0.3
Significant difference ;	*:P≤0.05	* : P ≤ 0.01		Test of Dunnett			

Group Name Administration week 22 26 26 Control 4.5± 0.3 4.5± 0.3 4.6± 0.3 200 ppm 4.5± 0.3 4.5± 0.3 4.6± 0.4 4.6± 0.2 4.5± 0.3 4.6± 0.2 4.5± 0.3 4.5± 0.3 4.6± 0.2					PAGE:
4.5± 0.3 4.5± 0.3 4.6± 4.5± 0.3 4.5± 0.3 4.6± 4.6± 0.2 4.5± 0.3 4.7± 4.6± 0.2 4.4± 0.3 4.7±	22	30	34	38	42
4.5± 0.3 4.5± 0.3 4.6± 4.6± 0.2 4.5± 0.3 4.7± 4.6± 0.2 4.4± 0.3 4.5±	0.3 4.6±	4.8± 0.3	4.9± 0.3	4.8± 0.3	4.8± 0.3
4.6 ± 0.2 4.5 ± 0.3 $4.7\pm$ 4.6 ± 0.2 4.4 ± 0.3 $4.5\pm$	0.3 4.6±	4.8± 0.3	4.9 ± 0.3	4.8± 0.3	4.7 ± 0.3
4.6 ± 0.2 4.4 ± 0.3 $4.5\pm$	0.3 4.7±	4.8± 0.3	4.9 ± 0.3	4.9± 0.4	4.8± 0.3
	0.3 4.5±	4,6± 0.3*	4.7 ± 0.3	4.6± 0.3**	4.6± 0.3**
TO THE THE PROPERTY OF THE PRO					
Significant difference ; $*:P \leq 0.05$ $*_{\!$	* : P ≤ 0.01	Test of Dunnett		**	

	SEX : MALE							PAGE :
$4.7\pm$ 0.3 $4.8\pm$ 0.3 $4.8\pm$ 0.3 $4.8\pm$ 0.3 $4.9\pm$ 0.2 $5.0\pm$ 0.3 $5.0\pm$ 0.3 $4.6\pm$ 0.3 $4.7\pm$ 0.3 $4.8\pm$ 0.3 $4.7\pm$ 0.3 $4.8\pm$ 0.3 $4.9\pm$ 0.3 $4.9\pm$ 0.3 $4.7\pm$ 0.3 $4.7\pm$ 0.3 $4.7\pm$ 0.3 $4.7\pm$ 0.5** $4.9\pm$ 0.4 $4.9\pm$ 0.4 $4.5\pm$ 0.3** $4.5\pm$ 0.3** $4.7\pm$ 0.3** $4.7\pm$ 0.3** $4.7\pm$ 0.3**	Group Name	Administration 46		54	28	62	99	70
4.6± 0.3 4.8± 0.3 4.7± 0.3 4.8± 0.3 4.7± 0.3 4.9± 0.3 4.9± 0.3 4.9± 0.3 4.9± 0.3 4.9± 0.4 4.9± 0.4 4.9± 0.4 4.9± 0.4 4.9± 0.4 4.9± 0.4 4.9± 0.4 4.9± 0.4 4.9± 0.4 4.9± 0.4 4.9± 0.3 4.9± 0.3** 4.7±		4.7± 0.3						
$4.7\pm$ 0.3 $4.7\pm$ 0.3 $4.7\pm$ 0.5** $4.9\pm$ 0.9 $4.9\pm$ 0.3** $4.9\pm$ 0.0 $4.9\pm$ 0								
4.5 \pm 0.3** 4.6 \pm 0.3** 4.5 \pm 0.3** 4.5 \pm 0.3** 4.5 \pm 0.3** 4.7 \pm 0.3** 4.7 \pm 0.3** 4.7 \pm 0.3** 4.7 \pm 0.3**								
* : P ≤ 0.05 ** : P ≤ 0.01								
*: P ≤ 0.05								
			**: P ≤ 0.01		Test of Dunnett			

Group Name	Administration week	week					
	74	78	82	98	06	94	86
Control	5.0 ± 0.4	5.2± 0.4	5.3 ± 0.4	5.0 ± 0.5	5.3士 0.4	5.0± 0.5	5.0± 0.6
100 ppm	4.9± 0.5	5.0± 0.5	5.2± 0.3	4.9± 0.6	5.1 ± 0.6	4.9± 0.6	4.9 ± 0.7
200 ррш	5.1± 0.5	5.2士 0.5	5.2± 0.6	5.1 ± 0.5	5.2± 0.9	5.2± 0.8	5.3± 0.7
400 ppm	4.8± 0.3**	4.9± 0.4**	5.0± 0.6**	4.7 ± 0.4*	4.9± 0.5**	4.8± 0.4*	4.9 ± 0.5
Significant difference ;	*: P ≤ 0.05	‡ : P ≤ 0.01	- The state of the	Test of Dunnett			

Group Name 102 102 104 Control 4.9± 0.9 5.1± 0.8 100 ppm 5.0± 0.6 5.0± 0.6 5.0± 0.6 4.0 ppm 5.1± 0.7 5.2± 0.6 4.0 ppm 7.7± 0.6* 5.1± 0.7	0 7001
Control 4.9± 0.9 5.1± 100 ppm 5.0± 0.6 5.0± 200 ppm 5.1± 0.7 5.2± 400 ppm 4.7± 0.6* 5.1±	
5.0± 0.6 5.0± 5.1± 0.7 5.2±	· δ.
200 ppm 5.1 \pm 0.7 5.2 \pm 400 ppm 4.7 \pm 0.6* 5.1 \pm	9.
4.7± 0.6*	φ.
	7.
Significant difference ; *: P \leq 0.05 **: P \leq 0.01	Test of Dunnett

TABLE E4

FOOD CONSUMPTION CHANGES: FEMALE

REPORT TYPE : A1 104	[<u>a</u>	PAGE: 7
Group Name	Administration week	on week						
	1	2	က	4	5	9	<u>L</u>	
			The state of the s					
Control	3.2± 0.2	3.2 ± 0.3	3.4 ± 0.2	3.5± 0.3	3.6± 0.3	3.7± 0.2	3.9± 0.3	
100 ppm	3.1± 0.3	3.2± 0.2	3.4± 0.2	3.5± 0.2	3.6± 0.3	3.8± 0.2	3.8+ 0.3	
200 ppm	3.1± 0.3	3.2± 0.2	3.4± 0.2	3.6± 0.3	3.8± 0.3*	3.8± 0.3	3.9± 0.3	
400 ррш	3.2± 0.2	3.2± 0.2	3.4± 0.2	3.5± 0.2	3.6± 0.2	3.7± 0.3	3.9± 0.3	
Significant difference;	; *:P≤0.05	☆ : P ≤ 0.01		Test of Dunnett				
(HAN260)		THE TAXABLE PROPERTY OF THE PR					Abbiliance of the control of the con	BAIS 4

Group Name	Administration wook	and the state of t						rage . 8
	8	6	10	11	12	13	14	
Control	3.9± 0.3	3.9± 0.2	3.9± 0.2	3.8± 0.3	4.1± 0.3	4.0± 0.3	3.9± 0.3	
100 ppm	3.84 0.3	3.9± 0.2	3.8± 0.3	3.7 ± 0.3	4.0 ± 0.3	3.9 ± 0.2	3.9 ± 0.3	
200 ppm	3.9± 0.3	3.9± 0.3	3.9 ± 0.3	3.8± 0.3	4.0 ± 0.2	4.0 ± 0.3	4.1± 0.3*	
400 ppm	3.84 0.3	4.0 ± 0.2	4.0± 0.3	3.6± 0.3**	4.0± 0.3	4.0± 0.3	4.1± 0.3**	
Significant difference ;	. P ≤ 0.05	p		Test of Dunnett				

SEX : FEMALE				•			_	PAGE:
Group Name	Administration week 18	week 22	26	30	34	38	42	
Control	4.1± 0.3	4.1 0.3	4.3± 0.4	4.4± 0.4	4.7± 0.4	4.5± 0.4	4.3± 0.4	
100 ppm	4.2± 0.3	4.0± 0.5	4.2± 0.3	4.4± 0.4	4.7 ± 0.4	4.4± 0.3	4.2± 0.5	
200 ррш	4.3± 0.3	4.2 ± 0.4	4.3 ± 0.4	4.5 = 0.4	4.7 ± 0.4	4.6± 0.4	4.5± 0.4	
400 ppm	4.3± 0.4*	4.2 ± 0.3	4.3± 0.3	4.4± 0.4	4.6± 0.5	4.3± 0.4	4.2± 0.4	
		The state of the s						
Significant difference;	*:P≤0.05	** : P ≤ 0.01		Test of Dunnett				
(HAN260)				THE PROPERTY OF THE PROPERTY O	The second secon			BAIS 4

Group Name	Administration wook	Joon a				T THE TAX A STATE OF THE TAX A S	
	46	50	54	58	29	99	70
Control	4.2± 0.5	4.4± 0.4	4.5± 0.4	4.2± 0.4	4.1± 0.5	4.4± 0.4	4.5± 0.4
100 ppm	4.2± 0.3	4.2± 0.4**	4.4± 0.5	4.4± 0.5	4.0± 0.5	4.5± 0.4	4.4 ± 0.7
200 ppm	4.3 ± 0.4	4.5± 0.5	4.5± 0.5	4.5± 0.4*	4.2± 0.5	4.5 ± 0.5	4.6± 0.5
400 ppm	4.2± 0.4	4.3 ± 0.4	4.1± 0.4**	4.2± 0.3	4.0 + 0.4	4.2 ± 0.5	4.4 ± 0.4
				THE PROPERTY OF THE PROPERTY O			
Significant difference;	*: P ≤ 0.05	** : P ≤ 0.01		Test of Numett			

T4 78 86 90 94 98 strol 4.5± 0.5 4.6± 0.5 4.4± 0.5 4.6± 0.5 4.6± 0.5 4.6± 0.6 4.5± 0.6 4.5± 0.6 4.5± 0.6 4.5± 0.6 4.5± 0.6 4.5± 0.6 4.5± 0.6 4.5± 0.6 4.5± 0.6 4.5± 0.6 4.5± 0.6 4.5± 0.6 4.5± 0.7 4.6±	Group Name	Administration week	n wook					TAGE . II
$4.5\pm$ 0.5 $4.6\pm$ 0.5 $4.4\pm$ 0.5 $4.6\pm$ 0.5 $4.5\pm$ 0.6 $4.5\pm$ 0.6 $4.7\pm$ 0.5 $4.7\pm$ 0.5 $4.8\pm$ $4.5\pm$ 0.6 $4.5\pm$ 0.6 $4.6\pm$ 0.5 $4.6\pm$ 0.5 $4.7\pm$ 0.7 $4.8\pm$ $4.4\pm$ 0.5 $4.5\pm$ 0.5 $4.5\pm$ 0.7 $4.6\pm$ 0.7 $4.6\pm$ 0.7 $4.6\pm$ 0.7 0.5 0		74		88	98	06	94	86
$4.5\pm \ 0.6$ $4.6\pm \ 0.6$ $4.6\pm \ 0.6$ $4.7\pm \ 0.6$ $4.7\pm \ 0.5$ $4.8\pm \ 0.5$ $4.6\pm \ 0.5$ $4.6\pm \ 0.5$ $4.7\pm \ 0.7$ $4.6\pm \ 0.5$ $4.7\pm \ 0.7$ $4.5\pm \ 0.5$ $4.6\pm \ 0.5$ $4.6\pm \ 0.5$ $4.6\pm \ 0.5$ $4.6\pm \ 0.7$	Control							4.5 ± 0.5
4.6 ± 0.6 4.5 ± 0.6 4.6 ± 0.5 4.6 ± 0.5 4.7 ± 0.7 4.6 ± 1.0 $5.0\pm 4.4\pm 0.5$ 4.5 ± 0.4 4.6 ± 0.5 4.5 ± 0.6 4.7 ± 0.7 4.5 ± 0.5 4.6 ± 0.5	100 ppm							4.8± 0.8*
4.4 ± 0.5 4.5 ± 0.4 4.6 ± 0.5 4.5 ± 0.6 4.7 ± 0.7 4.5 ± 0.5 $4.6\pm$	200 ppus							5.0± 0.8**
	400 ppm							4.6± 0.7
	Significant difference;	*: P ≤ 0.05	** : P ≤ 0.01		Test of Dunnett			

Administration week 102	
4.4± 0.6 4.5± 0.6	
4.6± 0.6 4.6± 0.5	
4.8± 0.6* 4.8± 0.5	
4.4± 0.6 4.7± 0.5	
Significant difference ; *: P \leq 0.05 **: P \leq 0.01	Test of Dunnett

TABLE F1

HEMATOLOGY: MALE

STUDY NO. : 0676 ANIMAL : MOUSE BGD2F1/Cr1j[Crj:BDF1] MEASURE. TIME : 1 SEX : MALE REPORT TYPE : A1	e bedefi/c _r i l Report	JF1/Cr1j[Crj:BDF1] REPORT TYPE : A1		HEMA ALL	HEMATOLOGY (SUMMARY) ALL ANIMALS (105W)	MMARY) 05W)								PAGE : 1
Group Name	NO. of Animals	RED BLOOD CELL 1 O ^s /µl	L HEMOGLOBIN g/dl	LOBIN	HEMATOCRIT %	RIT	MCV f. 2	- 1111/1744	мсн р g		MCHC g / dl		PLATELET 1 0³∕µl	
Control	30	9.57 ± 0.79	14.2±	1.4	41.5土	3.6	43.4±	1.3	14.8±	0.6	34.0±	0.8	1648±	384
100 ppm	30	9.35± 1.34	13.7±	1.8	40.5±	4.9	43.5 ±	2.4	14.7±	6.0	33.8±	6.0	1724±	260
200 ppm	33	9.43 ± 1.10	14.2±	1.2	41.8±	3.2	44,8±	4.4	15.2±	1.0	33.9+	1.2	1615±	446
400 ppm	39	9.25± 1.29	14.0±	1.9	40.8±	5.2	44.3±	1.8	15.1±	0.5	34.2±	0.9	1595±	344
Significant o	lifference;	Significant difference ; * : P ≤ 0.05	** : P ≤ 0.01	. 01		Vasional	Test of Dunnett	lett						

(HCL070)

	PAGE :						itt	BAIS 4
HEMATOLOGY (SUMMARY) ALL ANTMALS (105W)							**: P \leq 0.01 Test of Dunnett	
Cr.j:BDF1]	REPORT TYPE : A1	RETICULOCYTE %	2.1 + 0.5		2.8+ 2.9	2.7± 2.2	Significant difference ; * : P \leq 0.05	
'6 'SE B6D2F1/Cr1j['	REPORT T	NO. of Animals	30	30	33	39	difference;	
STUDY NO. : 0676 ANIMAL : MOUSE BGDZF1/Crlj[Crj:BDF1] MFASTIRF TTME : 1	SEX : MALE	Group Name	Control	100 ppm	200 ppm	400 ppm	Significant	(HCL070)

HEMATOLOGY (SUMMARY) ALL ANIMALS (105W)	PAGE : PA	17 $62\pm$ 17 $3\pm$ 1 $3\pm$ 2 $0\pm$ 0 $1\pm$ 1	13 $62\pm$ 15 $4\pm$ 6 $2\pm$ 1 $0\pm$ 0 $1\pm$ 1	11 $64\pm$ 12 $4\pm$ 3 $3\pm$ 2 $0\pm$ 0 1 \pm 1	10 $64\pm$ 11 $3\pm$ 2 $3\pm$ 2 $0\pm$ 0 $1\pm$ 2	≦ 0.01 Test of Dunnett
EMATOLOGY (SUMMARY) LL ANIMALS (105W)	0Hd (%)	17	15	12	11	Test
HBMA	Differential WBC NEUTRO LYMP					* : P ≤ 0.01
F1/Cr1;[Cr;:BDF1]	חצ	4. 65± 4. 45	3.74± 2.12	3.37± 1.67	$3.22\pm$ 1.44	
STUDY NO. : 0676 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1] MESURE. TIME : 1 SER : MAIE	NO. Anim	Control 30	100 ppm 30	200 ppm 33	400 ppm 39	Significant difference; *:P≦0.05

TABLE F2

HEMATOLOGY : FEMALE

4						BAIS 4
PAGE	r: g	367	376	364	317	
	PLATELET 1 0³ ∕ µℓ	1149±	∓086	∓686	1119±	
		1.9	1.1	1.5	1.1	
	MCHC g / d2	33.9±	34.2±	34.1±	34.4±	
		0.7	0.7	0.7	0.5	
	MCH p.g	15.2±	15.0±	15.2±	15.1±	-
		3.6	2.1	2. 2	2.1	nett
	MCV f &	44.9±	43.9±	44.5±	44.0±	Test of Dunnett
MMARY) (0547)	RIT	6.3	7.1	4.9	4.6	
HEMATOLOCY (SUMMARY) ALL ANIMALS (105W)	HEMATOCRIT	40.9	40.5±	40.9±	40.8	
HE AL	BIN	2.7	2, 6	1.9	1.8	1
	HEMOGLOBIN g / d2	14.0±	13.9±	$14.0 \pm$	$14.1\pm$	* : P ≤ 0.01
	RED BLOOD CELL 1 O ⁶ /µl	1.77	1.73	1.38	1.17	0.05
F1/Crlj[Crj:BDF1] REPORT TYPE : A1	RED BLOOD 1 O€ / µℓ	9.23±	9.24±	9.25	9.31±	* : P ≤ 0.05
B6D2F1/Cr1j(REPORT T	NO. of Animals	30	27	25	34	fference ;
STUDY NO. : 0676 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1] MEASURE. TIME : 1 SEX : FEMALE REPORT TYPE : A1	Group Name	Control	100 ppm	200 ppm	400 ppm	Significant difference : (HCL070)

STUDY NO. : 0676 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1] MEASUDE TIME : 1	; B6D2F1/Cr1j[C	%j:BDF1]	HEMATOLOGY (SUMMARY) ALL ANIMALS (1054)	
SEX : FEMALE	REPORT TYPE : A1	YPE : A1		PAGE: 5
Group Name	NO. of Animals	RETICULOCYTE %		
Control	30	4.0± 5.1	·	
100 pm	27	3.0± 2.4		
200 pm	25	4.1± 4.6		
400 ppm	34	3.0± 3.3		
Significant d	lifference ;	Significant difference; * : P ≤ 0.05	** : P ≤ 0.01 Test of Dunnett	nett
(HCL070)				BAIS 4

PAGE: 6						
		m	1	1	4	
	OTHER	5±	1+	 	5+2	
		0	0	0	0	
	BASO	#1	- -0	+0	+0	
		82	63	7	8	
	EOSINO	8+1	3+	#I %	3+	t.
		8			8	Test of Dunnett
C	MONO	#I +I	#I #I	3+	3+ +1	Test
HEMATOLOGY (SUMMARY) ALL ANIMALS (1054)	(%	16	10	16	15	
HEMATOLC ALL ANIM	WBC (%)	= 29	+ 99	62±	+ 49	estation -
	Differential)	15	11	14	14	0.01
	Di	25±	27±	31.	767	**: P ≤ 0.01
	ul	13.55	1.05	1.55	2.84	6 0.05
EF1/Crlj[Crj:BDF1] REPORT TYPE : Al	ΨΒC 1 0³∕μℓ	∓66 '9	2.67±	3.36±	3.32±	VII
B6D2F1/Crl. REPORT	NO. of Animals	30	27	52	34	fference ;
STUDY NO. : 0676 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] MEASURE. TIME : 1 SEX : FEMALE REPORT TYPE : A1	Group Name	Control	100 ppm	200 ppm	400 ppm	Significant difference; * : P ≤ 0.05

(HCL070)

TABLE G1

BIOCHEMISTRY: MALE

STUDY NO.: 0676 ANIMAL: MOUSE MEASURE. TIME: 1	B6D2	[Crj:BDF1]			***	BIOCHEMISTRY (SUMMARY) ALL ANIMALS (105W)	(SUMMARY) 105W)								
SEX : MALE	REPORT	REPORT TYPE : A1													PAGE: 1
Group Name	NO. of Animals	TOTAL P g / dl	TOTAL PROTEIN g⁄dl	ALBUMIN g / dl	N	A/G RATIO	TIO	T-BILIRUBIN mg/dl	RUBIN	GLUCOSE mg/dl		T-CHOLESTEROL mg/dk	STEROL	TRIGLYCERIDE mg/dk	ERIDE
Control	30	5.1+	0.5	2.5±	0.3	0.9+	0.1	0.12±	0.02	164土	39	106±	56	47±	24
100 ррп	31	5.4 +	6.0	2.6+	0.5	1.0±	0.1	0.13±	0.03	166±	46	132±	107	48±	23
200 ррш	34	5.3+	9.0	2.6±	0.3	1.0±	0.1*	0.13±	0.04	190±	25**	107±	36	45+	22
400 ppm	39	5.1±	0.4	2.6±	0.2	1.1+	0.1**	0.12±	0.03	188±	35**	101±	. 52	44±	22
Significant difference; *:P ≤ 0.05	ifference;	0 ∀I). 05	** : P ≤ 0.01	01			Test of Dunnett	nnett						

(HCL074)

STUDY NO. : 0676 ANIMAL : MOUSE MEASURE. TIME : 1	B6D2	i[Crj:BDF1]			BIOC ALL	BIOCHEMISTRY (SUMMARY) ALL ANIMALS (105W)	UMMARY) 15W)									
SEX : MALE	REPORT	REPORT TYPE : A1													PAGE:	2
Group Name	NO. of Animals	PHOSPHOLIPID mg/dl	LIPID	AST I U / g	9	ALT I U/2		LDH I U / 2		ALP I U / 2		G-GTP I U / 2		CK IU/2		
Control	30	189±	42	- 74 - 74 - 74 - 74 - 74 - 74 - 74 - 74	26	39∓	37	294 ±	335	239±	251	1 1	1	81+	103	
100 ppm	31	221 ±	137	148±	539	119±	246	504±	959	316±	341	+	83	1 62	92	
200 ppm	34	198±	23	±9 <i>L</i>	29	47±	53	229±	95	258±	256	#1	1	57±	22	
400 ppm	39	182 ±	37	77±	124*	36±	*69	283±	447	230±	218	#	1	52±	30*	
Significant difference ; * : P \leq 0.05	fference ;	* : P ≤ 0.	1. 05	** : P ≤ 0.01	1	The state of the s	T	Test of Dunnett	nett				And the second s			

(HCL074)

STUDY NO. : 0676 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1] MEASURE. TIME : 1	3 B6D2F1/Crlj	[Crj:BDF1]			BIOC ALL	BIOCHEMISTRY (SUMMARY) ALL ANIMALS (105W)	SUMMARY) 35W)							
SEX : MALE		REPORT TYPE : A1												PAGE: 3
Group Name	NO. of Animals	UREA NITROGEN mg/dl		SODIUM m Eq∕2		POTASSIUM m Eq / &	WG .	CHLORIDE m Eq / &		CALCIUM mg/de		INORGAN mg/d2	INORGANIC PHOSPHORUS	
Control	30	25.3± 9.9		153±	4,	4.2±	0.3	122±	ო	8. 8.	0.4	6.8	0.9	
100 ppm	31	25.4± 11.9		154±	2	4.1±	0.5	121±	4	9.0 +	0.7	6.7±	1.2	
200 ppm	34	22.6± 6.0		153±	ಣ	4.3±	0.4	122±	က	8.8+	0.4	€.7±	6.0	
400 ppm	39	24.4± 16.6*		153±	2	4.3±	0.5	122±	2	8.7±	0.3	6.5±	2. 3*	
Sionificant d	lifforence .	Significant difference * * 0 < 0.05	\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	100			£	9						
(HCL074)				70.01				Test of Dominett	115					BATS A
														# crva

TABLE G2

BIOCHEMISTRY: FEMALE

STUDY NO. : 0676 ANIMAL : MOUSE WEASIDE TIME : 1	: 0676 : MOUSE B6D2F1/Cr1j[Crj:BDF1]	[Crj:BDF1]		•	B	BIOCHEMISTRY (SUMMARY) ALL ANIMALS (105W)	(SUMMARY) 105W)								
SEX : FEMALE		REPORT TYPE : A1													PAGE:
Group Name	NO. of Animals	TOTAL PROTEIN g / dl	OTEIN	ALBUMIN g / dl		A/G RATIO	IIO	T-BILIRUBIN mg/dl	RUBIN	GLUCOSE mg/dl		T-CHOLE mg/dl	T-CHOLESTEROL mg/d2	TRIGLYCERIDE mg/dl	ERIDE
Control	30	5.1+	0.4	2.5士	0.3	1.0±	0.2	0.12±	0.02	121±	27	79.∓	25	. 32±	17
100 ppm	27	5.2	0.5	2.7±	0.3	1.1±	0.2	0.13±	0.07	128±	53	81±	45	27±	19
200 ppm	25	5.6+	1.7	2.5	0.2	1.0±	0.2	0.15±	0.17	126±	26	78±	34	37±	30
400 ppm	34	5.1±	0.4	2.6+	0.2	1.1	0.2	$0.12\pm$	0.03	134±	32	75±	26	28±	19
Significant difference ; *: P ≤ 0.05	ifference ;	* : P ≤ 0.0		*# : P ≤ 0.01			*	Test of Dunnett	nnett						

(HCL074)

STUDY NO. : 0676 ANIMAL : MOUSE	: 0676 : MOUSE B6D2F1/Crlj[Crj:BDF1]	j[Cr.j:BDF1]				BIOCHEMISTRY (SUMMARY) ALL ANIMALS (105W)	SUMMARY) 05W)									
SEX : FEMALE		REPORT TYPE : A1													PAGE:	2
Group Name	NO. of Animals	PHOSPHOLIPID mg/dl	OLIPID	AST I U / &	8	ALT I U / g		LDH I U / g	ā	ALP I U / g	8	6-6TP I U / 2		CK I U / g	2	
Control	30	135±	33	109 ±	62	51±	62	220 ±	181	305±	102	1+	1	117±	155	
100 ppm	27	149±	74	108±	91	46+	47	422±	961	328±	130	2+	4	132±	300	
200 ppm	25	135±	43	110±	81	∓89	83	344±	562	∓982	146	11	-	109	108	
400 ppm	34	135±	45	109	78	43 +1	30	329±	491	315±	157	#1	1	127±	291	÷
A P C C C C C C C C C C C C C C C C C C						TO 1.00 TO 1.0										Productions
Significant difference ; * : P \leq 0.05	ifference ;	* · P 🛇). 05	★ : P ≤ 0.01				Test of Dunnett	nett							

(HCL074)

STUDY NO. : 0676 ANIMAL : MOUSE BGDZFI/Crij[Crj:BDF1] MEASURE. TIME : 1	g B6D2F1/CrIj	[Crj:BDF1]		B.	BIOCHEMISTRY (SUMMARY) ALL ANIMALS (105W)	SUMMARY) 05W)							
SEX : FEMALE		REPORT TYPE : A1										PAGE :	9 : 1
Group Name	NO. of Animals	UREA NITROGEN	SODIUM m.Eq./ &	ē	POTASSIUM m.Eq./ &	NO.	CHLORIDE m Eq / 2		CALCIUM mg/dl	_	INORGANIC PHOSPHORUS	HOSPHORUS	
Control	30	25.6 ± 53.4	152±	က	4.1	0.9	121 ±	e	8.9+	0.4	6.4± 3.7	7	
100 ppm	27	16.4± 6.4	152±	87	3.9+	0.5	121±	23	9°0 +	0.5	6.4 ± 1.2	2	
200 ppm	52	20.0± 20.7	152±	82	4. 0 ±	0.4	121±	73	9.0∓	0.6	$6.6\pm$ 2.1	1	
400 ppm	34	17.5± 11.8	151±	63	4.1±	0.4	121±	2	8.7±	0.4	6.2 ± 1.0	0	
Significant difference ;	lifference ;	* : P ≤ 0.05	** : P ≤ 0.01	1		Ę	Test of Dunnett	1 1					
(HCL074)						THE PERSON NAMED IN COLUMN TWO IS NOT THE PERSON NAMED IN COLUMN TWO IS NAMED IN COLUMN TW							BAIS 4

TABLE H1

URINALYSIS: MALE

NO of ph No of Animals So 6.0 6.5 7.0 7.5 8.0 8.5 CHI Protein CHI CHI	MEASURE, TIME: 1 SEX: MALE	TIME: 1 REPORT TYPE: A1	PE : A	1 11											PAGE:
36 0 2 5 6 11 8 4 0 0 26 7 3 0 36 0 0 0 0 0 4 29 3 0 0 0 0 0 3 3 0 0 0 0 0 0 0 0 0 0 0	Group Name	NO. of Animals	5.0	6.0 (9.5	7.0 7.	5 8	1.0 8.		. 2+ 3+ 4+	CHI	2+ 3+ 4+	3+ 4+	Occult blood HI - ± + 2+ 3+	3+ CHI
32 0 1 4 6 5 13 3 0 0 3 18 10 1 0 32 0 0 0 0 0 0 9 22 1 0 0 0 0 0 3 3 7 0 0 0 0 0 0 0 0 0 0 0 0	Control	36	0	23	ιç				<u></u>			0 0 0 0 98		32 0 0 0	4
37 0 2 7 1 7 19 1 0 5 29 3 0 0 8 37 0 <td>100 ррш</td> <td>32</td> <td>0</td> <td></td> <td>4</td> <td></td> <td></td> <td></td> <td>~</td> <td></td> <td></td> <td>0 0 0</td> <td>1 0 0</td> <td>29 2 0 1</td> <td>0</td>	100 ррш	32	0		4				~			0 0 0	1 0 0	29 2 0 1	0
40 0 0 3 3 11 16 7 0 1 26 12 1 0 40 0 0 0 0 1 1 35 4 0 0 0	200 ppm	37	0	2	7	1	7 1	9 1		5 29 3 0 0	*	0 0 0 0	2 0 0	35 1 0 0	1
	400 ppm	40	0	0	က					0 1 26 12 1 0			1 35 4 0 0 0	36 0 1 0 3	က
Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of CHI SQUARE	Significant di	fference ;	*	A). 05	*	- d	VI 0	01		Test	of CHI SQUARE			

						Test of CHI SQUARE
UKINALYSIS	11					**: P ≤ 0.01 Test of C
ZF1/Cr1j[Crj:BDF1] REPORT TYPE : A1	Urobilinogen ± + 2+ 3+ 4+ CHI	0 0 0 0 98	32 0 0 0 0	37 0 0 0 0	40 0 0 0 0	
ANTMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] MEASURE. TIME : 1 SEX : MALE REPORT TYPE : A1	Group Name NO. of Animals	Control 36	100 ppm 32	200 ppm 37	400 ppm 40	Significant difference ; * : P ≤ 0.05

TABLE H2

URINALYSIS : FEMALE

TOWN . WO			Į		Ī				THE PROPERTY OF THE PROPERTY O				PAGE:
Group Name	NO. of Animals	5.0	6.0	6.5	7.0.7	7.5 8	pH 5.0 6.0 6.5 7.0 7.5 8.0 8.5	CHI	Protein — ± + 2+ 3+ 4+ CHI	Glucose	Ketone body - ± + 2+ 3+ 4+ CHI	0ccult blood [- ± + 2+ 3+ CHI	IH
Control	34	0	2	ന	2	8 11	12 7		0 25 5 3 1 0	34 0 0 0 0 0	23 3 8 0 0 0	32 0 0 1 1	
100 ppm	30	0			9	6	2 9		0 20 7 3 0 0	30 0 0 0 0 0	17 7 5 1 0 0	29 0 1 0 0	
200 ppm	56	0	-	က	4	9	8 4		0 14 10 1 1 0	26 0 0 0 0 0	19 3 4 0 0 0	25 0 0 1 0	
400 ррв	36	0	0	က	7 1	11 1	1 4		0 11 12 11 2 0 **	36 0 0 0 0 0	11 6 8 9 2 0 **	31 0 0 2 3	
Significant difference ;	ifference ;		*: P ≤ 0.05	0.05	*		* : P ≤ 0.01		1seI	Test of CHI SQUARE			

	PAGE: 4						BAIS 4
							Test of CHI SQUARE
							Test
URINALYSIS							
							** : P ≤ 0.01
		CHI					#
Crj:BDF1]	YPE : A1	Urobilinogen ± + 2+ 3+ 4+ CHI	34 0 0 0 0	30 0 0 0 0	26 0 0 0 0	36 0 0 0 0	*: P ≤ 0.05
B6D2F1/Cr1j[REPORT TYPE : A1	NO. of Animals	34	30	26	36	ifference ;
STUDY NO. : 0676 ANIMAL : MOUSE BEDZF1/Cr1j[Crj:BDF1] MEASURE. TIME : 1	SEX : FEMALE	Group Name	Control	пад 100	200 ррт	400 ppm	Significant difference ; (HCL101)

TABLE J1

ORGAN WEIGHT, ABSOLUTE : MALE

PAGE:	LUNGS KIDNEYS	± 0.112 0.712± 0.262	± 0.103 0.685± 0.246	± 0.064 0.683± 0.050	± 0.071 0.704± 0.332
		0.022 0.221±	0.031 0.217±	0.023 0.214±	0.026 0.213±
UMMARY)	HEART	38 0.229±	40 0.225±	35 0.231±	45 0.217±
ORGAN WEIGHT:ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (105W)	TESTES	0.208± 0.038	0.210± 0.040	0.204 ± 0.035	0.210± 0.045
ORGAN SURVIT	ADRENALS	0, 011± 0, 002	0.011± 0.003	0.011± 0.002	0.011 ± 0.002
j[Cr.j:BDFl]	Body Weight	45.8± 7.6	44.9± 8.6	46.5± 6.5	44.4± 5.5
e bedzfi/c _r i	NO. of Animals	30	31	34	39
STUDY NO. : 0676 ANTMAL : MOUSE BEDZF1/Crlj[Crj:BDF1] REPORT TYPE : Al SEX : MALE UNIT: g	Group Name	Control	100 ppm	200 ppm	400 ppm

BAIS 4

Test of Dunnett

*****★: P ≤ 0.01

Significant difference ; * : $P \le 0.05$

(HCL040)

PAGE: 2						tieut
ORCAN WEIGHT:ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (105W)	BRAIN	0.462± 0.019	0.460 ± 0.016	0.458± 0.019	0.456± 0.016	Test of Dunnett
ORGAN 1 SURVIV	LIVER	1.623 ± 0.281	2.080 ± 1.054	1.791 ± 0.567	1.679 ± 0.471	** : P ≤ 0.01
[Cr j: BDF1]	SPLEEN	0.163± 0.340	0.192 ± 0.449	0.102 ± 0.123	0.276 ± 0.781	*: P ≤ 0.05 **
STUDY NO. : 0676 ANUMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 SEX : MALE UNIT: g	Group Name NO, of Animals	Control 30	. 100 ppm 31	200 ppm 34	400 ppm 39	Significant difference ;

(HCL040)

TABLE J2

ORGAN WEIGHT, ABSOLUTE: FEMALE

NO. of Animals Body Weight ADRENALS OVARIES HEART LUNGS KIDNESS ontrol 30 29.1± 3.4 0.015± 0.003 0.201± 0.557 0.174± 0.026 0.213± 0.098 0.487± 0.219 0.219 00 ppm 27 33.2± 3.8** 0.015± 0.004 0.061± 0.067 0.043± 0.067 0.179± 0.023 0.196± 0.015 0.719 00 ppm 34 30.1± 4.5 0.013± 0.003 0.063± 0.060 0.175± 0.024 0.024 0.185± 0.024 0.196± 0.015 0.199± 0.018	STUDY NO. : 0676 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 SEX : FEMALE FAMILE	: B6D2F1/Cr1j	.Cr.j:BDF1]		ORGAN WE SURVIVAL	ORGAN WEIGHT:ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (105W)	FE (SUMMARY) JSW)							
Control 30 29.1± 3.4 0.015± 0.0201± 0.557 0.174± 0.026 0.213± 0.098 0.487± 0.219 100 ppm 27 33.2± 3.8** 0.015± 0.061± 0.061± 0.043 0.182± 0.034 0.186± 0.015 0.017 200 ppm 25 31.9± 4.6* 0.014± 0.007 0.079± 0.067 0.179± 0.023 0.196± 0.027 0.196± 0.027 0.196± 0.027 0.196± 0.027 0.196± 0.027 0.196± 0.027 0.196± 0.027 0.196± 0.027 0.196± 0.027 0.196± 0.027 0.196± 0.027 0.196± 0.027 0.196± 0.027 0.196± 0.027 0.196± 0.027 0.196± 0.027 0.196± 0.027 0.196± 0.019 0.196 0.027 0.196± 0.019 0.027 0.027 0.027 0.027 0.027 0.027 0.027 0.027 0.027 0.	Group Name	NO. of Animals	Body Weight		NALS	OVARI	ŒS	HEART		LUNGS		KIDNE	YS	PAGE: 3
100 ppm27 $33.2\pm$ 3.8**0.015±0.061±0.061±0.0430.182±0.0340.186±0.0150.458±0.071200 ppm25 $31.9\pm$ 4.6*0.014±0.0020.079±0.0670.179±0.0230.196±0.0270.503±0.241400 ppm3430.1±4.50.013±0.063±0.063±0.0500.175±0.0240.194±0.0180.459±0.138400 ppm3430.1±4.50.013±0.0030.063±0.0500.175±0.0240.194±0.0180.459±0.138	Control	30	29.1± 3.4	0.015土			0.557	0.174±	0.026	0.213士	0.098	0. 487±	0.219	
200 ppm 25 $31.9\pm$ 4.6* $0.014\pm$ 0.002 $0.079\pm$ 0.067 $0.179\pm$ 0.023 $0.196\pm$ 0.027 $0.503\pm$ 0.241 400 ppm 34 $30.1\pm$ 4.5 $0.013\pm$ 0.003 $0.063\pm$ 0.050 $0.175\pm$ 0.024 $0.194\pm$ 0.018 $0.459\pm$ 0.138 $0.459\pm$ 0.138 $0.194\pm$ 0.018 $0.459\pm$ 0.138 $0.194\pm$ 0.019	100 ppm	27	33.2± 3.8₩		0.004	0.061±	0.043	0.182±	0.034	0.186±	0.015	0.458±	0.071	
400 ppm 34 $30.1\pm$ 4.5 $0.013\pm$ 0.003 $0.063\pm$ 0.050 $0.175\pm$ 0.024 $0.194\pm$ 0.018 $0.459\pm$ 0.138 $1.199\pm$ 0.013 $1.199\pm$ 0.013 $1.199\pm$ 0.013 $1.199\pm$ 0.013 $1.199\pm$ 0.014 $1.199\pm$ 0.015 $1.199\pm$ 0.015 $1.199\pm$ 0.015 $1.199\pm$ 0.015 $1.199\pm$ 0.015 $1.199\pm$ 0.017 $1.199\pm$ 0.019 $1.199\pm$ 0.0	200 ppm	25	31.9± 4.6*	0.014±	0.002	€ 0.079	0.067	0.179±	0.023	$0.196\pm$	0.027	0. 503 ±	0.241	
Lificant difference ; *: P \leq 0.05 **: P \leq 0.01	400 ppm	34	30.1 ± 4.5	0.013±	0.003	$0.063\pm$	0.050	0.175±	0.024	$0.194\pm$	0.018	0.459±	0. 138	
	Significant d	lifference;	* : P ≤ 0.05	** : P ≤ 0.01			Test	of Dunnett						

ORGAN WEIGHT: ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (105W)	BRAIN	0.483 ± 0.018	0.490 ± 0.016	0.474 ± 0.016	0.483士 0.018	Test of Dunnett
ORG SUR	v LIVER	0.276 1.438 ± 0.248	0.218 1.731 ± 0.979	0.244 1.715± 1.070	0.148 1.417± 0.269	* : P ≤ 0.01
SIUDI NV. : UO/O ANIMAL : MOUSE BEDZF1/Crlj[Crj:BDF1] REPORT TYPE : A1 SEX : FEMALE UNIT: g	SPLEEN	0.246士 0	0.202± 0	0.232± 0	0.173± 0	e; *:P ≤ 0.05
AOUSE BEDZF1/	NO. of Animals	:01 30			opm 34	Significant difference ;
ANIMAL : WE ANIMAL : ME REPORT TYPE : SEX : FEMALE UNIT: &	Group Name	Control	100 ppm	200 ppm	400 ppm	Significa

BAIS 4

TABLE K1

ORGAN WEIGHT, RELATIVE: MALE

Group Name NO. of Body Weight Animals (g) Control 30 45.8± 7.6	ADRENALS 0.024± 0.007	TESTES				!
Animals Antimals Articl 30 46	ADVENTED 0.024± 0.007	153153	ec. ci.			PAGE: 1
30	0.024± 0.007	THE PERSON NAMED AND ADDRESS OF THE PERSON NAMED AND ADDRESS O	HEAKT	LUNGS	KIDNEYS	
		0.469土 0.132	$0.511\pm\ 0.090$	0.513± 0.376	1.624土 0.856	
100 ppm 31 44.9 ± 8.6	0.025± 0.010	$0.485\pm\ 0.136$	0.515± 0.112	0.519± 0.344	1.601± 0.814	
200 ppm 34 46.5± 6.5	0.023± 0.007	0.448± 0.108	0.501± 0.056	0.476± 0.218	1. 498± 0. 264	
400 ppm 39 44.4± 5.5	0.024± 0.006	0.476± 0.110	0.491 ± 0.059	0.484± 0.158	1.634± 1.034	
Significant difference ; *: P ≤ 0.05 **: P ≤ 0.01	≤ 0.01	Test o	Test of Dunnett			

3. 605 ± 0.717 1.039 ± 0.195 3. 605 ± 0.717 1.039 ± 0.195 3. 241 5. 125 ± 3. 803 1.064 ± 0.231 3. 325 3. 923 ± 1.549 1.004 ± 0.160 ** : P ≤ 0.01 ** : P ≤ 0.01 Took of Purmett	REPORT TYPE: A1 SEX: MALE UNIT: %			T I I I I I I I I I I I I I I I I I I I		PAGE: 2
0.392 ± 0.922 3.605 ± 0.717 1.039 ± 0.195 0.494 ± 1.241 5.125 ± 3.803 1.064 ± 0.231 0.234 ± 0.325 3.923 ± 1.549 1.004 ± 0.160 0.727 ± 2.271 3.862 ± 1.513 1.040 ± 0.127	Group Name	NO. of Animals	SPLEEN	LIVER	BRAIN	
0.494 ± 1.241 5.125 ± 3.803 1.064 ± 0.231 0.234 ± 0.325 3.923 ± 1.549 1.004 ± 0.160 0.727 ± 2.271 3.862 ± 1.513 1.040 ± 0.127 0.727 ± 2.271	Control		0.392± 0.922	3.605± 0.717	1.039土 0.195	
0.234 ± 0.325 3.923 ± 1.549 1.004 ± 0.160 0.727 ± 2.271 3.862 ± 1.513 1.040 ± 0.127 0.727 ± 0.05 0.05	100 ppm		0.494± 1.241	5.125士 3.803	1. $064\pm\ 0.231$	
0.727 ± 2.271 3.862 ± 1.513 1.040 ± 0.127 $*: P \leq 0.05$ $**: P \leq 0.01$	200 ppm	34	$0.234\pm\ 0.325$	$3.923\pm\ 1.549$	$1.004\pm\ 0.160$	
*:P \ 0.05	400 ppm	39	0.727 ± 2.271	$3.862\pm\ 1.513$	1.040 ± 0.127	
	Significant o	difference;	*: P ≤ 0.05 *	P ≤ 0.01	Test of Dunnett	

TABLE K2

ORGAN WEIGHT, RELATIVE : FEMALE

Group Name NO. of Animals Body Weight ADRENUES HEART LIDNGS KIDNEYS Control 30 29.1± 3.4 0.051± 0.013 0.655± 1.732 0.607± 0.123 0.744± 0.364 1.710± 0.932 100 ppm 27 33.2± 3.8** 0.044± 0.013 0.184± 0.132 0.549± 0.094 0.566± 0.065** 1.382± 0.179* 200 ppm 25 31.9± 4.6* 0.044± 0.008 0.258± 0.246 0.573± 0.108 0.631± 0.144 1.645± 1.052 400 ppm 34 30.1± 4.5 0.045± 0.013 0.208± 0.160 0.594± 0.119 0.658± 0.102 1.549± 0.443	ANIMAL : MOUSE BEDZF1/Crlj[Crj:BDF1] REPORT TYPE : Al SEX : FEMALE UNIT: %	SE BGDZF1/Crlj	[Cr.j:BDF1]	SURVIV	SURVIVAL ANIMALS (105W)				. 15V4
$ 29.1 \pm 3.4 \qquad 0.051 \pm 0.013 \qquad 0.655 \pm 1.732 \qquad 0.607 \pm 0.123 \qquad 0.744 \pm 0.364 $ $ 33.2 \pm 3.8 ** \qquad 0.044 \pm 0.013 \qquad 0.184 \pm 0.132 \qquad 0.549 \pm 0.094 \qquad 0.566 \pm 0.065 ** $ $ 31.9 \pm 4.6 * \qquad 0.044 \pm 0.008 \qquad 0.258 \pm 0.246 \qquad 0.573 \pm 0.108 \qquad 0.631 \pm 0.144 $ $ 30.1 \pm 4.5 \qquad 0.045 \pm 0.013 \qquad 0.208 \pm 0.160 \qquad 0.594 \pm 0.119 \qquad 0.658 \pm 0.102 $ $ ** : P \leq 0.05 \qquad ** : P \leq 0.01 $ Test of Durnett	Group Name	NO. of Animals	Body Weight (g)	ADRENALS	OVARIES	HEART	TUNGS	KIDNEYS	race .
$33.2\pm 3.8 **$ 0.044 ± 0.013 0.184 ± 0.132 0.549 ± 0.094 $0.566\pm 0.065 **$ $31.9\pm 4.6 *$ 0.044 ± 0.008 0.258 ± 0.246 0.573 ± 0.108 0.631 ± 0.144 0.045 ± 0.013 0.208 ± 0.160 0.594 ± 0.119 0.658 ± 0.102 $*: P \leq 0.05$ $**: P \leq 0.01$	Control		29.1+ 3.4	0.051 ± 0.013	0.655± 1.732	0.607± 0.123	0.744± 0.364	1.710± 0.932	·
$31.9\pm$ 4.6* $0.044\pm$ 0.008 $0.258\pm$ 0.246 $0.573\pm$ 0.108 $0.631\pm$ 0.144 $0.049\pm$ 0.045 $0.045\pm$ 0.013 $0.208\pm$ 0.160 $0.594\pm$ 0.119 $0.658\pm$ 0.102 $0.594\pm$ 0.01 $0.594\pm$ 0.01 $0.594\pm$ 0.01 $0.594\pm$ 0.01 $0.594\pm$ 0.01 $0.594\pm$ 0.01 $0.658\pm$ 0.02	100 ррш			0.044土 0.013	0.184土 0.132	0.549± 0.094	0.566± 0.065**	1.382± 0.179*	
$30.1\pm$ 4.5 $0.045\pm$ 0.013 $0.208\pm$ 0.160 $0.594\pm$ 0.119 $0.658\pm$ 0.102 $*: P \leq 0.05$ $*: P \leq 0.01$ Test of Dunnett	200 ррт			0.044± 0.008	0.258± 0.246	0.573± 0.108	0.631 ± 0.144	1.645士 1.052	
*: P ≤ 0.05 **: P ≤ 0.01	400 ррш		30.1± 4.5	$0.045\pm\ 0.013$	0.208± 0.160	0.594± 0.119	0.658± 0.102	$1.549\pm\ 0.443$	
	Significant	difference ;		# : P ≤ 0.01	Test	of Dunnett			

REPORT 1 SEX : FE UNIT: %	SEX: FEMALE UNIT: %					PAGE: 4
Group Name		NO. of Animals	SPLEEN	LIVER	BRAIN	
	Control	30	0.892土 1.154	$4.981\pm\ 0.945$	1. 682 ± 0. 194	
	100 ррш	27	0.599土 0.594	$5.181\pm\ 2.653$	I. 494± 0. 180**	
	200 ppm	25	0.777 ± 0.883	5.499± 3.664	1.516± 0.210*	
	400 ppm	34	$0.572\pm\ 0.454$	4.760± 0.864	$1.642\pm\ 0.267$	
Sign	Significant difference ;	ference ;	*: P ≤ 0.05 **:	**: P ≤ 0.01	Test of Dunnett	

TABLE L1

HISTOPATHOLOGICAL FINDINGS:

NON-NEOPLASTIC LESIONS: MALE

ALL ANIMALS

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

PAGE : 1	400 ppm 50 1 2 3 4 (%) (%) (%)
,	200 ppm 49 1 2 3 4 (%) (%) (%)
HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)	100 ppm 50 1 2 3 4 (%) (%) (%) (%)
HISTOPATHOLOGICAL FINDINGS :N ALL ANIMALS (0-105W)	Group Name Control No. of Animals on Study 50 Grade 1 2 3 4 (%) (%) (%) (%) (%)
STUDY NO. : 0676 ANIMAL : MOUSE BGDZF1/Cr1j[Crj:BDF1] REPORT TYPE : A1 SEX : MALE	OrganFindings

<pre>{Integumentary system/appandage) skin/app ulcer squamous cell hyperplasia subcutis inflammation asal cavit</pre>	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	(49) (4) (2) (0) (0) (0) (2) (0) (0) (0) (0) (2) (0) (0) (0) (0) (49) (0) (0) (0) (0) (0)	(50) 0 1 0 0) (2) (0) (0 0 0 0) (0) (0) ((50) 0 0 0 0) (0) (0) (
	(50) (50) 0 0 0 4 2 0 0 (0) (0) (0) (8) (4) (0) (0)	(49) 11 35 0 0 ** (22) (71) (0) (0)	<pre></pre>
mineralization		3 0 0 0 0 (9)	1 0 2) (0) (
inflammation			

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

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

(HPT150)

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

Croup Name	1				
y system) (50) eosinophilic change:olfactory epithelium 24 2 0 eosinophilic change:respiratory epithelium 17 0 0 inflammation:respiratory epithelium 1 0 0 inflammation respiratory metaplasia:olfactory epithelium 24 0 0 respiratory metaplasia:gland 36 0 0 respiratory metaplasia:gland 36 0 0	Animals on Study 50 (%) (%) (%) (%) (%)	100 ppm 50 1 2 3 4 (%) (%) (%)	200 ppm 49 1 2 3 4 (%) (%) (%) (%)	400 ppm 50	(%)
cosinophilic change:olfactory epithelium 24 2 0 eosinophilic change:respiratory epithelium 17 0 0 inflammation:respiratory epithelium 1 0 0 respiratory metaplasia:olfactory epithelium 24 0 0 respiratory metaplasia:gland 36 0 0 respiratory metaplasia:gland 36 0 0					
17 0 0 (34) (0) (0) (1 0 0 (2) (0) (0) (24 0 0 (48) (0) (0) (36 0 0 (72) (0) (0) ($\langle 50 \rangle$ 24 2 0 (48) (4) (0) (<50> 27 0 0 0 (54) (0) (0) (0)	<49> 13 1 0 0 (27) (2) (0) (0)	<pre></pre>	0 (0
1 0 0 (2) (0) (0) (24 0 0 (48) (0) (0) (36 0 0 (72) (0) (0) (17 0 0 (34) (0) (0) (17 0 0 0 (34) (34) (3) (3) (3)	40 2 0 0 *** (82) (4) (0) (0)	38 1 0 (76) (76) (2) (0) (** (0
24 0 0 (48) (9) (9) (9) (9) (72) (9) (9) (9) (9) (9) (9) (9) (9) (9) (9	1 0 0 2 2) (0) (0) (3 0 0 0 0 (9)	0 0 0 0 0	0 (0
36 0 0 (72) (72) (9) (9)	24 0 0 (48) (48) (60) (60) (60)	24 0 0 0 (48) (48) (60) (60)	38 0 0 0 *** (78) (0) (0) (0)	44 0 0 (88) (9) (9) (** (0
	0 0 0	39 1 0 0 (78) (2) (0) (0)	36 3 0 0 (73) (73) (6) (0)	39 6 0 (78) (12) (0) (* (0
squamous cell metaplasia:respiratory epithelium 100000 (2) (0) (0) (0)	1 0 0 (2) (3) (4) (5)	1 0 0 0 (2) (2) (3) (4)	12 0 0 0 ** (24) (0) (0) (0)	18 2 0 (36) (4) (0) (* (0
ulcer:respiratory epithelium 0 0 0 0 0 0 0 0 0 (\cdot 0) (0) (0) (0)	0 0 0 0		1 0 0 0 (2) (2) (3) (3)	0 0 1 (0) (0) (2) (0 (0
transitional cell hyperplasia 0 0 0 0 0 0 0 (0) (0) (0) (0) (0)	0 0 0		1 0 0 0 (2) (2) (3) (4)	1 0 0 (2) (2) (3) (4) (5) (4)	0 (0
Grade 1: Slight 2: Moderate 3: Marked 4: Severe $\langle a \rangle$ a: Number of animals examined at the site b : Number of animals with lesion (c) c: b/a * 100 Significant difference; *: P \leq 0.01 Test of Chi Square	farked 4:9				

(HPT150)

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

STUDY NO. : 067 ANIMAL : MOU REPORT TYPE : A1 SEX : MAL	: 0676 : MOUSE B6D2F1/Cr1j[Crj:BDF1] : A1 : MALE	H A	HISTOPATHOLOGICAL FINDINGS :N ALL ANIMALS (0-105W)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)		. PAGE :	ന
Organ	Findings	Group Name No. of Animals on Study Grade	Control 50 4 (%) (%) (%) (%)	100 ppm 50 (%) (%) (%) (%)	200 ppm 49 1 2 3 4 (%) (%) (%) (%)	400 ppm 50 1 2 3 4 (%) (%) (%) (%)	
{Respiratory system}	system)					110000000000000000000000000000000000000	
nasal cavit	xanthogranuloma		<50> (0) (0) (0) (0) (0)	(0)(0)(0)(0) 0 0 0 0 0 0 0 0	<49> 1 0 0 0 (2) (0) (0) (0)	(0)(0)(0)(0) 0 0 0 0 0 0 0 0	
	atrophy:olfactory epithelium			2 2 0 0 (4) (4) (0) (0)	18 29 0 0 ** (37) (59) (0) (0)	23 26 0 0 ** (46)(52)(0)(0)	v
	necrosis:respiratory epithelium			1 0 0 0 (2) (3) (4) (4)		(0)(0)(0)(0)	
nasopharynx	eosinophilic change		<50> 1 0 0 0 (2) (0) (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)	<49> 5 0 0 0 (10) (0) (0) (0)	(0)(0)(0)(0) 0 0 0 0 0 0 0 0	
lung	congestion		<50> (0) (0) (0) (0)	(0)(0)(0)(0) 0 0 0 0 0 0 0 0	(49) 1 0 0 0 (2) (0) (0) (0)	<50> 0 1 0 0 (0) (2) (0) (0)	
	hemorrhage		0 1 0 0 (0) (0) (0) (0)				
	inflammatory infiltration		1 0 0 0 (2) (2) (3) (4) (5)	1 0 1 0 (2) (3) (3) (4)	3 1 0 0 (6) (2) (0) (0)	0 1 0 0 (0) (0) (0) (0)	
Grade 1 : Slight <a> a : Number b b : Number (c) c c b / a * Significant difference;	2 : Moderate of animals examined of animals with lesi 1100 # : P ≤ 0.05	3 : Marked 4 : 9 at the site .on ** : P ≤ 0.01 Test of Chi	Severe i Square				

**: P ≤ 0.01

(HPT150)

4 : Severe

3 : Marked

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

STUDY NO. : 0676 ANIMAL : MOUSE BEDZF1/Cr1j[Crj:BDF1] REPORT TYPE : A1 SEX : MALE	HISTOPATHOLOGICAL FINDINGS :N ALL ANIMALS (0-105W)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)	W	PAGE:
OrganFindings	Group Name No. of Animals on Study Grade (%) (%) (%) (%)	100 ppm 50 1 2 3 4 (%) (%) (%)	200 ppm 49 1 2 3 4 (%) (%) (%) (%)	400 ppm 50 1 2 3 4 (%) (%) (%)
(Respiratory system) lung lymphocytic infiltration	<50> 1 0 0 0 (2) (0) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 (05)	(6) (0) (0) (0) (0) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 0 0 0 0
granulation		0 1 0 0 (0) (0) (0)		
squamous cell metaplasia			0 1 0 0 (0) (0) (0) (0)	
accumulation of foamy cells	1 0 0 0 (2) (3) (4) (5) (5) (6)		1 0 0 0 (2) (3) (4) (4)	1 0 0 0 (2) (2) (3) (4) (5)
bronchiolar—alveolar cell hyperplasia	a 0 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) (4)	3 1 0 0 (6) (2) (0) (0)	$\begin{pmatrix} 1 & 1 & 0 & 0 \\ (2) & (2) & (2) & (0) & (0) \end{pmatrix}$
(Hematopoietic system)				
bone marrow angiectasis	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	(0)(0)(0)(0) (0)(0)(0) (0)(0)(0)(0)(0)(0)(0)(0)(0)(0)(0)(0)(0)((49) 0 0 0 (0) (0) (0)	<00 (0) (0) (0) (0) (0)
increased hematopoiesis		1 0 0 0 (2) (3) (4) (6)	(0)(0)(0)(0)	1 0 0 0 (2) (2) (3) (4) (5)

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

STUDY NO. ANTMAL REPORT TYPE SEX	: 0676 : MOUSE B6D2F1/Cr1j[Crj:BDF1] : A1 : MALE	•	HISTOPATHOLOGICAL FINDINGS : ALL ANIMALS (0-105W)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)		PAGE :
Organ	Findings_	Group Name No. of Animals on Study Grade	Study 50 4 (%) (%) (%) (%)	100 ppm 50 1 2 3 4 (%) (%) (%)	200 ppm 49 1 2 3 4 (%) (%) (%)	400 ppm 50 1 2 3 4 (%) (%) (%) (%)
(Hematopoietic system)	ic system)					
spleen	deposit of melanin		<50> (0) (0) (0) (0)	<50> 2 0 0 (4) (0) (0) (0)	<49> 0 0 0 0 0 (0) (0) (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)
	extramedullary hematopoiesis		6 2 2 0 (12) (4) (4) (0)	12 8 0 0 * (24) (16) (0) (0)	11 3 0 0 (22) (5) (6) (0)	2 3 0 0 (4) (6) (0) (0)
	lymph-follicular hyperplasia		0 0 2 0 (0) (0) (4) (0)			(0)(2)(0)
(Circulatory system)	· system)					
heart	mineralization		<50> 0 1 0 (0) (2) (0) (0)	<50> 2 0 0 (4) (0) (0) (0)	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	(0) (0) (0) (0) 0 0 0 0 0 0 0 0
	myocardial fibrosis		1 0 0 0 (2) (2) (3) (4)	0 1 0 0 (0) (0) (0) (0)	1 0 0 0 (2) (2) (3) (4)	
(Digestive system)	ystem)					
tooth	dysplasia		<50> (0) (0) (0) (0) (0)	<50> (0) (0) (0) (0) (0) (0)	<49> 1 0 0 0 (2) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0)
Grade < a > b (c) Significant	Grade 1: Slight 2: Moderate $\langle a \rangle$ a: Number of animals examined at the b: Number of animals with lesion (c) c: b/a*100 Significant difference; *: P ≤ 0.05 **: P	3 : Marked site ≤ 0.01 Test of	4 : Severe Chi Square			

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

STUDY NO. ANTMAL REPORT TYPE SEX	: 0676 : MOUSE B6D2F1/Crlj[Crj:BDF1] : A1 : MALE		HISTOPATHOLOGICAL FINDINGS : ALL ANIMALS (0-105#)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105%)		PAGE :	9
Organ	Findings	Group Name No. of Animals on Study Grade	Control 50 4 (%) (%) (%) (%)	100 ppm 50 4 (%) (%) (%) (%) (%)	200 ppm 49 1 2 3 4 (%) (%) (%)	400 ppm 50 1 2 3 4 (%) (%) (%) (%)	<u> </u>
(Digestive system)	ystem)						l
tongue	arteritis		<50> 1 0 0 (2) (0) (0) (0)	(0) (0) (0) (0) 0 0 0 0 (20)	<49> 0 0 0 0 (0) (0) (0)	(0)(0)(0)(0) 0 0 0 0 0 0 0 0	•
salivary gl	lymphocytic infiltration		(50) 1 0 0 0 (2) (0) (0) (0)	<50> (0) (0) (0) (0) (0) (0)	<49> 0 0 0 . (0) (0) (0) (0)	<pre></pre>	
	xanthogranuloma					$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	
stomach	ulcer:forestomach		<50> 1 0 0 0 (2) (0) (0) (0)	<50> 0 1 0 0 (0) (2) (0) (0)	<49> (2) (0) (0) (0)	<pre></pre>	
	hyperplasia:forestomach			(0)(0)(0)(0)(0)	1 0 0 0 (2) (2) (3) (4) (5)	2 0 0 0 (4) (4) (6) (6) (6)	
	erosion:glandular stomach		8 0 0 0 (16)(0)(0)(0)	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	5 0 0 0 (10) (10) (10) (10)	7 2 0 0 (14) (4) (0) (0)	
	ulcer:glandular stomach			1 0 0 0 (2) (3) (4) (5)	2 0 0 0 (4) (4) (6) (6) (6)	1 0 0 0 (2) (2) (3) (4) (4)	
Grade <a>> b (c) Significant	Grade 1: Slight 2: Moderate 3: k (a > a : Number of animals examined at the site b : Number of animals with lesion (c) c: $b/a*100$ Significant difference; $*: P \le 0.05 **: P \le 0.05$	farked 01	4 : Severe Test of Chi Square				1

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

STUDY NO. ANIMAL REPORT TYPE SEX	: 0676 : MOUSE B6D2F1/Cr1j[Crj:BDF1] : A1 : MALE	HISTOPATHOLOGICAL FI ALL ANIMALS (0-105W)	CGICAL FINDINGS :NC (0-105%)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)	ı G	PAGE: 7
Organ	Findings	Group Name No. of Animals on Study Grade (%) (%) (%)	Control 50 3 4 6) (%) (%)	100 ppm 50 1 2 3 4 (%) (%) (%)	200 ppm 49 49 4 (%) (%) (%) (%)	400 ppm 50 1 2 3 4 (%) (%) (%) (%)
{Digestive system}	iystem)					
stomach	hyperplasia:glandular stomach	4 0 (8) (0	<50> 0 0 0 0) (0) (0)	<50> 12 0 0 0 (24) (0) (0) (0)	<49> 5 1 0 0 (10) (2) (0) (0)	<00> <00> 8 0 0 0 (16) (0) (0) (01)
liver	angiectasis	0 0 0	(0) (0) (0 0 0 0 (20) (20)	<pre></pre>	<49> 2 0 0 0 (4) (0) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 000
	necrosis:focal	1 0 (2) (00)	(0) (0) (0	0 1 0 0 (0) (0) (0) (0)		
	collapse	1 0 (2) (0 0)	(0) (0) (0			
	inflammatory infiltration	0 (0)	(0) (0) (0	0 1 0 0 (0) (0) (0) (0)	1 0 0 0 (2) (2) (3) (4)	
	granulation	0) (0)	(0) (0) (0	0 0 1 0 (0) (0) (2) (0)		0 1 0 0 (0) (0) (0)
	inflammatory cell nest	1 1 (2) (2)	1 0 0 2) (0) (0)	(0)(0)(0)(0)(0)		
	extramedullary hematopoiesis	1 0 (2) (0)	. (0) (0) (0	1 0 0 0 (2) (2) (3) (4)		1 0 0 0 (2) (3) (4) (6) (6)
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; $*: P \leq 0.05$ **: $P \leq 0.05$	3: Marked 4: Severe the site $: P \leq 0.01 $ Test of Chi Square				•

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

STUDY NO. ANIMAL REPORT TYPE SEX	STUDY NO. : 0676 ANIMAL : MOUSE BEDZF1/Crlj[Crj:BDF1] REPORT TYPE : A1 SEX : MALE	HISTOPATHOLOGICAL FINDINGS :1 ALL ANIMALS (0-105W)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105#)	Q	PAGE: 8
Or gan	Findings	Group Name Control No. of Animals on Study 50 Grade 1 2 3 4 (%) (%) (%) (%)	100 ppm 50 1 2 3 4 (%) (%) (%)	200 ppm 49 1 2 3 4 (%) (%) (%) (%)	
(Digestive system)					
liver	clear cell focus	<50> 1 0 0 0 (2) (0) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 000	(49) 0 2 0 (0)(4)(0)(0)	(0)(0)(0)(0) 0 0 0 0 (0)(0)(0)
	acidophilic cell focus	2 0 0 0 (4) (6) (6) (9)	4 1 0 0 (8) (7) (9) (9)	4 1 0 0 (8) (2) (0) (0)	5 0 0 0 (10) (10) (10) (10)
	basophilic cell focus		2 0 0 0 (4) (0) (0) (0)	1 0 0 0 (2) (2) (3) (4) (4)	2 0 1 0 (4) (0) (2) (0)
	hyperplasia:Ito-cell	0 1 0 0 (0) (0) (0) (0)			
gall bladd	cyst	(0) (0) (0) (0) 0 0 0 0 0 0 0 0	(0)(0)(0)(0) 0 0 0 0 0 0 0 0	(49) 1 0 0 0 (2) (0) (0) (0)	(0)(0)(0)(0) 0 0 0 0 (0)(0)(0)
pancreas	islet cell hyperplasia	<50> 1 0 0 0 (2) (0) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 (0) (0)	(49) 0 0 0 0 (0) (0) (0)	(0)(0)(0)(0) 0 0 0 0 (0)(0)(0)
	xanthogranuloma		(0)(0)(0)(0)	1 0 0 0 (2) (2) (3) (4) (4)	(0)(0)(0)(0)(0)

^{4 :} Severe Grade 1: Slight 2: Moderate 3: Marked $\langle a \rangle$ a: Number of animals examined at the site b : Number of animals with lesion (c) c: b/a*100 Significant difference; *: P \leq 0.05 **: P \leq 0.01 T

**: P ≤ 0.01

4 : Severe

3 : Marked

1: Slight 2: Moderate 3: Ma a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100

Grade 1: Slight 2: Moderate $\langle a \rangle$ a: Number of animals examine b b: Number of animals with le: (c) c:b/a*100 Significant difference; $*:P \leq 0.05$

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

IY NO. AL IRT TYPE	HISTOPATHOLOGICAL FINDINGS :NG ALL ANIMALS (0-105W)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105%)	X	
SEX : MALE				PAGE: 9
OrganFindings	Group Name Control No. of Animals on Study 50 Grade 1 2 3 4 (%) (%) (%) (%)	100 ppm 50 1 2 3 4 (%) (%) (%) (%)	200 ppm 49 1 2 3 4 (%) (%) (%)	400 ppm 50 1 2 3 4 (%) (%) (%)
{Urinary system}				
kidney hemorrhage	(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)	<49> 0 0 0 0 (0) (0) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 (0) (0)
thrombus			0 1 0 0 (0) (0) (0) (0)	
cyst	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$			
hyaline droplet		(0) (0) (0) (0). 0 0 0 0	1 0 0 0 (2) (2) (3) (4)	(2)(0)(0)(0)
basophilic change	1 0 0 0 (2) (3) (4) (5) (5) (6)		1 0 0 0 (2) (2) (3) (4)	
lymphocytic infiltration		1 0 0 0 (2) (2) (3) (4)		
inflammatory polyp	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	0 2 1 0 (0) (4) (2) (0)	(0)(2)(2)(0)	(0)(0)(0)(0)
hydronephrosis	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	0 3 6 0 (0)(6)(12)(0)	0 1 2 0 (0) (2) (4) (0)	(0) (2) (0) (0)

Grade 1: Slight 2: Moderate 3: Marked \langle a \rangle a : Number of animals examined at the site b : Number of animals with lesion (c) c: b/a * 100 Significant difference; *: P \leq 0.05 **: P \leq 0.01

(HPT150)

4 : Severe

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

STUDY NO. : 067 ANIMAL : MOU REPORT TYPE : A1 SEX : MALI	: 0676 : MOUSE B6D2F1/Crlj[Crj:BDF1] : A1 : MALE	HISTOPATHOLOGICAL F. ALL ANIMALS (0-105W)	INDINGS :NO	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)		PAGE: 10	0
Organ	Findings	Group Name Control No. of Animals on Study 50 Grade 1 2 3 (%) (%) (%)	rol (%)	100 ppm 50 1 2 3 4 (%) (%) (%)	200 ppm 49 (%) (%) (%) (%)	400 ppm 50 1 2 3 4 (%) (%) (%)	1
{Urinary system}	em)						1
kldney	dilated pelvis	(50) (2) (0) (0)	0 0	<50> 1 0 0 0 (2) (0) (0) (0)	(49) 0 0 0 (0) (0) (0)	(6) (0) (0) (0) 0 0 0 0 0 (0) (0) (0)	
urin bladd	dilatation	<50> 0 0 8 0 0 0 (0) (0) (16)	0 (0)	<50> (0) (0) (0) (0) (0)	<49> 0 0 2 0 (0) (0) (4) (0)	<00 (0) (0) (0	
	nodular hyperplasia:transitional epithelium	0 0 0 0 0 0 (0) (0) (0) (0)	0 (0)	(0) (0) (0) (0)	(0)(0)(0)(0)	1 0 0 0 (2) (3) (4) (5)	
(Endocrine system)	sten)						
pituitary	angiectasis	(6) (0) (0) 0 0 0 0 0 0 0 0 0	0 0	(49) 0 0 0 (0) (0) (0)	<49> 1 0 0 0 (2) (0) (0) (0)	<00) (0) (0) (0) 0 0 0 0 0 0 0 0 0 0	
	cyst	1 0 0 (2) (3) (6) (7)	0)	1 0 0 0 (2) (3) (4) (5)	1 0 0 0 0 (2) (2) (3) (3)	2 0 0 0 (4) (4) (6) (6)	
	hyperplasia	(0) (0) (0)	0 (0	1 0 1 0 (2) (3) (4)			

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Grade 1: Slight 2: Moderate 3: Marked $\langle a \rangle$ a: Number of animals examined at the site b : Number of animals with lesion (c) c: b/a*100 significant difference; \star : P \leq 0.05 $\star\star$: P \leq 0.01 $\star\star$

(HPT150)

4 : Severe

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

Composition	STUDY NO. ANIMAL REPORT TYPE SEX	: 0676 : MOUSE B6D2F1/Cr1j[Crj:BDF1] :: A1 : MALE	HISTOPATHOLOGICAL FINDINGS :N ALL ANIMALS (0-105W)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)	λ)	PAGE: 11
Table pouch Carlo Carlo	Organ	Findings	Name Control Animals on Study 50 1 2 3 (%) (%) (%)	100 ppm 50 2 3 (%) (%)	200 ppm 49 2 3 (%) (%)	
Pathike pouch Carol Caro	(Endocrine	system)				
Cost	pituitary	Rathke pouch	<50> 0 0 (0) (0)	<49> 1 0 (2) (0) (<49> 0 0 (0) (0) (\smile
Spindle-cell hyperplasia 11	parathyroid		(50) (0) (0) (0)	<50> 0 0 (0) (0) (<49> 0 0 (0) (0) (
hyperplassia:cortical cell hyperplassia	adrenal	spindle-cell hyperplasia	(50) (0) (0) (0)	<50> 0 0 (0) (0) (<49> 0 0 (0) (0) (\smile
(50)		hyperplasia:cortical cell) (0) (0)	1 0 (2) (0) (1 0 (2) (0) (\smile_{l}
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	(Reproductiv	Ve system)				
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	testis	mineralization	<00> (0) (0) (0) (0) (0) (0) (0) (<20> 0 0 (0) (0)	<49> 0 0 (0) (0) (\smile
		interstitial cell hyperplasia	1 0 (2) (0) (1 0 (2) (0) (0 (0)	\smile

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

STUDY NO. ANIMAL REPORT TYPE SEX	: 0676 : MOUSE B6D2F1/Crlj[Crj:BDF1] : A1 : MALE		HISTOPATHOLOGICAL FINDINGS :1 ALL ANIMALS (0-105W)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)	0	PAGE: 12
Organ	Findings	Group Name No. of Animals on Grade	Control 1 2 3 4 (%) (%) (%) (%)	100 ppm 50 1 2 3 4 (4) (4) (4)	200 ppm 49 1 2 3 4 (w) (w) (w)	400 ppm 50 3 4 40 (w) (w) (w) (w) (w)
5				(8)		(&) (&)
(Reproductive system) testis sperm	re system) spermatogenic granuloma		(0)(0)(0)(0)(0) 0 0 0 0 0 0 0 0 0	(0) (0) (0) (0) 0 0 0 0 0 <05>	<49> 1 0 0 0 (2) (0) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 0 0 0
epididymis	spermatogenic granuloma		(0) (0) (0) (0) 0 0 0 0 0 000	<pre></pre>	<49> 1 0 0 0 (2) (0) (0) (0)	<50> 1 1 0 0 (2) (2) (0) (0)
semin ves	hemorrhage		<50> 1 0 0 0 (2) (0) (0) (0)	(0) (0) (0) (0) 0 0 0 0 <05>	<49> 0 0 0 0 (0) (0) (0)	<20> (0) (0) (0) (0) (0) (0) (0) (0) (0) (0)
prostate	inflammatory infiltration		<00 (0) (0) (0) (0) (0) (0) (0) (<50> 1 0 0 0 (2) (0) (0) (0)	<49> 1 0 0 0 (2) (0) (0) (0)	<50> (0) (0) (0) (0) (0)
prep/cli gl	cyst		<50> 1 0 0 0 (2) (0) (0) (0)	<pre></pre>	49> 1 0 0 0 (2) (0) (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)
{Nervous system} brain	stem] hemorrhage		(0) (0) (0) (0) 0 0 0 0 0 (0) (0)	(0)(0)(0)(0)	49> 1 0 0 0 (2) (0) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 0 0 0
Grade <a>> (a > b) (c) Significant	Grade 1: Slight 2: Moderate 3:) <abahaa< td=""><td>farked 01</td><td>4 : Severe Test of Chi Square</td><td></td><td></td><td></td></abahaa<>	farked 01	4 : Severe Test of Chi Square			

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

STUDY NO. : ANIMAL : REPORT TYPE : SEX :	: 0676 : MOUSE B6D2F1/Crlj[Crj:BDF1] : Al : MALE	HISTOPATHOLOGICAL FINDINGS : ALL ANIMALS (0-105W)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)			PAGE : 13
Organ	Findings	Group Name Control No. of Animals on Study 50 Grade	100 ppm 50 1 2 3 4 (%) (%) (%)	200 ppm 49 1 2 3 4 (%) (%) (%) (%)	46 1 2 50 (%) (%)	400 ppm 50 2 3 4 %) (%) (%)
(Nervous system) brain	em) mineralization	<50> 18 0 0 0 (36) (0) (0) (0)	<50> 17 0 0 0 (34) (0) (0) (0)	21 0 0 0 (43) (0) (0) (0)	<50> 18 0 (36) (0) (0 0 0
{Special senseye	{Special sense organs/appendage} eye keratitis	<50> 0 1 0 0 (0) (2) (0) (0)	<50> 0 1 0 0 (0) (2) (0) (0)	<49> 0 0 0 0 (0) (0) (0)	(50) (0) (0) (0)	(O) (O O O
Harder gl	phthisis bulbi hyperplasia		0 0 0 1 (0)(0)(0)(2) (2) (50) (0)(0)(0)(0)	0 0 0 0 (0) (0) (0) (0) (0) (0) () (0) (0) - (20) - (20) 0 0	· (0) (0 (0 (0 (0 (0 (0 (0 (0 (0 (0 (0 (0 (0
(Musculoskeletal system) muscle	otal system} mineralization	<00 (0) (0) (0) (0) (0 (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)	(0) (0) (0) (0)	(50) (0) (0)	(O) (O
Grade 1 : Slight < a > a : Number b b : Number (c) c : b / a > Significant difference :	1: Slight 2: Moderate 3: 8 a : Number of animals examined at the site b : Number of animals with lesion c: b / a * 100 ifference : *: $P \le 0.05$ **: $P \le 0$	3 : Marked 4 : Severe : site . ≤ 0.01 Test of Chi Square				

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

PAGE: 14

STUDY NO. : 0676
ANIMAL : MOUSE BEDZF1/Crlj[Crj:BDF1]
REPORT TYPE : A1
SEX : MALE

	Group Name No. of Animals on Study	Control udv 50	100 ppm 50	200 ppm 49	400 ppm
OrganFindings	Grade	6) (%)	1 2 3 4 (%) (%) (%) (%)	1 2 3 4 (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)
{Musculoskeletal system}					
bone ostitis fibrosa		<pre></pre>	(0) (0) (0) (0) 0 0 0 0 0 <09>	<49> 0 0 0 0 0 0 0 0 0 0 0 0	(0) (0) (0) (0) 0 0 0 0 0 0 0 0
{Body cavities}					
peritoneum cyst		(0) (0) (0) (0) 0 0 0 0 0 0 0 0	<50> 1 0 0 0 (2) (0) (0) (0)	<49> 0 0 0 0 0 (0) (0) (0 0)	<50> (0) (0) (0) (0) (0)
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 4	: Severe : Severe Chi Square			

BAIS4

TABLE L4

HISTOPATHOLOGICAL FINDINGS:

NON-NEOPLASTIC LESIONS : FEMALE

ALL ANIMALS

(HPT150)

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

PAGE: 15 STUDY NO. : 0676
ANIMAL : MOUSE BEDZF1/Cr1j[Crj:BDF1]
REPORT TYPE : A1
SEX : FEMALE

	Group Name No. of Animals on Grade	Control Study 50	100 ppm 49 2 3	200 ppm 50 2 3	400 ppm 50 2 3
Organ	Findings	(%) (%) (%)	(%) (%) (%)	(%) (%) (%) (%)	(%) (%) (%)
(Respiratory system)	system)				
nasal cavit	ехидате	<50> 1 0 0 0 (2) (0) (0) (0)	<49> 6 7 2 0 ** (12) (14) (4) (0)	<50> 7 15 25 0 ** (14) (30) (50) (0)	<50> 15 23 10 0 ** (30) (46) (20) (0)
	mineralization		4 0 0 0 (8) (8) (9) (9)	2 0 0 0 (4) (4) (6) (6)	2 0 0 0 (4) (4) (6) (6) (7)
	inflammation			(0) (2) (0) (0)	
	eosinophilic change:olfactory epithelium	27 0 0 0 (54) (0) (0) (0)	20 0 0 0 (41) (41) (6) (6)	22 1 0 0 (44) (2) (0) (0)	45 1 0 0 ** (90) (2) (0) (0)
	eosinophilic change:respiratory epithelium	41 4 0 0 (82) (8) (0) (0)	19 1 0 0 ** (39) (2) (0) (0)	34 1 0 0* (68) (2) (0) (0)	41 3 1 0 (82) (6) (2) (0)
	inflammation:respiratory epithelium				1 1 0 0 (2) (2) (0) (0)
	respiratory metaplasia:olfactory epithelium	15 0 0 0 0 (30) (30) (30) (30)	23 0 0 0 (47) (70) (10) (10)	27 1 0 0 * (54) (2) (0) (0)	36 10 0 0 ** (72) (20) (0) (0)
	respiratory metaplasia:gland	34 0 0 0 (0) (0) (0) (0)	30 0 0 0 0 (61) (61) (0) (0) (0)	40 0 0 0 (80) (80) (90) (90)	47 0 0 0 ** (94) (0) (0) (0)
Grade 1 : Slight < a > a : Number b : Number (c) c : b / a * Significant difference ;	2 : Moderate 3 : Marked of animals examined at the site of animals with lesion : 100 $*: P \le 0.05$ **: $P \le 0.01$	4 : Severe Test of Chi Square			

(HPT150)

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

NY NO. IAL NRT TYPE	: 0676 : MOUSE B6D2F1/Cr1j[Crj:BDF1] : A1	HISTC ALL A	HISTOPATHOLOGICAL FINDINGS :: ALL ANIMALS (0-105#)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)		
SEX	: FEMALE			TO A	TO THE PARTY OF TH	PAGE: 16
Organ	Findings	Group Name No. of Animals on Study Grade	Control y 50 1 2 3 4 (%) (%) (%) (%)	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	200 ppm 50 1 2 4 (w) (w) (w)	400 ppm 50 1 2 4
			(8)	(V) (V)	(&) (&)	(%) (%)
(Respiratory system)	system)					
nasal cavit	squamous cell metaplasia:respiratory epithelium	<u> </u>	<50> 2 0 0 0 4) (0) (0) (0)	<49> 3 0 0 0 (6) (0) (0) (0)	<50> 19 1 0 0 ** (38) (2) (0) (0)	<50> 22 8 1 0 ** (44) (16) (2) (0)
	ulcer:respiratory epithelium	S	1 0 0 0 0 2) (0) (0)	(0)(0)(2)(0)	(0)(0)(0)(0)	1 0 3 0 (2) (3) (6) (9)
	atrophy:olfactory epithelium		(0)(0)(0)(0	6 5 1 0 ** (12) (10) (2) (0)	10 16 22 0 ** (20) (32) (44) (0)	7 33 7 0 ** (14) (66) (14) (0)
	necrosis:olfactory epithelium	Č	(0)(0)(0)(0		5 0 0 0 (10) (10) (10) (10)	2 1 0 0 (4) (2) (0) (0)
	necrosis:respiratory epithelium	S	(0)(0)(0)(0		7 1 0 0 * (14) (2) (0) (0)	5 0 0 0 (10) (10) (10) (10)
nasopharynx	eosinophilic change		<50> 4 0 0 0 8) (0) (0) (0)	<49> 2 0 0 0 (4) (0) (0) (0)	<50> 4 0 0 0 (8) (0) (0) (0)	<50> 1 1 0 0 (2) (2) (0) (0)
larynx	inflammatory infiltration		<50> (0) (0) (0) (0) (0) (0)	<49> (49> (2) (0) (0) (0)	<50> (0) (0) (0) (0)	<50> 0 0 0 0 (0) (0) (0)
Grade <a>> b (c) Significant of	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.	darked 4:5	severe			

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

STUDY NO. ANIMAL REPORT TYPE SEX	: 0676 : MOUSE B6D2F1/Crlj[Crj:BDF1] E : Al : FEMALE	HISTOPATHOLOGICAL FINDINGS :N ALL ANIMALS (0-105W)	HISTOPATHOLOCICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)	ζ,	PAGE: 17
Organ	Group Name No. of Anii Grade	Group Name Control No. of Animals on Study 50 Grade 1 2 3 4 (%) (%) (%) (%)	100 ppm 49 1 2 3 4 (%) (%) (%) (%)	200 ppm 50 1 2 3 4 (%) (%) (%) (%)	400 ppm 50 1 2 3 4 (%) (%) (%) (%)
(Respiratory system)	y system)				
trachea	eosinophilic change	<pre></pre>	(0) (0) (0) (0) 0 0 0 0 0 0 0 0	<50> 0 0 0 0 (0) (0) (0)	(0) (0) (0) (0) 0 0 0 0 (0) (0) (0)
lung .	inflammatory infiltration	<50> 2 0 0 (4) (0) (0) (0)	<49> 4 0 0 0 (8) (0) (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)	<550> 0 0 0 0 (0) (0) (0)
	lymphocytic infiltration	2 0 0 0 0 (4) (4) (6) (6)	1 0 0 0 (2) (2) (3) (4) (4)		4 0 0 0 (8) (9) (9) (9)
	accumulation of foamy cells	1 0 0 0 0 (2) (2) (3) (4) (4)			
	bronchiolar-alveolar cell hyperplasia		1 1 0 0 (2) (2) (0) (0)		$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
(Hematopoie bone marrow	tic s	<200>	. (46>)	(05)	<50>
	increased hematopoiesis		1 0 0 0 (2) (3) (3) (4)	1 0 0 0 (5) (5) (5) (5)	1 0 0 0 (2) (3) (0) (0)
Grade < a > b (c) Significant	Grade 1: Slight 2: Moderate 3: Marked $\langle a \rangle$ a : Number of animals examined at the site b : Number of animals with lesion (c) c: b/a * 100 c: b/a * 100 significant difference; *: P \leq 0.05 **: P \leq 0.01	4 : Severe Test of Chi Square			

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

STUDY NO. ANIMAL REPORT TYPE SEX	: 0676 : MOUSE BGDZF1/Cr1j[Crj:BDF1] PE : A1 : FEWALE	HISTOPATHOLOGICAL FINDINGS : ALL ANIMALS (0-105W)	STOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) L ANIMALS (0-105%)	(A:	PAGE	E: 18
Organ	Findings.	Group Name Control No. of Animals on Study 50 Grade 1 2 3 4 (%) (%) (%) (%)	100 ppm 49 1 2 3 4 (%) (%) (%) (%)	200 ppm 50 1 2 3 4 (%) (%) (%) (%)	400 ppm 50	(%)
(Hematopoie	(Hematopoietic system)					
bone marrow	т granulopoiesis∶increased	.<50> 1 0 0 0 (2) (0) (0) (0)	<49> 1 0 0 0 (2) (0) (0) (0)	(0)(0)(0)(0) 0 0 0 0 0 0 0 0	\$60\$\ 0 0 0 0 0 0 0 0 0	0
spleen	deposit of melanin	(0) (0) (0) (0) 0 0 0 0 0 0 0 0	<49> 0 0 0 0 0 0 0 0 0 0 0 0	(49) 0 0 0 0 (0) (0) (0)	<50> (50> (0) (0) (0) (0) (0) (0) (0) (0) (0) (0)	0 6
	extramedullary hematopoiesis	3 8 0 0 (6) (16) (0) (0)	6 2 0 0 (12) (4) (0) (0)	4 3 0 0 (8) (8) (0) (0)	6 1 0 (12) (2) (0) (* (0
	lymph-follicular hyperplasia		(0)(0)(0)(0)		2 0 0 (4) (4) (6) (7) (7)	0 (6
{Circulatory system}	ry system}					
heart	mineralization	<50> 0 0 0 0 (0) (0) (0) (0)	<pre></pre>	<pre></pre>	(20) (0) (0) (0) (0)	o (0
	myocardial fibrosis	2 0 0 0 (4) (4) (6) (6) (6)	1 0 0 0 (2) (3) (4) (4)	3 0 0 0 0 (0) (0) (0)	2 0 0	o (ô
Grade < a > b	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 e site P ≤ 0.01 Test of Chi Square				

5 0 (10) (10) (10)

4 0 0 0 (8) (8) (0) (0)

o 6 . .

• 6

2 (4) (-(

hyperplasia:glandular stomach

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

STUDY NO. : 0676 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1] REPORT TYPE : A1 SEX : FEMALE	HISTOPATHOLOGICAL FINDINGS :1 ALL ANIMALS (0-105W)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)	· G	PAGE: 19
OrganFindings	Group Name Control No. of Animals on Study 50 Grade (%) (%) (%) (%) (%)	100 ppm 49 1 2 3 4 (%) (%) (%) (%)	200 ppm 50 1 2 3 4 (%) (%) (%) (%)	400 ppm 50 1 2 3 4 (%) (%) (%) (%)
{Circulatory system} heart arthritis	(0) (0) (0) (0) 0 0 0 0 <05>	<49> 0 0 0 0 (0) (0) (0)	<50> 0 1 0 0 (0) (2) (0) (0)	(20) (0) (0) (0) 0 0 0 0 0 0 0 0
{Digestive system}				
salivary gl lymphocytic infiltration	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	<49> 1 0 0 0 (2) (0) (0) (0)	<pre></pre>	<50> 1 0 0 0 (2) (0) (0) (0)
stomach hyperplasia:forestomach	(0) (0) (0) (0) 0 0 0 0 <05>	<49> 0 0 0 0 0 0 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)
erosion:glandular stomach	(10) (2) (0) (0)	6 0 0 0 (12) (12) (13) (13) (13) (13)	4 3 0 0 (8) (8) (9) (0)	3 1 0 0 (6) (7) (7) (7)
ulcer:glandular stomach	0 0 1 0 (0) (0) (0) (0) (0)	0 1 0 0 (0) (0) (0)		0 1 1 0 (0) (2) (2) (0)

Test of Chi Square

^{4 :} Severe 3 : Marked Grade 1: Slight 2: Moderate 3: Me < a > a: Number of animals examined at the site b b: Number of animals with lesion (c) c: b/a * 100 Significant difference; $*: P \le 0.05$ **: $P \le 0.06$

^{**:} P ≤ 0.01

**: P ≤ 0.01

(HPT150)

Grade 1: Slight 2: Moderate 3: Me < 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

4 : Severe

3 : Marked

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

STUDY NO. : 0676 ANIMAL : MOUSE BGDZF1/Cr1j[Crj:BDF1] REPORT TYPE : A1 SEX : FEMALE		HISTOPATHOLOGICAL FINDINGS :NC ALL ANIMALS (0-105W)	HISTOPATHOLOCICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)	· · · · · · · · · · · · · · · · · · ·	PAGE: 20
OrganFindings	Group Name No. of Animals on Study Grade	Control 1 2 3 4 (%) (%) (%) (%)	100 ppm 49 1 2 3 4 (%) (%) (%)	200 ppm 50 1 2 3 4 (%) (%) (%)	400 ppm 50 1 2 3 4 (%) (%) (%)
{Digestive system} liver angiectasis		(50) 1 1 0 0 (2) (2) (0) (0)	<49> 2 0 0 0 (4) (0) (0) (0)	<50> 4 0 0 (8) (0) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 0 0 0
thrombus					0 1 0 0 (0) (0) (0) (0)
necrosis:focal		1 1 0 0 (2) (2) (2) (0) (0)	1 0 0 0 (2) (2) (0) (0) (0)		3 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
cyst				1 0 0 0 (2) (3) (4) (4)	
inflammatory infiltration	tion		1 0 0 0 (2) (3) (4) (5)		
lymphocytic infiltration	ion		1 0 0 0 (2) (3) (4) (5)		1 0 0 0 (2) (2) (3) (4)
inflammatory cell nest	÷:	1 0 0 0 (2) (2) (3) (4)	1 0 0 0 (2) (2) (3) (4)		
extramedullary hematopoiesis	poiesis	4 0 0 0 (8) (8) (9) (9)	2 0 0 0 (4) (4) (6) (6) (7)		$\begin{pmatrix} 1 & 0 & 0 & 0 \\ 2) & (0) & (0) & (0) \end{pmatrix}$

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

STUDY NO. : ANIMAL : REPORT TYPE : SEX :	: 0676 : MOUSE B6D2F1/Crlj[Crj:BDF1] : A1 : FEMALE		HISTOPATHOLOGICAL FINDINGS :: ALL ANIMALS (0-105W)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)		PAGE: 21
Organ	Findings	Group Name No. of Animals on Study Grade	on Study 50 (%) (%) (%) (%)	100 ppm 49 1 2 3 4 (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	400 ppm 50 (%) (%) (%) (%)
{Digestive system}	(stem)					
liver	clear cell focus ·		<50> (0) (0) (0) (0) (0)	<49> 2 0 0 0 (4) (0) (0) (0)	(0)(0)(0)(0) 0 0 0 0 0 0 0 0 0 0	<50> (0) (0) (0) (0) (0) (0) (0) (0) (0) (0)
	acidophilic cell focus		1 0 1 0 (2) (0) (2) (0)	3 0 0 0 0 (0) (0)	1 2 0 0 (2) (4) (0) (0)	1 2 1 0 (2) (4) (2) (0)
	bile duct hyperplasia		3 0 0 0 0 0 0 0 0	1 0 0 0 (2) (3) (6) (6)		
(Urinary system)	.em)		·			
kidney	cyst		<50> 1 0 0 (2) (0) (0) (0)	<49> 0 0 0 0 0 (0) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 0 0 0	(0) (0) (0) (0) 0 0 0 0 0 0 0 0
	hyaline droplet		13 1 0 0 (26) (26) (2) (0) (0)	6 0 0 0 0 (12) (12) (13) (13) (13) (14) (15)	12 0 0 0 (24) (24) (0) (0) (0)	(0)(0)(0)(91)
	lymphocytic infiltration		1 0 0 0 (2) (2) (3) (4) (4)	2 0 0 0 (4) (4) (6) (6)	1 0 0 0 (2) (3) (3) (4)	2 0 0 0 (4) (4) (6) (6)
	inflammatory polyp		(0)(0)(0)(0)	0 1 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	3 : Marked 4 : at the site on ** : P ≤ 0.01 Test of Chi	4 : Severe of Chi Square			

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

STUDY NO. ANIMAL REPORT TYPE SEX	: 0676 : MOUSE B6D2F1/Crlj[Crj:BDF1] : A1 : FEMALE	HISTOPATHOLOGICAL FINDINGS ALL ANTWALS (0-105W)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANTWALS (0-105W)	CA.		PAGE: 22
Organ	Findings	Group Name Control No. of Animals on Study 50 Grade 1 2 3 4 (%) (%) (%) (%) (%)	100 ppm 49 1 2 3 4 (%) (%) (%)	200 ppm 50 1 2 3 4 (%) (%) (%) (%)	400 ppm 50 50 (%) (%) (%) (%) (%) (%)	4 (%)
(Urinary system) kidhey	stem} hydronephrosis	<50> 1 2 0 0 (2) (4) (0) (0)	<49> (0) (2) (0) (0) (4) (2) (0)	<50> 0 2 1 0 (0) (4) (2) (0)	<pre></pre>	0 0
	glomerulosclerosis		0 0 1 0 (0) (0) (0)		(0) (0) (0)	0 0
urin bladd	dilatation	(0)(0)(0)(0) 0 0 0 0 0 0 0 0	<49> 0 0 0 0 0 0 (0) (0) (0) (0)	<50> 0 0 1 0 (0) (0) (2) (0)	(0) (0) (0) 0 0 0 (20)	(O)
	lymphocytic infiltration	1 0 0 0 (2) (3) (4) (6) (6) (6)	2 0 0 0 (4) (4) (6) (6)	1 0 0 0 (2) (2) (3) (4)	1 0 0 (2) (3) (4)	(0 0
(Endocrine system)	system)					
pituitary	angiectasis	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	<48>	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	<50> 4 0 0 (8) (0) (0)	0)
	hyperplasia	7 5 0 0 (14) (10) (0) (0)	6 1 0 0 (13) (2) (0) (0)	2 2 0 0 (4) (4) (0) (0)	0 2 0 (0) (4) (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.	$3:$ Marked $4:$ Severe he site $P \leq 0.01$ Test of Chi Square				

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

STUDY NO. ANIMAL REPORT TYPE SEX	: 0676 : MOUSE BGDZF1/Cr1j[Crj:BDF1] : A1 : FEMALE	HISTOP ALL AN	HISTOPATHOLOCICAL FINDINGS :1 ALL ANIMALS (0-105#)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)		PAGE: 23
Organ	Findings	Group Name No. of Animals on Study Grade (%)	Control 50 1 2 3 4 6 (%) (%) (%)	100 ppm 49 1 2 3 4 (%) (%) (%) (%)	200 ppm 50 1 2 3 4 (%) (%) (%) (%)	400 ppm 50 1 2 3 4 (%) (%) (%)
(Endocrine system)						
pituitary	Rathke pouch	6 (12)	(0) (0) (0) (0) (0)	<48> 1 0 0 0 (2) (0) (0) (0)	<50> 1 0 0 0 (2) (0) (0) (0)	<50> 2 0 0 0 (4) (0) (0) (0)
thyroid	cyst		<pre></pre>	<49> 0 0 0 0 (0) (0) (0) (0)	<50>	<50> 1 0 0 0 (2) (0) (0) (0)
	granulation	0	0 0 0 0 0	(0)(0)(0)(0)	1 0 0 0 (2) (2) (3) (4)	
	ultimobranchial body remanet		0 0 0 0 0	(0)(0)(0)(0)	1 0 0 0 (2) (2) (3) (4)	
adrena]	spindle-cell hyperplasia	16 (32)	<pre><50> 5 27 6 0 5) (54) (12) (0)</pre>	<49> 16 21 9 0 (33) (43) (18) (0)	<50> 16 31 3 0 (32) (62) (6) (0)	<50> 19 22 5 0 (38) (44) (10) (0)
	hyperplasia:cortical cell	0)	0 0 0 0 0	0 1 0 0 (0) (0) (0) (0)		(0)(0)(0)(0)
	focal fatty change:cortex	0 >	(0)(0)(0)(0	(0)(2)(0)(0)	0 3 0 0 0	0 0 2 0 (0) (0) (4) (0)
Grade < a > b (c) Significant	Grade 1: Slight 2: Moderate 3: ⟨a⟩ a: Number of animals examined at the sit b : Number of animals with lesion (c) c: b/a * 100 Significant difference; *: P ≤ 0.05 **: P ≤	3: Marked 4: Site Site ≤ 0.01 Test of Chi	severe Square			

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

ANTMAL REPORT TYPE SEX	. OO.70 . OOUSE B6D2F1/Crlj[Crj:BDF1] PE : A1 : FEMALE		HISTOPATHOLOGICAL FINDINGS : ALL ANIMALS (0-105W)	HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)	ÇA.	PAGE :
Organ	Findings	Group Name No. of Animals on Study Grade	S on Study 50 4 (%) (%) (%) (%)	100 ppm 49 (%) (%) (%) (%)	200 ppm 50 1 2 3 4 (%) (%) (%)	400 ppm 50
(Reproduct	(Reproductive system)					
ovary	thrombus		<50> (0) (0) (0) (0) (0)	<49> 0 1 1 0 0 0 2) (2) (0)	<pre></pre>	(0)(0)(0)(0)
	cyst		9 1 0 0 (18) (2) (0) (0)	8 0 0 0 (16) (16) (16) (16) (16) (16) (16) (16)	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	15 1 0 0 (30) (2) (0) (0)
	hyperplasia		(0)(2)(0)(0)	(2) (2) (0) (0)		0 1 0 0 (0) (0) (0)
uterus	cystic endometrial hyperplasia		<50> 34 0 0 0 (68) (0) (0) (0)	<49> 31 0 0 0 . (63) (0) (0) (0)	<50> 27 0 0 0 (54) (0) (0) (0)	<50> 34 0 0 0 (68) (68) (69) (69) (69) (69) (69) (69) (69) (69
{Nervous system}	:ystem)					
brain	necrosis:focal		<50> 0 0 0 0 (0) (0) (0)	<49> 2 0 0 0 (4) (0) (0) (0)	(0)(0)(0)(0) 0 0 0 0 0 (0)(0)	<50> 0 0 0 0 0 0 0 0 0 0 0 0
	mineralization		8 0 0 0 0 0 0 0 0 0	10 0 0 0 (20) (20) (0) (0)	9 0 0 6 (18) (18) (18)	11 0 0 0 (22) (22) (0) (0) (0)
Grade <a>(a <a>(b <a>(c	Grade 1: Slight 2: Moderate 3: M < a > a : Number of animals examined at the site b : Number of animals with lesion (c) c: b / a * 100 cs. * · · · · · · · · · · · · · · · · · ·	arked	4 : Severe			

PAGE: 25

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

STUDY NO. : 0676
ANIMAL : MOUSE BEDZF1/Cr1j[Crj:BDF1]
REPORT TYPE : A1
SEX : FEMALE

		Group Name	Control	100 ppm	200 ppm	400 ppm
Organ	Findings	No. of Animals on Study Grade (9		49 (%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)	50 1 2 3 4 (%) (%) (%) (%)
(Special sens	(Special sense organs/appendage)					
өхө	keratitis		(0) (0) (0) (0) 0 0 0 0 0 0 0 0	(49) 0 1 0 0 (0) (2) (0) (0)	(0)(0)(0)(0) 0 0 0 0 0 0 0 0	<00> (0) (0) (0) (0) (0) (0) (0) (0) (0) (0)
	mineralization:cornea		2 0 0 0 (4) (4) (0) (0)	3 0 0 0 0 0 0	3 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	7 0 0 0 0 (14) (14) (14) (15) (15)
Harder gl	hyperplasia		<50> 1 0 0 0 (2) (0) (0) (0)	<49> 0 0 0 0 0 (0) (0) (0)	(0)(0)(0)(0)	<50> 0 1 0 (0) (2) (0) (0)
(Musculoskeletal system)	etal system)					
muscle	mineralization		(0)(0)(0)(0) 0 0 0 0 0 0 0 0	<49> 1 0 0 (2) (0) (0) (0)	(0)(0)(0)(0) 0 0 0 0 0 0 0 0	(0) (0) (0) (0) 0 0 0 0 0 0 0 0
bone	ostitis fibrosa		<00 (0) (0) (0) (0) (0) (0)	<49> 2 0 0 (4) (0) (0) (0)	(0)(0)(0)(0)	3 0 0 (0) (9) (9) (9) (9)
Grade	1 : Slight 2 : Moderate	3 : Marked	4 : Severe			

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

BAIS4

TABLE O1

NEOPLASTIC LESIONS-INCIDENCE

AND STATISTICAL ANALYSIS: MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS		
9290	MOUSE B6D2F1/Cr1j[Crj:BDF1]	MALE
••	••	••
STUDY No.	ANIMAL	SEX

PAGE:

Tumor rate	SITE : lung TUMOR : bronchiolar—alveolar adenoma	EII			
0+11					
Overall rates(a)	4/50(8.0)	4/50(8.0)	3/49(6.1)	5/50(10.0)	
Adjusted rates(b)	10.00	12.90	6.82	11.11	
Terminal rates(c)	3/30(10.0)	4/31(12.9)	2/34(5.9)	4/39(10.3)	
Statistical analysis					
reto test	1				
Standard method(d)	h =				
Prevalence method(d)	P = 0.4064				
Combined analysis(d)	P =				
Cochran-Armitage test(e)	P = 0.7224				
Fisher Exact test(e)		P = 0,6425	P = 0.5114	P = 0.5000	
TERROPORTION TO THE PARTY OF TH	Transfer of the second	The second secon			
S					
	TUMOR : bronchiolar-alveolar carcinoma	пота			
Tumor rate					
Overall rates(a)	2/50(4.0)	3/50(6.0)	2/49(4.1)	3/50(6.0)	
Adjusted rates(b)			4.88	4.44	
Terminal rates(c)	2/30(6.7)	2/31(6.5)	1/34(2.9)	1/39(2.6)	
Statistical analysis					
Peto test					
Standard method(d)	P = 0.2873				
Prevalence method(d)	P = 0.5093				
Combined analysis(d)	P = 0.4034				
Cochran-Armitage test(e)	P = 0.7406				
Fisher Exact test(e)		P = 0.5000	P = 0.6837	P = 0.5000	
		The representative the control of th			
03 6		,			
Timor rate	lumun : bronchlolar-alveolar adeno	pronchiolar-alveolar adenoma, bronchiolar-alveolar carcinoma	•		
Overall rates(a)	6/50(12-0)	7/50(14 0)	5/40(10.9)	8/50(16.0)	
Adjusted rates(b)	16.67	10.35	11 36	0,001 10:0)	
Terminal rates(c)	5/30(16.7)	6/31(19.4)	3/34(-8.8)	5/39(12.8)	
Statistical analysis					
Peto test					
Standard method(d)	P = 0.2873				
Prevalence method(d)	P = 0.4278				
Combined analysis(d)	P = 0.3628				
Cochran-Armitage test(e)	P = 0.6162				
Fisher Exact test(e)		P = 0.5000	P = 0.5144	P = 0.3871	

Group Name	Control	100 ppm	200 ppm	400 ррш
	SITE : lymph node TUMOR : malignant lymphoma			
Tumor rate Overall rates(a)	9/50(18 0)	6/50/ 19 0)	(0 01)07/3	(0.00.)01/01
Adjusted rates(b)	13. 33	0,50(12.0)	0/49(12.2)	13/50(26. 0)
Terminal rates(c) Statistical analysis	4/30(13.3)	4/31(12.9)	3/34(8.8)	8/39(20.5)
Peto test Standard method(d)	0 + 0 2 - 4 2 - 7 - 7			
Prevalence method(d)				
Combined analysis(d)	P = 0.2188			
	P = 0.1805			
Fisher Exact test(e)		P = 0.2883	P = 0.3030	P = 0.2348
	SITE : liver			
Tumor rate	tomon . nepatocellular adenoma			
Overall rates(a)	6/50(12.0)	8/50(16.0)	18/49 (36,7)	10/50(20.0)
Adjusted rates(b)	13.16	23. 53	40.00	25.00
Terminal rates(c)	3/30(10.0)	6/31(19.4)	13/34 (38.2)	9/39(23.1)
ocatistical analysis Peto test				
Standard method(d)	P = 0.7256			
Prevalence method(d)	P = 0.1235			
Combined analysis(d)	P = 0.1708			
Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.2163	P = 0.3871	P = 0.0038**	P = 0.2070
THE PERSON NAMED IN COLUMN TWO IS NOT THE PERSON NAMED IN COLUMN TO THE PERSON NAMED IN COLUMN T	THE STATE OF THE S			
	SITE : liver			
	TUMOR : hemangiosarcoma			
lumor rate				
overall rates(a) Adiusted rates(h)	6/50(12.0)	3/50(6.0)	3/49(6.1)	3/50(6.0)
Terminal rates(c)	3/30/ 10 0)	7/21/ 6 5)	7,797	4.05
Statistical analysis Peto test	(0.01 (0.0)			1, 39 (6. 0)
Standard method(d)	P = 0.6802			
Prevalence method(d)	P = 0.8329			
Combined analysis(d)	P = 0.8576			
Cochran-Armitage test(e)	P = 0.3434			
Fisher Exact test(e)		D = 0 9/35	D - 0 9E9E	3076 V = Q

ANALYSIS
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NEOPLASTIC

STUDY No. : 0676
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]
SEX : MALE

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PAGE:

Group Name	Control	100 ppm	200 ppm	400 ppm
	SITE : liver TUMOR : hepatocellular carcinoma			
Overall rates(a)	5/50(10.0)	8/50 (16.0)	4/49(8.2)	2/50(4.0)
Terminal rates(c)	b. 06 1/30(3.3)	22. 58 7/31 (22. 6)	11.76 4/34(11.8)	2. 56 1/39(2. 6)
Statistical analysis Peto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Atmitare test(e)	P = 0.8877 P = 0.9115 P = 0.9654 P = 0.1333			
Fisher Exact test(e)		P = 0.2768	P = 0.5130	P = 0.2180
Const.	SITE : liver TUMOR : hemangioma, hemangiosarcoma			
Overall rates (a)	8/50(16.0)	3/50(6.0)	4/49(8.2)	4/50(8.0)
Adjusted rates(b) Terminal rates(c)	16. 67 5/30(16. 7)	6.45 2/31(6.5)	5.88 2/34(5.9)	6. 98 2/39(5. 1)
Statistical analysis Peto test				
Standard method(d) Prevalence method(d) Combined analysis(d)	P = 0, 6802 P = 0, 8621 P = 0, 8820			
Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.3111	P = 0.0999	P = 0.1882	P = 0.1783
	SITE : liver TUMOR : hepatocellular adenoma, hepatocellular carcinoma	ocellular carcinoma		
Tumor rate Overall rates(a)	10/50(20.0)	16/50 (32.0)	19/49(38.8)	11/50(22.0)
Adjusted rates(b) Terminal rates(c)	17.65 4/30(13.3)	44.12 13/31(41.9)	42.86 14/34(41.2)	25. 00 9/39(23. 1)
Statistical analysis Peto test Standard method(d) Prevalence method(d)	P = 0.9233 P = 0.4353			
Combined analysis (d) Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.6669 P = 0.9940	P = 0.1271	P = 0. 0331*	P = 0. 5000
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NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSI	
STUDY No. : 0676 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1] SFY : MAIF	

Group Name	Control	100 ppm	200 ppm	400 ppm	
	SITE : Harderian gland		The state of the s		
Tumor rate					
Overall rates(a) Adjusted rates(b)	2/50(4.0)	4/50(8.0)	4/49(8.2)	4/50(8.0)	
Terminal rates(c) Statistical analysis	0/30(0.0)	0/31(0.0)	4/34(11.8)	10. 2b 4/39(10. 3)	
Peto test Standard method(d)	P =				
Prevalence method(d) Combined analysis(d)	P = 0.2771 P =				
Cochran-Armitage test(e) Fisher Exact test(e)	P = 0,5108	P = 0.3389	P = 0.3292	P = 0.3389	
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Standard method : Death analysis

⁽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.

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.

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: 0676 : MOUSE BGD2F1/Cr1j[Crj:BDF1] : MALE

STUDY No. ANIMAL

SEA . MALE		TANA TOTAL T	The state of the s	PAGE:
Group Name	Control	100 ppm	200 ppm	400 ppm
	SITE : ALL SITE			
Tumor rate Overall rates(a) Adjusted rates(h)	3/50(6.0)	2/50(4.0)	2/49(4.1)	4/50(8.0)
Terminal rates(c) Statistical analysis	0/30(0.0)	0.0 0/31(0.0)	0.0 0/34(0.0)	7. 69 3/39(7. 7)
Standard method(d) Prevalence method(d) Combined analysis(d)	P = 0.8481 P = 0.0067** P = 0.3525			
Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.5631	P = 0.5000	P = 0.5097	P = 0.5000
Throw woth	SITE : ALL SITE TUMOR : malignant lymphoma		The state of the s	
overall rates(a) Adjusted rates(h)	9/50(18.0)	6/50(12.0)	7/49(14.3)	13/50 (26. 0)
Terminal rates(c) Statistical analysis Peto test	4/30(13.3)	4/31 (12. 9)	11. (b 4/34(11. 8)	20.51 8/39(20.5)
Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e)	P = 0.4453 P = 0.1723 P = 0.2180 P = 0.1752			
Fisher Exact test(e)		P = 0.2883	P = 0.4101	P = 0.2348

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

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⁽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.

TABLE O2

NEOPLASTIC LESIONS-INCIDENCE

AND STATISTICAL ANALYSIS: FEMALE

ANALYSIS
STATISTICAL
AND
LESI ONS-INCIDENCE
NEOPLASTIC

STUDY No. : 0676
ANIMAL : MOUSE B6D2F1/Cr1;[Cr;:BDF1]
SEX : FEMALE

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Group Name	Control	100 ppm	200 ppm	400 ppm
Timor rate	SITE : lymph node TUMOR : malignant lymphoma			
Overall rates(a) Adjusted rates(b)	15/50(30.0)	14/49 (28. 6)	15/50(30.0)	13/50(26.0)
Terminal rates(c) Statistical analysis	25.81 8/31(25.8)	18. 52 5/27 (18. 5)	34.62 9/26(34.6)	20.59 7/34(20.6)
Peto test Standard method(d) Prevalence method(d) Combined analysis(d)	P = 0. 6912 P = 0. 5969 P = 0. 7065			
Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.6748	P = 0, 5259	P = 0.5862	P = 0.4120
Timor vato	SITE : liver TUMOR : hepatocellular adenoma			
Overall rates(a) Adjusted rates(b)	1/50(2.0)	5/49(10.2)	3/50(6.0)	3/50(6.0)
Terminal rates(c) Statistical analysis	1/31(3.2)	18. 52 5/27 (18. 5)	10.00 2/26(7.7)	8.82 3/34(8.8)
Peto test Standard method(d) Prevalence method(d)	P = P = 0.3705			
Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e)	P = 0, 6944	P = 0.0976	P = 0.3087	P = 0.3087
	SITE : liver			
Tumor rate	TOWNS THE HEAT STORY THE HEAT STATE OF THE S			
Overall rates(a) Adjusted rates(b)	0/50(0.0)	2/49(4.1)	4/50(8.0)	3/50(6.0)
Terminal rates(c) Statistical analysis	0/31(0.0)	2/27(7.4)	4/26(15.4)	3/34(8.8)
Peto test Standard method(d) Prevalence method(d) Combined analysis(d)	P = 0.1100 P = 0.1100			
Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.1524	P = 0.2424	P = 0.0587	P = 0.1212
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STUDY No. : 0676
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
SEX : FEMALE

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400 ppm	3/50(6.0) 8.82 3/34(8.8)	P = 0.3087	12/50 (24. 0) 27. 91 7/34 (20. 6)	P = 0, 4048	14/50 (28. 0) 30. 23 8/34 (23. 5)	P = 0. 2415
200 ppm	3/50(6.0) 10.00 2/25(7.7)	P = 0.3087	13/50(26.0) 33.33 8/26(30.8)	P = 0.3176	13/50 (26. 0) 33. 33 8/26 (30. 8)	P = 0.3176
100 ppm	: liver : hepatocellular adenoma, hepatocellular carcinoma 0(2.0) 5/49(10.2) 3.23 18.52 1(3.2) 5/27(18.5)	P = 0. 0976	11/48(22. 9) 39. 29 10/27(37. 0)	P = 0, 4577	a 11/48(22. 9) 39. 29 10/27(37. 0)	P = 0. 4577
Control	SITE : liver TUMOR : hepatocellular adenoma 1/50(2.0) 3.23 1/31(3.2)	P = 0.3705 P = 0.3705 P = 0.6944	SITE : pituitary gland TUMOR : adenoma 10/50(20.0) 29.03 9/31(29.0)	P = 0.4099 P = 0.3709 P = 0.3632 P = 0.6379	SITE : pituitary gland TUMOR : adenoma, adenocarcinoma 10/50(20.0) 29.03 9/31(29.0)	P = 0.1406 P = 0.2827 P = 0.2030 P = 0.3347
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)	Tumor rate Overall rates(a) Adjusted rates(b) Terminal rates(c) Statistical analysis	Peto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e)	Tumor rate Overall rates(a) Adjusted rates(b) Terminal rates(c) Statistical analysis	Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e) (HFT360A)

Group Name	The state of the s				PAGE:
	Control	100 mag	200 ppm	400 ppm	
SITE	SITE : ovary		100000		
Tumor rate					
Overall rates(a)	1/50(2,0)	(0 0)67/0			
Adjusted rates(b)	3.23		(0.0)00/0	3/50(6.0)	
Terminal rates(c)	1/31(3.2)	0/27(0,0)	0.0	1/34(2.0)	
Statistical analysis					
reto test Standard method(A)					
-					
	P = 0.0564				
	P =				
(e)	P = 0.0893				
Fisher Exact test(e)		P = 0.5051	P = 0.5000	P = 0.3087	
SITE	H : IItemis		ANGLE REGISTER CONTRACTOR CONTRAC		
TUM	• • •				
Overall rates(a)	9/50(18.0)	7/49 (14.3)	14/50(28.0)	8/50(16 0)	
Adjusted rates(b)	3.23	14.81	3 82	(2) 10: (2)	
Terminal rates(c)	1/31(3.2)	4/27(14.8)	1/96(3.8)	3/34(= 0)	
Statistical analysis Peto test					
method(d)	P = 0 4707				
(P)	2 = 0, 5451				
	P = 0.4987				
(e)	P = 0.9654		•		
Fisher Exact test(e)		P = 0.4101	P = 0.1710	P = 0.5000	

: 0676 : MOUSE B6D2F1/Cr1j[Crj:BDF1] : FEMALE

STUDY No. ANIMAL SEX

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400 ppm	2/50(4.0) 4.44 1/34(2.9)	P = 0.5000
200 ppm	3/50(6.0) 8.57 2/26(7.7)	F = 0.308/
100 ppm	0/49(0.0) 0.0 0/27(0.0)	10001
Control	SITE : Harderian gland TUMOR : adenoma 1/50(2.0) 2.44 0/31(0.0) P = P = 0.1767 P = 0.3306	
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)	

(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

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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 cochinal 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.

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: 0676 : MOUSE B6D2F1/Cr1j[Crj:BDF1] : FEMALE

STUDY No. ANIMAL SEX

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	400 ppm	9) 82 8) 0) 59 6)
	400	
TOTAL TANKS TO THE PARTY TO THE	200 ppm	16/50(32.0) 3.85 1/26(3.8) P = 0.2522 9/26(34.6) P = 0.5862
And the second s	100 ppm	10/49(20. 4) 14.81 4/27(14.8) P = 0. 4258 14/49(28. 6) 18. 52 5/27(18. 5) P = 0. 5259
The state of the s	Control	SITE : ALL SITE TUMOR : histiocytic sarcoma 12/50(24.0) 9.68 3/31(9.7) P = 0.5317 P = 0.6540 P = 0.6540 P = 0.6053 P = 0.8073 SITE : ALL SITE TUMOR : malignant lymphoma 15/50(30.0) 25.81 8/31(25.8) P = 0.6912 P = 0.6912 P = 0.6948 P = 0.6748
1000	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) Fisher Exact test(e) Tumor rate Overall rates(a) Adjusted rates(b) Terminal rates(c) Statistical analysis Peto test Standard method(d) Prevalence method(d) Cochran-Armitage test(e) Fisher Exact test(e) Fisher Exact test(e) Feto test Standard method(d) Cochran-Armitage test(e) Fisher Exact test(e)

N.C.:Statistical value cannot be calculated and was not significant.

⁽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

TABLE Q1

CAUSE OF DEATH : MALE

PAGE: I				RATSA
COUSE OF DEATH (SUMMARY) (0-105W)	400 ppm	111	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	TATAL TRANSPORT TO THE PROPERTY OF THE PROPERT
00	200 ppm	15	000 # 0 0 1	
	100 ppm	19	0147011008110	republica and representations
: 0676 : MOUSE B6D2F1/Cr1j[Crj:BDF1] : MALE	Control	20	0 0 0 0 22 1 3 3 0 1 1 0 0 0 22 1 1 3 3 0 0 1	
STUDY NO. : 0676 ANIMAL : MOUSE B6D21 SEX : MALE	Group Name	Number of Dead and Moribund Animal	no microscop confirm renal lesion urinary retention hydronephrosis tumor d:leukemia tumor d:lump node tumor d:lymph node tumor d:lymph node tumor d:lymph calinary tumor d:pituitary tumor d:pituitary tumor d:pleura	(BI0120)

BAIS4

TABLE Q2

CAUSE OF DEATH: FEMALE

					PAGE: 2
Group Name	Control	100 ppm	200 ppm	400 ppm	
Number of Dead and Moribund Animal	19	22	24	16	
no microscop confirm	1	2	0	0	
renal lesion	0		0	, , c	
urinary retention	0	0			
hydronephrosis	0	1	0		
tumor d:leukemia	2	6	9	, , ,	
tumor d:subcutis	0	2	0		
tumor d:lung	_	0	0		
tumor d:1ymph node	0	1	0	0	
tumor d:spleen	0	0		0	
tumor d:liver	-	0	0		
tumor d:pituitary	0	0	_		
tumor d:ovary	_	0	0	0	
tumor d:uterus	8	က	13		
tumor d:vagina	0	1	0		
tumor d:spinal cord	0	0	_	. 0	
tumor d:periph nerv	0		0	. 0	
tumor d:bone	0	0	0		
tumor d:peritoneum	0	1	1		

FIGURES

FIGURE 1	2,4-PENTANEDIONE VAPOR GENERATION SYSTEM AND
	INHALATION SYSTEM
FIGURE 2	SURVIVAL ANIMAL RATE OF MALE MICE IN THE 2-YEAR
I	NHALATION STUDY OF 2,4-PENTANEDIONE
FIGURE 3	SURVIVAL ANIMAL RATE OF FEMALE MICE IN THE 2-YEAR
	INHALATION STUDY OF 2,4-PENTANEDIONE
FIGURE 4	BODY WEIGHT CHANGES OF MALE MICE IN THE 2-YEAR
I IGUIL 4	INHALATION STUDY OF 2,4-PENTANEDIONE
FIGURE 5	BODY WEIGHT CHANGES OF FEMALE MICE IN THE 2-YEAR
FIGURE 3	INHALATION STUDY OF 2,4-PENTANEDIONE
EKCLUDE (
FIGURE 6	FOOD CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 2,4-PENTANEDIONE
FIGURE 7	FOOD CONSUMPTION CHANGES OF FEMALE MICE IN THE
	2-YEAR INHALATION STUDY OF 2,4-PENTANEDIO

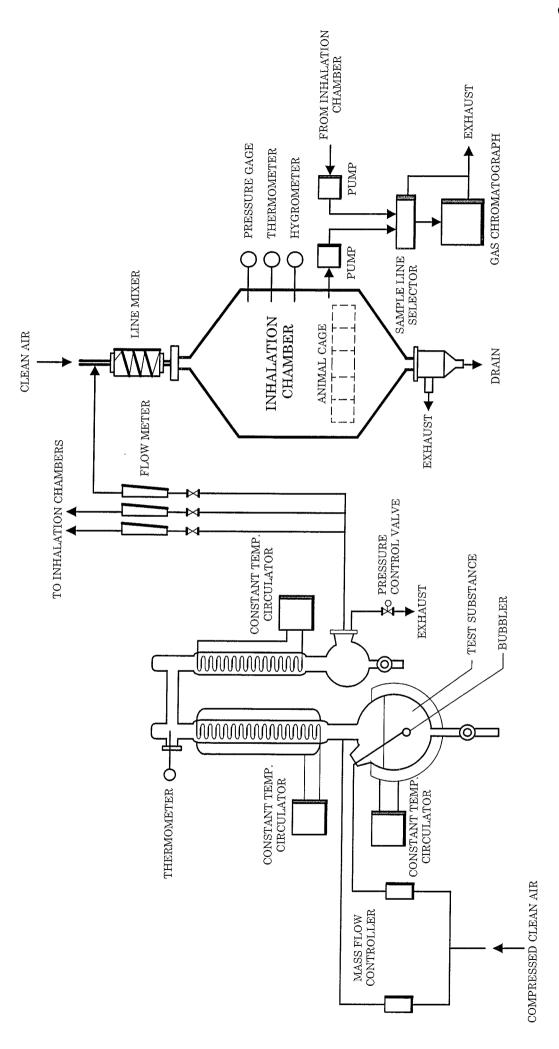


FIGURE 1 2,4-PENTANEDIONE VAPOR GENERATION SYSTEM AND INHALATION SYSTEM

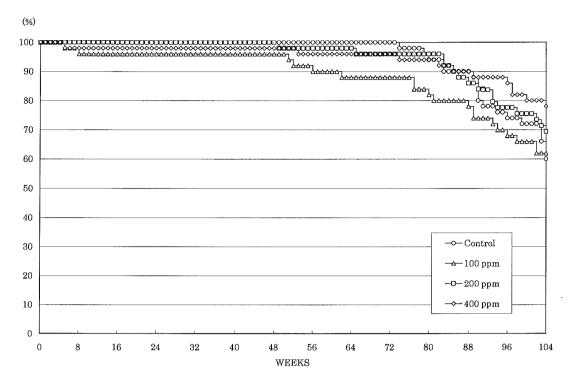


FIGURE 2 SURVIVAL ANIMAL RATE OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 2,4-PENTANEDIONE

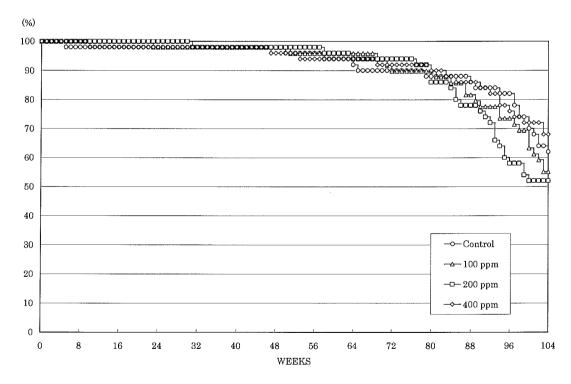


FIGURE 3 SURVIVAL ANIMAL RATE OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 2,4-PENTANEDIONE

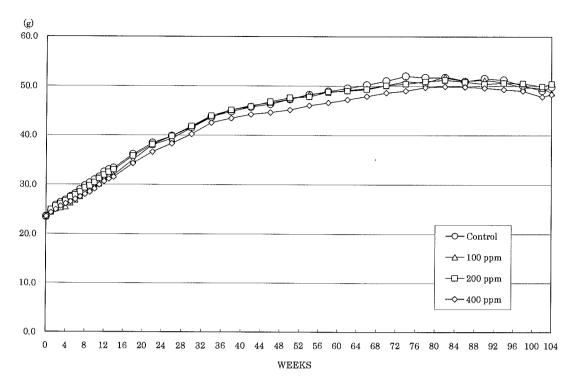


FIGURE 4 BODY WEIGHT CHANGES OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 2,4-PENTANEDIONE

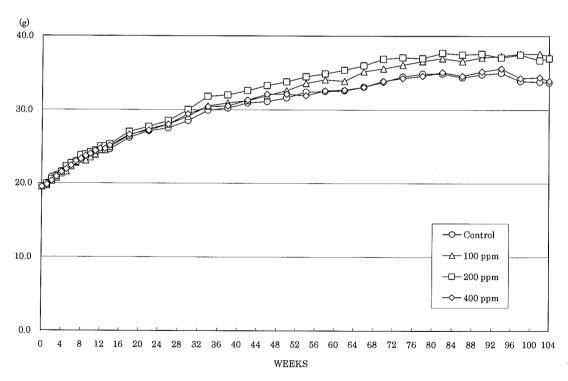


FIGURE 5 BODY WEIGHT CHANGES OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 2,4-PENTANEDIONE

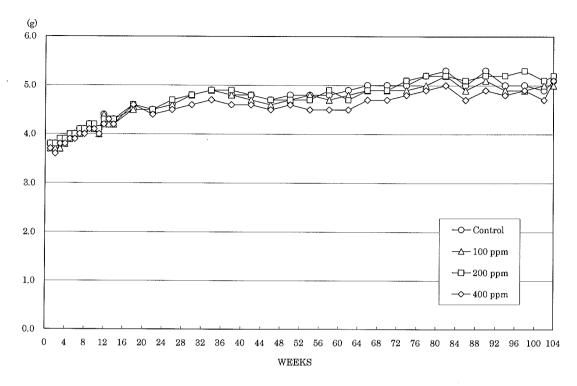


FIGURE 6 FOOD CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 2,4-PENTANEDIONE

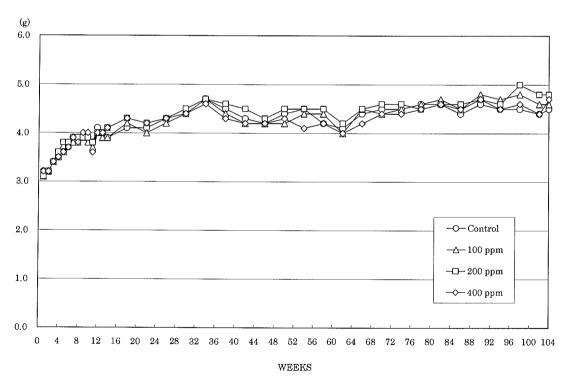
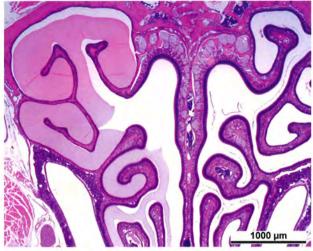
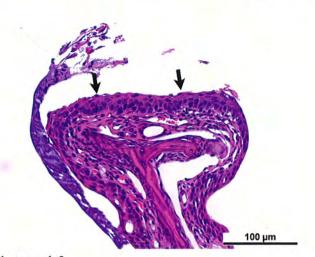


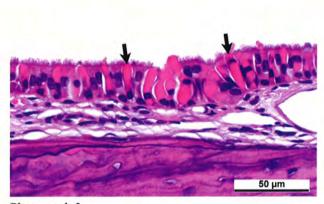
FIGURE 7 FOOD CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 2,4-PENTANEDIONE



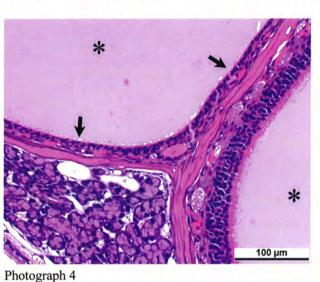
Photograph 1
Nasal cavity (Level 3): Exudate
Mouse, Male, 100 ppm, Animal No. 0676-1141 (H&E)



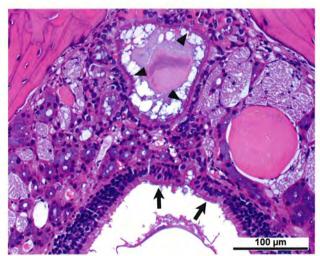
Photograph 2 Nasal cavity (Level 1): Squamous metaplasia (arrows) of the respiratory epithelium Mouse, Female, 400 ppm, Animal No. 0676-2314 (H&E)



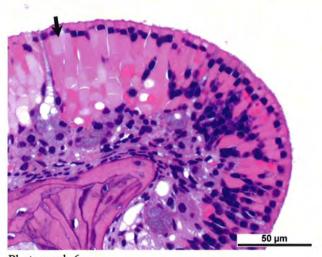
Photograph 3 Nasal cavity (Level 1): Eosinophilic change (arrows) of the respiratory epithelium Mouse, Male, 200 ppm, Animal No. 0676-1202 (H&E)



Nasal cavity (Level 3): Atrophy of the olfactory epithelium (arrows) and exudate (*)
Mouse, Male, 100 ppm, Animal No. 0676-1141 (H&E)



Photograph 5 Nasal cavity (Level 3): Respiratory metaplasia of the olfactory epithelium (arrows) and gland (arrowheads) Mouse, Female, 400 ppm, Animal No. 0676-2314 (H&E)



Photograph 6
Nasal cavity (Level 3): Eosinophilic change of the olfactory epithelium (arrow)
Mouse, Female, 400 ppm, Animal No. 0676-2344 (H&E)