### Summary of Drinking Water Carcinogenicity Study

of 3-Aminophenol

in B6D2F1 Mice

July 2012

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 July 31, 2012.

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

### Summary of Drinking Water Carcinogenicity Study of 3-Aminophenol in B6D2F1 Mice

#### Purpose, materials and methods

3-Aminophenol (CAS No. 591-27-5) is a white to pale gray crystals and with a melting point of 122°C. It is soluble in water, alcohol, and ether.

The carcinogenicity and chronic toxicity of 3-aminophenol were examined in B6D2F1/Crlj mice. Groups of test animals were administered 3-aminophenol in their drinking water for 2 years (104 weeks). Each group consisted of either 50 male or 50 female mice. The drinking water concentration of 3-aminophenol were 0, 625, 1250 or 2500 ppm (w/w). Both sexes were administered each concentration of 3-aminophenol. 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 3-aminophenol used in these experiments was confirmed by both infrared spectrometry and mass spectrometry. The chemical was analyzed by high performance liquid chromatography before and after use to affirm its stability. The concentrations of 3-aminophenol in the drinking water were determined by high performance liquid chromatography at the time of preparation and on the 4th day after preparation while stored at room temperature. The animals were observed daily for clinical signs and mortality. Body weight, water consumption and food consumption were measured once a week for the first 14 weeks and every 4 weeks thereafter. Animals found dead, in a moribund state, or surviving to the end of the 2-year administration period underwent complete necropsy. Urinalysis was performed near the end of the administration period. Hematology and blood biochemistry analysis were performed at the terminal necropsy: surviving animals were fasted overnight and bled under 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. Three 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 3-aminophenol 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, water consumption, 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 were found between any of the groups administered 3-aminophenol and their respective controls. Brown urine was observed in the males and females administered 1250 ppm and above. Body weights were supressed in the males and females administered 2500 ppm throughout the 2-year administration period, and body weights were supressed in the males administered 1250 ppm in the middle of administration period. Body weights were also supressed in the females administered 1250 ppm sporadically. Food consumption was decreased in the males administered 2500 ppm throughout the 2-year administered 1250 ppm throughout the 2-year administration period, food consumption was decreased in the females administered 1250 ppm and above sporadically. Water consumption of males and females administered 2500 ppm were suppressed throughout the 2-year administration period. Water consumption was decreased in the males administered 2500 ppm were suppressed throughout the 2-year administration period. Water consumption was decreased in the males administered 2500 ppm were suppressed throughout the 2-year administration period. Water consumption was decreased in the males administered 625 ppm in many of the 2-year administration period.

The incidences of selected neoplastic lesions in male and female mice are presented in the tables below. No significant increase in the incidence of neoplastic or neoplasm related lesions was found in any 3-aminophenol-administered group of either sex as compared with the respective control.

In blood and hematopoietic system, methemoglobin concentration was increased in the males and females administered 2500 ppm 3-aminophenol. Red blood cell count and hemoglobin concentration was decreased in females administered 2500 ppm. Mean corpuscular volume was increased in males administered 1250 ppm and above. Mean corpuscular hemoglobin was increased in males administered 2500 ppm. Mean corpuscular hemoglobin concentration was decreased in females administered 1250 ppm and above. Reticulocyte was increased in males administered 2500 ppm and above. Reticulocyte was increased in males administered 2500 ppm and females administered 1250 ppm and above.

In the spleen, deposit of hemosiderin was increased in males and females administered 1250 ppm and above. Increased extramedullary hematopoiesis was significantly observed in males and females administered 2500 ppm. Deposit of brown pigment was increased also in liver and follicular cell in thyroid in males and females administered 2500 ppm.

Using blood and hematopoietic system as endpoint markers, the no-observed-adverse-effectlevel (NOAEL) of 3-aminophenol in the drinking water was 625 ppm (64 mg/kg body weight per day for male and 81 mg/kg body weight per day for female).

#### **Conclusions**

There was no evidence for carcinogenicity of 3-aminophenol in male and female mice.

	Dose (ppm)	0	625	1250	2500	Peto test	Cochran- Armitage test
	Number of examined animals	50	50	50	50		
benign tumor							
lung	bronchiolar-alveolar adenoma	6	2	3	6		
spleen	hemangioma	1	3	1	1		
liver	hemangioma	2	3	3	1		
	hepatocellular adenoma	16	8	9	1 **		$\downarrow\downarrow$
Harderian	adenoma	2	3	4	0		
gland							
malignant tur	lor						
lung	bronchiolar-alveolar carcinoma	10	9	2 *	3 *		$\downarrow$
lymph node	malignant lymphoma	7	4	9	6		
liver	histiocytic sarcoma	6	2	4	1		
	hepatocellular carcinoma	7	6	5	2		
lung	bronchiolar-alveolar						
	adenoma +	16	10	5 **	0		
	bronchiolar-alveolar	10	10	5 **	9		
	carcinoma						
liver	hepatocellular adenoma +	21	12	10 *	2 **		11
	hepatocellular carcinoma	<i>∠</i> 1	13	12 *	5 ***		$\downarrow\downarrow$

Incidences of selected neoplastic lesions of male mice in the 2-year drinking water carcinogenicity study of 3-aminophenol

Significant difference

*: p≦0.05		**: p≦0.01		(Fisher test)
1: p≦0.05	increase	$\uparrow\uparrow:p \leq 0.01$	increase	(Peto, Cochran-Armitage test)
$\downarrow: p \leq 0.05$	decrease	$\downarrow\downarrow:p \leq 0.01$	decrease	(Cochran-Armitage test)

	Dose (ppm)	0	625	1250	2500	Peto test	Cochran- Armitage test
]	Number of examined animals	50	50	50	50		
benign tumor							
lung	bronchiolar-alveolar adenoma	2	3	1	1		
liver	hemangioma	1	1	1	3		
	hepatocellular adenoma	4	6	4	5		
pituitary	adenoma	4	9	6	7		
ovary	papillary adenoma	1	0	4	1		
uterus	endometrial stromal polyp	3	2	2	2		
Harderian	adenoma	1	0	4	3		
gland							
malignant tum	or						
lung	bronchiolar-alveolar carcinoma	1	4	1	2		
lymph node	malignant lymphoma	18	17	21	10		
liver	histiocytic sarcoma	2	3	0	1		
ovary	histiocytic sarcoma	16	14	12	12	↑ <sup>a</sup>	
mammary	adenocarcinoma	0	1	0	3	↑ (	↑
gland	adenosquamous carcinoma	0	1	0	1		
mammary gland	adenocarcinoma+ adenosquamous carcinoma	0	2	0	4	1	↑

Incidences of selected neoplastic lesions of female mice in the 2-year drinking water carcinogenicity study of 3-aminophenol

a :Significant only in Prevalence method in Peto test.

Significant difference

*: p≦0.05		**: p≦0.01		(Fisher test)
1: p≦0.05	increase	$\uparrow\uparrow:p \leq 0.01$	increase	(Peto, Cochran-Armitage test)
$\downarrow: p \leq 0.05$	decrease	$\downarrow\downarrow:p \leq 0.01$	decrease	(Cochran-Armitage test)

### SELECTED TABLES

- TABLE C 1 BODY WEIGHT CHANGES AND SURVIVAL ANIMAL NUMBERS: MALE
- TABLE C 2BODY WEIGHT CHANGES AND SURVIVAL ANIMAL NUMBERS:<br/>FEMALE
- TABLE C 3 BODY WEIGHT CHANGES: MALE
- TABLE C 4 BODY WEIGHT CHANGES: FEMALE
- TABLE D 1
   FOOD
   CONSUMPTION
   CHANGES
   AND
   SURVIVAL
   ANIMAL

   NUMBERS:
   MALE
- TABLE D 2FOODCONSUMPTIONCHANGESANDSURVIVALANIMALNUMBERS:FEMALE
- TABLE D 3FOOD CONSUMPTION CHANGES: MALE
- TABLE D 4FOOD CONSUMPTION CHANGES: FEMALE
- TABLE E 1
   WATER
   CONSUMPTION
   CHANGES
   AND
   SURVIVAL
   ANIMAL

   NUMBERS:
   MALE
- TABLE E 2WATER CONSUMPTION CHANGES AND SURVIVAL ANIMAL<br/>NUMBERS: FEMALE
- TABLE E 3WATER CONSUMPTION CHANGES: MALE
- TABLE E 4WATER CONSUMPTION CHANGES: FEMALE
- TABLE F 1 CHEMICAL INTAKE CHANGES: MALE
- TABLE F 2CHEMICAL INTAKE CHANGES: FEMALE
- TABLE G 1HEMATOLOGY: MALE
- TABLE G 2HEMATOLOGY: FEMALE
- TABLE H 1 BIOCHEMISTRY: MALE
- TABLE H 2BIOCHEMISTRY: FEMALE

### SELECTED TABLES (CONTINUED)

- TABLE I 1 URINALYSIS: MALE
- TABLE I 2URINALYSIS: FEMALE
- TABLE K 1 ORGAN WEIGHT, ABSOLUTE: MALE
- TABLE K 2ORGAN WEIGHT, ABSOLUTE: FEMALE
- TABLE L 1ORGAN WEIGHT, RELATIVE: MALE
- TABLE L 2ORGAN WEIGHT, RELATIVE: FEMALE
- TABLE M 1HISTOPATHOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS:<br/>MALE: ALL ANIMALS
- TABLE M 4HISTOPATHOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS:<br/>FEMALE: ALL ANIMALS
- TABLE P 1
   NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS:

   MALE
- TABLE P 2NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS:<br/>FEMALE
- TABLE RHISTORICALCONTROLDATAOFSELECTEDNEOPLASTICLESIONS IN JAPANBIOASSAYRESEARCHCENTER:B6D2F1/CrljFEMALEMICE
- TABLE S 1 CAUSE OF DEATH: MALE
- TABLE S 2CAUSE OF DEATH: FEMALE

### TABLE C 1

## BODY WEIGHT CHANGES AND SURVIVAL ANIMAL NUMBERS: MALE

PAGE																																				
		No. of	Surviv.	50/50	50/50	50/50 50/50	50/50	50/50	50/50	00/20 50/50	49/50	49/50	49/50	49/50	49/50	49/50	49/50	49/50	49/50	49/50 40/50	49/50	49/50	49/50	49/50	49/50 40/50	49/50	48/50	48/50	48/50	47/50	46/50	46/50	45/50	44/5U 40/50	40/ JU 39/50	
	Шdd	% 0f	cont. <50>	100	96 0	96 96	97	96	94	94 03	6	94	94	93	93	06 06	91	06	83	68 00	0°	89	89	89	88	60	6	06	91	91	94	6	68	86	87	
JRV I VAL	2500	Av. Wt.		24. 2 (50)	24.2 (50)	25.5 (50)	26.4 (50)	27.1 (50)	27.4 (50)	28 7 (50)	29.2 (49)	30.1 (49)	30.5 (49)	31.3 (49)	32.1 (49)	34.8 (49)	36.4 (49)	37.9 (49)	39.3 (49)	40.6 (49)	43. 4 (49)	44.2 (49)	44.8 (49)	45.4 (49)	45.0 (49) A6.2 (40)	46.7 (49)	46.9 (48)	47.1 (48)	47.8 (48)	47.5 (47)	47.8 (46)	47.0 (46)	45.7 (45)	44.4 (44) 43 3 (40)	43.0 (39)	A ROUNDARY AND
elghts and su		No. of	Surviv.	50/50	50/50	00/20 20/50	50/50	50/50	50/50	3U/3U 50/50	50/50	50/50	50/50	50/50	50/50 50/50	50/50	50/50	50/50	50/50	50/50 50/50	50/50	50/50	50/50	49/50	49/50	47/50	47/50	45/50	45/50	44/50	44/50	43/50	40/50	38/5U 21/50	31/50	
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	Ē	% of	cont. <50>	100	100 80	100	101	100	101	100	100	100	100	001	001	66	66	66	66 6	66 60	66	98	<u> 8</u> 8	98 28	90	66	66	98	66	100	103	701	99 0 C	CR 20	97	
(Crj:80F1)	625 pp	Av.Wt.		24.2 (50)	25.0 (50) 25.7 (50)	26.5 (49)	27.5 (49)	28.4 (49)	29.2 (49) 30 1 (40)	30.8 (49)	31.4 (49)	32.0 (49)	32.6 (49)	33.6 (49)	34.4 (49) 34.9 (49)	37.7 (49)	39.7 (49)	41.5 (49)	43. 5 (48)	45. U (48) 46. 7 (48)	48.1 (48)	48.8 (48)	49.5 (47)	49.9 (47) E0 E (47)	51 7 (45)	51.9 (44)	51.6 (44)	51.8 (44)	52.0 (43)	51.9 (42)	52.4 (41)	52.4 (39)	51.0 (38)	46.3 (30) A7 R (35)	47.9 (32)	
2 SE B6D2F1/Cr1j  104 E	rol	t. No. of	Surviv. <50>	(50) 50/50	(50) 50/50 (50) 50/50	(50) 50/50	(50) 50/50	(50) $50/50$	(50) 50/50 (50) 50/50	(50) 50/50	(50) 50/50	(50) 50/50		(50) 50/50	(50) 50/50 (50) 50/50	(50) 50/50	(50) 50/50	(50) 50/50	00/00 /00)	(50) 50/50	(49) 49/50	(49) 49/50	(49) 49/50	(49) 49/50	(48) 48/50	(48) 48/50	(47) 47/50	(47) 47/50	(45) $45/50$	(43) 43/50	(41) 41/50	131) 31/50 (37) 39/ED	(32) 32/50 (70) 20/E0	(27) 20/50	(24) 24/50	
: 071; : MOU(; : g : g : MALE	Contr	Av. W1		24.2	25.   25. 9	26.6	27.3	28.3	30.0	30.8	31.5	32.0	32.6	33 -	35 3 35 3	37.9	40.1	42.0	44 1 1	43. 3	48.5	49.6	50.5	51.0	52.0	52.2	52.2	52.6	52.4	52. U	5 U C E 1 J	01.4 51.5	51.0 71.0	1.10	49.4	
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### TABLE C 2

## BODY WEIGHT CHANGES AND SURVIVAL ANIMAL NUMBERS: FEMALE

Matrix Figua         Matrix Figua<	udy no. 11mal 11t	: 0712 : MOUSE	B6D2F1/Cr1,	j [Crj:BDF1]			W	AN BODY WE	eights and si	URV I VAL				
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	ORT TYPE	EMALE											PAGE :	2
		Control		625	Dpm		1250	Шdd		2500	Шdd			
Mark         Mark         Option         Option         Option         Option         Option         Option         Option           7         11         00	-	Av. Wt.	No. of	Av. Wt.	% of	No. of	Av. Wt.	% of	No. of	Av. Wt.	% of	No. of		
1         11         11         11         10         11         10 </th <th>ek-Day I Study</th> <th></th> <th>Surviv. &lt;50&gt;</th> <th></th> <th>cont. &lt;50&gt;</th> <th>Surviv.</th> <th></th> <th>con t. &lt;50&gt;</th> <th>Surviv.</th> <th></th> <th>cont. &lt;50&gt;</th> <th>Surviv.</th> <th></th> <th></th>	ek-Day I Study		Surviv. <50>		cont. <50>	Surviv.		con t. <50>	Surviv.		cont. <50>	Surviv.		
1         10         21         20         21         200         21         200         21         200         2	0-0	20.1 (5	(0) 50/50	20.1 (50	1) 100	50/50	20.1 (50)	100	50/50	20.1 (50)	100	50/50		-
7.7         7.1 <td>1-7</td> <td>20.5 (5</td> <td>50/50</td> <td>20.2 (50</td> <td>66 (I</td> <td>50/50</td> <td>20.1 (50)</td> <td>98</td> <td>50/50</td> <td>19.9 (50)</td> <td>97</td> <td>50/50</td> <td></td> <td></td>	1-7	20.5 (5	50/50	20.2 (50	66 (I	50/50	20.1 (50)	98	50/50	19.9 (50)	97	50/50		
	2-7	21.2 (5	50/ 50/50	20.8 (5(	) 98 (0	50/50	20.8 (50)	86 8	50/50	20.5 (50)	<u>16</u>	50/50		
	3-1 4-7	21.1 (5)	00 50/50	21. b (51 21 g (50	001 (1	50/50 50/50	21.2 (50) 21 9 (50)	96 90	50/50 50/50	21.0 (50)	97	50/50		
F-1         22.2         600         70/1         200         200         200         200           F-1         22.8         600         70/2         22.7         600         7         900           F-1         22.8         600         70/3         7         7         900         7         900           F-1         22.8         600         70/3         72.8         600         70         700         900         7         900           F-1         22.8         600         70/3         72.4         600         70         700         900         7	5-7	22.7 (5	0) 50/50	22.5 (50	66 (l	50/50	22.3 (50)	06 85	50/50	21. / (50) 22 1 (50)	86 07	5U/5U 50/50		
7.7         2.34         610         950         917         917         917         910         91         910         91         910         91         910         91         910         91         910         91         910         91         910         91         910         91         910         91         910         91         910         91         910         91         910 <t< td=""><td>6-7</td><td>23.2 (5</td><td>0) 50/50</td><td>23.3 (50</td><td>100</td><td>50/50</td><td>22.7 (50)</td><td>86 86</td><td>50/50</td><td>22. 6 (50)</td><td>26</td><td>50/50</td><td></td><td></td></t<>	6-7	23.2 (5	0) 50/50	23.3 (50	100	50/50	22.7 (50)	86 86	50/50	22. 6 (50)	26	50/50		
Priv         ZiA (50)         5/7         6/1         6	7-7	23.8 (5	0) 50/50	23.6 (50	66 (I	50/50	23.2 (50)	97	50/50	23. 1 (50)	67	50/50		
9-7         2.45         6.0         5.74         6.00         5.7         6.05         7         6.05           17-7         2.48         6.00         5.70         2.41         6.00         37         50.50           17-7         2.48         6.00         5.70         2.41         6.00         37.60         2.47         6.00         37         50.50           17-7         2.48         6.00         5.70         3.41         5.00         3.70         3.41         5.00         37.70         3.41         5.00         37.70         3.41         5.00         37.60         37.70	8-7	24.4 (5	10) 50/50	24.2 (50	66 (I	50/50	23.8 (50)	98	50/50	23.7 (50)	26	50/50		
10-7         2.4         6.0         5.0         5.4         6.0         97         50/5           17-7         2.6         5.0         5.0         5.1         500         2.4         500         7         50/5           17-7         2.6         5.0         5.0         5.0         50         5.0         50 <td< td=""><td>6-7</td><td>24.6 (5</td><td>50/50</td><td>24.4 (5(</td><td>66 ((</td><td>50/50</td><td>24.1 (50)</td><td>98</td><td>50/50</td><td>23.9 (50)</td><td>97</td><td>50/50</td><td></td><td></td></td<>	6-7	24.6 (5	50/50	24.4 (5(	66 ((	50/50	24.1 (50)	98	50/50	23.9 (50)	97	50/50		
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	107	24.9 (5	50/50	24.8 (51	100	50/50	24.5 (50)	98	50/50	24.1 (50)	67	50/50		
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	/-[]	24.8 (5	50/50 50/50	24.7 (50	100	50/50	24.2 (50)	98	50/50	24.2 (50)	88	50/50		
17         16.0         10.0         50.70         15.6         10.0         17         50.70         15.7         10.0         10.7         50.70         10.0         10.7         50.70         10.0         10.7         50.70         10.0         10.7         50.70         10.0         10.7         10.0         10.7         10.0         10.7         10.0         10.7         10.0         10.7         10.0         10.7         10.0         10.7         10.0         10.7         <	1-71	() () () () () () () () () () () () () () () () () () () (	00 20/20	25. U (5)	00 (r	50/50	24.6 (50)	16	50/50	24.4 (50)	96	50/50		
11.         25.6         630         57.7         530         25.7         55.0         50.7         50.7         50.7         50	13-7 14-7	25. 8 (5 26. 0 (5	0) 50/50	25.4 (5( 75.9 (5()	100 (r	50/5U 50/50	25. 1 (50) 25. 8 (50)	/6 00	50/50 50/50	25.0 (50) 25.3 (50)	97 70	50/50 E0/50		
277         38.6         (49)         49750         28.7         (50)         0.0         50/50         27.7         50.50 <td>18-7</td> <td>26.6 (5</td> <td>0) 50/50</td> <td>27.2 (50</td> <td>102</td> <td>50/50</td> <td>26.3 (50)</td> <td>66</td> <td>50/50</td> <td>26. 0 (50) 26. 0 (50)</td> <td>6</td> <td>50/50 50/50</td> <td></td> <td></td>	18-7	26.6 (5	0) 50/50	27.2 (50	102	50/50	26.3 (50)	66	50/50	26. 0 (50) 26. 0 (50)	6	50/50 50/50		
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	22-7	28.6 (4	19) 49/50	28.7 (50	) 100	50/50	28.1 (50)	98	50/50	27.1 (50)	95	50/50		
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	26-7	29.3 (4	19) 49/50	29.6 (50	101 (0	50/50	28.8 (50)	98	50/50	27.5 (50)	94	50/50		
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	5U-1 5 4-7	30. 5 (4 39 1 14	19/ 49/50	30.5 (5( 11 7 (FO		50/50 50/50	30.1 (50)	66 66	50/50	28.4 (50)	93	50/50		
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	38-7	33 3 (4	10, 49/50	31.7 (51 33.0 (50	66 (r	5U/5U 50/50	31.0 (50) 31 7 (50)	97 05	50/50 E0/E0	29.3 (50) 20.3 (50)	6 6	50/50		
$66^{-7}$ $34.9$ $(49)$ $49.50$ $34.5$ $50.90$ $50.50$ $31.5$ $50.90$ $50.50$ $87^{-7}$ $35.4$ $49760$ $35.5$ $509$ $100$ $50.70$ $32.5$ $50.70$ $32.7$ $50.90$ $50.750$ $32.7$ $50.90$ $32.7$ $50.90$ $32.7$ $50.70$ $32.7$ $50.750$ $32.7$ $40.750$ $32.6$ $40.750$ $32.6$ $40.750$ $32.6$ $40.750$ $32.7$ $40.750$ $32.7$ $40.750$ $32.7$ $40.750$ $32.7$ $40.750$ $32.7$ $40.750$ $32.7$ $40.7$	42-7	34.0 (4	19) 49/50	33.9 (50	100	50/50	32.5 (50)	96	50/50	30. 9 (50) 30. 9 (50)	91 16	50/50		
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	467	34.9 (4	19) 49/50	34.5 (50	66 (I	50/50	32.9 (50)	94	50/50	31.5 (50)	60	50/50		
3-7 $31$ $49$ $99$ $49/50$ $31$ $50$ $93$ $50/50$ $32$ $7(50)$ $88$ $50/50$ $37.1$ $47/50$ $31.1$ $49/50$ $31.7$ $50/50$ $32.7$ $500$ $88$ $50/50$ $77.1$ $47/50$ $31.7$ $49/9$ $99$ $48/50$ $34.7$ $49/9$ $33.7$ $50/50$ $88$ $50/50$ $77.1$ $41/7$ $38.6$ $48/9$ $99$ $48/50$ $34.7$ $48/9$ $32.7$ $500$ $88$ $50/50$ $77.1$ $14/1$ $47/50$ $38.7$ $48/9$ $92$ $48/50$ $32.7$ $500$ $88$ $50/50$ $77.1$ $14/1$ $47/50$ $38.4$ $48/50$ $34.3$ $48/50$ $32.7$ $48/50$ $88$ $50/50$ $77.1$ $31.3$ $14/750$ $37.6$ $48/50$ $32.7$ $48/50$ $32.7$ $48/50$ $88/50$ $50/50$ $78-7$ $38.6$ $37/50$ $37/6$ $37.7$ $41/750$	50-7	35.4 (4	19) 49/50	35.5 (50	) 100	50/50	33.6 (50)	95	50/50	32.1 (50)	91	50/50		
37.3 $43750$ $36.1$ $(49)$ $99$ $44750$ $33.1$ $(50)$ $88$ $50750$ $77.1$ $41750$ $36.9$ $48750$ $34.5$ $487$ $92$ $48750$ $33.1$ $(50)$ $88$ $50750$ $70-7$ $37.1$ $411$ $41750$ $36.9$ $48750$ $34.5$ $487$ $92$ $48750$ $33.2$ $(50)$ $88$ $50750$ $70-7$ $37.6$ $439$ $99$ $48750$ $34.5$ $48$ $92$ $48750$ $33.2$ $(50)$ $88$ $50750$ $70-7$ $37.6$ $439$ $99$ $48750$ $34.7$ $40$ $92$ $48750$ $32.7$ $(48)$ $85$ $50750$ $78-7$ $38876$ $37.7$ $477$ $92$ $44750$ $32.7$ $48750$ $85$ $48750$ $78-7$ $38876$ $37.7$ $477$ $92$ $44750$ $32.7$ $48750$ $88$ $50750$ $78-7$ $331750$ $331750$ $332.7$ $4$	54-7 ro -7	36.6 (4	19) 49/50	36.3 (49	66 (6	49/50	33.9 (50)	93	50/50	32.7 (50)	68	50/50		
71 $31.6$ $41.7$ $31.5$ $44.9$ $34.5$ $44.9$ $34.5$ $44.9$ $34.5$ $44.9$ $34.5$ $44.9$ $34.5$ $44.9$ $34.5$ $44.9$ $34.5$ $44.9$ $34.5$ $44.9$ $34.5$ $44.9$ $34.5$ $44.9$ $34.5$ $44.9$ $34.5$ $34.5$ $44.9$ $34.5$ $44.9$ $34.5$ $34.5$ $44.9$ $34.5$ $44.9$ $34.5$ $44.9$ $34.5$ $44.9$ $34.5$ $34.5$ $44.9$ $34.5$ $44.9$ $34.5$ $34.5$ $44.9$ $34.5$ $34.5$ $44.9$ $34.5$ $34.5$ $44.9$ $34.5$ $34.5$ $44.75$ $34.7$ $44.75$ $34.7$ $44.75$ $34.7$ $44.75$ $34.7$ $44.75$ $34.7$ $44.75$ $34.7$ $44.75$ $34.7$ $44.75$ $34.7$ $44.75$ $34.7$ $44.75$ $34.7$ $44.75$ $34.75$ $34.75$ $34.75$ $34.75$ $34.75$ $34.75$ $34.75$ $34.75$ $34.75$ $34.75$ $34.75$ $34.75$ $34.75$	20-1 59-7	31.3 (4	13) 49/50	31.1 (45	() AA	49/50	34.7 (49)	6	49/50	33. 0 (50)	88	50/50		
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	05 I	36.8 (4	41/30 16) 46/50	36 6 (48	00 (i	46/50 48/50	34.3 (48) 34.5 (48)	76	48/50	32. / (5U) 32 / (50)	80	0/DC		
$74^-7$ $37.6$ $(39)$ $3950$ $36.8$ $(47)$ $98$ $47/50$ $35.0$ $(45)$ $93$ $45/50$ $32.1$ $(48)$ $85$ $4850$ $78^-7$ $38.5$ $37.5$ $(47)$ $98$ $47/50$ $35.4$ $(42)$ $93$ $42/50$ $32.5$ $(48)$ $85$ $48/50$ $82^-7$ $38.0$ $(38)$ $39/50$ $37.0$ $(47)$ $98$ $47/50$ $35.0$ $(42)$ $92$ $42/50$ $32.7$ $(48)$ $85$ $48/50$ $86^-7$ $37.8$ $(33)$ $39/50$ $37.2$ $(41)$ $93$ $41/50$ $32.7$ $(48)$ $85$ $48/50$ $86^-7$ $37.8$ $(33)$ $38/50$ $37.3$ $(43)$ $99$ $43/50$ $33.7$ $(41)$ $92$ $41/50$ $32.7$ $(47)$ $87$ $91^-7$ $37.8$ $(33)$ $38/50$ $37.7$ $(41)$ $92$ $41/50$ $32.7$ $(45)$ $85$ $45/50$ $94^-7$ $37.3$ $33.350$ $35.7$ $(33)$ $96$ $33.750$ $33.7$ $(42)$ $82$ $45/50$ $94^-7$ $37.3$ $33.3550$ $35.7$ $(33)$ $96$ $33.750$ $33.7$ $(41)$ $92$ $40/50$ $94^-7$ $37.3$ $33.3550$ $35.7$ $(33)$ $96$ $33.750$ $33.7$ $(42)$ $82$ $45/50$ $96^-7$ $37.5$ $33.9$ $96$ $33.750$ $33.7$ $(42)$ $82$ $45/50$ $96^-7$ $33.750$	2-02	37.1 (4	1) 41/50	36.3 (45	86	48/50	34, 3 (46)	92	46/50	32.0 (50)	98	50/50		
$78^-7$ $38.2$ $(39)$ $37.5$ $(47)$ $98$ $47/50$ $35.4$ $(42)$ $93$ $42/50$ $32.5$ $(48)$ $85$ $48/50$ $82^-7$ $38.0$ $38.750$ $37.0$ $47/7$ $97$ $47/50$ $35.0$ $(42)$ $92$ $42/50$ $32.4$ $(48)$ $85$ $48/50$ $86^-7$ $38.8$ $38.750$ $37.3$ $43.99$ $43750$ $35.2$ $(41)$ $93$ $41/50$ $32.7$ $(47)$ $87$ $47/50$ $90^-7$ $37.8$ $(38)$ $38/50$ $35.7$ $(40)$ $92$ $40/50$ $32.7$ $(47)$ $87$ $45/50$ $90^-7$ $37.8$ $38.3350$ $35.7$ $(48)$ $85$ $45/50$ $45/50$ $34.7$ $(40)$ $92$ $40/50$ $32.1$ $(42)$ $87$ $45/50$ $90^-7$ $37.150$ $35.7$ $38.9$ $96$ $38/50$ $31.7$ $(40)$ $92$ $40/50$ $32.1$ $(42)$ $87$ $45/50$ $96^-$	74-7	37.6 (3	19) 39/50	36.8 (47	7) 98	47/50	35.0 (45)	93	45/50	32. 1 (48)	85	48/50	,	
82-7       38. 0       (38)       38/50       37. 0       (47)       97       47/50       35. 0       (42)       92       42/50       32. 4       (48)       85       48/50         86-7       37. 8       (38)       38/50       37. 3       (43)       99       43/50       35. 2       (41)       93       41/50       32. 7       (47)       87       47/50         90-7       37. 8       (38)       39       97       39/50       34. 7       (40)       92       40/50       32. 1       (45)       85       45/50         94-7       37. 3       33       35.6       (39)       96       38/50       33. 7       (40)       92       40/50       32. 1       (45)       85       45/50         94-7       37. 3       33       35.0       96       38/50       33. 7       (40)       92       40/50       32. 1       (45)       85       45/50         94-7       37. 3       31       313       31/50       35.7       38.4       43/50         96-7       37. 4       (33)       96       33.7       38.9       91       38.7       4.2       56         36. 3       25.556 <td>7-87</td> <td>38.2 (3</td> <td>19) 39/50</td> <td>37.5 (47</td> <td>7) 98</td> <td>47/50</td> <td>35.4 (42)</td> <td>93</td> <td>42/50</td> <td>32.5 (48)</td> <td>85</td> <td>48/50</td> <td></td> <td></td>	7-87	38.2 (3	19) 39/50	37.5 (47	7) 98	47/50	35.4 (42)	93	42/50	32.5 (48)	85	48/50		
$85^{-7}$ $37.8$ $(38)$ $38/50$ $37.3$ $(43)$ $99$ $43/50$ $35.2$ $(41)$ $97$ $41/50$ $32.7$ $(47)$ $87$ $47/50$ $90^{-7}$ $37.3$ $37/50$ $36.6$ $(39)$ $97$ $39/50$ $34.7$ $(40)$ $92$ $40/50$ $32.1$ $(45)$ $85$ $45/50$ $94^{-7}$ $37.3$ $33.50$ $35.7$ $(38)$ $91$ $38/50$ $32.1$ $(40)$ $92$ $40/50$ $32.1$ $(42)$ $85$ $45/50$ $94^{-7}$ $37.1$ $(31)$ $31/50$ $35.7$ $(33)$ $96$ $33/50$ $32.9$ $40/50$ $32.1$ $(42)$ $82$ $45/50$ $94^{-7}$ $37.1$ $(24)$ $96$ $33.7/50$ $31.4$ $(33)$ $82$ $39/50$ $96^{-7}$ $37.0$ $(24)$ $96$ $23.4$ $(33)$ $92$ $33.750$ $30.4$ $(42)$ $82$ $39/50$ $70$ $24/50$ $34.4$ $(33)$ $93$ $3$	82-7	38.0 (3	18) 38/50	37.0 (47	.) 97	47/50	35.0 (42)	92	42/50	32.4 (48)	85	48/50		
90-7 37.8 (37) 37/50 36.6 (39) 97 39/50 34.7 (40) 92 40/50 32.1 (45) 85 45/50 94-7 37.3 (33) 33/50 35.7 (38) 96 38/50 33.9 (38) 91 38/50 31.2 (43) 84 43/50 98-7 37.1 (31) 31/50 35.5 (33) 96 33/50 33.9 (35) 91 35/50 30.4 (42) 82 42/50 02-7 36.3 (25) 25/50 34.8 (24) 96 24/50 33.7 (33) 93 33/50 30.8 (39) 85 39/50 02-7 37.0 (24) 24/50 34.5 (21) 93 21/50 34.4 (33) 93 33/50 30.5 (38) 82 38/50	86-7	37.8 (3	<b>38/50</b>	37.3 (4;	3) 66	43/50	35.2 (41)	93	41/50	32.7 (47)	87	47/50		
94-7 3.7.3 (3.3) 33/50 35.7 (38) 96 38/50 33.9 (38) 91 38/50 31.2 (43) 84 42/50 98-7 37.1 (31) 31/50 35.5 (33) 96 33/50 33.9 (35) 91 35/50 30.4 (42) 82 42/50 02-7 36.3 (25) 25/50 34.8 (24) 96 24/50 33.7 (33) 93 33/50 30.8 (39) 85 39/50 04-7 37.0 (24) 24/50 34.5 (21) 93 21/50 34.4 (33) 93 33/50 30.5 (38) 82 38/50	2-12	37.8 (3	87) 37/50	36.6 (35	26 (6	39/50	34.7 (40)	92	40/50	32.1 (45)	85	45/50		
98-7 3.1.1 31/50 35.5 (33) 96 33/50 3.9 (35) 91 35/50 30.4 (42) 82 42/50 02-7 36.3 (25) 25/50 34.8 (24) 96 24/50 33.7 (33) 93 33/50 30.8 (39) 85 39/50 04-7 37.0 (24) 24/50 34.5 (21) 93 21/50 34.4 (33) 93 33/50 30.5 (38) 82 38/50	94-7 22 7	37.3 (3	(3) 33/50	35.7 (38	3) 96	38/50	33.9 (38)	91	38/50	31. 2 (43)	84	43/50		
$04^{-7}$ 37. 0 (24) 24/50 34. 5 (21) 93 21/50 34. 4 (33) 93 33/50 30. 5 (38) 82 38/50 04-7 37. 0 (24) 24/50 34. 5 (21) 93 21/50 34. 4 (33) 93 33/50 30. 5 (38) 82 38/50	98-/ 02-7	31.1 (3	(1) 31/50	35.5 (3:	3) 96	33/50	33.9 (35)	91	35/50	30.4 (42)	82	42/50		
	04-7	37.0 (2	4) 24/50	34. 5 (21 34. 5 (21		21/50	33. / (33) 34. 4 (33)	56 76 76	33/50 33/50	30. 8 (39) 30 5 (38)	85 87	39/5U 38/50		
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## TABLE C 3

## BODY WEIGHT CHANGES: MALE

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j UNIT : g REPORT TYPE : A1 104 SEX : MALE	(Crj :80F1)		BODY WEIGHT CHANGES ALL ANIMALS	(SUMMARY)			PAGE
Group Name	Administration 0-0	n week-day	2-7	3-7	4-7	5-7	
							-
Control	24. 2 ± 0. 7	25.1± 0.9	<b>25.9</b> ± 0.9	<b>26.6</b> ± 1.1	<b>27.3</b> ± <b>1.3</b>	28. 3土 1. 4	<b>29.</b> 0 ± 1. 5
625 ррт	$24,2\pm$ 0.7	$25. 0 \pm 0.7$	<b>25.</b> 7 ± 1. 0	<b>26.</b> 5 ± 1. 1	<b>27.5</b> ± <b>1.1</b>	28. 4 ± 1. 2	<b>29</b> . 2 ± <b>1</b> . 2
1250 ррт	24. 2 ± 0. 7	24.9± 0.9	<b>25</b> .7 ± 0.9	$26.4\pm$ 1.0	27. 4 ± 1. 1	<b>28.</b> 2 ± 1. 2	28.9土 1.3
2500 ррт	24.2± 0.7	24. 2 ± 1. 0 <b></b> **	24.8± 1.4**	25. 5 土 1. 3**	26.4土 1.5**	27. 1 土 1. 5**	27.4土 1.8**
Significant difference	بر ال بر ال ال ال ال	, ** 10 0 ∧ 11		Acc T			
	20 × 11	** · I == 0.01		IEST OF DUNNETL			

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STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j UNIT : & REPORT TYPE : A1 104 SEX : MALE	[Crj :BDF1]		BODY WEIGHT CHANGES ALL ANIMALS	(SUMMARY)			PAGE : 2
Group Name	Administratic	on week-day					
	L-1	8-7	6–7	10-7	11-7	12-7	13-7
Control	<b>30.</b> 0 ± <b>1.</b> 6	30. 8 土 1. 7	<b>31.</b> 5 ± <b>1.</b> 9	32. 0 ± 2. 0	32.6十 2.1	33.7 ± 2.2	34.5士 2.4
625 ррт	30.1± 1.4	30. 8 土 1. 5	<b>31.</b> 4 ± 1. 7	<b>32.</b> 0 ± 1. 7	<b>32.</b> 6± 1.7	33.6土 1.9	<b>34. 4</b> ± 2. 0
1250 ррт	29.6土 1.5	30. 3土 1. 6	30.9土 1.8	$31.6\pm 2.0$	<b>32.</b> 2 ± 2. 1	<b>33.</b> 3⊥ <b>2.</b> 3	34.1± 2.4
2500 ррт	28.1± 2.1 <b>*</b> *	28. 7 ± 2. 2**	<b>29.</b> 2 ± 1. <b>9 * *</b>	<b>30.</b> 1 ± 2. 1 <b>* *</b>	30. 5 土 2. 2**	31. 3 ± 2. 3**	32.1士 2.5**
Significant difference ;	* : P ≦ 0.05	** : P ≦ 0.01		Test of Dunnett			

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STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j UNIT : s REPORT TYPE : A1 104 SEX : MALE	[Crj : BDF1]		BODY WEIGHT CHANGES ALL ANIMALS	(SUMMARY)			PAGE
Group Name	Administration 14-7	n week-day	2-66	26-7	30-7	34-7	7.00
			-	-		2-40	30-I
Control	35. 3 ± 2. 5	37.9土 2.6	40.1 ± 3.1	42.0 ± 3.4	<b>44.</b> 0 ± 3. 7	45.5士 3.6	47.2 ± 3.5
625 ррт	$34.9\pm$ 2.0	37.7± 2.6	<b>39.</b> 7 ± <b>2.</b> 8	41.5士 3.1	<b>43.</b> 5 ± 3. 5	45.0± 3.5	46.7 ± 3.5
1250 ррт	34.8 ± 2.4	<b>37.1</b> ± <b>2.8</b>	$39.\ 0\pm 3.4$	40.7 ± 3.8	<b>42.5</b> ± 4.1	43. 7± 4. 2*	45.3土 4.2*
2500 ррт	32. 8 ± 2. 5**	34. 8 土 2. 7**	36.4± 3.0**	37.9士 3.4**	<b>39.</b> 3 ± 3. 6 <b>* *</b>	<b>40.</b> 6 ± 3. 7 <b>* *</b>	<b>42.</b> 3 ± 3. 9 <b>* *</b>
Significant difference ;	* : P ≦ 0.05	** : P ≦ 0.01		Test of Dunnett			

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STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j UNIT : g REPORT TYPE : A1 104 SEX : MALE	[Crj:BDF1]		BODY WEIGHT CHANGES ALL ANIMALS	(SUMMARY)			PAGE : 4	
Group Name	Administratio 42-7	in week-day46-7	50-7	54-7	58-7	62–7	66-7	
Control	48.5 土 3.5	49.6± 3.6	50.5土 3.7	<b>51.</b> 0± 3.4	52.2 土 3.6	52.0土 3.6	<b>52.</b> 2 ± 3. 9	
625 ppm	<b>48. 1 ± 3. 6</b>	48.8 土 3.6	49.5 ± 3.7	49.9 4 4	<b>50.6</b> ± 5.4	<b>51.</b> 7 ± 3. 5	<b>51.9</b> ± <b>3.3</b>	
1250 ррт	<b>46.</b> 3 ± 4. 0*	47.0± 4.2 <b>*</b> *	<b>48.</b> 0 ± 4. 7 <b>*</b> *	48.8士 5.0*	49.8土 5.1*	49. 7 ± 5. 4*	50.0	
2500 ррт	43. 4	44. 2 士 4. 2 * *	44.8± 4.5 <b>*</b>	45.4土 5.5**	46. 0 ± 5. 5 <b>* *</b>	46. 2 土 5. 5**	46.7 ± 5.7 <b>*</b> *	
Significant difference .				Toot of Discontinue				

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STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j UNIT : g REPORT TYPE : A1 104 SEX : MALE	[Crj:BDF1]		BODY WEIGHT CHANGES ALL ANIMALS	(SUMMARY)			PAGE : 5
Group Name	Administratio 70-7	n week-day 74-7	78-7	82-7	86-7	2-06	94-7
Control	52. 2 ± 4. 6	52.6土 4.7	52.4± 5.5	52. 0± 5. 5	50.8+ 7.6	51.4+ 7.3	51 6+ 7 7
625 ppm	<b>51.6± 3.6</b>	<b>51.</b> 8土 4. 2	$52.0\pm5.0$	51.9± 5.5	$52.4\pm 5.3$	52.4+ 5.1	
1250 ррт	50.2 ± 5.5	<b>50.</b> 8 ± 6. 1	<b>51.</b> 8± 6.0	52. 0± 5. 9	51. 3 ± 6. 4	49.5± 7.9	$49.5 \pm 7.2$
2500 ppm	46.9 土 4.9**	47.1 ± 5.3 **	47.8± 5.6 <b>*</b> *	47. 5± 6. 0 <b>*</b> *	47.8± 6.3	47.0 <u>十</u> 6.5*	45. 7 +
Significant difference :	* : P ≦ 0.05	** : P ≦ 0.01		Test of Dunnett			

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Test of Dunnett

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STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Crlj. UNIT : g REPORT TYPE : A1 104 SEX : MALE	(Cr.j.:80F1]		BODY WEIGHT CHANGES ALL ANIMALS	(SUMMARY) PAGE · 6
Group Name	Adminictratio	nn week-dav		
	98-7	102-7	104-7	
Control	51.7± 6.4	49.5 土 7.5	<b>49.</b> 4 ± 7. 6	
625 ppm	<b>48.9</b> ± 6.6	47.8± 6.4	$47.~9\pm6.~2$	
1250 ррт	<b>48.</b> 3 ± 7.9	<b>4</b> 6. 8 ± 8. 2	<b>46.</b> 3 ± 9. 3	
2500 ppm	44.4 土 7.5**	<b>4</b> 3. 3 ± − 7. 6 <b>*</b> *	<b>43. 0</b> ± 7. 8 <b>*</b> ∗	
Significant difference ;	* : P ≦ 0.05	** : P ≤ 0.01		Test of Dunnett
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### TABLE C 4

### BODY WEIGHT CHANGES: FEMALE

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j UNIT : g REPORT TYPE : A1 104 SEX : FEMALE	[Crj:BDF1]		BODY WEIGHT CHANGES ALL ANIMALS	(SUMMARY)			PAGE : 7
Group Name	Administration 0-0	n week-day	2-7	3-7	4-7	57	6-7
Control	<b>20.</b> 1 ± 0. 8	20.5士 0.8	21. 2 土 1. 1	21.7 ± 1.1	22. 2 土 1. 3	22.7 土 1.4	23. 2 ± 1. 3
625 ppm	<b>2</b> 0.1 ± 0.8	<b>20.</b> 2 ± 0. 8	<b>20</b> .8± <b>1</b> .0	<b>21.</b> 6± 1.1	21.9土 1.1	22.5± 1.1	<b>23.3</b> ± <b>1.3</b>
1250 ppm	$20.1\pm0.8$	<b>2</b> 0. 1 ± 0. 9 <b>∗</b>	<b>20.8</b> ± 0.9	<b>21.</b> 2 ± <b>1.</b> 0	<b>21.</b> 8± <b>1.</b> 0	22. 3± 1. 1	22. 7± 1. 1
2500 ррм	<b>20.1</b> ± 0.8	<b>19. 9</b> ± 0. 8 <b>**</b>	$20.5 \pm 0.8 * *$	<b>21.</b> 0± 0.9**	<b>21</b> . 7 ± <b>1</b> . <b>0</b>	22. 1 土 1. 0*	$22.6 \pm 1.2$
Significant difference ;	* : P ≦ 0.05	** : P ≦ 0.01		Test of Dunnett			

BAIS 4

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Crij UNIT : g REPORT TYPE : A1 104 SEX : FEMALE	[Crj:B0F1]		BODY WEIGHT CHANGES ALL ANIMALS	(SUMMARY)			PAGE : 8
Group Name	Administratic 7-7	on week-day	0-7	10-7	11-7	10 7	г с <b>*</b>
	-	-	-	1-0-1	<i>i</i> _ 1	1-71	13-7
Control	23.8± 1.5	24.4土 1.7	24.6土 2.2	24.9± 2.0	24. 8 ± 2. 1	25.3± 2.3	25.8± 2.7
625 ррт	23.6土 1.4	<b>24.</b> 2 <u>+</u> <b>1. 5</b>	24.4土 1.5	24.8± 1.7	24.7 ± 1.6	<b>25.</b> 0 ± 1. 7	25.4± 2.0
1250 ррт	<b>23.</b> 2 ± 1. 2*	23. 8 土 1. 1	24.1 ± 1.3	<b>24.5</b> ± <b>1.3</b>	24.2 ± 1.5	24.6土 1.5	25.1土 1.6
2500 ррт	23.1± 1.2*	<b>23</b> . 7 ± <b>1</b> . <b>3</b>	23.9土 1.4	24.1士 1.4*	24. 2 土 1. 5	24.4土 1.7*	<b>25.</b> 0 ± 1. 7
Significant difference ;	* : P ≦ 0.05	** : P ≦ 0.01		Test of Dunnett			

(HAN260)

Test of Dunnett

BAIS 4

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j UNIT : g REPORT TYPE : A1 104 SEX : FEMALE	[Crj:BDF1]		BODY WEIGHT CHANGES ALL ANIMALS	(SUMMARY)			PAGE
Group Name	Administration 14-7	week-day 18-7	22-7	26-7	30-7	34-7	38-7
Control	26.0 <b>±</b> 2.7	<b>26.6</b> ± 2.9	28.6十 3.8	<b>29.</b> 3 ± 3. 9	<b>30.5</b> ± 4.7	32. 1 ± 5. 1	<b>33.</b> 3⊥ <b>4.</b> 9
625 ррт	25.9± 2.1	27. 2 ± 2. 1	<b>28</b> . 7 ± 2. 7	29.6土 3.4	30.5士 3.5	31.7 ± 3.9	33.0士 4.4
1250 ррт	25.8 ± 1.7	<b>26.</b> 3 ± 2. <b>0</b>	<b>28.1</b> ± <b>2.3</b>	28.8土 2.8	<b>30.1</b> ± <b>3.2</b>	$31.0\pm 3.5$	<b>31.</b> 7主 3.4
2500 ppm	<b>25.</b> 2 ± 1. 9	<b>26.</b> 0± 2. 1	27.1± 2.3 <b>*</b>	27.5± 2.6*	28.4士 2.7*	<b>29.</b> 3 ± 2. 8 <b>* ∗</b>	30.3土 2.8**
Significant difference ;	* : P ≤ 0.05	** : P ≦ 0.01		Test of Dunnett			

(HAN260)

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BAIS 4

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Crlj. UNIT : g REPORT TYPE : A1 104 SEX : FEMALE	(Crj : BDF1)		BODY WEIGHT CHANGES ALL ANIMALS	(SUMMARY)			PAGE - 10
Group Name	Administratic 42-7	on week-day 46-7	50-7	54-7	58-7	62-7	66-7
Control	34.0± 5.9	34.9土 5.9	35.4 ± 6.3	<b>36. 6</b> ± <b>6.</b> 5	<b>37.3</b> ± <b>5.9</b>	37.1± 4.8	36.8土 4.9
625 ррт	<b>33.9</b> ± <b>4.1</b>	34.5± 4.3	35.5 土 4.6	<b>36. 3</b> ± <b>4. 6</b>	<b>37.1</b> ± <b>4.8</b>	36.9土 4.8	36.6土 5.2
1250 ррж	32.5士 3.6	<b>32.</b> 9 ± 3. 7	33.6土 4.1	33.9± 4.2	<b>34.</b> 7 ± <b>4</b> . 8	<b>34. 3</b> ± 4. 5 <b>*</b> +	34.5土 4.8
2500 ррм	<b>30.</b> 9 ± 3. 0 <b>* *</b>	<b>31.</b> 5 ± <b>3.</b> 1**	32.1土 3.5**	<b>32.</b> 7 ± 3. 3 <b>* *</b>	33.0土 3.4**	32.7 土 3.4**	32.4 ± 3.2**
Significant difference;	* : P ≦ 0.05	** : P ≤ 0,01		Test of Dunnett			

BAIS 4

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j UNIT : g REPORT TYPE : A1 104 SEX : FEMALE	(Crj :80F1)		BODY WEIGHT CHANGES ALL ANIMALS	(SUMMARY)			PAGE
Group Name	Administratic	on week-dav					
	2-02	74-7	78-7	82-7	86-7	2-06	94-7
Control	37.1 ± 5.2	37.6土 4.9	<b>38.2</b> ± <b>4.9</b>	38.0土 4.9	37.8土 4.6	37.8± 5.4	<b>37.3± 6.2</b>
625 ррт	<b>36.3</b> ± 5.3	<b>36.</b> 8 ± 5. 0	37.5 ± 5.3	<b>37.0</b> ± <b>5</b> .8	<b>37.3</b> ± <b>5.6</b>	<b>36.6</b> ± <b>6.3</b>	<b>35.</b> 7 ± 6. 8
1250 ppm	34、3 土 4、7 *	35.0	35.4	35.0± 5.6 <b>*</b>	<b>35.</b> 2 ± 5. 8	34.7 土 5.8*	33. 9 ± 6. 0 <b>*</b>
2500 ррт	32.0士 3.9**	32. 1 土 4. 1 **	<b>32.</b> 5 ±     4. 7 <b>* *</b>	32.4土 4.5**	32.7 ± 5.1 **	<b>32.</b> 1± <b>4.</b> 5 <b>**</b>	31.2± 4.7**
Significant difference ;	* : P ≤ 0.05	** : P ≤ 0.01		Test of Dunnett			

BAIS 4

S (SUMMARY)
CHANGE
BODY WEIGHT ALL ANIMALS
STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : & REPORT TYPE : A1 104 SEX : FEMALE

PAGE : 12 

Group Name	Administration	1 week-day	
	987	102-7	104-7
Control	37.1 ± 5.8	<b>36. 3</b> ± <b>6. 3</b>	37.0 ± 7.0
625 ррт	35.5土 6.4	34.8± 6.0	34.5± 5.7
1250 ррт	<b>33.</b> 9 ± 5. 9	33.7土 5.8	34.4 ± 7.3
2500 ррт	30.4土 4.6**	30. 8 土 4. 3**	30.5士 4.6**
Significant difference ;	* : P ≤ 0.05	** : P ≦ 0.01	Test of Dunnett

BAIS 4

Test of Dunnett

### TABLE D 1

## FOOD CONSUMPTION CHANGES AND SURVIVAL ANIMAL NUMBERS: MALE

STUDY NO. ANIMAL UNIT REPORT TYPE	: 0712 : MOUSE : 8 : A1 104	B6D2F1/Cr1j	j [Crj :BDF1]			MEA	N FOOD CC	NSUMPT I ON (FC	) AND SURVIV	۲۲		
SEX	: MALE											PAGE : 1
	Contro	_	62	5 ppm		1250	шdd		2500 1	Шdc		
	Av. FC.	No. of	Av. FC.	% of	No. of	Av. FC.	% of	No. of	Av. FC.	% of	No. of	
week-uay on Study		ыгили. <50>		cont. <50>	Surviv.		con t. <50>	Surviv.		cont. <50>	Surviv.	
1-7	4.0 (5	0) 50/50	3.9 (5)	0) 98	50/50	3.9 (50)	98	50/50	3.5 (50)	88	50/50	
2-7	3.9 (E	10) 50/50	3.8 (5	0) 97	50/50	3.8 (50)	26	50/50	3.7 (50)	95	50/50	
3-7		50) 50/50	3.7 (4	97 97	49/50	3.7 (50)	26	50/50	3.6 (50)	95	50/50	
4-1 5-7	2) 2) 2) 2) 2) 2) 2) 2) 2) 2) 2) 2) 2) 2	0) 50/50		9) 100 100 (c	49/50 40/50	3.8 (50) 3.8 (50)	100	50/50 E0/50	3.7 (50)	97 01	50/50	
6-7	3.9 (5	0) 50/50	3.8 (4)	16 (6	49/50	3.8 (50)	16	30/30 50/50	3.7 (50)	55 95	5U/5U F0/F0	
7-7	4.0 (5	0) 50/50	3.9 (4	96 (6	49/50	3.9 (50)	98	50/50	3.7 (50)	63	50/50	
8-7	4.0 (E	10) 50/50	3.9 (4:	6) 98	49/50	3.9 (50)	98	50/50	3 8 (50)	95	50/50	
9-7 1 2 2 1	4.2	50/ 50/50	4.0 (4	9) 95	49/50	4.0 (50)	66	50/50	3.9 (49)	93	49/50	
11-7	4.2.4	0) 50/50	4.1 (4	6) 86 (6	49/50	4.1 (50)	98 3	50/50	3.9 (49)	93	49/50	
12-7	4 7 (5	01 50/50	4. 1 (4 A 1 (4	96 (t	49/50 40/50	4. 1 (5U) 4 1 (50)	86 80	50/50 50/50	4.0 (49)	95	49/50	
13-7	4.2 (5	0) 50/50	4.1.(4)	6 (f	49/50	4.1 (50)	0.6 86	50/50	4.0 (43) 4.0 (49)	95 95	43/3U /Q/FN	
14-7	4.2 (E	0) 50/50	4.1 (4	96 (6	49/50	4.2 (50)	100	50/50	4.1 (49)	86	49/50	
18-7	4.2 (5	50) 50/50	4.2 (4	9) 100	49/50	4.1 (50)	98	50/50	4.0 (49)	95	49/50	
1-77	4 v v v f	0) 50/50	4.1 (4.	9) 95 3)	49/50	4.1 (50)	95	50/50	4.0 (49)	93	49/50	
30-7	4 4 5 1 2 1 2	0) 50/50	4. 1 (4	9) 98 3) 95	49/5U 48/50	4. U (5U) A 1 (50)	45 29	50/50 50/50	3.9 (49) A D (40)	93	49/50 40/50	
34-7	4.5 (5	0) 50/50	4.5 (4)	3) 100	48/50	4.4 (50)	r 86	50/50	4.3 (49)	16 96	43/ 3U 49/50	
38-7	4.5 (5	0) 50/50	4.5 (4;	8) 100	48/50	4.4 (50)	98	50/50	4.4 (49)	86	49/50	
42-7	4.6	(9) 49/50	4.6 (4.	8) 100	48/50	4.5 (50)	98	50/50	4.4 (49)	96	49/50	
40-/ 50-7	4. / (4	19/ 49/50	4.6	8) A8	48/50	4.5 (50)	96 9	50/50	4.4 (49)	94	49/50	
54-7	4.6 (4	9) 49/50	4, 7 (4	7) 102	41/50 47/50	4. / (50) 4. 6. (49)	98 100	5U/5U 49/50	4.5 (49) A 6 (40)	94 100	49/50	
58-7	5.0 (4	18) 48/50	4.9 (4)	26 (2	47/50	4.8 (49)	96 96	49/50	4.6 (49)	92	49/50	
62-7	4,7 (4	8) 48/50	4.7 (4:	5) 100	45/50	4.6 (48)	98	48/50	4.5 (49)	96	49/50	
1-99 70 7	4 / 4	18) 48/50 7) 47/50	4.7.4	4) 100	44/50	4.5 (47)	96	47/50	4.4 (49)	94	49/50	
74-7	7 0 V	7) 47/50	4.8 (4	4) 98	44/50	4. ( (41)	96 9	47/50	4.5 (48)	32	48/50	
78-7	4 4 7 8 7	5) 45/50	4.0 (4)	3) 98	44/ 50	4.0 (45) 4.7 (45)	06 86	45/50 45/50	48) C.4 48) A.48)	94 07	48/5U 48/FD	
82-7	4.7 (4	3) 43/50	4.7 (4)	2) 100	42/50	4.6 (44)	86	44/50	4.4 (47)	64	47/50	
86-7	4.6 (4	11) 41/50	4.9 (4	1) 107	41/50	4.7 (44)	102	44/50	4.6 (46)	100	46/50	
2-06	4 8 6	(7) 37/50	4.7 (3.	9) 98	39/50	4.7 (43)	98	43/50	4.6 (46)	96	46/50	
94-/ 00 7	- 4 	(2) 32/50 0) 20/50	4.6 (3.	8) 68	38/50	4.7 (40)	100	40/50	4.4 (45)	94	45/50	
90-7 102-7	4 4 7 8 7 9	28/20 7) 27/50	4 A Q (3)	100	36/50 35/50	4. (38)	96 96	38/50 24/50	4.5 (44) 4.5 (44)	92	44/50	
104-7	4.8 (2	4) 24/50	4.8 (3;	2) 100	32/50	4.7 (31)	0 8 6	31/50	4.0 (40) 4.4 (39)	92 92	40/50 39/50	
	<b> </b> ~	>:No.of ef	fective an	imals, ( ):	No.of measur	ed animals	Av	FC. : g				

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### TABLE D 2

## FOOD CONSUMPTION CHANGES AND SURVIVAL ANIMAL NUMBERS: FEMALE

AND SURVIVAL	
CONSUMPTION (FC)	
N FOOD	
MEA	

2

PAGE																											
		No. of Surviv.	50/50 50/50 50/50	50/50 50/50	50/50 50/50	50050	50/50 50/50	50/50 50/50	50/50	50/50 50/50	50/50	50/50 50/50	50/50	50/50	50/50 50/50	50/50	50/50 50/50	50/50	50/50	50/50	40/30 48/50	48/50	47/50	45/50	43/50	42/5U 30/5D	38/50
	2500 ppm	Av. FC. % of cont. <50>	3. 3 (50) 92 3. 4 (50) 100 3. 3 (50) 07	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	3.6 (50) 100 3.7 (50) 100	3.8 (50) 100	3.8 (50) 9/ 3.8 (50) 100	3.9 (50) 100 3.8 (50) 100	3. 9 (50) 100	3.8 (50) 100 3.8 (50) 100	3.8 (50) 97	3.5 (50) 95 3.6 (50) 95	4. 0 (50) 98	4.0 (50) 93	4. 2 (50) 100	4.1 (50) 98	4.1 (50) 98 4.1 (50) 100	4. 0 (50) 95	3.8 (50) 97	3.8 (50) 95	3. 8 (48) 90 3. 8 (48) 90	3. 9 (48) 93	3.8 (47) 88	3.9 (45) 93	3.9 (43) 98	3.9 (42) 89 4 0 (30) 95	4.1 (38) 95
	) ррт	% of No.of cont. Surviv. <50>	97 50/50 100 50/50 97 50/50	97 50/50 100 50/50	97 50/50 97 50/50		100 50/50 100 50/50	97 50/50 97 50/50	97 50/50	100 50/50 100 50/50	97 50/50	97 50/50 97 50/50	98 50/50	95 50/50	98 50/50	98 50/50	98 50/50 100 49/50	93 48/50	97 48/50	95 46/50 BD 4E/ED	95 42/50	95 42/50	91 41/50	93 40/50	98 38/50	98 35/50 08 33/50	105 33/50
	1250	of Av. FC. v.	50         3.5         (50)           '50         3.4         (50)           '50         3.3         (50)	(50 3. 4 (50) (50 3. 5 (49)	(50 3.5 (50) (50 3.6 (50)	(50 3.8 (50)	50 3.8 (50)	50         3.8         50           50         3.7         50	50 3.8 (50)	50 3.8 (50) 50 3.8 (50)	50 3.8 (50)	50 3.6 (50) 50 3.7 (50)	50 4.0 (50)	(50 4.1 (50)	50 4.1 (50)	50 4.1 (50)	50 4.1 (50) 50 4.1 (49)	50 3.9 (48)	50 3.8 (48)	50 3.8 (46) 5.7 (45)	50 4.0 (42)	50 4.0 (42)	50 3.9 (41)	50 3.9 (40)	50 3.9 (38)	50 4.5 (33) 50 4.1 (33)	50 4.5 (33)
	nqq	% of No.c cont. Survi <50>	) 97 50/ ) 100 50/ ) 100 50/	) 100 50/	) 100 50/ ) 97 50/	) 97 50/	) 100 50/	) 97 50/ 97 50/	97 50/	) 100 50/ ) 97 50/	97 50/	) 100 50/ ) 95 50/	98 50/	) 95 50/ ) 100 50/	) 100 50/	) 105 50/	) 100 49/	98 48/	97 48/	) 98 48/ 08 47/	) 98 47/	102 47/	98 43/	) 100 39/	) 100 38/	1 100 33/ 102 24/	) 105 21/
	625	o.of Av.FC. rviv. >	50/50 3.5 (50 50/50 3.4 (50 50/50 3.4 (50	50/50 3.5 (50) 50/50 3.5 (50)	50/50 3.6 (50) 50/50 3.6 (50)	50/50 3.7 (50 50/50 3.7 (50	50/50 3.8 (50,	50/50 3.8 (50) 50/50 3.7 (50)	50/50 3.8 (50	50/50 3.8 (50) 50/50 3.7 (50)	49/50 3.8 (50	49/50 3.7 (50) 19/50 3.6 (50)	49/50 4.0 (50)	49/50 4.1 (50 19/50 4.2 (50)	<b>19/50 4.</b> 2 (50)	49/50 4.4 (50)	49/50 4.2 (49)	4.1 (48,	46/50 3.8 (48	41/50 5.9 (48 10/50 A D (47)	39/50 4.1 (47)	38/50 4.3 (47,	38/50 4.2 (43.	37/50 4.2 (39	33/50 4.0 (38 21/50 4.1 (38)	25/50 4.3 (24)	24/50 4.5 (21)
: g TYPE : A1 104 : FEMALE	Control	y Av. FC. No v (50)	3. 6 (50) 3. 4 (50) 3. 4 (50) 5	3.5 (50) ( 3.5 (50) (	3.6 (50) 5 3.7 (50) 5	3.8 (50) (	3.8 (50) 5	3.9 (50) 5 3.8 (50) 5	3.9 (50)	3.8 (50) 3.8 (50) 3.8 (50)	3. 9 (49) 4	3. / (49) 4 3. 8 (49) 4	4.1 (49) 2	4.3 (49) 4	4. 2 (49) 4	4.2 (49) 2	4. 2 (43) 4. 4. 1 (49) 4.	4.2 (47) 4	3.9 (46) 2	4. U (41) 4 4 1 (39) 3	4 2 (39) 5	4.2 (38) 🤅	4.3 (38)	4 2 (37)	4.0 (33)	4.2 (25) 2	4.3 (24)
UNIT REPORT SEX		Week-Da) on Stud	1-7 2-7 3-7	4-7 5-7	2-7 7-7	8-7 0-7	3 / 10-7	11-7 12-7	13-7	14-/ 18-7	22-7	20-7 30-7	34-7	38-7 42-7	46-7	50-7 51-7	58-7 58-7	62-7	20-2	74-7	7-87	82-7	86-7	2-06	94-/ 08-7	102-7	104-7

BAIS 4

(B10040)

TABLE D 3

### FOOD CONSUMPTION CHANGES: MALE

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j UNIT : g REPORT TYPE : A1 104 SEX : MALE	[Crj:80F1]	FOO	D CONSUMPTION CHANGE ANIMALS	(S (SUMMARY)			PAGE
Group Name	Administration 1-7(7)	week-day(effective) 2-7(7)	3-7 (7)	4-7 (7)	2-7 (7)	(1) 2-9	(1) 7-7
Control	4.0± 0.3	3.9± 0.2	<b>3.</b> 8± 0.3	<b>3</b> . 8⊥ 0. <b>3</b>	<b>3.</b> 9± 0.3	3.9土 0.2	<b>4.</b> 0± 0.3
625 ррт	<b>3.</b> 9 ± 0. 2	<b>3.</b> 8 ± 0. 4	3.7± 0.4	<b>3.</b> 8 ± 0. 2	3.8 ± 0.2	<b>3.</b> 8 ± 0. 3	3.9士 0.2
1250 ррт	<b>3.</b> 9 ± 0. 3 <b>*</b>	<b>3.</b> 8± 0.3	3.7± 0.3	3.8± 0.4	3.8± 0.3	3.8士 0.2	3.9± 0.3 <b>*</b>
2500 ррт	3.5土 0.2**	3.7± 0.3*	<b>3.</b> 6± <b>0.</b> 3	3.7 土 0.3**	<b>3.</b> 7 ± <b>0.</b> 3 <b>* *</b>	<b>3.</b> 7土 0. 3 <b>*</b> *	3.7士 0.3**
Significant difference ;	* ™ 10.05	#* : P ≦ 0.01		Test of Dunnett			

Test of Dunnett \*\* : P ≦ 0.01

BAIS 4

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j UNIT : g REPORT TYPE : A1 104 SEX : MALE	[Grj:BDF1]	FO	DD CONSUMPTION CHANGE - ANIMALS	S (SUMMARY)			
Group Name	Administratic 8-7(7)	on week-day(effective) 9-7(7)	10-7 (7)	(2) 2-11	12-7 (7)	13-7 (7)	PAGE : 2 14-7 (7)
CONTROL	$4.0 \pm 0.3$	4.2 ± 0.3	4.2± 0.3	<b>4.</b> 2 ± <b>0.</b> 3	4.2± 0.3	4. 2 士 0. 3	$\textbf{4.} \ \textbf{2} \pm  \textbf{0.} \ \textbf{3}$
625 ррт	<b>3.</b> 9 ± 0. 3	$4. \ 0 \pm 0. \ 2$	<b>4</b> , 1± 0. 3	4.1 ± 0.3	<b>4</b> .1± 0.3	<b>4.1</b> ± 0.3	4.1 ± 0.3
1250 ррт	<b>3.</b> 9 ± 0. <b>3</b>	<b>4.</b> 0 ± 0. 3	<b>4.1</b> ± 0.3	4.1± 0.3	4.1± 0.3 <b>∗</b>	4. $1 \pm 0.3$	4. 2 土 0. 3
2500 ррт	3.8± 0.3 <b>*</b> *	3.9± 0.2 <b>*</b> *	3.9± 0.3**	<b>4.</b> 0 ± 0. 3 <b>* *</b>	4. $0 \pm 0.3 * *$	4.0 - 0.3**	<b>4.1</b> ± 0.3
Significant difference ;	* : P ≦ 0.05	** : P ≦ 0.01		Test of Dunnett			

(HAN 260)

BAIS 4

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j UNIT : g REPORT TYPE : A1 104 SEX : MALE	[Crj:BDF1]	F0 ALI	DD CONSUMPTION CHANGES L ANIMALS	S (SUMMARY)			 PAGE
Group Name	Administration 18-7(7)	week-day (effective) 22-7 (7)	26-7 (7)	30-7 (7)	34-7 (7)	38-7 (7)	42-7 (7)
Control	<b>4.</b> 2 ± 0. 3	<b>4</b> . 3 ± 0. 3	$\textbf{4.}\ \textbf{2}\pm  \textbf{0.}\ \textbf{3}$	4.4 ± 0.3	<b>4.</b> 5 ± 0. 3	<b>4.</b> 5 ± 0. 3	<b>4.</b> 6± 0.3
625 ppm	4.2 ± 0.3	<b>4.</b> 1 ± 0. 3 <b>*</b>	4.1 ± 0.2 *	<b>4</b> . 2 ± 0. 3	$4.5\pm 0.3$	4.5士 0.3	<b>4.</b> 6± 0.3
1250 ррт	<b>4.</b> 1 ± 0. 3	4.1± 0.3**	<b>4.</b> 0 ± 0. 3 <b>* *</b>	4.1土 0.4**	4.4 土 0.4	4.4± 0.3	<b>4</b> .5± 0.4 <b>*</b>
2500 ppm	<b>4.</b> 0 ± 0. 2 <b>* *</b>	4. 0 $\pm$ 0. 3**	3.9土 0.3**	<b>4</b> , 0 ± 0. 3 <b>*</b> ∗	4. $3\pm$ 0. $3**$	4.4士 0.3*	<b>4</b> . 4 ± 0. 3 <b>* *</b>
Significant difference ;	* : P ≦ 0.05	** : P ≦ 0.01		Test of Dunnett			

(HAN260)

Test of Dunnett

BAIS 4

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j1 UNIT : g REPORT TYPE : A1 104 SEX : MALE	(crj :80F1]	FOC	DD CONSUMPTION CHANGE ANIMALS	ES (SUMMARY)			PAGE : 4	
Group Name	Administration 46-7(7)	week-day (effective) 50-7(7)	54-7 (7)	58-7 (7)	62-7 (7)	(1) 2-99	(1) 2-02	
Control	4.7 ± 0.3	4.8士 0.4	$4.6\pm  0.4$	5.0 ± 0.3	<b>4</b> . 7± 0. 3	<b>4.</b> 7 ± 0. 5	<b>4.</b> 9± 0.4	
625 ррт	4. $6 \pm$ 0. 3	<b>4.</b> 7 ± 0. 3	4. $7 \pm 0.3$	<b>4.</b> 9⊥ 0. 4	<b>4</b> . 7 ± 0. 3	4.7 土 0.3	<b>4.</b> 8 ± 0. 3	
1250 ррт	<b>4.</b> 5 ± 0. 4 <b>* ∗</b>	4.7 十 0.5	4.6±0.4	<b>4.</b> 8± 0.4	$4,6\pm  0.4$	<b>4.</b> 5 ± 0. 6	4.7 土 0.4*	
2500 ррт	4.4士 0.3**	<b>4.</b> 5 ± 0. 4 <b>* *</b>	4.6± 0.4	4.6土 0.4**	4.5 ± 0.4 **	<b>4.</b> 4 ± − 0. 4 <b>* *</b>	<b>4.</b> 5 ± 0. 4 <b>* *</b>	
Significant difference ;	* * : P ≦ 0.05	** : P ≦ 0.01		Test of Dunnett				

(HAN260)

Test of Dunnett

BAIS 4
STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j UNIT : g REPORT TYPE : A1 104 SEX : MALE	[Crj:B0F1]	F0 ALL	DD CONSUMPTION CHANGE: L ANIMALS	s (summary)			 PAGE
Group Name	Administration	week-day (effective)					
	74-7 (7)	(2) 2-82	82-7 (7)	86-7 (7)	(2) 2-06	94-7 (7)	64-7 (7)
Control	<b>4.</b> 8 ± 0.4	<b>4.</b> 8 ± 0. 7	4.7 ± 0.5	<b>4.</b> 6± 1. 1	<b>4.</b> 8⊥ 0.5	4.7 ± 0.9	<b>4</b> .9± 0.5
625 ppm	4.6± 0.4	4.7± 0.4	4.7 ± 0.4	<b>4</b> .9± 0.5	4.7 ± 0.7	4.6± 0.4	4.9 ± 0.5
1250 ррт	4. $6 \pm$ 0. 4*	4.7 土 0.4	4.6± 0.4	4.7± 0.5	<b>4</b> . 7 ± 0. 5	<b>4</b> . 7 ± <b>0</b> . 7	<b>4</b> . 7 ± 0. 7
2500 ррт	4. 5 $\pm$ 0. 3**	4. 4± 0. 4 <b>*</b> *	4, 4 ± 0. 5 <b>*</b> ∗	<b>4.</b> 6 ± 0. 5	4.6 $\pm$ 0.5*	4.4土 0.5*	4.5士 0.6*
Significant difference ;	 10 10 10 10 10 10 10 10 10 10 10 10 10	** : P ≤ 0.01		Test of Numett			
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BAIS 4

(HAN260)

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j UNIT : g REPORT TYPE : A1 104 SEX : MALE	[Cr.j : BDF1]	FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS	PAGE : 6
Group Name	Administration 102-7 (7)	n week-day(effective) 104-7(7)	
Control	4.8±0.5	4.8 ± 0.7	
625 ррт	$4.~9\pm0.~8$	4.8± 0.6	
1250 ppm	4, 7 ± 0.8	4.7 ± 0.7	
2500 ppm	$4.5\pm  0.6$	4.4± 0.4**	
Significant difference ;	* : P ≤ 0.05	** : P ≤ 0.01 Test of Dunnett	

(HAN260)

Test of Dunnett

BAIS 4

TABLE D 4

## FOOD CONSUMPTION CHANGES: FEMALE

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/CrIj UNIT : g REPORT TYPE : A1 104 SEX : FEMALE	(Crj:80F1]	FOC	DD CONSUMPTION CHANGE - ANIMALS	ES (SUMMARY)			PAGE : 7
Group Name	Administration 1-7(7)	week-day (effective) 2-7 (7)	3-7 (7)	4-7 (7)	5-7 (7)	(1) 2-9	(1) 1-1
Control	$3.6\pm$ 0.3	3. 4 ± 0. 3	$3.4\pm 0.3$	3.5土 0.4	3.5± 0.3	<b>3.6</b> ± <b>0.3</b>	<b>3</b> . 7 ± 0. 3
625 ррт	<b>3.</b> 5 ± 0. 2	3.4土 0.2	$3.4\pm 0.2$	3.5士 0.2	3. 5 ± 0. 2	3.6 土 0.3	<b>3.</b> 6 ± 0. 3
1250 ррт	3.5 ± 0.3	<b>3. 4</b> ± <b>0.</b> 3	<b>3</b> . 3 ± <b>0</b> . 2	3.4± 0.2	3.5±0.2	3.5 ± 0.2	3.6土 0.3
2500 ppm	3. 3 ± 0. 3 <b>* *</b>	<b>3.</b> 4 ± 0. 2	3. 3 土 0. 2	3.5 ± 0.2	$3.5\pm$ 0.2	3.6 ± 0.2	3.7 ± 0.2
Significant difference ;	* : P ≦ 0.05	** : P  ∆ 0.01		Test of Dunnett			

(HAN260)

Test of Dunnett

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j[ UNIT : g REPORT TYPE : A1 104 SEX : FEMALE	Crj :80F1]	FDO	JD CONSUMPTION CHANGE - ANIMALS	ES (SUMMARY)			PAGE : 8
Group Name	Administration 8-7(7)	week-day (effective) 9-7(7)	10-7 (7)	(2) 2-11	12-7 (7)	13-7 (7)	14-7 (7)
Control	<b>3.</b> 8± 0.3	3.9±0.4	3.8± 0.3	3.9± 0.3	3.8土 0.4	<b>3.</b> 9± 0.4	3. 8 土 0. 4
625 ppm	3. 7 ± 0. 3	<b>3.</b> 8 ± 0. 3	3.8± 0.3	3.8± 0.3	3.7 土 0.3	<b>3.</b> 8± <b>0.</b> 3	<b>3.</b> 8± 0.3
1250 ppm	3.8± 0.2	3.9± 0.2	$3.8\pm$ 0.3	<b>3.</b> 8 ± 0. 3	<b>3.</b> 7 ± <b>0. 3</b>	3.8土 0.2	3. 8 土 0. 3
2500 ррт	$3.8\pm0.3$	<b>3.</b> 8 ± 0. 3	3. 8 土 0. 3	3.9土 0.3	3.8± 0.3	3.9± 0.3	3.8± 0.3
Significant difference ;	* : P ≦ 0.05	** : P ≦ 0.01		Test of Dunnett			

(HAN260)

BAIS 4

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Crlj. UNIT : g REPORT TYPE : A1 104 SEX : FEMALE	.Crj:BDF1]	FOC	D CONSUMPTION CHANGE: ANIMALS	S (SUMMARY)			DAGE PAGE
Group Name	Administration 18-7(7)	N week-day (effective) 22-7 (7)	26-7 (7)	(2) 2-08	34-7 (7)	38-7 (7)	42-7 (7)
Control	3.8十 0.3	3.9土 0.4	3. 7 ± 0. 4	3.8± 0.4	<b>4.</b> 1 ± 0. 5	<b>4.</b> 3 ± 0. 4	<b>4.</b> 2 ± 0. 5
625 ppm	<b>3</b> . 7 ± <b>0</b> . 4	$3.8\pm$ 0.4	3.7 ± 0.4	3.6± 0.5 <b>*</b>	4.0± 0.5	4.1 ± 0.5	<b>4</b> . 2 ± 0. 4
1250 ppm	3.8 ± 0.3	$3.8\pm$ 0.3	3.6± 0.3	<b>3</b> . 7 ± <b>0</b> . 4	<b>4.</b> 0 ± 0. 4	4.1± 0.4	4.2 ± 0.6
2500 ррт	<b>3.</b> 8 ± <b>0. 3</b>	3.8± 0.3	3.5土 0.3**	<b>3.</b> 6 ± 0. 4	<b>4</b> . 0 ± 0. 3	4.0 ± 0.4	<b>4.</b> 2 ± 0. 3
Significant difference ;	* : P ≦ 0.05	t: P ≤ 0.01		Test of Dunnett			

(HAN260)

Test of Dunnett

BAIS 4

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j UNIT : g REPORT TYPE : A1 104 SEX : FEMALE	(Crj:BDF1]	FDO	JD CONSUMPTION CHANG	ES (SUMMARY)			PAGE : 10
Group Name	Administration 46-7(7)	week-day (effective) 50-7 (7)	54-7 (7)	58-7 (7)	(1) (1)	(1) 2-99	(2) 2-02
Control	<b>4.</b> 2 ± 0. 5	<b>4.</b> 2 ± 0. 6	4, 2 十 0. 5	<b>4.</b> 1 ± 0. 4	<b>4</b> . 2 ± 0. 6	3.9±0.5	<b>4.</b> 0± 0.6
625 ррт	4. $2 \pm 0.4$	<b>4</b> . 4 ± 0. 7	<b>4</b> . 2 ± 0. 6	<b>4</b> . 2 ± 0. 5	<b>4</b> .1 ± 0.5	3.8± 0.6	<b>3.</b> 9± 0.6
1250 ррт	<b>4</b> . 1 ± 0. 4	4.1± 0.5	4.1± 0.6	<b>4.</b> 1 ± <b>0. 6</b>	<b>3.</b> 9± <b>0.</b> 5 <b>**</b>	3.8 ± 0.5	3. 8 土 0. 4
2500 ррт	<b>4.</b> 2 ± 0. 5	<b>4</b> . 1 ± 0. 4	$4.1 \pm 0.4$	<b>4.</b> 1 ± 0. 5	<b>4.</b> 0 ± 0. 4	3.8 <b>⊥</b> 0.4	3.8土 0.4
Significant difference ;	* : P ≦ 0.05	** : P ≦ 0.01		Test of Dunnett			

(HAN260)

Test of Dunnett

BAIS 4

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j UNIT : g REPORT TYPE : A1 104 SEX : FEMALE	[Crj:BDF1]	FOO	DD CONSUMPTION CHANGE . ANIMALS	S (SUMMARY)			PAGE : 11
Group Name	Administration 74-7(7)	week-day (effective) 78-7(7)	82-7 (7)	(2) 2-98	(1) 7-06	94-7 (7)	(1) 7–86
Control	<b>4.</b> 1 <u>⊥</u> 0. 6	<b>4.</b> 2 ± 0. 5	<b>4.</b> 2 ± 0. 5	4.3± 0.7	<b>4.</b> 2 ± 0. 6	<b>4.</b> 0 ± 0. 8	<b>4</b> .4⊥ 1.0
625 ррт	$4.0 \pm 0.4$	4.1 士 0.7	<b>4</b> . 3 ± 1. 1	<b>4.</b> 2 ± 0. 7	· 4,2± 0.7	<b>4.</b> 0 <b>⊥</b> 0. 8	<b>4.</b> 4 ± 0.9
1250 ррт	3. 7 ± 0. 7 <b>* *</b>	<b>4</b> . 0 ± 0. 5	4. $0\pm$ 0. 6	3.9土 0.6*	<b>3.</b> 9 ± 0. 6	3.9± 0.6	<b>4.</b> 3 ⊥ 0. 6
2500 ррт	3.7± 0.5*	3. 8 土 0. 5**	<b>3.</b> 9 ± 0. 4 <b>*</b>	3. 8土 0. 5**	$3.9\pm0.5$	3.9± 0.7	3.9土 0.8**
Significant difference ;	* : P ≦ 0.05	** : P ≦ 0.01		Test of Dunnett			

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Test of Dunnett

BAIS 4

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

PAGE : 12

Group Name	Administration 102-7(7)	week-day (effective)	
Control	2 U +6 V		
60E		0 D D D D D D D D D D D D D D D D D D D	
010 DDM	4, 3 ±	4.5 ± 0.7	
1230 PPM	4. 1 ± 0. b	4.5 H 0.8	
		0 	
Significant difference ;	* : P ≦ 0. 05	** : P ≦ 0.01	Test of Dunnett

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\*\* : P ≦ 0.01

Test of Dunnett

BAIS 4

#### TABLE E 1

# WATER CONSUMPTION CHANGES AND SURVIVAL ANIMAL NUMBERS: MALE

STUDY NO. ANIMAL UNIT REPORT TYPE	: 0712 : MOUSE : g A1 104	B6D2F1/Cr1	j [Crj :80F1]			MEA	N WATER C	ONSUMPTION (W	IC) AND SURVIV	AL		
SEX	: MALE											PAGE : 1
	Cont ro	_	625	mqq i		1250	mqq		2500 p	Шd		
	Av. WC.	No. of	Av. WC.	% of	No. of	Av. WC.	% of	No. of	Av. WC.	% of	No. of	
eek-uay on Study		50>		cont. <50>	Surviv.		cont. <50>	Surviv.		cont. (50)	Surviv.	
1-7	4.7 (	50) 50/50	4.1 (50	1) 87	50/50	3.4 (50)	72	50/50	2.7 (50)	57	50/50	
2-7	44	49) 50/50	3.7 (50	) 84	50/50	3.4 (50)	22	50/50	2.6 (50)	59	50/50	
3-1 4-7	4 3 4	48) 50/50 18) 50/50	3.9 (45	16 (1	49/50 40/50	3.4 (50) 3.3 (50)	62 70	50/50	2.7 (50) 2.7 (50)	63	50/50 F0/F0	
5-7	44	50) 50/50	3.9 (49	68 (	49/50	3.4 (50)	21 21	50/50	2. 8 (50) 2. 8 (50)	04 64	5U/5U 50/50	
2-9	4.2 (	50) 50/50	3.8 (49	06 (	49/50	3.4 (50)	81	50/50	2.8 (50)	29	50/50	
2-7 7-7	4 1 4	50) 50/50	3.7 (45	06 (	49/50	3.5 (50)	85	50/50	2.9 (50)	11	50/50	
81 0-7	- 4 - 1 - 1	50/50 50/50	3.7 (45	) 63	49/50	3.3 (50)	83	50/50	2.8 (50)	02	50/50	
3-1 10-7	4 4 7	50/ 50/50 50/ 50/50	3.1 (45	06 (	49/50 40/60	3.5 (50) 3.E (E0)	85	50/50	2.9 (49)	17	49/50	
11-7	4 0 4	50) 50/50	3.8 (49	62	49/50	3. 3 (50)	00 22	00/00 50/50	2 0 (40)	11	49/50	
12-7	3.9 (1	50) 50/50	3.6 (49	92	49/50	3.4 (50)	87	50/50	2.9 (49)	74	49/50	
13-7	3.9 (!	50) 50/50	3.6 (49	) 92	49/50	3.4 (50)	87	50/50	3.0 (49)		49/50	
14-7	ئے مہر م	50) 50/50	3.5 (49	92	49/50	3.3 (50)	87	50/50	2.8 (49)	74	49/50	
10-1 22-7	, 1 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	20/ 50/ 50 20/ 50/50	3.4 (45	16 (1	49/50	3.2 (50)	91	50/50	2.7 (49)	77	49/50	
26-7	, e 9 9 9 9 9 9	50/ 50/50	37 (45 3 4 (45	76 (	49/50 40/50	3.3 (50)	8/	5U/50 50/50	2.8 (49)	74	49/50	
30-7	3.5 (	50) 50/50	3.4 (48	26 (	48/50	3.2 (50)	6	50/50	2 8 (49) 2 8 (49)	0 / U	49/30 49/50	
34-7	3.7 (	50) 50/50	3.6 (48	16 (	48/50	3.4 (50)	92	50/50	3.0 (49)	81	49/50	
38-7	3.7	50) 50/50	3.6 (48	26 (	48/50	3.4 (50)	92	50/50	3.0 (49)	81	49/50	
42-1 46-7	ے دے منہ	49) 49/50	3.7 (48	26 ()	48/50	3.5 (50)	92	50/50	3. 2 (49)	84	49/50	
50-7		10/27 (01 10/50	3. 5 (48	1 9/	48/50 47/50	3.6 (50) 3.5 (50)	92 0	50/50 50/50	3.1 (49)	62	49/50	
54-7	4.0 (4	19) 49/50	4.0 (47	100	47/50	3.6 (49)	06 76	20/20 49/50	3.7 (49)	70 80	49/ 30 49/50	
58-7	4.1 (2	18) 48/50	4.0 (46	.) 98	47/50	3.7 (49)	06	49/50	3. 2 (49)	78	49/50	
62-7 55 -7	4 1 7 7 7	48) 48/50	4.0 (45	98	45/50	3.7 (48)	06	48/50	3.2 (49)	78	49/50	
70-7	+ -  	101 48/50	4.3 (44	001	44/50	4.0 (47)	63 03	47/50	3.4 (49)	62	49/50	
74-7	4 9 7 9 7	17) 47/50	4.3 (44	06 (	44/50 AA/50	4.3 (41)	96 80	4//50 46/50	3.5 (48) 2.6 (40)	78	48/50	
78-7	4.7 (4	12) 45/50	4.4 (42	) 94	43/50	4.3 (43)	6	45/50	3 8 (48)	81	46/ 30 48/50	
82-7	4.5 (2	11) 43/50	4.3 (39	96 (	42/50	4.2 (43)	63	44/50	3.8 (47)	84	47/50	
86-7	4.6 (	40) 41/50	4.5 (39	) 98	41/50	4.5 (43)	98	44/50	4.0 (46)	87	46/50	
7-06	9 7 7 7 7 7	35) 37/50	4.7 (38	96 ()	39/50	4.5 (41)	92	43/50	4.0 (45)	82	46/50	
94-1 08-7	- ⊂ - ⊂	06/26 (10	4.9 (30 F 1 (31	104	38/50	4.9 (39)	104	40/50	4.0 (44)	85	45/50	
30-1 102-7	2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	15) 27/50	15) 1.C 0() 0 0	90 (	30/5U 35/50	4.8 (3b) 4.4 (20)	96 86	38/50 24/50	4.2 (42)	84	44/50	
104-7	5.4 (2	2) 24/50	5.1 (27	) 94	32/50	4.7 (28)	87	34/ JU 31/50	4. 1 (31) 4. 2 (36)	00 78	40/30	
	~	>:No. of et	ffective ani	mals.().	No of measur	ed animals	<u> </u>	دی. M				
101 001 1,								۵				
(B10040)												RAICA

#### TABLE E 2

# WATER CONSUMPTION CHANGES AND SURVIVAL ANIMAL NUMBERS: FEMALE

SURVIVAL
AND
CONSUMPTION (WC)
WATER
MEAN

STUDY NO. ANIMAL UNIT	: 0712 : MOUSE : g	B6D2F1/Cr1j	[Crj:BDF1]			MEAL	I WATER CO	NSUMPTION (W	C) AND SURVIN	/AL			
REPORT TYPE SEX	: A1 104 : FEMALE											PAGE : 2	2
	Control		625 p	md		1250 F	md		2500	ШШ			1
	Av. WC.	No. of	Av. WC.	% of	No. of	Av. WC.	% of	No. of	Av. WC.	% of	No. of		
week-Jay on Study		surviv. <50>		cont. <50>	Surviv.		cont. <50>	Surviv.		cont. <50>	Surviv.		
1-7	4.3 (5.	0) 50/50	4.0 (50)	93	50/50	3.6 (50)	84	50/50	2.7 (50)	63	50/50		I
2-7	4.1 (5	0) 50/50	3. 6 (50)	88	50/50	3.4 (50)	83	50/50	2.7 (50)	66	50/50		
3-7 A-7	4.1 (5 4.0 (5	0) 50/50 1) 50/50	3.7 (50)	06	50/50	3.5 (50)	85	50/50	2.8 (50)	68	50/50		
5-7	4 0 (3)	0) 50/50	3. 7 (50)	0688	5U/5U 50/50	3.6 (50) 3.7 (50)	90 88	50/50 50/50	2.9 (50) 2.0 (50)	73	50/50 50/50		
6-7	4.0 (5)	0) 50/50	3.7 (50)	93 93	50/50	3.6 (50)	06	50/50	3.0 (50)	75	10/00 50/50		
7-7	4.1 (5)	0) 50/50	3.7 (50)	6	50/50	3.7 (50)	06	50/50	3.1 (50)	9Z	50/50		
8-7	4.1 (5	0) 50/50	3.6 (50)	88	50/50	3.6 (50)	88	50/50	3.1 (50)	2.6	50/50		
2-6	4.2	0) 50/50	3.7 (50)	88	50/50	3.6 (50)	86	50/50	3.1 (50)	74	50/50		
7-01 11 2	4.1 (5	0) 50/50	3.7 (50)	06 0	50/50	3.7 (50)	06	50/50	3.1 (50)	76	50/50		
19-7	4. 1 (5 4 2 (5)	0) 50/50 0) 50/50	3. / (50) 2. 6. (50)	90 98	50/50 50/50	3.7 (50) 3.E (E0)	06 6	50/50	3.1 (50)	2.6 7.6	50/50		
13-7	4.2 (5)	0) 50/50	3.7 (50)	88	50/50	3.6 (50)	03 86	50/50 50/50	3. 1 (5U) 2 1 (50)	74	50/50 E0/E0		
14-7	4.0 (5)	0) 50/50	3.6 (50)	60	50/50	3.6 (50)	606	50/50	3.0 (50)	75	30/30 50/50		
18-7	3.8 (5	0) 50/50	3.4 (50)	89	50/50	3.2 (50)	84	50/50	2.9 (50)	2.6	50/50		
22-7	4.1 (4.	9) 49/50	3.5 (50)	85	50/50	3.3 (50)	80	50/50	3.0 (50)	73	50/50		
30-7	3. 9 (4	9) 49/50 2) 40/50	3.3 (50) 2.2 (E0)	65 29	50/50	3.1 (50)	62	50/50	2.8 (50)	72	50/50		
34-7	4,1 (4,	9) 49/50	3.4 (50)	6 6 6 6	50/50	3.2 (50)	28 80	50/50 50/50	2.8 (5U) 3.0 (50)	27	50/50 50/50		
38-7	4.0 (4:	9) 49/50	3.4 (50)	85	50/50	3.3 (50)	83	50/50	2.9 (50)	23	50/50		
42-7	4.1 (4.	9) 49/50	3.6(50)	88	50/50	3.3 (50)	80	50/50	3.0 (50)	73	50/50		
40-1 50-7	4   (4	9) 49/50 3) 40/50	3.6 (50)	888	50/50	3.4 (50)	83	50/50	3.0 (50)	73	50/50		
54-7	4.0 (4)	9) 49/50	3.4 (49)	85 85	30/ 30 49/50	3.2 (50) 3.3 (50)	83	50/50	2.8 (50) 2.9 (50)	68 73	50/50 50/50		
58-7	3.9 (4:	9) 49/50	3.5 (49)	90	49/50	3.2 (49)	82	49/50	2.8 (50)	72	50/50		
62-7	3.9 (4	7) 47/50	3.5 (48)	06	48/50	3.2 (47)	82	48/50	2.8 (50)	72	50/50		
1-99 20-7	3.9 (4)	6) 46/50	3.7 (48)	95 97	48/50	3.4 (47)	87	48/50	3. 0 (50)	22	50/50		
74-7	4 1 (3(	1) 41/30 30/50	(48) C.S. 27 (45)	88	48/50	3.4 (46) 3.5 (44)	85 10	46/50 45/50	3.1 (50)	82	50/50		
7-8-7	4.2 (3)	9) 39/50	3.9 (44)	63	47/50	3.8 (39)	06	43/30 42/50	3. 3 (46) 3. 9 (45)	00 26	46/5U 48/50		
82-7	4.2 (3	7) 38/50	4.1 (43)	98	47/50	4.1 (40)	98	42/50	3.4 (46)	81	48/50		
86-7	4.2 (3:	5) 38/50	4.2 (39)	100	43/50	4.2 (37)	100	41/50	3.5 (44)	83	47/50		
90-7 04-7	4.3 (3	5) 3//50	4.1 (34)	95	39/50	4.0 (33)	93	40/50	3.8 (43)	88	45/50		
98-7	4 - 10 7 - 10	0/ 33/30 3/31/50	4 I (3U) A 2 (97)	001	38/5U 22/50	4. b (35)	112	38/5U 35/50	3.6 (40)	88	43/50		
102-7	4.4 (2)	1) 25/50	4.1 (19)	6 66	24/50	4.0 (30)	50	33/50 33/50	3. 8 (40) 4 2 (36)	80 02	42/5U 20/5A		
104-7	4.5 (2)	0) 24/50	4.0 (15)	89	21/50	4. 2 (21)	93	33/50	4. 2 (36)	63 7	38/50		
	<b>\</b>	>:No.of eft	<sup>F</sup> ective anima	ls, ( ) :N	lo. of measure	d animals	Av.	WC. : g					1

# TABLE E 3

### WATER CONSUMPTION CHANGES: MALE

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j UNIT : g REPORT TYPE : A1 104 SEX : MALE	(Crj:BDF1)	ALL	ER CONSUMPTION CHANGE ANIMALS	S (SUMMARY)			PAGE .
Group Name	Administration 1-7(3)	1 week-day (effective) 2-7(3)	3-7 (3)	4-7 (3)	5-7 (3)	6-7 (3)	7-7 (3)
Control	<b>4</b> . 7 ± 1. 1	<b>4.</b> 4± 0. 7	<b>4.</b> 3 ± 0. 7	<b>4.</b> 2 ± 0. 7	<b>4</b> . 4 ± 0. 8	<b>4.</b> 2.⊥ 0. 8	<b>4.1</b> ± 0.6
625 ppm	4.1土 0.4**	3.7± 0.5**	<b>3.</b> 9± 0.6 <b>*</b>	3.9± 0.8 <b>*</b> *	3.9土 0.6**	<b>3.</b> 8± 0.6 <b>*</b> *	3.7± 0.6**
1250 ррт	3.4土 0.4**	3. 4 ± 0. 5**	<b>3.</b> 4 ± 0. 6 <b>* *</b>	<b>3.</b> 3 ± 0. 6 <b>*</b> ∗	3. 4 ± 0. 5**	3. 4土 0. 4**	<b>3.5</b> ± 0.5 <b>*</b> *
2500 ррт	2.7土 0.3**	2. 6 ± 0. 5**	2.7 土 0.5**	2.7 土 0.5**	<pre>2.8± 0.5**</pre>	2.8±0.5**	2.9± 0.5 <b>*</b> *
Significant difference ;	* : P ≦ 0.05	** : P ≦ 0.01		Test of Dunnett			

(HAN260)

Test of Dunnett

BAIS 4

ANIMAL : MOUSE B6D2F1/Crlji UNIT : g REPORT TYPE : A1 104 SEX : MALE	Crj:80F1]	WAT ALL	ER CONSUMPTION CHANGES ANIMALS	S (SUMMARY)			PAGE
Group Name	Administration 8-7(3)	week-day (effective) 9-7 (3)	10-7 (3)	11-7 (3)	12-7 (3)	13-7 (3)	14-7 (3)
Control	4.0± 0.6	4.1 ± 0.7	<b>4.</b> 1 ± 0. 6	<b>4</b> . 0 ± 0. 7	<b>3.</b> 9± <b>0</b> .6	3.9± 0.6	3.8土 0.5
625 ppm	3. 7 ± 0. 7**	<b>3</b> . 7士 0. 6**	3.7± 0.7**	3.8± 0.6	<b>3.6</b> ± <b>0.6**</b>	3.6土 0.6*	3.5土 0.6**
1250 ррт	3. 3 ± 0. 4 * *	3. 5 ± 0. 5**	3.5± 0.4**	3. 4土 0. 4**	<b>3.</b> 4 ± 0. 4 <b>* *</b>	3. 4土 0. 4**	3.3士 0.3**
2500 ррт	2.8士 0.4**	2.9± 0.5 <b>*</b> *	2.9± 0.5 <b>*</b> ∗	<b>3.</b> 0 ± 0. 4 <b>**</b>	2.9± 0.4 <b>*</b> *	3.0土 0.5**	<b>2.</b> 8⊥ 0.4 <b>*</b> *
Significant difference ;	* P ⊠ 0.05	** 		Test of Dunnett			

(HAN260)

BAIS 4

STUDY N0. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j UNIT : g REPORT TYPE : A1 104 SEX : MALE	[Crj:BDF1]	HAT ALL	ER CONSUMPTION CHANGE: ANIMALS	s (summary)			PAGF
Group Name	Administration 18-7 (3)	1 week-day(effective) 22-7(3)	26-7 (3)	30-7 (3)	34-7 (3)	38-7 (3)	42-7 (3)
Control	3. 5 ± 0. 4	3.8± 0.4	3.6± 0.4	3.5± 0.4	3.7±0.4	<b>3</b> . 7 ± <b>0</b> . 3	<b>3.</b> 8± 0.3
625 ppm	3.4土 0.5	<b>3.</b> 5 ± 0. 4 <b>* *</b>	<b>3.4</b> ± 0.5*	3. 4土 0. 5	<b>3.</b> 6± 0.5	3.6土 0.4	3.7±0.4
1250 ррт	3. 2 ± 0. 3**	<b>3.</b> 3 ± 0. 3 <b>*</b> ∗	<b>3.</b> 4± 0. 3 <b>*</b>	3. 2 ± 0. 3**	3.4 ± 0.3**	3.4± 0.3**	3.5士 0.4**
2500 ррт	<b>2</b> . 7 ± 0. 4 <b>*</b> *	<b>2</b> . 8 ± 0. 4**	2.8土 0.4**	2.8± 0.4**	3. 0± 0. 5 <b>*</b> *	3.0± 0.4 <b>*</b> *	3.2±0.5**
Significant difference ;	* : P ≦ 0.05	** : P ≦ 0.01		Test of Dunnett			

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BAIS4

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j UNIT : g REPORT TYPE : A1 104 SEX : MALE	[Crj :80F1]	MA. ALI	TER CONSUMPTION CHANGE L ANIMALS	S (SUMMARY)			PAGF -
Group Name	Administratio 46-7(3)	n week-day(effective) 50-7(3)	54-7 (3)	58-7 (3)	62-7 (3)	66-7 (3)	70-7 (3)
Control	3.9± 0.4	3.8土 0.3	<b>4.</b> 0 ± 0. 4	<b>4.</b> 1 ± 0. 5	<b>4.</b> 1 ± 0. 6	4. 3 ± 0. 7	<b>4.5</b> ± 0.6
625 ррт	3.8±0.5	<b>3.</b> 7 ± <b>0.</b> 5	4.0土 0.8	<b>4.</b> 0 ± 0.8	<b>4.</b> 0 ± 0. 6	<b>4</b> . 3 ± 0. 6	<b>4.</b> 3 ± 0. 6
1250 ppm	3.6± 0.4**	3.5士 0.5**	3.6± 0.4 <b>*</b> €	<b>3.</b> 7 ± 0. 4 <b>* *</b>	3. 7 ± 0. 5 <b>*</b> ∗	<b>4.</b> 0 ± − 1. 1 <b>* *</b>	<b>4</b> . 3 ± 1. 2**
2500 ррт	3.1土 0.4**	<b>3.</b> 1 ± 0. 5 <b>* *</b>	3. 2 土 0. 5**	<b>3.</b> 2 ± 0. 5 <b>* *</b>	<b>3.</b> 2 ± 0. 4 <b>* *</b>	3. 4± 0. 4 <b>*</b>	3.5士 0.5**
Significant difference ;	* : P <u> </u> ∧ 0.05	** … P 0.01		Test of Dunnett			

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(HAN260)

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j UNIT : g REPORT TYPE : A1 104 SEX : MALE	[Crj:80F1]	ALLI ALLI	ter consumption change. L'ANIMALS	S (SUMMARY)			PAGE 
Group Name	Administration 74-7(3)	week-day (effective) 78-7 (3)	82-7 (3)	86-7 (3)	6) –7 (3)	(2) <u>(</u> 3)	0
Control	$\textbf{4. } \textbf{6} \pm \textbf{0. } \textbf{9}$	<b>4</b> . 7 ± 1. 0	4.5 ± 0.9	<b>4</b> . 6 ± 1. 7	<b>4.</b> 9⊥ 1.0	<b>4</b> . 7土 <b>1</b> . 5	5.0土 0.8
625 ppm	4.2 ± 0.8	4.4士 0.8	4.3土 0.6	4.5士 0.7	<b>4.</b> 7 ± 0.9	<b>4.</b> 9⊥ 1. 5	5.1± 1.3
1250 ррт	4.1土 0.6**	<b>4</b> . 3 ± 0. 6	4.2 ± 0.8	<b>4.</b> 5 ± 1. 0	<b>4.</b> 5± <b>1.</b> 0	4.9土 1.5	4.8土 1.1
2500 ppm	3.6± 0.6**	3.8± 0.6 <b>*</b> *	3.8± 0.9 <b>*</b>	<b>4</b> . 0 ± − 1. 1 <b>*</b> *	<b>4.</b> 0 ± <b>1.</b> 0**	4. 0 $\pm$ 1. 0**	4.2 土 1.0**
Significant difference ;	* : P ≦ 0.05	** : P ≦ 0.01		Test of Dunnett			

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STUDY NO.	••••	0712 M0116E	0609E1 /0/1   [0/2]
	·	NUUSE	מטטברו/ טרון נערן . מערון
		t	

	104		
50	: A1		
UNIT	REPORT TYPE	SEX : MALE	

PAGE : 6

Group Name	Administration we 102-7(3)	ieek-day (effective)
Control	<b>5.</b> 1 ± 0. 8	5.4 ± 1.1
6.0E		
Wdd C70	4. 9	5. 1± 1. 0
1250 ppm	4.4 土 1.2 *	<b>4.</b> 7± 1. 2
2500 ррт	4.1士 1.0**	4. 2± 1. 0**

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

(HAN260)

TABLE E 4

#### WATER CONSUMPTION CHANGES: FEMALE

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Crlj UNIT : g REPORT TYPE : A1 104 SEX : FEMALE	CrJ : BDF1]	ALLI	ER CONSUMPTION CHANGES - ANIMALS	S (SUMMARY)			PAGE : 7
Group Name	Administration 1-7 (3)	week-day (effective) 2-7 (3)	3-7 (3)	4-7 (3)	5-7 (3)	6-7 (3)	7-7 (3)
Control	<b>4</b> .3 ± 0.4	<b>4.</b> 1 ± 0. 5	<b>4</b> .1 ± 0.5	<b>4.</b> 0 ± 0. 5	<b>4</b> . 2 ± 0. 5	<b>4.</b> 0 ± 0. 4	4.1 ± 0.4
625 ppm	4.0 ± 0.4**	3.6土 0.3**	3.7± 0.4 <b>*</b> *	3.6± 0.3 <b>*</b> *	3.7± 0.4**	3.7± 0.3**	3.7± 0.4 <b>*</b> *
1250 ррт	$3.6\pm 0.3**$	3.4土 0.4**	3.5 ± 0.5**	3.6土 0.5**	<b>3.</b> 7 ± 0. 4 <b>* *</b>	3.6± 0.5 <b>*</b> ≭	3.7± 0.6 <b>*</b> *
2500 ррт	2.7 ± 0.3**	2. 7± 0. 3 <b>*</b> *	2.8± 0.3 <b>*</b> *	2.9± 0.3 <b>**</b>	3. 0 士 0. 4**	3.0土 0.4**	3.1土 0.4**
Significant difference ;	* : P ≦ 0.05	** : P ≦ 0.01		Test of Dunnett			

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STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j UNIT : g REPORT TYPE : A1 104 SEX : FEMALE	(Crj : BDF1]	ALIA ALIA	TER CONSUMPTION CHANGE. - ANIMALS	S (SUMMARY)			PAGE
Group Name	Administration 8-7(3)	week-day (effective) 9-7 (3)	10-7 (3)	11-7 (3)	12-7 (3)	13-7 (3)	14-7 (3)
Control	<b>4.</b> 1 ± 0. <b>4</b>	$4.~2\pm  0.~5$	<b>4.</b> 1 ± 0. 5	<b>4</b> , 1	4.2 土 0.7	<b>4.</b> 2 ± 0.6	4.0 ± 0.4
625 ppm	$3.6\pm$ 0.4**	<b>3</b> . 7 ± 0. 4 <b>*</b> ±	<ol> <li>3. 7 ± 0. 4**</li> </ol>	<b>3.</b> 7 ± 0. 4 <b>* *</b>	3.6± 0.5 <b>*</b> *	3.7 土 0.4**	3.6± 0.4**
1250 ppm	3.6土 0.3**	$3.6\pm$ 0.4**	3.7 土 0.4**	3. 7 ± 0. 6 <b>*</b> *	3.5 <b>± 0.4</b> **	3.6± 0.4 <b>*</b>	<b>3.6</b> ± <b>0.6**</b>
2500 ррш	<b>3.</b> 1± 0.4 <b>*</b> ±	3.1± 0.4 <b>*</b> *	3.1土 0.4**	3. 1 ± 0. 4**	3. 1 ± 0. 5**	3. 1 ± 0. 5**	3.0± 0.3 <b>*</b> *
Significant difference ;	* : P ≦ 0.05	** : P ≦ 0.01		Test of Dunnett			

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Test of Dunnett

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STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j UNIT : g REPORT TYPE : A1 104 SEX : FEMALE	[Crj:80F1]	HLT ALL	ER CONSUMPTION CHANGE ANIMALS	ES (SUMMARY)			PAGE
Group Name	Administration	week-day (effective)					
	18-7 (3)	22-7 (3)	26-7 (3)	30-7 (3)	34-7 (3)	38-7 (3)	42-7 (3)
Control	3.8 ± 0.4	<b>4.1</b> ± <b>0.6</b>	<b>3.</b> 9 ± 0. 6	3.9 ± 0.7	<b>4</b> , 1 ± 0.8	<b>4</b> . 0 ± 0. 7	4,1± 0.7
625 ррм	3.4 ± 0.3**	3.5± 0.5**	3. 3 土 0. 4**	<b>3.</b> 3 ⊥ 0. 5**	<b>3.</b> 4 ± 0. € <b>* *</b>	3. 4 ± 0. 4**	3.6± 0.4 <b>*</b> *
1250 ррт	3. 2 ± 0. 3**	3. 3土 0. 4**	3.1± 0.3**	3. 2 ± 0. 4**	<b>3.</b> 3 ± 0. 3 <b>* *</b>	3. 3 <b>± 0. 4*</b>	3. 3 ± 0. 4**
2500 ррт	2.9± 0.4**	3. 0 土 0. 4**	2. 8 土 0. 4**	2.8± 0.3**	$3.0 \pm 0.4 * *$	$2.9\pm 0.4**$	3.0十 0.3**
Significant difference ;	* : P ≦ 0.05	** : P ≤ 0.01		Test of Numett			

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STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j[ UNIT : g REPORT TYPE : A1 104 SEX : FEMALE	Crj:B0F1]	ALLA	ER CONSUMPTION CHANGE. - ANIMALS	S (SUMMARY)			PAGE : 10
Group Name	Administration 46-7(3)	week-day (effective) 50-7 (3)	54-7 (3)	58-7 (3)	62-7 (3)	66-7 (3)	70-7 (3)
Control	<b>4</b> . 1 ± 0. 8	<b>4</b> . 1 ± 0. 8	4. $0 \pm$ 1. $0$	<b>3.</b> 9 ± 0.6	$3.9\pm0.8$	<b>3.</b> 9 ± 0. 8	<b>4.0</b> ± <b>0.8</b>
625 ppm	3.6 ± 0.5**	3.6± 0.5 <b>*</b> *	3. 4 土 0. 5**	3.5∓ 0.5 <b>*</b> *	<ol> <li>3. 5 ± 0. 6*</li> </ol>	<b>3</b> . 7 ± 0. 7	3.5士 0.8*
1250 ppm	3.4土 0.7**	3. 2 ± 0. 4 <b>*</b> *	3. 3 ± 0. 7**	3.2± 0.8 <b>*</b>	3. 2 土 0. 5**	3. 4 ± 0. 7**	3.4± 0.9 <b>*</b> *
2500 ррт	3.0土 0.4**	2.8± 0.4 <b>*</b> *	2. 9 <b>±</b> 0. 5 <b>*</b> *	2.8± 0.4**	2. 8 土  0. 5**	3. 0 土 0. 7**	3.1土 1.0**
Significant difference ;	* : P ≦ 0.05	** : P ≦ 0.01		Test of Dunnett			

(HAN260)

Test of Dunnett

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j UNIT : g REPORT TYPE : A1 104 SEX : FEMALE	[Cr]:BDF1]	ALLA ALLA	IER CONSUMPTION CHANGE - ANIMALS	S (SUMMARY)			PAGE 11
Group Name	Administration 74-7(3)	n week-day(effective) 78-7(3)	82-7 [3]	86-7 (2)	(5) (3)	(c) Z VO	10/ 7 00
					(c) 1-06	34-7 (3)	96-1 (J)
Control	4.1± 0.8	4, 2± 0.8	<b>4.</b> 2 ± 1. 0	<b>4.</b> 2 ± 0. 9	<b>4.</b> 3 ± 0. 9	4.1± 1.1	4.4土 1.1
625 ррт	3.7± 0.9	3.9±0.9	4.1土 1.2	4.2 ± 1.2	<b>4.</b> 1 ± 1.4	4,1± 1.4	<b>4</b> . 3 ± 1. 5
1250 ppm	3.5± 1.0**	3. 8 土 1. 2**	<b>4</b> , 1 <b>⊥ 1</b> . <b>5</b>	4.2 <b>±</b> 1.4	<b>4.</b> 0 ± 1. 3	4.6± 1.8	4.6± 1.6
2500 ppm	3.3士 1.4**	3. 2 ± 1. 1**	3.4土 1.5**	3.5± 1.6 <b>*</b> *	3.8± 1.7**	3.6± 1.7*	3. 8 土 1. 8
Significant difference :	* . P S 0.05	** · P 🛆 0.01		Toot of Dumott			

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2	<pre>SE B6D2F1/Cr1j [Crj:BDF1]</pre>		1 104	
0712	MOUS	50	Al	
••	••	•••	ΥPE	MALE
20				Щ
STUDY	ANIMAL	UNIT	REPORT	SEX :

	104	
	٨l	
)		
	比	

Group Name

PAGE : 12

: 1.2 4.5土 1.1	
・ 1.6 4.0土 1.1 、	
: 1.4 4.2± 1.4	
· 1.7 4.2± 1.8	
1.6	4.0±       1.1         4.2±       1.4         4.2±       1.8

Test of Dunnett	
** : P ≦ 0.01	
* : P ≦ 0.05	
Significant difference ;	(HAN260)

BAIS 4

#### TABLE F 1

## CHEMICAL INTAKE CHANGES: MALE

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Crlj[Crj:E UNIT : mg/kg/day REPORT TYPE : A1 104 SEX : MALE	BDF1]			CHEMICA ALL ANII	- INTAKE CH AALS	Hanges (1	SUMMARY)							PAGE : 1
Group Name	Administ	ration (wee	eks)											
	-		2		e.		4		5		6		7	
Control	0 +	0	+0	0	$^+$ 0	0	+ 0	0	+  0	0	+  0	0	+  0	0
625 ррт	<b>103</b> ±	10	<b>30</b> ±	Ξ	$92\pm$	14	$88 \pm$	19	$85\pm$	15	81+	14	17土	12
1250 ppm	173±	19	167 ±	25	<b>15</b> 9 ±	29	151±	23	153土	21	147 土	19	147 土	21
2500 ррт	$283\pm$	32	<b>258</b> ±	47	263土	50	<b>256</b> ±	47	$259\pm$	45	<b>258</b> ±	51	$262\pm$	50

(HAN300)

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j[Crj∷ UNIT : mag∕kag∕d a y REPORT TYPE : A1 104 SEX : MALE	8DF1]			CHEMI ALL A	CAL INTAKE NIMALS	CHANGES	(SUMMARY)							PAGE : 2
Group Name	Administ 8	tration	(weeks)9		10		11		12		13		14	
Control	0+	0	0	0	+  0	0	十 0	0	+  0	0	+0	0	<b>0</b>	0
625 ррт	$74\pm$	15	74±	13	73土	14	73 ±	13	∓L9	13	99	12	$63\pm$	12
1250 ррт	<b>1</b> 39±	20	$142 \pm$	20	<b>138</b> ±	20	135 ±	19	127土	18	126±	18	<b>119</b> ±	13
2500 ррт	245±	43	250土	46	$242\pm$	40	$244\pm$	41	<b>232</b> ±	41	<b>2</b> 32 ±	43	<b>218</b> ±	37

(HAN300)

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Crlj[Crj:! UNIT : ma∠kg∕day REPORT TYPE : A1 104 SEX : MALE	BDF1]			CHEMI ALL A	CAL INTAKE NIMALS	CHANGES	(SUMMARY)							PAGE : 3
Group Name	Administ 18	tration	(weeks)22		26		30		34		38		42	
Control	+! 0	0	+  0	0	+ 0	0	+ 0	0	0	0	+0	0	0+	0
625 ppm	$56\pm$	6	<b>56</b> ±	8	<b>52</b> ±	6	$\pm 05$	ø	$50\pm$	æ	$49\pm$	7	<b>49</b> ⊥	7
1250 ppm	110±	14	<b>106</b> ±	13	104 土	12	<del>1</del> 96	12	<b>97</b> ±	13	<del>9</del> 6	14	<del>1</del> 96	13
2500 ppm	196+	36	<b>195</b> ±	32	187±	30	$178\pm$	31	186土	31	179土	28	<b>18</b> 3±	34

(HAN300)

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Crlj[Crj:B UNIT : mg/kg/day REPORT TYPE : A1 104 SEX : MALE	30F1]			CHEMIC ALL AN	al intake ( imals	CHANGES	(SUMMARY)							PAGE : 4
Group Name	Administ	ration (w	veeks)											
	46		50		54		58		62		66		70	
Control	$0\pm$	0	+  0	0	+0	0	+0	0	$0^+$	0	+0	0	$0^{\mp}$	0
625 ppm	<b>50</b> ±	8	$47\pm$	ø	51±	18	$50\pm$	17	<b>4</b> 8±	7	<b>52</b> ±	7	$52\pm$	8
1250 ppm	$95\pm$	13	$92 \pm$	13	<b>93</b> ±	13	<b>9</b> 4 ±	12	<b>95</b> ++	16	<b>103</b> ±	42	111 H	55
2500 ppm	178±	27	176土	30	十77十	28	<b>172</b> ±	26	177±	25	<b>183</b> ±	26	<b>189</b> ±	35

(HAN300)

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:L UNIT : mc/kg/d a y REPORT TYPE : A1 104 SEX : MALE	BDF1]			CHEM I ALL AI	CAL INTAKE NIMALS	CHANGES	(SUMMARY)							PAGE	
Group Name	Administ 74	tration	(weeks) 78		82		86		06		94		98		
Control	+  0	0	0 ⊥	0	-i 0	0	0+	0	$0^+$	0	+  0	0	0	0	
625 ррт	<b>52</b> ±	13	<b>53</b> +	12	51+	10	53 ±	12	56∺	15	<b>62</b> ±	27	<b>64</b> ±	22	
1250 ррт	++ 66	16	$104\pm$	18	<b>102</b> ±	24	110±	34	117±	39	128±	56	<b>127</b> ±	48	
2500 ррт	<b>196</b>	42	$202\pm$	48	$203\pm$	74	<b>215</b> 土	87	219土	76	227 土	83	236±	72	

(HAN300)

0712	AOUSE B6D2F1/Cr1j[Crj:BDF1]	ng/kg/day	: A1 104	
tudy No. :	NIMAL :		EPORT TYPE	EX : MALE

CHEMICAL INTAKE CHANGES ALL ANIMALS

19

 $65\pm$ 

19

 $64\pm$ 

55

 $\mathbf{131} \pm$ 

37

 $116\pm$ 

1250 ppm

625 ррш

Control

0

++ 0

0

+|

104

Administration (weeks) 102 1(

Group Name

86

 $250\pm$ 

81

 $242\pm$ 

2500 ppm

(SUMMARY)	
e changes	

PAGE : 6

BAIS 5

(HAN300)

#### TABLE F 2

### CHEMICAL INTAKE CHANGES: FEMALE

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Crlj[Cr UNIT : mg/kg/diay REPORT TYPE : A1 104 SEX : FEMALE	j : BDF1]			CHEN	AICAL INTAKE ANIMALS	CHANGES	(SUMMARY)							4	2 10
Group Name	Adminis	tration	(weeks)												
	-		5		ε		4		2		9		7		
Control	++	0	0+	0	+0	0	<b>0</b> ±	0	0+	0	<b>0</b> ±	0	$0\pm$	0	
625 ppm	123 土	=	<b>1</b> 09 ±	5	<b>106</b> ±	6	$102\pm$	10	103±	11	<b>98</b> ±	σ	+ 66	10	
1250 ррт	$225\pm$	25	202 ±	21	210+	30	206±	33	208±	25	1 99 <del>+</del>	28	<b>201</b> ±	34	
2500 ррт	$340\pm$	32	${\bf 333}\pm$	33	335+	39	$333\pm$	39	$339\pm$	46	$333\pm$	46	$336\pm$	48	
(UUZIVI)															
STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Crij[Crj:¦ UNIT : mag∕kag∕day REPORT TYPE : A1 104 SEX : FEMALE	BDF1]			CHEMICA ALL ANI.	L INTAKE C WALS	HANGES (:	SUMMARY)							PAGE : 8	
--	--------------	--------------	--------------	---------------------	---	-----------	-------------	----	------------	----	---	----	-------------	--------------	
Group Name	Administ	tration (wei	eks)		and the second se						T PROVIDE A CONTRACT OF A C				
	8		6		10		11		12		13		14		
Control	0+	0	++ 0	0	$^+$ 0	0	+0	0	<b>0</b> +	0	$0\pm$	0	+0	0	
625 ррт	95±	10	<b>95</b> ++	10	94+	=	<b>95</b> ±	6	<b>91</b>	11	<b>91</b> ±	10	<b>86</b> +	<del>4</del>	
1250 ррт	<b>192</b> ±	20	$186\pm$	23	<b>1</b> 87±	22	191+	33	180土	23	<b>180</b> ±	25	176 土	32	
2500 ррт	$328\pm$	50	$328\pm$	49	322土	47	325 ±	45	320土	54	$314\pm$	50	301土	40	

(HAN300)

BAIS 5

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Crlj[Crj:! UNIT : mag∕kag∕day REPORT TYPE : A1 104 SEX : FEMALE	BDF1]			CHEMIC ALL AR	CAL INTAKE VIMALS	CHANGES	(SUMMARY)							PAGE :	<b>~</b>
Group Name	Administ	ration (w	veeks)		HARD- VALUE										ş
	18		22		26		30		34		38		42		1
															1
Control	+0	0	+  0	0	0 <i>±</i> 0	0	+0	0	+1 0	0	$0^+$	0	+0	0	
625 ppm	<b>79</b> ±	10	$78\pm$	13	71±	10	$68\pm$	13	$\pm$ 69	15	99 ⊹	Ξ	₩29	12	
1250 ррт	<b>155</b> ±	20	150±	23	137±	21	<b>1</b> 34±	23	135±	21	131±	23	128±	21	
2500 ррт	279±	43	274 土	43	<b>259</b> ±	44	$247\pm$	39	$255\pm$	43	244土	45	242±	33	

(HAN300)

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j[Crj: UNIT : mg/kg/day REPORT TYPE : A1 104 SEX : FEMALE	BDF1]			CHEM	ICAL INTAKE ANIMALS	CHANGES	(SUMMARY)							PAGE : 1	0
Group Name	Administ	Iration	(weeks)												1
	46		50		54		58		62	1997)	99		20		1
									NUMBER OF A LOCAL AND A						1
Control	÷0	0	<b>0</b> +	0	<b>0</b>	0	+ 0	0	<b>0</b> ±	0	+  0	0	+  0	0	
625 ppm	+ 29	14	63+	12	+09	13	ţ	10	4 13	L T	Ĺ	د ۲	ç	î	
	5		2	<u>-</u>	-	2		71	10	61	H 60	9	∓ 7 <b>9</b>	17	
1250 ppm	$129\pm$	30	119±	17	<b>124</b> 土	40	119±	48	118±	24	124±	32	<b>1</b> 30±	60	
														1	
2500 ррт	$239\pm$	38	$224\pm$	39	$224\pm$	42	$216\pm$	34	$220\pm$	47	$237\pm$	69	$247\pm$	109	

(HAN300)

BAIS 5

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : mg/kg/d a y REPORT TYPE : A1 104 SEX : FEMALE

Group Name	Administr	ation (	weeks)					THE PARTY IN CASE OF A DESCRIPTION OF A	TRANSPORT AND A DESCRIPTION OF A DESCRIP		The second se			
	74		78		82		86		06		94		98	
	Workshold A. L. L. All.			and the second sec				PROVIDE THE PROVIDENCE AND						
Control	+0	0	<b>0</b> ±	0	<b>0</b>	0	+0	0	++	0	<b>0</b> +	0	<b>0</b> +	0
625 ppm	$64\pm$	22	66±	21	±01	27	72±	30	71 +	38	72 ±	39	76±	35
1250 ррт	129±	52	137±	63	156十	84	156±	80	<b>148</b> ±	72	182 ±	101	177±	93
2500 ppm	267±	152	256土	143	$280\pm$	178	$281\pm$	169	$309\pm$	188	$307\pm$	191	$337\pm$	209

(HAN300)

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:1 UNIT : mæ/kæ/d a y REPORT TYPE : A1 104 SEX : FEMALE	BDF1]			CHEMICAL INTAKE CHANGES ALL ANIMALS	(SUMMARY)
Group Name	Adminíst 102	tration	(weeks) 104		
Control	+0	0	+0	0	
625 ppm	74±	37	71±	21	
1250 ррт	<b>156</b> ±	78	<b>152</b> ±	68	
2500 ррт	$356\pm$	192	$360\pm$	200	

(HAN300)

BAIS 5

# TABLE G 1

## HEMATOLOGY: MALE

STUDY NO. : 0712 ANIMAL : MOUSI MEASURE. TIME : i SEX : MALE	E B6D2F1/Cr1j 1 REPORT	[Crj:BDF1] TYPE : A1		ALL	ATOLOGY (SU . ANIMALS (1	MMARY) 05W)								- - - -
Group Name	NO. of Animals	RED BLOOD CELL 1 O <sup>€</sup> ∕µℓ	$\frac{1}{g \wedge d\ell}$	<b>DBIN</b>	HEMATOC %	RIT	MCV f 2		MCH છ		MCHC g ∕ dℓ		PLATELET 1 0³ / μℓ	
Control	24	<b>9.</b> 24 ± 1. 47	13. 1 ±	2. 0	<b>4</b> 3. 2 <u>⊥</u>	6.5	<b>46.</b> 9⊥	3. 4	14.2±	0.9	<b>30.</b> 2 ±	0.9	1921 ±	524
625 ppm	32	8. 83 ± 1. 00	<b>12</b> . 7 ±	1. 5	<b>4</b> 2. 4⊥	4. 2	<b>48.</b> 1 ±	1.7	14.4 <i>±</i>	0. 5	<b>30.</b> 0 ±	0.9	<b>1850</b> ±	391
1250 ррт	31	8. 63 ± 1. 35	<b>12.</b> 7 ±	1. 8	<b>42.</b> 1土	5. 3	<b>4</b> 9. 1 ±	2. 9**	14. 7 ±	0. 7	<b>30. 0</b> ±	1. 0	1955	488
2500 ррт	38	<b>8.</b> 42 ± 1. 33	<b>12</b> . 3 ±	1. 9	<b>41</b> . 2 ±	5.5	<b>49.</b> 2 $\pm$	2. 8**	14.6±	0. 7*	<b>29.</b> 7 ±	1. 0	1876±	490
Significant c (HCL070)	lifference;	* : P ≦ 0.05	** : P ≦ 0.0	5			Fest of Dunn	let t						BAIS 5

STUDY NO. : 0712 ANIMAL : MOUSE MEASURE. TIME : 1 SEX : MALE	E B6D2F1/Cr1j REPORT -	[Crj:BDF1] TYPE : A1		HEMATOLOGY (SUMMARY) ALL ANIMALS (105W)	PAGE
Group Name	NO. of Animals	RETICULOCYTE %	₩E ₩E	HEMOGLOB I N	
Control	24	<b>3</b> . 7 ± <b>3</b> . 7	0.4	± 0.1	
625 ppm	32	3.5土 1.6	0.5.	± 0.2	
1250 ррт	31	<b>4</b> . 3 ± 4. 1	0.5:	+ 0.3	
2500 ppm	38	4.8± 3.3:	** 0. 7 :	土 0.3**	
Significant d	lifference ;	* : P ≦ 0.05	∨∥ ∟ **	0.01	Test of Dunnett

BAIS 5

(HCL 070)

STUDY NO. : 0712 ANIMAL : MOUS MEASURE. TIME : SEX : MALE	E B6D2F1/Crlj 1 REPORT	j [Crj : BDF1] TYPE A1			HEMATOLOG ALL ANIMA	Y (SUMMAR) LS (105W)	C								
Group Name	NO. of Animals	WBC 1 0³∕µl <sup>2</sup>	Di	fferential	WBC (% LYMPHO		ONOM		EOS I NO		BASO		OTHER		PAGE : 3
Control	24	<b>7.</b> 74土 13. 36	<b>3</b> 0±	14	<b>62</b> ±	16	3 3	2	3+	e	-H 0	0	3+	-D	
625 ррт	32	<b>5.</b> 36 ± 3. 91	28±	16	$63\pm$	19	33  +	2	<b>4</b> +	=	0 ±	0	$3\pm$	4	
1250 ррт	31	<b>4</b> . 37 土 2. 40	<b>34</b> ±	18	57±	20	3 1+	2	<b>2</b> ±	2	0+	0	<b>4</b>	9	
2500 ррш	38	<b>3. 66</b> ± 1. 99 <b>∗</b>	<b>34</b> ±	18	+ 20+	17	<del>د</del> ا+	2	+	2	+0	C	+ ~	Ρ	
														-	
Significant	difference;	* : P ≦ 0.05	VI  *	0. 01			Test	of Dunnet	ب						
(HCL 070)															RAISS

TABLE G 2

#### HEMATOLOGY: FEMALE

STUDY NO. : 0712 ANIMAL : MOUSE MEASURE. TIME : 1 SEY · EEMALE	B6D2F1/Cr1j[	Crj:B0F1]			AL	EMATOLOGY (SU L ANIMALS (1	JMMARY) 05W)								
		IFC . AI													PAGE : 4
Group Name	NO. of Animals	RED BL( 1 0 <sup>6</sup> ∕1	اللا 00D CELL	B / d2	0B   N	HEMATOC %	RIT	MCV f 2		MCH P g		MCHC g 📈 d2		PLATELE <sup>-</sup> 1 0 <sup>3</sup> /JL	2
										NAME AND A DESCRIPTION OF A DESCRIPTION OF A DESCRIPTION OF A DESCRIPTIONO			AND PARAMENTAL ADDRESS OF THE OWNER ADDRESS OF		
Control	22	<b>9</b> . 14±	1. 10	<b>13</b> . 3 ±	1.6	<b>4</b> 3. 5 ±	4. 1	47. 9 $\pm$	3. 1	<b>14.6</b> ±	0.6	<b>30.</b> 4±	1. 2	<b>1081</b> ±	353
625 ррт	21	<b>9</b> . 21⊥	0. 75	<b>13</b> . 1 <u>+</u>	1. 2	44. 2 ±	3. 5	<b>48.</b> 1⊥	1.9	14. 3 <del>+</del>	0. 7	<b>29.</b> 7 ±	1. 0	1262 ±	400
1250 ppm	28	8.64±	1. 25	12. 3±	1.9	<b>41.</b> 8 $\pm$	5. 4	<b>48.</b> 6 ±	3. 0	<b>14.</b> 3 ±	0. 9	<b>29</b> . 4⊥	1. 2*	1150+	413
2500 ррт	38	8. 31+	1. 43*	11.8±	2. 3*	<b>40.</b> 2 ±	6. 2	<b>48</b> . 7 <u>+</u>	4.7	<b>14</b> . 3 ±	1. 3	<b>29.</b> 3 ±	1. 5**	<b>1232</b> ±	485
Significant di	fference ;	* : P ≦ (	0. 05	** : P ≦ 0.(	01			Test of Dun	nett						
(חטרטיט)															BAIS 5

STUDY NO. : 0712 ANIMAL : MOUSE MEASURE. TIME : 1	B6D2F1/Cr1j[	[Cr] :B0F1]			HEMATOLOGY (SUMMARY) All animals (105W)	
SEX : FEMALE	REPORT I	'YPE : A1			fd	AGE : 5
Group Name	NO. of Animals	RETICUL %	OCYTE	Methemogl ( %	00.081N	
Control	22	<b>3</b> . 7 $\pm$	4.1	0. 3 ± (	0.1	
625 ррт	21	<b>3.</b> 5 ±	1. 2	0.4± (	0. 2	
1250 ррт	28	<b>4</b> . 7 ±	2. 0**	0.5± (	0. 2	
2500 ррт	38	6.5±	5. 3**	0.6±	0.3**	
Significant d (HCL070)	fference ;	0 √∥  *	. 05	** : P ≦ 0.01	11 Test of Dunnett	BAIS 5

STUDY NO. : 0712 ANIMAL : MOUS MEASURE. TIME : SEV : FFWARF	E B6D2F1/Cr1j	[Crj:BDF1]		_ ~	HEMATOLOG <sup>,</sup> ALL ANIMAL	/ (SUMMARY) .S (105W)									
JEA : FEMALE	KEFUKI	IYPE : AI													PAGE : 6
Group Name	NO. of Animals	₩ВС 1 0 <sup>3</sup> ∕/µℓ	Differ NEUTRO	ential Wi	BC (%) LYMPHO		ONOM		EOS I NO		BASO		OTHER		
				Annound in the second sec	an and a second s										
Control	22	<b>5.</b> 36 ± 6. 67	<b>25</b> 土 1	5	61+	22	3+ 3	2	<b>2</b> ±	ę	+0	0	10±	21	
625 ppm	21	8. 13 ± 11. 97	<b>22</b> ± <b>1</b>	2	57 土	20	+  8	ę	+	-	+- 	0	17土	28	
1250 ррш	28	$3.61\pm 2.06$	$32\pm$ 2	0	53 +	25	2土	2	+  	-	$\pm 0$	0	13+	Ξ	
2500 ррт	38	<b>4.</b> 37 ± 5. 71	29 土 1	80	$53 \pm$	22	<b>3</b>  +	<b>2</b> .	2土	2		0	14 土	21	
Significant	difference;	<b>*</b> : P ≦ 0.05	** : P ≦ 0.0	-			Test (	of Dunnett							
(HCL 070)			PERMIT												BAIS 5

AIS 5

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# TABLE H 1

#### **BIOCHEMISTRY: MALE**

STUDY NO. : 0712 ANIMAL : MOUSE MEASURE. TIME : 1	B6D2F1/Cr1j	j [Crj :80F1]				BIOCHEMISTRY ALL ANIMALS (1	(SUMMARY) 105W)									
SEX : MALE	REPORT	TYPE : A1													PAGE :	-
Group Name	NO. of Animals	T0TAL g ∕dℓ	PROTEIN 2	ALBUM & ⁄di	L L	A/G RAT	10	T-BILI mg/d2	RUBIN	GLUCOSE mg/dl		T−CHOLES mg∕dl	TEROL	TRIGLYCI mg∕dℓ	ERIDE	-
Control	24	5. 4±	0. 7	2.6±	0. 4	<b>0</b> .9±	0. 2	0. 11 ±	0. 04	$156\pm$	37	<b>149</b> ±	11	<b>4</b> 7 ±	21	
625 ррт	32	5.1+	0.5*	2.4±	0. 3	0. <del>9</del> +	0.1	0. 10±	0. 03	$158\pm$	37	119±	28	43 土	28	
1250 ррш	31	<b>5</b> . 1 ±	0.5*	<b>2</b> . 4⊥	0.3	1. 0+	0. 2	<b>0.</b> 10±	0. 02	$157\pm$	45	127±	27	48 土	28	
2500 ррт	38	5. 0 ±	0. 5**	2.4±	0. 3	<b>1</b> . 0 <i>±</i>	0. 1	<b>0.12</b> ±	0. 04	153 ±	37	129±	31	$49 \pm$	35	
Significant d	ifference ;	∨⊓ ⊾ *	0. 05	** : P ≦ 0.	01			Test of Du	nnett							
(HCL 074)					The second se	· · · · · · · · · · · · · · · · · · ·										

STUDY NO. : 0712 ANIMAL : MOUSE MEASURE. TIME : 1	B6D2F1/Cr1j	[Crj:BDF1]				BIOCHEMISTRY ( ALL ANIMALS (1	SUMMARY) 05W)									
SEX : MALE	REPORT	TYPE : A1													PAGE :	2
Group Name	NO. of Animals	PHOSPHC mg∕dℓ	0LI PI D	AST U/L		ALT U/L				ALP U/L		G-6TP U∕L		CK CK		THE OWNER AND A REAL PROPERTY OF
Control	24	<b>247</b> ±	86	85 ±	11	<b>44</b> ±	49	$268\pm$	134	<b>264</b> ±	276	+1		<b>51</b>	21	
625 ppm	32	206±	48	<b>100</b> +	155	<b>64</b> ±	164	$314\pm$	603	<b>191</b> ±	99	+	0	19土	191	
1250 ррт	31	210±	52	$240\pm$	833	136±	493	$516\pm$	1557	175 ±	47	+1	-	£9 ±	38	
2500 ррт	38	214士	50	$94\pm$	126	<b>4</b> 3 ±	81	$\textbf{282}\pm$	344	178±	51	<del>.  </del>	-	73±	128	
Significant d (HCL074)	ifference;	0 √I  *	). 05	** : P ≦ 0.0	_			Test of Dur	mett						B/	AIS 5

STUDY NO. : 0712 ANIMAL : MOUSE MEASURE. TIME : 1 SEY - MALE	B6D2F1/Cr1j	i [Crj:BDF1] TVDF			BI	IOCHEMISTRY L ANIMALS (	(SUMMARY) 1 05W)							
Group Name	NO. of	UREA NITR	ROGEN	SODIUM		POTASS	MU	CHLORIDE		CALCTU		INORGA	LLC PHOSPHORUS	PAGE : 3
	Animais	mg∕ ar		intq 2		un Eq 🗸	Б	mEq 2		mg/dl		mg/dl		
Control	24	<b>24.</b> 8 ±	5. 8	154 土	2	<b>4</b> . 3⊥	0.4	121±	3	9.2	0.5	<b>6</b> . 0 ±	0. 8	
625 ррт	32	26.6土 1	13. 4	<b>154</b> ±	2	4.3+	0.6	<b>123</b> ±	3	8.9 <b>∺</b>	0. 3	5.8	0. 9	
1250 ppm	31	30. 2 土 1	16.9	154±	2	<b>4</b> . 4 $\pm$	0.8	123±	4	8. 9+	0. 3	6. 0 ±	1. 2	
2500 ppm	38	28.5± 1	16.3	$155\pm$	4	<b>4</b> . 3 <u>+</u>	0.6	<b>12</b> 3±	ъ	8.9+	0. 5	<b>6</b> . <b>0 </b> +	0. 7	
Significant d (HCL074)	ifference ;	* . P ≦	05	** : P ≦ 0.01				Test of Dunr	net t					BAIS 5

TABLE H 2

#### **BIOCHEMISTRY: FEMALE**

STUDY NO. : 0712 ANIMAL : MOUSE MEASURE. TIME : 1 SEX : FEMALE	B6D2F1/Cr1j REPORT T	[Crj:BDF1] 'YPE : A1			Ð	ALL ANIMALS (10	UMMARY) 1514)									
Group Name	NO. of Animals	TOTAL H g / d£	PROTEIN	albumin g ∕ d£		A/G RATI	0	T-BILI mg⁄d2	RUBIN	GLUCOSE mg/d2		T-CHOLES mg/d2	STEROL	TRIGLYCI mg∕dℓ	ERIDE	4
Control	22	5.0±	0. 5	<b>2</b> . 6 ±	0. 2		0. 2	<b>0</b> . 10 <u>+</u>	0. 02	118±	34	<b>83</b>	26	<b>31</b>	15	
625 ррт	21	$5.2\pm$	0.6	2. 4±	0. 3	0.9+	0. 2	0.11±	0. 05	<b>106</b> ±	30	100±	29	<b>40</b> ±	24	
1250 ррт	28	5. 1±	0.6	2.6±	0. 2	1. 1 	0. 2	0. 11  +	0. 02	121±	28	110土	48*	£4 ⊥	75	
2500 ррт	38	5.2士	0.8	2.6+	0. 3	<b>1</b> . 0 ±	0. 2	0. 13 <i>±</i>	0. 04*	<b>119</b>	24	<b>112</b> ±	39**	<b>49</b> ±	55	
Significant d	ifference ;	0   V    -   *	<u>)</u> . 05	** . P ≤ 0.0				Tect of Du	++							
(HCL074)				•												

STUDY NO. : 0712 ANIMAL : MOUS MEASURE. TIME :	E B6D2F1/Crlj 1	[Crj:BDF1]			Ξ×	310CHEMISTRY ( ALL ANIMALS (1	(SUMMARY) 05W)									
SEX : FEMALE	REPORT	TYPE : A1													PAGE	<b>و</b>
Group Name	NO. of Animals	hdSOHd PHOSPH	OLIPID	AST U/L		ALT U/L		UM UM		ALP U/L		1∕∩ 9-6TP		CK CK		
Control	22	151±	43	<b>115</b> ±	67	44	36	255+	145	<b>412</b> ±	290	+1	-	84 ±	63	
625 ррт	21	174土	43	114土	61	<b>42</b> ±	28	$292\pm$	187	<b>330</b> ±	220	+	-	<b>211</b> ±	458	
1250 ррт	28	197±	81**	<b>115</b> ±	95	$41\pm$	35	<b>394</b> ±	640	319 土	176	+	-	159±	222	
2500 ррт	38	188土	59*	148 土	154	22 <del>  </del>	67	<b>631</b> ±	1182	$251\pm$	111	+1	-	97 ±	74	
Significant	difference ;	– ∨∣  *	0. 05	** : P ≦ 0.1	10			Test of Dur	nett							
(HCL074)	Note that a second second second second second					Contraction of the local distance of the loc										BAIS 5

STUDY NO. : 0712 ANIMAL : MOUSE MEASURE. TIME : 1 SEX : FEMALE	B6D2F1/Cr1j REPORT	[Crj:BDF1] TYPE : A1				BIOCHEMISTRY ALL ANIMALS	(SUMMARY) (105W)							PAGE
Group Name	NO. of Animals	UREA N mg⁄dℓ	I TROGEN	SOD!UM In Eq∕£		P0TAS InEq∠	SIUM 2	CHLORIDE In Eq / 2		CALCIU mg/d2	~	I NORGANIC mg∕dℓ	PHOSPHORUS	
Control	22	<b>23.</b> 6±	16. 2	152±	33	4. 1+	0.6	121±	3	9. 2 $\pm$	0. 5	<b>6</b> . 1 ±	1. 3	
625 ррт	21	27.9土	25. 2	153±	2	<b>4</b> . 0 ±	0. 4	<b>123</b> ±	3	<b>9</b> .6	1.4	7.4	2. 9	
1250 ррт	28	31.6土	24.7	153±	4	4.1±	0. 3	$123\pm$	4	<b>9.</b> 5	0. 7	<b>9</b> .9	1. 9	
2500 ррт	38	28.8土	17.6	<b>15</b> 3±	2	4 1+	0.5	122±	3	<b>9.</b> 6 ⊥	0.9	7.3±	2.5	
Significant d (HCL074)	ifference;	√   □_ ・・ **	0. 05	** : P ≦ 0.01				Test of Dunn	lett					BAIS 5

TABLE I 1

## URINALYSIS: MALE

STUDY NO. : 0712 ANIMAL : MOUS MEASLIDE TIME :	E B6D2F1/Cr1j	[Crj :Bl	DF1]						URINA	'FYSIS						
SEX : MALE	REPORT	TYPE :	A1													PAGE : 1
Group Name	NO. of Animals	рН 5. 0	6. 0	6.5	7.0	7. 5	8.0	8.5	СНІ	$\frac{\text{Protein}}{- \pm + 2 \pm 3 \pm 4 \pm 0}$	СНІ	Glucose 61ucose 61	Ketone body - ± + 2+ 3+ 4+	СН	0ccult blood - ± + 2+ 3+	СНІ
Control	25	0	5	8	ŝ	-	œ	0		0 5 16 2 2 0		25 0 0 0 0 0	10 14 0 1 0 0		25 0 0 0 0	
625 ррт	33	0	7	11	9	4	4	-		0 5 18 8 2 0		33 0 0 0 0 0	9221100		29 2 0 1 1	
1250 ррш	32	0	9	13	5	7		0	*	0 2 17 12 1 0	*	32 0 0 0 0 0	7195100		30 0 0 0 2	
2500 ррш	39	0	12	12	6	2	-	0	*	0 1 22 14 2 0	*	39 0 0 0 0 0	5 22 7 5 0 0	*	39 0 0 0 0	
Significant (	difference ;	*	VI a 	0.05		**	∨I	0. 01			Test o	if CHI SQUARE				
(HCL 101)							PERSONAL DIVISION OF ALL ADDRESS									DAICE

STUDY NO. : 071	2 51 DEDOF1 (0 1.1		URINALYSIS	
MEASURE. TIME :	SE BOUZFI/Grij 1	[Cr] : BUF1]		
SEX : MALE	REPORT	TYPE : A1		PAGE : 2
Group Name	NO. of Animals	Urobilinogen ± + 2+ 3+ 4+ (	GHI	
Control	25	25 0 0 0 0		
625 ррт	33	33 0 0 0 0		
1250 ppm	32	32 0 0 0 0		
2500 ррт	39	39 0 0 0 0		
Significant	dìfference ;	* : P ≦ 0.05	<b>**</b> : P ≦ 0.01 Test	t of CHI SQUARE

94

(HCL101)

TABLE I 2

#### URINALYSIS: FEMALE

STUDY NO. : 0712									UR I NA	SISA					
ANIMAL : MOUS MEASURE TIME ·	RE B6D2F1/Cr1j1	(Crj :BD	0F1]												
SEX : FEMALE	. REPORT T	TYPE :	A1											PAGE :	<del>د</del>
Group Name	NO. of Animals	рН 5. 0	6. 0	6.5	7.0	7.5 8	3.0 8	2	CHI	Protein - ± + 2+ 3+ 4+ CHI	Glucose - ± + 2+ 3+ 4+	CHI Ket	one body ± + 2+ 3+ 4+ CHI	Ccult blood 0ccult blood - ± + 2+ 3+ CHI	
Control	25	0	9	9	-		2	4		2 7 10 4 2 0	25 0 0 0 0 0	12	67000	23 2 0 0 0	
625 ррт	21	0	0	9	4	7		° m	*	276600	21 0 0 0 0 0	6	6 6 0 0 0	21 0 0 0 0	
1250 ррт	33	0	8	12	2	ŝ	9	2		3 10 12 8 0 0	33 0 0 0 0 0	15	7 10 1 0 0	31 0 0 1 1	
2500 ppm	38	0	6	6	7	2	с т			1 10 11 9 6 1	38 0 0 0 0 0	12	911 3 3 0	37 0 0 0 1	
Significant (HCL101)	difference ;	*		0. 05		н  *	0	10		Tec	st of CHI SQUARE			B	MIS5

STUDY NO. : 071 ANIMAL : MOU MEASURE. TIME : SEX : FEMALF	2 SE B6D2F1/Cr1j 1 RFP0RT 3	[Crj:BDF1] TYPE · A1	URINALYSIS	
				PAGE : 4
Group Name	NO. of Animals	Urobilinogen ± + 2+ 3+ 4+	CHI	
Control	25	25 0 0 0 0		
625 ррт	21	21 0 0 0 0		
1250 ррт	33	33 0 0 0 0		
2500 ррт	38	38 0 0 0 0		
Significant	difference	* : P ≤ 0.05	** : P ≦ 0.01	Test of CHI SQUARE

(HCL 101)

# TABLE K 1

# ORGAN WEIGHT, ABSOLUTE: MALE

STUDY NO. : 071 ANIMAL : MOU REPORT TYPE : A	12 JSE B6D2F1/Cr1j V1	[Crj:BDF1]		ORGAN WE SURVIVAL	.IGHT:ABSOLUT ANIMALS (10	TE (SUMMARY) )5W)								
sea : male UNIT: g													PAGE :	-
Group Name	NO. of Animals	Body Weight	ADRE	:NAL S	TESTE	S	HEART		LUNG	S	KIDN	EYS		
Control	24	44.9 ± 7.9	<b>0.</b> 010 ±	0. 003	<b>0</b> . 235±	0. 047	0. 215±	0. 022	<b>0</b> . 259 <u>+</u>	0. 167	0.662±	0. 081		
625 ррш	32	44. 0 ± 6. 2	<b>0</b> . 010 ±	0. 002	0. 239±	0. 049	<b>0</b> . 207 ±	0. 021	<b>0</b> . 224±	0. 075	<b>1</b> . 087 ⊥	1. 970		
1250 ррт	31	42.3 土 9.6	0. 009 <u>+</u>	0. 002	0. 248 <i>±</i>	0. 074	0. 216±	0. 027	0.208±	0. 043	0.696±	0. 252		
2500 ррт	38	39. 3 ± 7. 8 <b>*</b>	0. 010 ±	0. 002	$0.232\pm$	0. 034	0. 205±	0. 033	<b>0</b> . 214±	0. 048	0. 945 土	1. 196		
Significant	: difference ;	* : P ≦ 0.05	** : P ≦ 0.01			Test o	of Dunnett							
(HCL040)					TANK AND DURING BUILDING TANK							ANY MONTH AND ANY	RA	5

-

B6D2F1/Cr1j [Crj:BDF1]	
0712 MOUSE : A1	
STUDY NO. : ANIMAL : REPORT TYPE	SEX : MALE UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (105W)

(105W)	
NIMALS	
AL A	

BRAIN

LIVER

SPLEEN

NO. of Animals

Group Name

PAGE : 2

BAIS 5

Test of Dunnett

\*\* : P ≦ 0.01

\* : P ≦ 0.05

Significant difference ;

(HCL 040)

0.013

0.454±

0.442

**1**. 777 ±

0.231

 $0.147\pm$ 

31

1250 ppm

 $0.455 \pm 0.012$ 

1.  $584 \pm$  0. 219

0.137± 0.149

38

2500 ppm

 $0.455\pm 0.015$ 

0.283

**1.**679±

0.114

0.145 ±

32

625 ррш

**0.** 454± **0.** 013

1.  $853 \pm$  0. 470

 $0.139 \pm 0.142$ 

24

Control

# TABLE K 2

# ORGAN WEIGHT, ABSOLUTE: FEMALE

STUDY NO. : 0712 ANIMAL : MOUS REPORT TYPE : A1 SEX : FEMALE UNIT: g	E B6D2F1/Crlj.	[Crj:BDF1]		ORGAN WE SURVIVAL	IGHT:ABSOLUT ANIMALS (10	e (Summary) 15W)							3 9 0 7 0 7 0
Group Name	NO. of Animals	Body Weighi	ADRE	NALS	OVARI	ES	HEART		ILUNG	S	KIDN	EYS	2
Control	22	<b>33.</b> 1 ± 6. 3	<b>0</b> . 014 <b>±</b>	0. 002	0. 044 <i>±</i>	0. 056	<b>0</b> . 17 <b>3</b> ±	0. 025	0. 206 ±	0. 076	0. 455 ±	0. 110	
625 ppm	21	30.9 ± 5.7	0. 013±	0. 002	0. 045±	0. 032	0. 175±	0. 026	0.247±	0. 139	<b>0.</b> 535 ±	0. 263	
1250 ррт	30	<b>30.</b> 9± 5.9	0. 013±	0. 002	0. 044 <i>±</i>	0. 033	0. 171 ±	0. 022	<b>0</b> . 210 ±	0. 041	<b>0</b> . 504 ±	0.190	
2500 ррт	38	27.7 ± 3.9**	k 0. 013⊥	0. 002	0.088±	0. 221	0. 166±	0. 022	<b>0.</b> 203 ±	0. 038	0. 515 <u>+</u>	0. 239	
Significant (HCL040)	difference;	* : P ≦ 0.05	** : P ≦ 0.01			Test	of Dunnett						BAISS

PAGE						Dunnett
:ABSOLUTE (SUMMARY) Mals (105W)	BRAIN	76± 0.018	<b>81</b> ± 0.017	74士 0.016	<b>6</b> 3± 0.016 <b>*</b>	Test of
ORGAN WEIGHT SURVIVAL ANI	LIVER	± 0.427 0.4	± 0.199 0.4	± 0.313 0.4	± 0.612 0.4	10
	7	). 150 1. 534	0. 160 1. 449	). 385 1. 568	). 573 1. 550	** : P ≦ 0.
j [Cr.j :B0F1]	SPLEE	0. 214 ± (	<b>0.</b> 217 ± 1	<b>0.</b> 311 ± (	0.340± (	+ : P ≦ 0.05
0712 MOUSE B6D2F1/Cr1j : A1	NO. of Animals	22	21	30	38	int difference;
STUDY NO. : 1 ANIMAL : 1 REPORT TYPE : SEX : FEMALE UNIT: g	Group Name	Control	625 ррт	1250 ррш	2500 ррт	Significa

(HCL040)

# TABLE L 1

# ORGAN WEIGHT, RELATIVE: MALE

STUDY NO. : 071. ANIMAL : MOU: REPORT TYPE : A: SEX : MALE	2 SE B6D2F1/Crlj 1	[Crj:BDF1]	ORGAN W SURVIVA	VEIGHT:RELATIVE (SUMMAR) AL ANIMALS (105W)	\$			
UNIT: % Group Name	NO. of Animals	Body Weight (g)	ADRENALS	TESTES	HEART	LUNGS	KIDNEYS	PAGE : 1
Control	24	44. 9 <b>±</b> 7. 9	<b>0.023</b> ± <b>0.006</b>	0. 534 <b>± 0.</b> 124	0. 490± 0. 080	0. 604 ± 0. 476	<b>1.516</b> ± 0.323	
625 ррш	32	$44.\ 0 \pm 6.\ 2$	0.023 ± 0.006	<b>0.</b> 553± 0. 126	<b>0.</b> 478± 0. 062	0. 529 ± 0. 226	<b>2.</b> 526 ±  4. 711	
1250 ррт	31	42.3 <b>±</b> 9.6	0.024± 0.010	0.607± 0.184	0.537±0.159	$0.530\pm 0.220$	1. 707 土 0. 584	
2500 ppm	38	39. 3 土 7. 8*	$0.026\pm 0.007$	$0.612\pm 0.146$	0. 533± 0. 100	0.571±0.187	2. 587 <b>±</b> 3. 600 <b>∗</b>	
Significant (HCL042)	difference ;	* : P ≤ 0.05	** : P ≦ 0.01	Τes	t of Dunnett			BAIS5

STUDY NO. : 0712 ANIMAL : MOUSI REPORT TYPE : A1 SEX : MALE	E B6D2F1/Cr1j[	Crj:BDF1]	ORGAN WE SURVIVAL	EIGHT:RELATIVE (SUMMARY) L ANIMALS (105W)	
Group Name	ND OF	SPI FEN	I I VED	PAGE	: 2
	Animals			DKATIN	
	r c				
00111101	47	U. 332 Ⅲ U. 380	4.318土 1.0/8	1. U43 ± U. 189	
625 ррт	32	<b>0</b> . 341 ± 0. 290	<b>3. 885 ± 0. 864</b>	1.056主 0.167	
1250 ррш	31	$0.353\pm0.430$	<b>4.</b> 331± 1. 161	1.136± 0.301	
	ç				
mdd nnc7	38	U. 358± U. 362	4. 163± 1. 012	1.204± 0.240*	
SIGNITICANT	difference ;	: ** ℃0.00 *** :	P 🔝 0. 01	Test of Dunnett	
(HCL 042)					BAIS5

STUDY NO: : 0712
# TABLE L 2

# ORGAN WEIGHT, RELATIVE: FEMALE

0

STUDY NO. : 07 ANIMAL : MOU REPORT TYPE : / SEX : FEMALE	12 USE B6D2F1/Crlj A1	[CrJ:BDF1]	ORCAN V SURVIVI	WEIGHT:RELATIVE (SUMMARY AL ANIMALS (105W)	6			
UNIT: %								PAGE : 3
Group Name	NO. of Animals	Body Weight (දූ)	ADRENALS	OVARIES	HEART	TUNGS	KIDNEYS	
Control	22	<b>33.</b> 1 <b>⊥</b> 6. 3	0.042 ± 0.008	0.135 ± 0.164	0. 537± 0. 105	<b>0. 650</b> ± 0. 318	<b>1</b> . 399 ± 0. 343	
625 ppm	21	30.9土 5.7	$0.042\pm0.008$	$0.150\pm 0.105$	<b>0.</b> 582 ± 0. 129	0.837± 0.515	<b>1. 841 ± 1. 190</b>	
1250 ррт	30	30.9 ± 5.9	$0.043\pm 0.008$	0. 150± 0. 115	0. 570± 0. 113	0.708± 0.202	1.715± 0.890	
2500 ррт	38	27.7 ± 3.9**	0. 047 ± 0. 009 <b>*</b>	$0.\ 300\pm\ 0.\ 678$	0.608± 0.087	0. 757 ± 0. 213	1. 903 ± 0. 971 **	
Significan <sup>†</sup> (HCL 042)	t difference ;	 	** : P ≦ 0.01	Test	of Dunnett			BAIS 5

(SUMMARY)	
TIVE	(105W)
GHT : RELA	<b>AN I MAL S</b>
WE I	VAL /
ORGAN	SURVI

PAGE : 4

Group Name	NO. of Animals	SPLEEN	LIVER	BRAIN	
	· · ··································				
Control	22	0.673±0.523	4. 684	1.484± 0.260	
625 ррт	21	0.713± 0.584	<b>4</b> . 772 ± 0. 735	1. 606± 0. 302	
1250 ррт	30	<b>0.</b> 971 ± 1. 038	5. $201 \pm 1.219$	1.587 ± 0.290	
2500 ррт	38	1. 257 ± 2. 205	5. 600 ± 1. 938	1.701± 0.224 <b>*</b> *	
Significant	difference ;	* : P ≦ 0.05 ** :	P ≦ 0.01	Test of Dunnett	
(HCL 042)				RAISS	15.5

# TABLE M 1

# HISTOPATHOLOGICAL FINDINGS:

## NON-NEOPLASTIC LESIONS:

# MALE: ALL ANIMALS

STUDY NO. ANIMAL REPORT TYPE SEX	: 0712 : MOUSE B6D2F1/Crlj[Crj:BDF1] : Al : MALE	Η¥	I STOPATHOL LL ANIMALS	.0GICAL F (0-105W)	INDINGS : NO	N-NEOPLAST	C LESION	is (su <b>m</b> aary								PAG		
		Group Name No. of Animals on S	Cont tudy	rol 50		625	ppm 50			1250 pi	ES			2500	mqq 105			
Organ	. Findings	Grade	(%) (%)	2+ 3+ (%) (%)	4+ (%)	(%) (%) ()	2+ 3+ %) (%)	4+ (%)	<del>%</del>	2+ (%)	3+	4+ (%)	- 6)	±	2+2	÷	4+ (%)	
{ ntegument	ary system/appandage}																	
skin/app	ulcer		1 (2) (	<pre>&lt;50&gt; 0 0) 0</pre>	0 )	) (0 ) 0	<50> 2 0 4) ( 0)	0 )	1 (2)	( 7 7	0 0 (0)	0 )	) )		) ( ) ( 20>		0 (0	
	erosion		) (0 )	0) 00) 00	0 0	1 (2) (	2 4) ( 0)	0 0	0 0	2 ( 4)	0 0 )	0	<u> </u>		5 - 5		0 0	
	inflammation		) (0 0 )	0) (0 0 0	0 0	) (0 ) 0	0 0 0	0 0	0 0	1 (2)	0 0 )	0)	- -				0 (0	
	squamous cell hyperplasia		) 0 )	0 ) 0 0	0 0	) (0 ) 0	0 0 0	0 0	4 (8)	0 0	0 0 )	0 )	- -				0 (0	
	scab		3 (6){	0 ) 0 0	0 )	1 (2) (	(0 0 ) 0	0 0	(0 0	(0 0	0 0 )	0)	) }		 		0 (0	
	epidermal cyst		) (0)	0) (0 0	0 (0 	) (0 ) 0	2 4) ( 0)	0 0 )	1 (2)	0 0	0 (0 )	0 (0	_		 0 (i)		0 (0	
subcutis	hematoma		) (0) )	<pre>&lt;50&gt; 0 0 0 0</pre>	0 )	) (0 ) 0	<pre>&lt; 50&gt;</pre> <pre>0</pre> <p< td=""><td>0 0</td><td>0 )</td><td>( <sup>1</sup></td><td>0 0 0)</td><td>0 0</td><td>-</td><td></td><td>0) &lt;20</td><td></td><td>0</td><td></td></p<>	0 0	0 )	( <sup>1</sup>	0 0 0)	0 0	-		0) <20		0	
	inflammation		) (0 0 )	0) (0 0	0 )	) (0 ) 0	1 2) ( 0)	0 0	0 0	0 0 )	0 (C) 	(0 0	<u> </u>		0		0 ()	
Grade < a > b ( c ) Significant	1+ : Slight2+ : Moderate $a$ : Number of animals examined at th $b$ : Number of animals with lesion $c$ : $b / a \pm 100$ $c$ : $b / a \pm 100$ $c$ : $b / a \pm 100$	3+ : Marked 4+ : he site P ≦ 0.01 Test of Ch	Severe i Square															
(HPT150)																	BAIS5	

STUDY NO. ANIMAL REPORT TYPE : SEX	0712 MAUSE B6D2F1/Cr1j[Crj:BDF1] A1 MALE	HISTOPATHOLOGI ALL ANIMALS (0	CAL FIND 1-105W)	INGS : NON-	NEOPLASTIC LES	LIONS (SUMMARY)							PA	۰ با	~
	-														
Organ	uroup Name No. of Animals on Grade	Control Study 5 1+ 2+	ھَ <del>3</del> + 0	4+	625 ppm 50 1+ 2+	3+ 4+	1+ 12	50 ppm 50 2+ 2/	3+	+.	250 1+	0 ppm 50 24	3+	4+	
		1 m (m) -	ies	101	(v) (v)	(@) (@)	(9)	(8)	(¥) (¥)		(%)	(%)	(%)	(%)	I.
{ ntegumentar	y system/appandage)														
subcutis	xanthogranu loma	( 0) ( 0)	) (0 ) 0 <0	0 (0	(50) (50) (50) (50) (50)	(0) 00 0	( 1 ( 2) (	<50> 0 0 (	0 0	-	0	<50> 0 0) (	) 0	0 0	
(Respiratory	system]														
nasal cavit	eosinophilic change:olfactory epithelium	<pre>&lt;5 &lt;16 &lt;16 &lt;132) &lt;10)</pre>	) (0 ) 0 <0	0 (0	( 26) ( 0) (	(0 0 0	13 (26) (	<50> 0 0) (	0 )	-	14 28) (	<pre>&lt;50&gt; 0 0</pre>	-) 0 (0	0 0	
	eosinophilic change:respiratory epithelium	23 0 (46) (0)	) (0 ) 0	0 (0	21 0 (42) (0) (	(0) 00000	19 (38) (	) 0	0 ) (0		18 36) (	) 0	) 0	0 (0	
	inflammation:foreign body	1 0 (2) (0)	) (0 0 )	0 (0	) (0 ) (0 ) 0 0	0) (0 0	) (0 )	) 0	0 ) (0	-	0	~ 0 (0	) 0	0 (0	
	respiratory metaplasia:olfactory epithelium	9 1 (18) (2)	) (0)	0 0	5 0 (10) (0) (	(0) 0) 0 0	7 (14) (	) 0	0 0 0 0	-	5 10) (	) 0	_ 0	0 (0	
	respiratory metaplasia:gland	9 1 (18) (2)	) (0 ) 0	0 0	8 0 (16) (0) (	(0) 00000000000000000000000000000000000	7 (14) (	1 2) (	0 0 0 0	-	10 20) (	) 0	- 0	0	
nasopharynx	eosinophilic change	( 0) ( 0)	) (0 ) 0 <0	0 (0	<pre></pre>	0 ) 0 0	) (0 )	<pre></pre>	0 ) 0 0	-	0	<50> 0 0) (	_ 0	0	
Grade Grade < a > b ( c ) Significant d	1+: Slight2+: Moderate3+: Marked4+1: Number of animals examined at the site $a$ : Number of animals with lesion $c$ : $b > a : 100$ $a = 0.01$ 1: Ifference : $a : P \leq 0.05$ $a : P \leq 0.01$ Test of C	: Severe in Square													I

(HPT150)

STUDY NO. Animal Report type Sex	: 0712 : MOUSE B6D2F1/Cr1j[Crj:BDF1] : A1 : MALE	HISTOPATHOLOGICAL FINDINGS : ALL ANIMALS (0-1054)	NON-NEOPLASTIC LESIONS (SUMMAR	8	DAACF · 3
	Group Name No. of Animals	Control on Study 50	625 ppm 50	1250 ppm 50	2500 ppm 50
Organ	Grade Grade	1+         2+         3+         4+           (%)         (%)         (%)         (%)	1+ 2+ 3+ 4+ (%) (%) (%) (%)	1+ 2+ 3+ 4+ (%) (%) (%) (%)	1+ 2+ 3+ 4+ (%) (%) (%) (%)
(Respiratory	system)				
lung	congestion	( 0) ( 0) ( 0) ( 0)	$\begin{pmatrix} < 50 \\ 0 \\ 1 \\ 0 \end{pmatrix} \begin{pmatrix} < 0 \\ 0 \end{pmatrix}$	( 0) ( 0) ( 0) 0 0 0 0 ( 0) ( 0) ( 0)	$\begin{pmatrix} <50 \\ 0 \\ 0 \\ 0 \end{pmatrix} \begin{pmatrix} <0 \\ 0 \end{pmatrix} \begin{pmatrix} <0 \\ 0 \end{pmatrix}$
	hemorrhage	(0) (0) (0) (0) 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	1 0 0 0 (2) (0) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0 0 0
	deposit of amyloid	4 0 0 0 (8) (0) (0) (0)	6 0 0 0 (12) (0) (0) (0)	4 0 0 0 (8) (0) (0) (0)	8 0 0 0 (16) (0) (0) (0)
	inflammatory infiltration	2 1 0 0 { 4} ( 2) ( 0) ( 0)	2 0 0 0 (4) (0) (0) (0)	3 0 0 0 (6)(0)(0)(0)	1 0 0 0 (2)(0)(0)(0)
	bronchiolar-alveolar cell hyperplasia	2 0 0 0 (4) (0) (0) (0)	2 0 0 0 (4) (0) (0) (0)	1 0 0 0 (2)(0)(0)(0)	1 0 0 0 (2) (0) (0) (0)
	eosinophilic change:bronchial epithelium	1 0 0 0 0 ( 2) ( 0) ( 0)	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	(0) (0) (0) (0) 0 (0) (0)	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
(Hematopoiet	ic system)				
bone marrow	congestion	$\begin{pmatrix} < 50 \\ 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0$	$\begin{pmatrix} 50 \\ 0 \\ 1 \\ 0 \end{pmatrix} \begin{pmatrix} 50 \\ 1 \\ 0 \\ 0 \end{pmatrix} \begin{pmatrix} 0 \\ 0 \\ 0 \end{pmatrix}$	( 0) ( 0) ( 0) ( 0)	<pre>&lt; &lt;50&gt;</pre> <pre>&lt; &lt;50&gt;</pre> <pre>0 0 0 0</pre> <pre>0 0</pre>
Grade Grade < a > b ( c ) Significant o	1+ : Slight 2+ : Moderate 3+ : Marked a : Number of animals examined at the site b : Number of animals with lesion c : b / a ± 10 d5 ± ± : P ≤ 0.01 Test o	4+ : Severe f Chi Sourare			
(HPT150)					BAIRE

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712	0USE B6D2F1/Cr1j [Crj:BDF1]	1	AIE
			7
NO.		ΤΥΡΕ	
Σ	MAL	ORT	

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STUDY NO. Animal Report type : Sex	0712 MOUSE B6D2F1/Cr1j[Crj:BDF1] A1 MALE	HISTOPATHOLOGICAL FINDINGS : ALL ANIMALS (0-10540)	ION-NEOPLASTIC LESIONS (SUMMAR	8	PA	GE : 4
Organ	Findings	Group Name Control No. of Animals on Study 50 Grade 1+ 2+ 3+ 4+ (%) (%) (%) (%)	625 ppm 50 1+ 2+ 3+ 4+ (%) (%) (%) (%)	1250 ppm 50 1+ 2+ 3+ 4+ (%) (%) (%)	2500 ppm 50 50 1+ 2+ 3+ (%) (%)	4+ (%)
(Hematopoieti	c system}					
bone marrow	increased hematopoiesis	$\begin{array}{ccccc} & \langle 50 \rangle & \\ 12 & 0 & 0 \\ (24) & (0) & (0) & (0) \end{array}$	$\begin{array}{cccc} \langle 50\rangle & \\ 11 & 0 & 0 \\ (22) & (0) & (0) & (0) \end{array}$	$\begin{array}{cccc} <50 \\ 10 & 0 & 0 \\ (20) & (0) & (0) & (0) \end{array}$	<pre><pre><pre><pre><pre><pre><pre><pre></pre></pre></pre></pre></pre></pre></pre></pre>	0
	granu opoiesis:increased	2 0 0 0 (4) (0) (0) (0)	6 0 0 0 (12) ( 0) ( 0) ( 0)	4 0 0 0 0 (8) (0) (0) (0)	2 0 0 ( 4) ( 0) ( 0) (	0
lymph node	lymphaden ítis	$\begin{array}{cccc} \langle 50 \rangle & \\ 1 & 0 & 0 \\ ( 2 ) & ( 0 ) & ( 0 ) \\ \end{array}$	$\begin{array}{ccc} \langle 50\rangle \\ 0 & 1 & 0 \\ ( & 0) & ( & 2) & ( & 0) & ( & 0) \end{array}$	<pre>&lt; 50&gt; </pre> ( 0) ( 0) ( 0)	<pre></pre>	0
thymus	atrophy	$\begin{pmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 &$	$\begin{pmatrix} < 50 \\ 0 \\ 1 \\ 0 \end{pmatrix} \begin{pmatrix} < 50 \\ 0 \\ 0 \end{pmatrix}$	<pre>&lt; 0) &lt; 0) &lt; 0) &lt; 0) &lt; 0)</pre>	( 0) ( 0) ( 0) (	0
spleen	deposit of hemosiderin	$\begin{array}{ccccc} <50> & <50> \\ 20 & 0 & 0 \\ (40) & (0) & (0) \\ \end{array}$	$\begin{array}{cccc} < 50 \\ 26 & 0 & 0 \\ (52) & (0) & (0) \end{array}$	<pre> &lt;60&gt; &lt;50&gt; &lt;50&gt; &lt;30 &lt;4 0 0 **   (60) (8) (0) (0)</pre>	<pre></pre>	** ()
	deposit of melanin	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	1 0 0 0 (2)(0)(0)(0)	(0) (0) (0) 0 0 0 0 0 0 0	) (0 ) (0 ) 0 0 0 0	0
	fibrosis:focal		(0) (0) (0) (0) 0 0 0 0 0	1 0 0 0 ( 2) ( 0) ( 0) ( 0)	) (0 ) (0 ) 0 0 0 0	0
Grade <a> b (c) Significant d</a>	1+ : Slight $2+$ : Moderate a : Number of animals examined at the b : Number of animals with lesion c : b / a $\pm 100$ ifference ; $\pm$ : P ≤ 0.05 $\pm\pm$ : P	34 : Marked 44 : Severe s site ≥ ≦ 0.01 Test of Chi Square				
(HPT150)						BAICE

114

STUDY NO. ANIMAL REPORT TYPE SEX	: 0712 : MOUSE B6D2F1/Cr1j[Crj:BDF1] : A1 : MALE		HISTOPATI ALL ANIM	HOLOGICAL F Als (0-105W	indings in	ON-NEOPLAS	TIC LES 10	VS (SUMMARY	-					<u>م</u>	: age
		Group Name No. of Animals	on Study	ontrol 50		62	5 ppm 50		1	250 ppm 50			2500 pp	EQ	
Organ	Findings	urade	± 🛞	5+ (%) (%)	4+ (%)	* €	5+ (%) (%)	+ 4+	+ (%)	2+ (%)	3+ 4+ %) (%)	- 36	() (%) (%)	3+ %	4+ %
{Hematopoiet	tic system)														
spleen	extramedullary hematopoiesis		11 ( 22)	<pre>&lt;50&gt; 11 0 ( 22) ( 0)</pre>	0 (0 )	14 (28) (	<50> 8 0 16) ( 0)	(0 0	13 ( 26)	<50> 10 ( 20) (	1 2) ( 0)	20 ( 40	) 12 () 24)	0> 1 (2)(	0
	follicular hyperplasia		- 5 4)	(0) (0) (0)	0 (Ö 	3 ( 6) (	0 0 0	(0) 0	1 (2)	) (0 0	0) (0 0	1 ( 2	00)	) (0 )	0 ()
(Circulatory	r system)														
heart	deposit of amyloid		2 (4)	<pre>&lt;50&gt; 0 0 0 0</pre>	0 (0	5 (10) (	<50> 0 0 0) ( 0)	(0) 0	5 (10)	<pre>&lt;50&gt; 0 ( 0) (</pre>	(0 0 0	7 (14	, 0 <2	) (0 ) (0 )	0 0
	mineralization		2 ( 4)	1 0 (2) (0)	0	) (0 )	0 0 0	0 0	1 (2)	) 0 )	0 ) 0 0	0 ~		) 0 )	0
	myocardial fibrosis		17 (34)	(0) (0) 0 0	0 (Ö )	10 (20) (	(0 0 ) (0 0	0 0	19 (38)	) 0 )	0) 00) 00	13 (26	0)	) (0 )	0 0
	arteritis		1 ( 2)	(0) (0) 0 0	0 (Ö ~	1 (2)	(0 0 ) 0	0 0	1 (2)	) 0	0) 00) 00	0 )	) 1 ) (2)	) 0 )	0 0
artery/aort	mineralization		0 )	<pre>&lt;50&gt; 0 0 ( 0) ( 0)</pre>	0 )	) 0 )	<50> 0 0 0) ( 0)	0 0	(2)	<pre></pre>	(0) 0000	0)	) ( 0)	) (0 ) 0 <0	0
Grade < a > b ( c ) Significant (HPT150)	1+: Slight 2+: Moderate a : Number of animals examined at th b : Number of animals with lesion c : b / a $\pm 100$ difference ; $\pm : P \leq 0.05$ *# :	3+:Marked , he site P≦0.01 Testo:	L+ : Severe Chi Square												

STUDY NO. ANIMAL REPORT TYPE SEX	: 0712 : MOUSE B6D2F1/Cr1j[Crj:BDF1] : A1 : MALE		HISTOPATHOLOGIC ALL ANIMALS (0-	AL FIND 105W)	INGS : NON	-NEOPLAST I	C LESIO	DNS (SUMMARY	-							PAGE :	9
Or gan	F ind ings	Group Name Group Name No. of Animals on S Grade	Control Study 50 (%) (%)	(%) (%)	44 (%)	625 1+ (%) (	ррт 50 %) (3	3+ 4+ (%) (%)	(%) + *	250 ppm 50 2+ (%)	3+ 2 (%) (9	+ <del>3</del>	2! (%)	500 ppr 5( (%)	÷	4+ (%)	
(Digestive s	system)																
oral cavity	hema toma		<pre></pre>	) 0 0 0	0	) (0 ) 0	<50> 1 2) ( (	0 (0 0 (1	0 )	<pre>&lt;50&gt;</pre>	0 (0	a â	0 0 )	( 0) <2(	0 (0 (1)	0	
tooth	dysplasia		( 0) ( 0) (	 0 (0 ^	0	1 (2){	<pre>&lt;50&gt; 0 ( 0 )</pre>	0 ((	0 )	( 0) ( 0 ( 0) (	0	- A	( 2)	( 0) <2(	0 (0 (0)	0 )	
tongue	squamous cell hyperplasia		0 0 (0) (	- 0 0	0	1 (2) (	<pre></pre>	(0) ((	0 (0	<pre>&lt; 50&gt;</pre>	0	98	0	( 0) <2(	0 (0 (0)	0	
	epidermal cyst		) (0 ) (0 ) 0 0	) 0	0	1 (2) {	0	0 (0	(0 0	) 0 )	) ) 0	a â	0 0	0 ()	0)	0	
	arteritis		1 0 ( 2) ( 0) (	) 0	0	) (0)	) ) ) 0	0 (0	1 ( 2)	) (0)	0	- <b>G</b>	0 0 )	0 (0	0 (O	0 0	
stomach	ulcer:forestomach		0 0 (0) (10) (10) (10) (10) (10) (10) (1	) 0 0	0	) (0 ) 0 )	( ( ( (	(0) ((	1 (2)	<pre>&lt; 50&gt;</pre> <pre>&lt; 50&gt;</pre> <pre>( 0) (</pre>	0 0	- A	0 0 )	( 0) <2(	0 (0 (0)	0 0	
	hyperplasia:forestomach		0 1 ( 0) ( 2) (	) 0	0	2 (4) (	0	0 0	1 (2)	) (0)	0	08	( 2)	0)	0 (0	0 )	
Grade < a > b ( c ) Significant	<pre>1+ : Slight 2+ : Moderate a : Number of animals examined at 1 b : Number of animals with lesion c : b / a * 100 c : b / a * 100 difference ; * : P ≤ 0.05 ** :</pre>	3+:Marked 4+: the site :P≦0.01 Test of Ch	: Severe ii Square														

(HPT150)

STUDY NO. ANIMAL REPORT TYPE SEX	: 0712 : MOUSE B6D2F1/Crlj[Crj:BDF1] : A1 : MALE	HISTOPATHOLOGICAL FINDING ALL ANIMALS (0-105%)	GS :NON-NEOPLASTIC LESIONS (SUMMARY		PAGE :	. 7
Organ	F ind ings.	Group Name Control No. of Animals on Study 50 Grade (%) (%) (%) (%) (%) (%)	625 ppm 50 50 50 1+ 2+ 3+ 4+ (%) (%) (%) (%)	1250 ppm 50 1+ 2+ 3+ 4+ (%) (%) (%)	2500 ppm 50 50 44 1+ 2+ 3+ 4+ (%) (%) (%) (%)	
(Digestive s stomach	iystem] erosion:glandular stomach	<pre>(20)</pre>	3 0 0 0	4 0 0		
	hyperplasia:glandular stomach		$\begin{array}{cccccccccccccccccccccccccccccccccccc$	( 8) ( 0) ( 0) ( 0) 9 0 0 0 ( 18) ( 0) ( 0) ( 0)	(2) (0) (0) (0) 14 0 0 0 (28) (0) (0) (0)	
small intes	ulcer	$\langle 50 \rangle$ $\begin{pmatrix} 60 \\ 1 \\ 0 \end{pmatrix}$ $\begin{pmatrix} 0 \\ 2 \end{pmatrix}$ $\begin{pmatrix} 0 \\ 0 \end{pmatrix}$	<pre> &lt;50&gt; &lt;50&gt; &lt;50&gt; (50) (50) (50) (50) (50) (50) (50) (50)</pre>	<pre><code (0)="" (0)<="" color="" td=""><td><pre></pre></td><td></td></code></pre>	<pre></pre>	
	hemorrhage			1 0 0 0 (2) (0) (0) (0)	(0) (0) (0) (0) 0 (0) (0) (0)	
liver	angiectasis	$\begin{array}{ccccc} \langle 50 \rangle \\ 1 \\ 1 \\ 2 \\ 2 \\ 1 \\ 2 \\ 1 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0$	(10) (10) (10) (10) (10) (10) (10) (10)	<pre><code color="1"><code color="1"><code color="1"></code></code></code></pre>	<pre> &lt;50&gt; &lt;50&gt; &lt;50&gt; (50) (50) (50) (50) (50) (50) (50) (50)</pre>	
	necrosis:central		1 0 0 0 ( 2) ( 0) ( 0) ( 0)	(0) (0) (0) (0) 0 0 0 0)	(0)(0)(0) 0 0 0 0) 0 0 0)	
	necrosis:focal	2 0 0 0 (4) (0) (0) (0)	1 1 0 0 ( 2) ( 2) ( 0) ( 0)	2 0 0 0 (4) (0) (0) (0)	2 0 0 0 (4)(0)(0)(0)	
Grade	1+ : Slight 2+ : Moderate a : Number of animals examined at th b : Number of animals with lesion c : b / a ± 100 difference : ± : P ≤ 0.05 ±± :	3+ : Marked 4+ : Severe he site P ≤ 0.01 Test of Chi Square				
(HPT150)					Ē	BAIS5

STUDY NO. ANIMAL REPORT TYPE SEX	: 0712 : MOUSE B6D2F1/Cr1j[Crj:BDF1] : A1 : MALE		HISTOPATHOLOC ALL ANIMALS	31CAL F1 (0105W)	NDINGS :N	ON-NEOPLA ST	IC LES	IONS (SI	MMARY)								PAGE	œ 
Organ	Findings	Group Name No. of Animals Grade	on Study Contro 1+ 2+ (%) (%)	1 50 (%)	4+ (%)	625 (%)	i ppm 50 (%)	(%) (%)	+ ~	(%) (%)	50 ppr 50 2+ (%)	3+ (%)	4+ (%)	(%)	2500 p 2+ (%)	50 (%) 3+	4 %	+ ~
(Digestive	system)																	
liver	necrosis:single cell		> (0 0 (0 0 )	50> 0 ( 0)	0 0 )	) (0 0	<50> 0 0) (	00		0	( 0) - <	0 O	0 (0	1 (2)	° 0 6 _	50> 0 ( 0)	0 0 	(
	collapse		(0) (0) 000	0 0	0 0	1 (2) (	) (0	0 0	-	00	00	00	0 0	0 )	0 0	0 0	00	-
	inflammatory infiltration		0 1 ( 0) ( 2)	0 0	0 )	) (0 0 )	) 0	0 0		00	0 (0	0 0	0 0	(0) 0	0 0	0 0	00	-
	inflammatory cell nest		11 0 (22) (0)	0 0	0 )	9 (18) (	) 0 (0	0 0		8 ( 16)	0 6	00	0 (0	13 (26)	1 (2)	0 0	00	-
	clear cell focus		(0) (0) 000	0 0	0 (0	1 (2) (	) 0 (i)	0 ) (0		0 Ô	00	00	00	0 )	0 (î )	0 0 )	00	-
	acidophilic cell focus		(0) (0) 0 0	0 0 )	0 0 )	) (0 0	) 0	0 ) 0		0 (0	00	00	0 (0	1 (2)	0 0 )	00 0	00	-
	basophilic cell focus		1 0 (2) (0)	0 )	0 (O )	6 (12) (	1 2) (	0 ) 0 (0	-	( 6) 3	2)	0	0 (0	2 ( 4)	0 0	0 0	00	-
	mixed cell focus		(0) (0) 0 0	0 )	0 (î	1 (2) (	) 0 (0	0 ) (0	-	0 ()	0 (0	0 0	0 (0	1 (2)	(0 0	0 0	0 )	-
Grade	1+ : Slight2+ : Moderatea : Number of animals examined at theb : Number of animals with lesionc : b $/$ a $* 100$ c : b $/$ a $* 100$ difference ; $*$ : $P \leq 0.05$	3+ : Marked he site P≦ 0.01 Test	4+ : Severe of Chi Square															
(DG114H)																		BAIS5

STUDY NO. ANIMAL REPORT TYPE Sex	: 0712 : MOUSE B6D2F1/Cr1j [Crj:BDF1] : A1 : MALE	ALL A	PATHOLOGICAL NIMALS (0-10	FINDINGS :NO 5W)	DN-NEOPLAST I (	CLESION	s (Summary)					
											X.	
		Group Name No. of Animals on Study	Control 50		625 p	50 50		12	50 ppm		2500 ppm 50	
Organ	Findings	Grade	1+ 2+ %) (%) ((	3+ 4+ %) (%)	1+ (%)	2+ 3+ 3) (%)	4+ (%)	1+ (%)	2+2 (%)	3+ 4+ %) (%)	(x) (x) (x) (x) (x)	4+ (%)
(Digestive s	ystem)											
liver	biliary cyst		2 (50) 4) ( 0) ( 1	0 ) 0 (0	1 (2) (0	<pre>&lt;50&gt; 0 0 0 0</pre>	0 )	) (0 ) 0 )	<pre>&lt;50&gt; 0 0</pre>	0 ) (0 0 0	<pre></pre>	0 0
	intestinal metaplasia:bile duct	_	0 1 0) ( 2) ( 1	0 ) 0 )	0) (0)	0)	0 0	) (0 )	) 0	0 ) 0 ) 0	) (0 ) (0 ) (0 ) 0 0 0	0 (0
	deposit of brown pigment	~		0 ) ((	0 ) (0 ) 0 )	000	0 0 )	) (0 0 )	) (0	0 0	10 0 0 (20) (0) (0) (	** (0
pancreas	cyst	<u> </u>	0 ( 0) ( (	0 ) ((	0 (0) (2	<50> 0 0 ( 0)	0 0	) (0 )	<pre>&lt;50&gt; 0 0</pre>	0 ) 0 ) 0	<pre>&lt; 50&gt; </pre> <pre>&lt; 50&gt; </pre> <pre>( 0) ( 0) (</pre>	0
(Urinary sys	tem)											
k i dney	atrophy		0 ( ( ( ( ( ( ( ( ( ( ( ( ( ( ( ( ( ) ) (	0 0	0 ) (0 ) 0 0	<pre>&lt;50&gt; 0 (0)</pre>	0 (0	) (0 0	<50> 0 0) (	0 )	<pre>&lt;50&gt; &lt;50&gt; </pre> (50) (4) (0) (4) (50)	0 (0
	cyst	~		0)(0)	0 ) (0 ) 0 0	0 )	0 0	) (0 0	) 0	0 ) (0	1 0 0 ( 2) ( 0) ( 0) (	0 (0
Grade Grade ( a ) ( c ) Significant	1+ : Slight2+ : Moderatea : Number of animals examined at theb : Number of animals with lesionc : b / a $\pm 100$ difference ; $\pm : P \leq 0.05 \pm : P$	3+ : Marked 4+ : Sev site ≦ 0.01 Test of Chi Sa	ere uare									
(HPT150)												RAISS

	E B6D2F1/Cr1j [Crj:BDF1]		
0712	MOUSE	A1	1.111
• •	• •	• •	
Ч0.		TYPE	
Γ	MAL	ORT	

STUDY NO. ANIMAL REPORT TYPE	: 0712 : MOUSE B6D2F1/Cr1j [Crj:BDF1] : A1 : A1	HISTOPATHOLOGICAL ALL ANIMALS (0-10	. FINDINGS :NO 15W)	DN-NEOPLASTIC LESION	IS (SUMMARY)									
SEA	: MALE												PAGE :	10
Organ	Findings.	Group Name Control No. of Animals on Study 50 Grade (%) (%) (%)	3+ 4+ %) (%)	625 ppm 50 1+ 2+ 3+ (%) (%) (%)	4+	(%) (%) (%)	50 ppm 50 2+ (%)	3+ (光) (兆)	<b>* •</b>	2; (%)	500 ppr 51 (%)	(%) 3 1 0	4+ (%)	
(Urinary sy	.tem)													
k i dney	hyaline droplet	(2) $(0)$ $(1)$ $(2)$ $(2)$ $(1)$	(0) 0) 00	<pre></pre>	0 )	5 (10) (	<pre>&lt;50&gt; 0 0</pre>	0 0 0	-	( 2 (	( 0) <sup>(</sup> 2(	0 () ()	0 )	
	deposit of amyloid		0 ) 0 0	(0)(0)(0) 000 000	0 0	) (0 0 )	_ 0 0	0)	-	0 (0	1 (2)	0 (O	0)	
	hyaline cast	1 0 1 (2) (0) (-	0 ) 0 0	(0)(0)(0) 0000	0)	1 (2) (	) 0	0 ) 0 0	-	0 (0	0 (0	0 () )	0 (O	
	inflammatory infiltration		0) 00)	(0) (0) (0) 0 0 0	(0 0	) (0 )	2) (	000000000000000000000000000000000000000		0 0	0 (0	0 () )	0 () 	
	lymphocytic infiltration		0 ) 0 0	2 0 0 (4) (0) (0)	0 0	) (0 0	) 0 (0	0 0 0 0		1 (2)	0 (0)	0 (0	0 (0	
	scar		0 ) 0 0	2 3 0 (4) (6) (0)	0 0	4 (8) (	) 0	0 0 0 0	-	(2)	( 9) 3	000	0 (0	
	inflammatory polyp	0 2 0	4 0 8) ( 0)	1 3 2 ( 2) ( 6) ( 4)	0 0	1 (2) (	4 8) (	0 0 0 0	-	( 2)	, 1 , 2)	1 (2)	0 (0	
	hydronephrosis	1 2 1 (2) (4) (1)	6 1 2) (2)	0 3 8 ( 0) ( 6) (16)	0 0	) (0 )	4 8) (	3 6) ( 0	-	0 (0	5 (10)	( 4)	0 (0	
Grade Grade < a > b ( c ) Significant (HPT150)	1+: Slight 2+: Moderate a : Number of animals examined at the b : Number of animals with lesion c : b / a * 100 c : b / a * 100 difference ; * : P ≦ 0.05 ** : P	3+:Marked 4+:Severe e site P≦0.01 Test of Chi Square												3
													õ	CC I V

STUDY NO. Animal Report type Sex	: 0712 : MoUSE B6D2F1/Cr1j[Crj:BDF1] : A1 : MALE	HISTOPATHOLOGICA ALL ANIMALS (0-1	AL FINDINGS :NO 05W)	ON-NEOPLASTIC LESIONS (SUMMARY	-					PAG	ية 11
Organ	Findings	Group Name Control No. of Animals on Study 50 Grade (%) (%) (%)	3+ 4+ (%) (%)	625 pom 50 1+ 2+ 3+ 4+ (%) (%) (%)	1250 1+ 2 (%)	ррт 50 1) (%)	4+ (%)	25 (%)	00 ррт 50 (%)	3+ (%)	(%) (%)
(Urinary syst	tem)										
k i dney	Dyelonephritis	(50) 0 1 (0) (2) (	(0) 000	<pre></pre>	1 2 (2) (4	<50> ( 0) (	0	0 (O 	( 0) (	) 0	0
	mineralization:papilla	) (0 ) (0 ) 0 0	0) (0 0 0	1 0 0 0 (2) (0) (0) (0)	0 ) (0 ) 0 )	) (0) (1)	0 (0	0 )	0	) 0	0 (0
	mineralization:cortex	2 0 (4) (0) (	(0) 0(0) 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 ) 0 )	) (0) (	0	0 (0	0	) 0	0
	regeneration:proximal tubule	19 1 (38) (2) (	(0 0 (0 0	17 2 0 0 (34) (4) (0) (0)	17 1 (34) (2	) (0 ) (	0 (0	21 (42)	0 (0	) 0	0 (0
	urothelial hyperplasia:pelvis	0 0 0	(0) 0 (0	1 0 0 0 (2) (0) (0) (0)		) (0 ) (	0 (0	0	0	) 0	0
urin bladd	dilatation	<pre></pre>	(0 0 0 0	$\begin{pmatrix} < 50 \\ 0 \\ 7 \\ 0 \end{pmatrix} \begin{pmatrix} < 50 \\ 7 \\ 0 \end{pmatrix} \begin{pmatrix} 0 \\ 0 \end{pmatrix}$	1 4 (2) (8	<50> 0 ( 0) (	0	0	<50> 2 4) (	) 0	0 (0
	ulcer	) (0 ) (0 ) 0 0	0) 0000 0000	(0)(0)(0)(0) 0 0 0 0) 0 0	0 ( 0) ( 2	) (0 0 ) (	0 0	0	0 (0	) 0 (0	0
	simple tubule hyperplasia	1 0 ( 2) ( 0) (	0) (0 0 0	1 0 0 0 (2) (0) (0) (0)	0 ) (0 ) 0 )	) (0 ) (	0 0	0	2) (	_ 0 (i)	0
Grade < a > b ( c ) Significant d	$1+$ : Slight $2+$ : Moderate $1+$ : Slight $2+$ : Moderate $a$ : Number of animals examined at thu $b$ : Number of animals with lesion $c$ : $b / a \pm 100$ $c$ : $b / a \pm 100$ $tifference$ ; $*$ : $P \leq 0.05$	3+ : Marked 4+ : Severe e site P ≦ 0.01 Test of Chi Square									
(HPT150)											BALSS

BAI S5

	8602F1/Cr1j [Crj :8DF1]		
0712	MUUSE A1	MALE	
STUDY NO.	ANIMAL REPORT TYPE	SEX	

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

PAGE : 12

	Group Name Control No of Animals on Study En	625 ppm	1250 ppm	2500 ppm
Organ Findings	Grade Minimers of Study 34 44	50 (%) (%) (%) (%) (%)	50 1+ 2+ 3+ 4+ (%) (%) (%) (%)	50 1+ 2+ 3+ 4+ (%) (%) (%) (%)
{Urinary system}				
urin bladd xanthogranuloma	$\begin{pmatrix} \langle 50 \rangle \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix} \begin{pmatrix} \langle 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}$	$\begin{pmatrix} < 50 \\ 0 &   & 0 \\ 0 &   & 0 \\ ( & 0) & ( & 0) \\ \end{pmatrix}$	$\begin{pmatrix} & 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0$	<pre>&lt; 450&gt; </pre> ( 0) ( 0) ( 0)
[Endocrine system]				
pituitary Rathke pouch	$\begin{array}{ccccc} \langle 50 \rangle \\ 2 & 0 & 0 \\ ( 4 ) & ( 0 ) & ( 0 ) \\ \end{array}$	$\langle 50\rangle$ $\begin{pmatrix} <50\rangle\\ 0 & 0\\ ( 0) & ( 0) & ( 0) \\ 0 & ( 0) & ( 0) \\ \end{pmatrix}$	<pre>&lt; 0 ( 0) ( 0) ( 0)</pre>	$\begin{pmatrix} \langle 49 \rangle \\ 0 & 0 \\ \langle 0 \rangle & 0 \\ \langle 0 \rangle & \langle 0 \rangle \\ \langle 0 \rangle & \langle 0 \rangle & \langle 0 \rangle & \langle 0 \rangle \\ \langle 0 \rangle & \langle 0 \rangle & \langle 0 \rangle & \langle 0 \rangle \\ \langle 0 \rangle & \langle 0 \rangle & \langle 0 \rangle & \langle 0 \rangle \\ \langle 0 \rangle & \langle 0 \rangle & \langle 0 \rangle & \langle 0 \rangle \\ \langle 0 \rangle & \langle 0 \rangle & \langle 0 \rangle & \langle 0 \rangle & \langle 0 \rangle \\ \langle 0 \rangle & \langle 0 \rangle \\ \langle 0 \rangle & \langle 0 \rangle$
thyroid cystic thyroid follicle	$\begin{pmatrix} < 50 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 $	$\begin{array}{cccc} \langle 50\rangle & & \\ & \langle 50\rangle & & 0 \\ 1 & 0 & 0 & 0 \\ ( & 2) & ( & 0) & ( & 0) \\ \end{array}$	$\begin{array}{cccc} \langle 50 \rangle \\ ( 0) & ( 0) & ( 0) \\ ( 0) & ( 0) & ( 0) \\ \end{array}$	$ \begin{array}{cccc} & ( & 0 ) & ( & 0 ) & ( & 0 ) \\ & & & & ( & 0 ) \\ & & & & ( & 0 ) \\ & & & & ( & 0 ) \\ & & & & & ( & 0 ) \\ & & & & & ( & 0 ) \\ & & & & & ( & 0 ) \\ & & & & & & ( & 0 ) \\ & & & & & & & & \\ & &$
deposit of brown pigment	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	1 0 0 0 0 0 ( 2) ( 0) ( 0)	10 0 0 0 ** (20) (0) (0) (0)
adrenal hyperplasia:medulla	$\begin{array}{cccc} <50 \\ 0 & 1 & 0 \\ ( & 0) & ( & 2) & ( & 0) \\ \end{array}$	<pre>&lt; 60 &lt; 60 &lt; 60 &lt; 60 &lt; 60 </pre>	<pre>&lt;30&gt;</pre> (50) (60) (60) (70) (70) (70)	<pre>&lt;30&gt;</pre> (10) (10) (10) (10)
{Reproductive system}				
testis mineralization	$\begin{array}{ccccc} & \langle 50 \rangle & \\ 2 & 0 & 0 \\ ( 4 ) & ( 0 ) & ( 0 ) \\ \end{array}$	<pre>&lt;60&gt; <!--50--> </pre> (0) (0) (0) (0)	<pre>&lt;50&gt; &lt;1 0 </pre> (2) (0) (0) (0)	<pre>&lt;50&gt; <!--50--> </pre> (2) (2) (0) (0)
Grade 1+: Slight 2+: Moderate $\langle a \rangle a$ : Number of animals examined at b : Number of animals with lesion (c) b / $a \pm 100$ Significant difference ; $\pm : P \leq 0.05$ ##	3+:Marked 4+:Severe t the site n ≠:P ≦ 0.01 Test of Chi Square			

BAI S5

STUDY NO. ANIMAL REPORT TYPE SEX	: 0712 : MOUSE B6D2F1/Cr1j[Crj:BDF1] : A1 : MALE	HISTOPATHOLOGICAL FINDINGS : ALL ANIMALS (0-105W)	:NON-NEOPLASTIC LESIONS (SUMMAR	()	
					PAGE : 13
		Group Name Control No. of Animals on Study 50	625 ppm 50	1250 ppm 50	2500 ppm 50
0rgan	Findings	Grade 1+ 2+ 3+ 4+ (%) (%) (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	1+ 2+ 3+ 4+ (%) (%) (%) (%)	00 (%) (%) (%) (%) (%)
(Rep roduc t )	ve system}				
testis	xanthogranuloma	$\begin{pmatrix} 50 \\ 0 \\ 1 \\ 0 \end{pmatrix} \begin{pmatrix} 50 \\ 0 \\ 0 \end{pmatrix} \begin{pmatrix} 0 \\ 0 \end{pmatrix}$	$\begin{pmatrix} < 50 \\ 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0 \\ < 0$	$\begin{array}{cccc} & <50 \\ 0 & 1 & 0 & 0 \\ ( & 0) & ( & 2) & ( & 0) \\ \end{array}$	$\langle 0 \rangle \langle 0 $
epididymis	spermatogenic granuloma	$\begin{array}{cccc} \langle 50 \rangle \\ 4 & 2 & 0 & 0 \\ (8) & (4) & (0) & (0) \end{array}$	$\langle 50\rangle$ $\begin{pmatrix} <50\rangle\\ 0 & 1 & 0 & 0\\ ( & 0) & ( & 2) & ( & 0) & ( & 0) \\ \end{pmatrix}$	<pre>&lt;50&gt; 3 2 0 0 ( 6) ( 4) ( 0) ( 0)</pre>	<pre>&lt;50&gt;</pre>
prostate	inflammation	$\begin{pmatrix} < 50 \\ 0 & 1 & 0 \\ 0 & ( & 2 ) & ( & 0 ) & ( & 0 ) \\ ( & 0 ) & ( & 2 ) & ( & 0 ) & ( & 0 ) \\ \end{pmatrix}$	$\begin{pmatrix} 0 & -1 & -2 & 0 \\ 0 & -1 & 0 & 0 \\ 0 & 0 & -1 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 &$	$\begin{pmatrix} < 50 \\ 0 \\ 0 \end{pmatrix}$ $\begin{pmatrix} < 50 \\ 2 \\ 0 \end{pmatrix}$ $\begin{pmatrix} < 0 \\ 0 \end{pmatrix}$ $\begin{pmatrix} 0 \\ 0 \end{pmatrix}$	<pre>&lt;50&gt; (50) (50) (50) (50) (50) (50) (50) (50)</pre>
prep/clig	duct ectasia	$\begin{array}{cccc} \langle 50\rangle & & \\ 1 & 0 & 0 \\ ( & 2) & ( & 0) & ( & 0) \\ \end{array}$	<pre>&lt;50&gt; 2 0 0 ( 4) ( 0) ( 0)</pre>	<pre>&lt;50&gt; 1 0 0 ( 2) ( 0) ( 0)</pre>	<pre>&lt;50&gt;</pre>
{Nervous sy: brain	stem) hamorrhaeo	, (05) ,	(50)	<20>	<60>
	memorriase mineralization		( 0) ( 0) ( 0) ( 0) ( 0) ( 0) ( 0) ( 0) ( 22) ( 0) ( 0) ( 0) ( 0)	0 0 0 0 0 0 1 0 1 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 ( 0) ( 0) ( 0) ( 0) 11 0 0 0 ( 22) ( 0) ( 0) ( 0)
Grade Grade ( a ) b ( c ) Significant	<pre>1+ : Slight 2+ : Moderate 3 a : Number of animals examined at the : b : Number of animals with lesion c : b / a * 100 c : b / a * 100 difference ; * : P ≤ 0.05 ** : P;</pre>	∵:Marked 4+:Severe ite ≦0.01 Test of Chi Square			
(HPT150)					RAISE

2		
2		

B6D2F1/Cr1j [Crj:BDF1]	
0712 MOUSE A1 MALE	
STUDY NO. Animal Report type Sex	

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-10540)

	• WVLLL							PAGE :	14
0rgan	G R Findings	oup Name Control 2. of Animals on Study 50 ade 1+ 2+ 3+ (%) (%) (%)	4+ (%)	625 ppm 50 1+ 2+ 3+ 4+ (%) (%) (%) (%)	1250 ppm 50 1+ 2+ 3+ 4+ (%) (%) (%) (%)	255 (%)	0 ppm 50 (%) (%)	44	
(Special sen	se organs/appendage								
eye	cataract	2 (20) (0) ( 2 0 0 (10) (20) (20) (20) (20) (20) (20) (20) (2	0 (0	$ \begin{array}{cccc} \langle 50\rangle \\ 2 & 0 \\ 4 & ( 0 ) & ( 0 ) \\ \end{array} $	$\begin{array}{cccc} \langle 50 \rangle & & \\ & \langle 50 \rangle & & \\ & 1 & 0 & 0 & \\ & (2) & (0) & (0) & (0) \end{array}$	2 4) (	<50> 0 0 0) ( 0)	0 0	
	keratitis		0	(0) (0) (0) (0) 0 0 0 0 (0)	0 1 0 0 ( 0) ( 2) ( 0) ( 0)	) (0 0	(0 0 ) (0	0 0	
Harder gl	lymphocytic infiltration	$\langle 50\rangle$ $\langle 50\rangle$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$	0 () 	$\begin{pmatrix} < 50 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix} \begin{pmatrix} < 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}$	$\begin{array}{ccccc} \langle 50\rangle \\ 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \\ \end{array}$	2 ( 4) (	<50> 0 0 0) ( 0)	0 0	
	hyperplasia	1 0 0 ( 2) ( 0) ( 0) (	0 (0	1 0 0 0 0 ( 2) ( 0) ( 0)	(0) (0) (0) 0 0 0 0) 0 0)	) (0 0	0 ) 0 (0	(0 0	
(Musculoskel	etal system)								
muscle	mineralization	$\begin{array}{cccc} < 50 \\ 1 & 0 & 0 \\ ( & 2) & ( & 0) & ( & 0) \\ \end{array}$	0 (0	$\begin{pmatrix} \langle 50 \rangle \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}$	<pre>&lt; 450&gt;</pre>	) (0 0	<50> 0 0 0) ( 0)	0 0	
bone	osteoscierosis	$\begin{array}{cccc} \langle 50\rangle \\ 1 & 0 \\ (2) & (0) & (0) \end{array}$	0	<pre>&lt;50&gt; <!--50--> </pre> (50) (0) (0) (0) (0) (0)	<pre></pre>	) (0 0	<50> 0 0 0) ( 0)	0	
Grade Crade b ( c ) Significant o	$1+$ : Slight $2+$ : Moderate $3+$ : $a$ : Number of animals examined at the sitt $b$ : Number of animals with lesion $c$ : $b / a * 100$ $difference$ ; $*$ : $P \leq 0.05$	Marked 4+ : Severe .01 Test of Chi Square							

BAIS5

(HPT150)

# TABLE M 4

#### HISTOPATHOLOGICAL FINDINGS:

# NON-NEOPLASTIC LESIONS:

#### FEMALE: ALL ANIMALS

STUDY NO. ANIMAL REPORT TYPE : SEX	0712 MOUSE B6D2F1/Crlj[Crj:BDF1] Al FEMALE	HISTOPATH ALL ANIMA	10L0G1CAL F1 ALS (0-105W)	ND I NGS I NO	N-NE0PLAST I C	LESIONS	(SUMMARY)								PAGE	 
Organ	Group Na No. of A Grade Findings	me Co nimals on Study 1+ (%)	ntrol 50 2+ 3+ (%) (%)	4+ (%)	625 pp 1+ 2+ (%) (%)	(%) (%) (%)	4+ (%)	12 (%)	50 ppm 50 2+ (%)	34	(%)	- <del>-</del> - <del>-</del> - <del>-</del> - <del>-</del> - <del>-</del>	2500 F 21 (%)	50 %	* C	<del>4</del> 3
{ ntegumentar	v system/appandage)															
skin/app	epidermal cyst	0 0	<pre>&lt;50&gt; 0 0 ( 0) { 0}</pre>	0	> 0 (0 ) 0 (0 )	50> ( 0)	(0) 0	0	<50) 1 2) (	) 0 (0	0 (0	1 (2)	× 0 60 	(50) ( 0	-	<u> </u>
(Respiratory	system}															
nasal cavit	eosinophilic change:olfactory epithelium	4 ( 8)	<pre>&lt;50&gt; 0 0 0 0</pre>	0 )	3 1 (6)(2)	50> 0 0	0	( 5 ( 4)	<pre>&lt;50&gt; 0 0</pre> ()	 0 (0	0 (0	6 ( 12)	( <sup>1</sup>	(50) ( 0	-	0.8
	eosinophilic change:respiratory epithelium	28 (56)	8 0 (16) (0)	0 (0	26 2 (52)(4)	0 0	0 (0	28 (56) (	3 6) (	 0 (0	0 0	33 ( 66)	5 (10)	- 1	- -	<b>.</b> .
	inflammation:respiratory epithelium	0	0 ) 0 0	0 )	1 0 (2) (0)	0 0	0	0	) 0	) 0	0 0	(0 )	0 0	00	-	<u>.</u>
	respiratory metaplasia:olfactory epithelium	(2)	0 ) 0 0	(0 0	(0) (0) (0)	0 0	0)	2 ( 4)	) 0	- 0	0 0	3 ( 6)	0 0	00		0.0
	respiratory metaplasia:gland	9 ( 18) (	0 (0 ) 0 0	0 (0	11 0 (22) (0)	0)	0	10 (20) (	) 0 (0	) 0	00	9 (18)	0 0 )	00	-	<u> </u>
nasopharynx	eosinophilic change	9 9 1	<pre>&lt; 50&gt; </pre> <pre>&lt; 50&gt; </pre> 0 0 <pre></pre>	0	<pre></pre>	50> 0 0	0	1 (2)	( 0 0) (	- 0 (0	o ô	4 S	× 0 8	(50) (0)	-	

(HPT 150)

 $\begin{array}{ccccc} \mbox{Grade} & 1+: \mbox{Slight} & 2+: \mbox{Moderate} & 3+: \mbox{Marked} & 4+: \mbox{Severe} \\ \mbox{$\langle a \ensuremath{>} a : \ensuremath{Number} of animals examined at the site $b$ & b: \mbox{Number} of animals with lesion $(c)$ & c: b/a * 100 $(c)$ & c: b/a * 100 $(c)$ & s*: \ensuremath{P} \leq 0.01 $(c)$ & for $c$ & for $$ 

IDUY NU: : U/TZ NIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] EPORT TYPE : A1 EX : FEMALE	HISTOPATHOLOGICAL FINDINGS : ALL ANIMALS (0-1054)	NON-NEOPLASTIC LESIONS (SUMMAR	<b>W</b>	PAGE
Group N No. of Grade	Name Control Animals on Study 50 1+ 2+ 3+ 4+ (%) (%) (%) (%)	625 ppm 50 1+ 2+ 3+ 4+ (%) (%) (%) (%)	1250 ppm 50 51 31 41 (\$) (\$) (\$) (\$) (\$)	2500 ppm 50 50 44 50 50 50 50 50 44 (%) (%) (%) (%) (%)
Respiratory system}				
ung congestion	$\begin{pmatrix} & < 50 \\ 0 & 0 \\ 0$	$\begin{pmatrix} 50 \\ 0 \\ 0 \\ 0 \end{pmatrix} \begin{pmatrix} 50 \\ 0 \\ 0 \\ 0 \end{pmatrix} \begin{pmatrix} 0 \\ 0 \\ 0 \end{pmatrix}$	<pre>&lt;50&gt; </pre> (50) (50) (60) (60) (60) (70) <	$\begin{array}{cccc} \langle 50 \rangle \\ 1 & 0 & 0 \\ ( 2 ) & ( 0 ) & ( 0 ) \\ \end{array} $
deposit of amyloid	3 0 0 0 (6) (0) (0) (0)	3 0 0 0 0 (6) ( 0) ( 0)	7 0 0 0 0 (14) ( 0) ( 0)	5 0 0 0 (10) (10) (10) (10)
inflammatory infiltration	3 0 0 0 (6) (0) (0) (0)	0 1 0 0 ( 0) ( 2) ( 0) ( 0)	3 0 0 0 ( 0) ( 0)	2 0 0 0 (1) (4) (0) (0) (0)
lymphocytic infiltration	0 0 0 0 0 0 0 0 0 0	(0) (0) (0) 0 0 0 0 0 0 0 0		2 0 0 0 (4) (0) (0) (0)
bronchiolar-alveolar cell hyperplasia	0 0 0 0 0 0 0 0 0 0	0 0 0 0 0	(0) (0) (0) (0) 0 0 0 0	1 0 0 0 (2)(0)(0)(0)
Hematopoietic system}				
one marrow granulation	$\begin{pmatrix} 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 &$	<pre>&lt;50&gt; <!--50--> </pre> 0 1 0 0 ( 0) ( 2) ( 0) ( 0)	$\begin{array}{cccc} \langle 50 \rangle \\ 2 & 0 \\ 4 & ( 0 ) & ( 0 ) \\ \end{array} $	$\begin{pmatrix} < 50 \\ 0 & 1 \\ 0 & 1 \\ 0 & 0 \\ 0 & 0 \end{pmatrix}$
increased hematopoiesis	10 0 0 0 (20) (0) (0) (0)	13 0 0 0 (26) (0) (0) (0)	11 0 0 0 0 0 ( 22) ( 0) ( 0) ( 0)	8 0 0 0 (16) (0) (0) (0)
rade 1+:Slight 2+:Moderate 3+:Marke a > a :Number of animals examined at the site b b :Number of animals with lesion c b a ±100	ed 4+ : Severe			

DY NO.	• •	0712	
MAL	• •	MUUSE	B6D2F1/Cr1j [C
ORT TYPE	• •	A1	

STUDY NO. ANIMAL REPORT TYPE SEX	: 0712 : MOUSE B6D2F1/Cr1j[Crj:BDF1] : A1 : FEMALE	HISTOPATHOLOC ALL ANIMALS	GICAL FIN (0-10514)	ID I NGS : N	ON-NEOPLASTIC I	- ESIONS (SUMMAAI	(V)				AGE : 17
0rgan	Findings	Group Name Contro No. of Animals on Study 1+ 2+ Grade (%) (%)	50 50 (%)	4+ (%)	625 ppr 625 ppr 1+ 2+ (%) (%)	50 34 (%) (%)	1250 ppm 50 1+ 2+ (%) (%)	(%) (%) (%)	25 1+ (%)	(00 ррт 50 (%) (%)	(%) (%)
(Hematopoie	tic system)										
bone marrow	granul opoiesis: increased	5 (10) (0)	(50) (0)	0 0	3 ( 6) ( 0)	(0) (0) 0 (0)	<pre>&lt;50&gt; 4 0 ( 8) ( 0) (</pre>	0 ) (0 0 0	5 (10)	<pre>&lt; 50&gt; </pre> ( 0) ( 0)	0 (O )
lymph node	lymphadenitis		<pre>(50) ( 0) </pre>	0 (0	<pre></pre>	(0) (0) 0 (0)	<pre></pre>	0 ) 0 0	0	<pre>&lt;50&gt; 1 0 2) ( 0)</pre>	0
spleen	deposit of hemosiderin	30 (0) (0) (0) (0)	( 0) ( 0 (	0 (0	<pre>&lt;5 &lt;5 34 34 (68) (6)</pre>	(0) (0) 0 (0)	<pre>&lt;50&gt; 38 6 ( 76) ( 12) (</pre>	(0) (0 ** 0 0	30 ( 60) (	<pre>&lt;50&gt; 12 5 24) (10)</pre>	** (0 )
	deposit of melanin	1 0 ( 2) ( 0)	0	0 (0	1 0 ( 2) ( 0)	(0) (0) 000	) (0 ) (0 ) 0 0	(0) 0000	0	0 ) 0 ) 0 ;	0
	extramedullary hematopoiesis	7 11 (144 (22)	1 (2) (	0 (0	13 13 (26) (26)	2 0 (4) (0)	13 10 (26) (20) (	(0) 00000000000000000000000000000000000	19 (38) (	12 0 24) ( 0)	* (0 )
	follicular hyperplasia	1 1 (2) (2)	0	0	(0) (0) (0)	(0) (0) (0)	1 2 ( 2) ( 4) (	0 ) 0 0	1 (2) (	0 0 0	0 (0
(Circulator: heart	y system} thrombus		(50) (0)	0 0	3 ( 6) ( 0)	(0) (0) 0 (0) <0;	<pre></pre>	0 0 0 0 0	0	<pre><code <="" pre=""></code></pre> <pre><code <="" pre=""><pre><code <="" pre=""><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre></pre><pre><td>0</td></pre></code></pre></code></pre>	0
Grade 6 a > b ( c ) Significant	1+ : Slight 2+ : Moderate a : Number of animals examined at the b : Number of animals with lesion c : b / a ± 100 difference ; ± : P ≤ 0.05 ±± : P	3+ : Marked 4+ : Severe le site P≦0.01 Test of Chi Square									

BAIS5

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: MUUSE E TYPE : A1	B602F1/Cr1J[Cr]:B0F1] A	ALL AN
: Female		
	Group Name	į

STUDY NO. :: ANIMAL :: Report type : Sex ::	0712 MOUSE B6D2F1/Cr1j[Crj:BDF1] A1 FEMALE	ΗΨ	iISTOPATHOLOGICAL FIN ALL ANIMALS (0-10540)	DINGS : NON	-NEOPLASTIC LI	esions (summi	(RY)						• •
													•
		Group Name No. of Animals on S	Control itudy 50	:	625 ppm 51		-	250 ppm 50			2500 ppm 50		
Organ	Findings	ur ade	1+ 2+ 3+ (%) (%) (%)	4+ (%)	1+ 2+ (%) (%)	3+ 4+ (%) (%)	¥ 34	2+ (%)	3+ 4+ (%) (%)	1+ (%)	2+ (%)	3+ (%) (%	±0
{Circulatory :	system)												
heart	deposit of amyloid		<pre></pre>	0 0	<pre></pre>	(0) (0)	6 ( 12)	<pre>&lt;50&gt; 1 ( 2) ( 0</pre>	0 )	5 (10)	<pre>&lt;50&gt;</pre>	0 0 0	
	mineralization		2 0 0 (4) (0) (0) (	0 (0	4 0 (8) (0)	0 (0 ) 0 0	1 (2)	) ) (0 )	0 (0	1 (2)		0	
	inflammatory infiltration		1 0 0 (2) (0) (0) (	0 ()	(0) (0) 000	(0) (0) 000	0	) ) (0 )	0)(0)	0 0 )	) (0) )	0 ) 0 0	- 5
	myocardial fibrosis		13 0 0 (26) (0) (0) (	0	13 0 (26) (0)	(0) 00) 00)	20 (40)	0	0 ()	17 (34)	) (0)	0 ) (0 0	
	arteritis		1 0 0 (2) (0) (0) (	0 (0	1 0 ( 2) ( 0)	(0) (0) (0)	- 5 (+ 4)	0 )	0)(	(0) 0	) (0 0 )	0 ) 0 0	- 6
(Digestive sys	s t em]												
tongue	inflammatory infiltration		<pre>&lt;50&gt; <!--50--> </pre> <pre>( 2) ( 0) ( 0) (</pre>	0 (0	( 0) ( 0)	(0) 0) 0) 0)	(0 )	<pre>&lt;50&gt;</pre>	0)	0 0	<50> 0 ( 0) (	0 ) 0 (0	
	arteritis		) (0 ) (0 ) 0 0 0 0	0 8	(0) (0) (0)	(0) 0(0) 0	1 (2)	0	0)(	(0 )	) (0)	0 ) 0 (0	
Grade Grade b ( c ) Significant di	1+: Slight 2+: Moderate 3: a : Number of animals examined at the : b : Number of animals with lesion c : b / a ± 100 fifterence ; ± : P ≦ 0.05 ** ; P ;	+: Marked 4+: site ≤ 0.01 Test of Ch	Severe i Square										
(HPT 150)													BAIS5

STUDY NO. Animal Report type SfX	: 0712 : MOUSE B6D2F1/Cr1j[Crj:BDF1] : A1 : FFWAIF	ALI	STOPATHOLOGI ANIMALS (0	CAL FINE -105W)	DINGS : NON	I-NEOPLAST I	C LESIO	NS (SUMMARY)									
																PAGE	. 19
		Group Name No. of Animals on Stu	Control Idy 5			625	50		1	250 ppm 50				500 pt	E 03		
0rgan	Findings	Grade	1+ 2+ (%) (%)	3+ (%)	4+ (%)	(%) +	% 3 % 3	+ 4+ (%)	1+ (%)	2+ (%)	3+ (%)	¥+ %	1+ (%)	2+ (%)	<del>%</del> 3+	44	* -
(Digestive s	vs tem)																
stomach	hyperplasia:forestomach	_	$\begin{pmatrix} 1 & <5\\ 2 & 0 \end{pmatrix}$	) 0) (0)	0 0	3 ( 6) (	<50> 0 0) ( 0	0)	2 4)	<pre></pre>	) 0 0	0 (0	2 ( 4)	×06	50> 0 ( 0)	0	_
	erosion:glandular stomach	_	2 0 (4) (0)	) (0)	0 (0	1 (2) (	0 ) (0	0 ) (	1 (2)	) 0 )	) 0 (0	0 (0	3 ( 6)	0)	0 0	0 0	_
	hyperplasia:glandular stomach		8 0 (16) (0)	) (0)	0 0	11 (22) (	0 ) 0	0)	12 (24)	) 0 (î) )	) 0	0 6	12 (24)	0 0	(0 0	0 0	_
small intes	adhesion		0 1 (5) ( 0) ( 2)	) (0 )	0 0	) (0 ) 0	<pre>&lt;20&gt; 0 0) ( 0</pre>	0 )	(0) 0	(0) ((	, 0 (0	0 (0	1 ( 2)	<sup>3</sup> ∕060 ∵	50> ( 0)	0 (0	
liver	angiectasis		1 3 2) ( 6)	) (0 ) 0 <(	0 0	1 (2) (	<50> 3 0 6) ( 0	0)	1 ( 2)	<50) 2 (4) (	00	0 (0	(0 0	() () () () () () () () () () () () () (	50> ( 0)	0 0 )	
	necrosis:central	_	0 ) (0 0 )	) (0)	0 0	) (0 0 )	1 2) ( 0	0 )	0	。 0 0	) 0	0 (0	0 0	0 0	0 0	0	-
	necros is: foca		0 ) (0 ) 0 0	) (0 )	0 0	1 (2) (	0 ) 0 (0	0 )	1 (2)	0 0 0	_ 0 (0	0 (0	1 (2)	0 (O )	0 0	0 0 )	
Grade Grade ( c ) Significant	1+: Slight 2+: Moderate a: Number of animals examined at th b: Number of animals with lesion c : b / a * 100 difference ; * : P ≦ 0.05 **:	3+ : Marked 4+ : S le site P≦0.01 TestofChi	evere Square														

(HPT150)

STUDY NO. ANIMAL REPORT TYPE SEX	: 0712 : MOUSE B6D2F1/Cr1j[Crj:BDF1] : FEMALE : FEMALE		HISTOPATHOLOGICAL F ALL ANIMALS (0-10541)	INDINGS : NO	ON-NEOPLASTIC	LESIONS (	SUMMARY)							PAGE	: 20
Organ	. Findings	Group Name No. of Animal: Grade	s on Study Control 1+ 2+ 3+ (%) (%) (%) (%)	4 + (%)	625 pr 1+ 2+ (%) (%)	50 (%) (%)	<b>(%)</b>	(%) 11 12	50 ppm 50 (%)	3+ 4+ (%) (%)	- -	2500 1+ (%)	(%) ppm (%) 2+ 3 (%) (%	+ (3	± 9
(Digestive	system)														
liver	inflammatory infiltration		<pre></pre>	0)	1 0 2) ( 0)	(50) (0) (	0 (0	0 0	<pre>&lt;50&gt; 0 0 (</pre>	0 ) 0 (0	)	 0 (0	<pre>&lt;50&gt; 0 0 0</pre>	0 0	
	lymphocytic infiltration		0 0 0 0 0 0 0	0 0	(0) (0) (0)	) (0 0	0	) (0 )	0	(0) 0) 0		2) (	0 0 0	0 	
	inflammatory cell nest		14 0 0 (28) (0) (0)	00	14 0 {28) (0)	) (0 0	0 (0	12 (24)	) 0	(0) 00000000000000000000000000000000000	}	17 34) (	1 2) ( 0	0 )	
	acidophilic cell focus		0 0 0 0 0 0 0 0	0 0	(0) (0) 000	) (0 ) 0	0 0	0 0	) ()	(0) 0(0)	2	1 2)	0 ) 0	0 )	- 5
	biliary cyst		0 0 0 0 0 0 0	0 0 )	(0) (0) 0 0	) (0 0	0 0	) (0 )	) (0	0) 00) 0	2	4) (	0 ) 0 (0	0 )	
	deposit of brown pigment		(0)(0) 000 000	0 0	(0) (0) 0 0	) (0 ) 0	0 (0	) (0 )	) 0	0) 0) 0	Ç	10 20) (	0 ) 0 0	0 )	** (
(Urinary sy:	steml														
k i dney	cyst		$\begin{pmatrix} 60 \\ 0 \\ 0 \\ 0 \end{pmatrix} \begin{pmatrix} 50 \\ 0 \\ 0 \end{pmatrix}$	0 (0	> 0 ) 0 ) 0 )	50> 0 ( 0) (	0 (0	) (0 )	<50> 0 0) (	0 ) 0 0	2	( 4) 5	<pre>&lt; 50&gt; 0 0) ( 0</pre>	0 0	- C
Grade		3+:Marked he site P≦0.01 Test	4+ : Severe of Chi Square												

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$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$	TUDY NO. : 0712 NIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 SEX : FEMALE	HISTOPATHOLOGICAL FINDINGS ALL ANIMALS (0-10549)	:NON-NEOPLASTIC LESIONS (SUMMAR	2	PAGE :
$ \begin{array}{llllllllllllllllllllllllllllllllllll$	rgan Findings	Group Name Control No. of Animals on Study 50 Grade (%) (%) (%) (%)	625 ppm 50 1+ 2+ 3+ 4+ (%) (%) (%) (%)	1250 ppm 50 1+ 2+ 3+ 4+ (%) (%) (%) (%)	2500 ppm 50 1+ 2+ 3+ 4+ (\$) (\$) (\$) (\$)
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$	(Urinary system)				
Parline cast         [2] <t< td=""><td>cidney hyaline droplet</td><td><math display="block">\begin{array}{cccc} \langle 50\rangle &amp; &amp; \\ 14 &amp; 0 &amp; 0 \\ (28) &amp; (0) &amp; (0) &amp; (0) \end{array}</math></td><td><pre> &lt;50&gt; &lt;50&gt; (50)</pre> <pre> 9 0 0 (0)</pre> <pre> (18) (0) (0)</pre></td><td><pre>&lt;50&gt; 10 0 0 (20) ( 0) ( 0) ( 0)</pre></td><td><pre>&lt;50&gt; &lt;50&gt; &lt;10) ( 0) ( 0) * </pre></td></t<>	cidney hyaline droplet	$\begin{array}{cccc} \langle 50\rangle & & \\ 14 & 0 & 0 \\ (28) & (0) & (0) & (0) \end{array}$	<pre> &lt;50&gt; &lt;50&gt; (50)</pre> <pre> 9 0 0 (0)</pre> <pre> (18) (0) (0)</pre>	<pre>&lt;50&gt; 10 0 0 (20) ( 0) ( 0) ( 0)</pre>	<pre>&lt;50&gt; &lt;50&gt; &lt;10) ( 0) ( 0) * </pre>
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	hyaline cast	1 0 0 0 (2) (0) (0) (0)	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	(0)(0)(0) 0 0 0 0 0)(0)	3 0 0 0 (6)(0)(0)(0)
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	inflammatory infiltration	(0) (0) (0) (0) 0 (0) (0) (0)	1 0 0 0 (2) (0) (0) (0)	(0) (0) (0) (0) (0)	(0) (0) (0) (0) 0 0 0 0 0
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	lymphocytic infiltration	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	4 0 0 0 (8) (0) (0) (0)	1 0 0 0 (2)(0)(0)(0)	3 0 0 0 (6) (0) (0) (0)
Star       (5) (10) (0) (0) (0) (0) (0) (0) (0) (0) (0) (	osseous metaplasia	1 0 0 0 (2) (0) (0) (0)	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	(0) (0) (0) (0) 0 0 0 0 0	1 0 0 0 ( 2) ( 0) ( 0) ( 0)
inflammatory polyp       inflammatory polyp       1       0       0       0       3       0	scar	3 5 0 0 ( 6) ( 10) ( 0) ( 0)	4 5 0 0 (8) {10} {0) (0)	2 9 1 0 ( 4) (18) ( 2) ( 0)	6 5 0 0 (12) (10) ( 0) ( 0)
hydronephrosis       0       3       1       0       5       1       0       1       6       1       6       1       0         Grade       1 + : Slight       2 + : Moderate       3 + : Marked       4 + : Severe       (0)       (10)       (2)       (0)       (2)       (0)       (2)       (0)         Ca>       a : Number of animals examined at the site       b : Number of animals with lesion       4 + : Severe       (2)       (2)       (2)       (0)       (2)       (0)       (2)       (12)       (2)       (0)         Ca>       a : Number of animals examined at the site       b : Number of animals with lesion       (2)       (2)       (2)       (0)       (2)       (2)       (0)       (2)       (0)       (2)       (0)       (2)       (0)       (2)       (0)       (2)       (0)       (2)       (2)       (0)       (2)       (0)       (2)       (0)       (2)       (0)       (2)       (0)       (2)       (0)       (2)       (0)       (2)       (0)       (2)       (0)       (2)       (0)       (2)       (0)       (2)       (0)       (2)       (0)       (2)       (0)       (2)       (0)       (2)       (0) <t< td=""><td>inflammatory polyp</td><td>1 0 0 0 (2) (0) (0) (0)</td><td>3 0 0 0 (6)(0)(0)(0)</td><td>4 0 0 0 (8) (0) (0) (0)</td><td>5 0 0 0 (10) (0) (0) (0)</td></t<>	inflammatory polyp	1 0 0 0 (2) (0) (0) (0)	3 0 0 0 (6)(0)(0)(0)	4 0 0 0 (8) (0) (0) (0)	5 0 0 0 (10) (0) (0) (0)
Grade     1+: Slight     2+: Moderate     3+: Marked     4+: Severe       < a > a: Number of animals examined at the site     b     b     Number of animals with lesion       (c)     c: b/ a * 100     c: b/ a * 100     rest of Chi Shuare       Significant difference     a : p ≤ 0.01     Test of Chi Shuare	hydronephrosis	0 3 1 0 ( 0) ( 6) ( 2) ( 0)	0 5 1 0 ( 0) ( 10) ( 2) ( 0)	1 4 2 0 ( 2) ( 8) ( 4) ( 0)	1 6 1 0 ( 2) (12) ( 2) ( 0)
	Grade 1+:Slight 2+:Moderate < a > a :Number of animals examined a b :Number of animals with lesion (c ) c : b / a * 100 Significant difference : ★ P ≤ 0.05 ★	3+ : Marked 4+ : Severe ut the site on ± · D < O D1 Test of Chi Source			

	FEMALE											<u>а</u>	AGE :
gan	F indings	Group Name Control No. of Animals on Study 50 Grade (%) (%)	3+ 4+ (%) (%)	625 ppn 625 ppn 1+ 2+ (%) (%)	0 3+ (%) (%)	+ -	1250 1+2 (%) (%	ррт 50 (%)	(%) (%)	(%) (%)	2500 pp 5 + 2+ (%)	÷ (%)	4+ (%)
inary syste	em)												
dney	tubular necrosis	<pre></pre>	(0) 0 (0	<pre>&lt;5 1 0 ( 2) ( 0)</pre>	(0) (0) (0)	_	0	<50> 0 0 0	0 )	0 )	( 0) <2	0 0 0	0
	papillary necrosis	3 0 (6) (0) (	0) 00) 0	1 0 (2) (0)	(0) (0) (0)		7 14) (2	0) (	(0 0	6 ( 12)	1 (2)	0	0
	mineralization:papilla	) (0 ) (0 ) 0 0	(0) 0) 0	(0 <sup>-</sup> ) (0 ) 0 0	(0) (0) 0 0	_	0 ) 0 (0	0) (	0)	1 (2)	0 0	0	0 0
	glomerulosclerosis		0) 00) 00	0 1 ( 0) ( 2)	(0) (0) 0 0	2	0 ) 0 (0	0) (	0 )	0 )	1 (2)	00	0 0
	regeneration:proximal tubule	2 0 ( 4) ( 0) (	0 ) 0 0	1 1 ( 2) ( 2)	(0) (0) (0)	2	0 ) 0 (0	0)	0)	4 (8)	1 (2)	0	0 0
	desquamation:pelvis	0 0 0	(0) 00) 00	1 0 ( 2) ( 0)	(0) (0) 0 0	_	0 ) 0 (0	0 0	0 0	1 (2)	0 0	0 (0	0 (0
	urothelial hyperplasia:pelvis	2 0 (14) (10) (14)	0 ) 0 0	1 0 ( 2) ( 0)	(0) (0) 0 0	~	1 2) ( 0	0 )	0 0	2 ( 4)	0 )	00	0
ter	dilatation	( 0) ( 0) ( 20>	(0) 0000	( 2) ( 0)	(0) (0) 0 (0) <0	~	0 ) 0 (0	<50> 0 ( 0)	0	0 )	<pre></pre>		0 (0
de 1	1+ : Slight 2+ : Moderate a : Number of animals examined at the b : Number of animals with lesion	3+ : Marked 4+ : Severe site											

BAI S5

STUDY NO. ANIMAL REPORT TYPE SEX	: 0712 : MOUSE B6D2F1/Crij[Crj:BDF1] : A1 : FEMALE		HI STOPAT ALL ANIA	THOLOGICAL ALS (0-1051 ALS (0-1051	FINDINGS : N	DN-NEOPLAS	FIC LES	ons) summa	RY)								PAGE	: 23
0rgan	Findings	Group Name No. of Animals Grade	on Study (%)	ontrol 50 2+ 3 (%) (%)	+ + + (%)	62! (%)	і ррм 50 2+ (%)	3+ 4+ (%) (%)	<del></del>	1250 + 2 ) ( <del>1</del>	ррш + 50 (%	+ 4+ (%)		25 (%)	00 ppr 50 2+ (%)	(% <sup>3</sup>	4+ (%)	
{Urinary sys	stem											A 100 10 10 10						
urin bladd	dilatation		1 (2)	<pre>&lt; 0) ( 0)</pre>	0 )	) (0 0	<50> 1 2) (	(0) 0000	-	- (	<50> 0 0 0	0 )	}	0	$0 \\ \leq 20$	0 ô	0 (O )	
	lymphocytic infiltration		(0 0	(0) (0) 0 0	0	) (0 0		(0) 0) 0	- -		0 )	0)	J	4) (	0 (0	0 (0	0 (0 )	
	xanthogranu loma		(0 )	1 0 (2) (0)	0)	) (0 0	) 0	0 (0 0 (0	~	-	0 0	0)	_	0 (0	0 0	0 (O	0 (O )	
{Endocrine s	sys tem)																	
pítuitary	angiectasis		0 0	<pre>&lt; 0) ( 0)</pre>	0 0	) (0 )	<50> 0 0) (	0) (0 0	1	0 ) (	<50> ( 0	0 (0	2	00	0 0	0 (0 (1)	0 (0	
	cyst		(0 0	(0) (0) 0 0	0 0 _	) (0 0 )	 0 (0	(0) 0 (0	-	0 0	0 )	0	<u> </u>	1 (2)	00	0	0 0 )	
	hyperplasia		3 (9)	(0) (0) 0 0	0 0	3 ( 6) (	4) (	(0) 00000	4 )	2	0 0	0 )	2	4 8) (	2)	0	0 0 )	
	Rathke pouch		0 0	(0) (0) (0)	0 (0	) (0 0 )	) 0 (0	(0) 0 (0 0	2	0 ) (	0 )	0 )	_	0 (0	0 Ô	0 (0	0 0 )	
Grade Grade b ( c ) Significant	1+Slight2+: ModerateaNumber of animals examined at 1bNumber of animals with lesioncb $a + 100$ difference $a + 100$	3+ : Marked the site :P≦0.01 Testo	4+ : Severe f Chi Squar	D. D.														

(HPT150)

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STUDY NO. ANIMAL REPORT TYPE SEX	: 0712 : MOUSE B6D2F1/Cr1j[Crj:BDF1] : A1 : FEMALE	HISTOP ALL AN	ATHOLOGICAL IMALS (0-105)	FINDINGS	NON-NEOPLASTIC LESIONS (SI	MMARY)						Ĭ	й
		na sense a sens						ļ					r . <sup>7</sup> 4
		Group Name No. of Animals on Study	Control 50		625 ppm 50		1250 pp 5	εc		5	500 ppm		
Organ	Findings	Grade 1. (%)	+ 2+ 3- (%) (%)	+ 4+ (%)	1+ $2+$ $3+$ $4$ (%) (%) (%) (9)	± 0	1+ 2+ (%) (%)	% <del>3</del>	4+ (%)	1+ (%)	2+ (%)	3+	4+ (%)
(Endocr ine ;	system)												
thyroid	arteritis	0 0 ~	<pre><co></co></pre>	0	<pre></pre>	- 6	1 0 (2) (0)	) () ()	0 0	0 )	<pre></pre>	) 0	0 (0
	deposit of brown pigment	0	(0) (0) (0)	0 (0	) (0 ) (0 ) (0 ) 0 0 0 0		0 ) (0 ) 0 0	0 (0	0 ()	7 (14)	) (0 ) 0 )	) 0	* (0
adrenal	spindle-cell hyperplasia	4 (	<pre>&lt;60&gt; (0) (0)</pre>	0	<pre> &lt;50&gt;</pre>		<pre></pre>	) (0 (0)	0 0	1 (2)	<pre>&lt;50&gt;</pre> <pre>(50) {</pre>	) 0	0 (0
	fatty change:corticomedullary junctio	0) uo	0 (0 )	0 (0		-	0 1 0) (2)	0 )	0 0	0 0	) 0 )	) 0	0
(Rep roduct iv	re system}												
ovary	thrombus	0 0	<pre>&lt;20&gt; </pre> ( 0) ( 0)	0)	<pre> &lt;50&gt; &lt;50&gt; (50&gt; (50)</pre> <pre> ( 0) ( 4) ( 0) ( 0) ( 0) ( 0) ( 0) ( 0)</pre>	-	0 (0) (0 0 (0)	) (0 (0	0 ()	(0 0	<pre>&lt; 50&gt;</pre> <pre></pre> <pre>( 0) (</pre>	) 0	0
	cyst	3 (9)	(0) (0) (0)	0	8 0 0 0 ( (16) ( 0) ( 0) ( 0	-	5 0 10) ( 0)	0	0 0	7 (14)	) 0 (0 )	) 0	0 (0
Grade < a > b ( c ) Significant	1 + : Slight2 + : Moderate31 + : Slight2 + : Moderate3a : Number of animals examined at the tb : Number of animals with lesionc : b / a $\pm 100$ c : b / a $\pm 100$ difference ; $\pm : P \leq 0.05$	+ : Marked 4+ : Sever site ≦ 0.01 Test of Chi Squ	<u>ں</u> ب										

BAIS5

(HPT 150)

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

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j(Crj:BDF1] REPORT TYPE : A1 SEX : FEMALE		HISTOPATHOLOGICAL FINDINGS : ALL ANIMALS (0-105W)	:NON-NEOPLASTIC LESIONS (SUMMAR	()	:
					PAGE : 25
	Group Name No. of Anim	Control als on Study 50	625 ррт 50	1250 ppm 50	2500 ppm 50
OrganFindings	Grade	1+         2+         3+         4+           (%)         (%)         (%)         (%)         (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	1+ 2+ 3+ 4+ (%) (%) (%) (%)
{Reproductive system}					
uterus dilatation		(0)(0)(0)(0)	<pre> &lt;50&gt; &lt;50&gt; (50) (0) (0)</pre> (0) (0) (0) (0) (0) (0) (0) (0) (0) (0)	$\begin{array}{cccc} \langle 50\rangle & \\ 0 & 1 & 0 & 0 \\ ( 0) & ( 2) & ( 0) & ( 0) \end{array}$	<pre>&lt;50&gt; (50) (0 1 0 (0) (2) (0) (0)</pre>
cystic endometrial hyperp	lasia	9 4 0 0 (18) (8) (0) (0)	8 0 0 0 (16) ( 0) ( 0)	11 1 0 0 (22)(2)(0)(0)	11 2 0 0 (22) (4) (0) (0)
(Nervous system)					
brain mineralization		<pre>&lt;50&gt; 12 0 0 (24) ( 0) ( 0) ( 0)</pre>	<pre>&lt;50&gt; 11 0 0 0 ( 22) ( 0) ( 0) ( 0)</pre>	<pre>&lt;50&gt; &lt;13 0 0 </pre> 13 0 0  (26) (0) (0)	<pre>&lt;50&gt; &lt;10</pre>
spinal cord gliosis		<pre></pre>	<pre></pre>	<pre>&lt;50&gt; 1 0 0 ( 2) ( 0) ( 0)</pre>	<pre>(0) (10) (20) (20) (20) (20) (20) (20) (20) (20)</pre>
(Special sense organs/appendage)					
eye keratitis		( 0) ( 0) ( 0) ( 0) ( 0) ( 0) ( 0) ( 0)	<pre> &lt;50&gt; &lt;50&gt; (50) (0) (0) (0)</pre>	<pre>&lt;50&gt; 1 0 0 ( 2) ( 0) ( 0)</pre>	<pre>&lt;50&gt; &lt;1 0 0 </pre> (2) (0) (0) (0)
Grade 1+:Slight 2+:Moder: <abra>&gt; a:Number of animals examined b b:Number of animals with (c) c:b/a ± 100</abra>	ate 3+:Marked ned at the site lesion **:P≤0.01 Te	4+ : Severe st of Chi Square			
(HPT150)					BAIS5

STUDY NO. ANIMAL REPORT TYPE SEX	: 0712 : MOUSE B6D2F1/Crlj[Crj:BDF1] : A1 : FEMALE	HISTOPATHOLOGICAL FIND ALL ANIMALS (0-1059)	INGS :NON-NEOPLASTIC LESIONS (SUMMAR	8	PAGE : 26
Organ	Findings	Group Name Control No. of Animals on Study 50 Grade (*) (*) (*)	625 ppm 625 ppm 44 1+ 24 34 44	1250 ppm 50 1+ 2+ 3+ 4+	2500 ppm 50 1+ 2+ 3+ 4+
Special sen	ise or gans/appendage			(2) (2) (2)	(3) (3) (3)
Harder gl	lymphocytic infiltration	<pre>&lt; 50&gt;</pre>	0 1 (50) 0 1 0 0 0) (2) (0) (0) (0)	<pre>&lt; 450&gt; </pre> <pre>&lt; 450&gt; </pre> 0 <p0< p=""></p0<>	$\begin{array}{cccc} \langle 50 \rangle \\ 2 & 0 & 0 \\ (4) & (0) & (0) & (0) \end{array}$
	hyperplasia	) (0 ) (0 ) 0 0 0 )	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	1 0 0 0 (2)(0)(0)(0)	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
(Musculoske)	fetal system}				
muscle	hema toma	$\begin{pmatrix} 60 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 $	(0) (0) (0) (0) (0) (0) (0) (0) (0) (0)	$\begin{array}{cccc} & <50 \\ 0 & 1 & 0 & 0 \\ ( & 0) & ( & 2) & ( & 0) & ( & 0) \end{array}$	<pre>&lt; 50&gt;</pre>
	mineralization	1 0 0 (2) (0) (0) (	0 3 0 0 0 0) ( 6) ( 0) ( 0)	1 0 0 0 (2) ( 0) ( 0) ( 0)	1 0 0 0 (2) (0) (0) (0)
bone	osteoscierosis	<pre>&lt;60&gt; </pre> (0) (0) (0) (	0 (0) (0) (0) (0) (0)	<pre>&lt;50&gt; 2 0 0 ( 4) ( 0) ( 0) ( 0)</pre>	<pre>&lt;50&gt; <!--50--> </pre> ( 0) ( 0) ( 0) ( 0)
{Body caviti	esl				
pleura	inflammation	$\begin{pmatrix} 0 & 0 \\ 0 $	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccc} < 50 \\ 0 & 1 & 0 \\ ( & 0) & ( & 2) & ( & 0) \\ \end{array}$	( 0) ( 0) ( 0) ( 0)
Grade < a > b ( c ) Significant	$\begin{array}{llllllllllllllllllllllllllllllllllll$	3+ : Marked 4+ : Severe he site P≦0.01 Test of Chi Square			
(HPT150)					DAICE

STUDY NO. : 0712 ANIMAL : MOUSE B6D2F1/Cr1j (Crj:BDF1) REPORT TYPE : A1 SEX : FEMALE	HISTOPATHOLOGICAL FINDINGS :N ALL ANIMALS (0-10500)	ion-neoplastic lesions (su <b>m</b> mar	(X	PAGE : 27
	Group Name Control No. of Animals on Study 50	625 ppm 50	1250 ppm	2500 ppm
Organ Findings	Grade 1+ 2+ 3+ 4+ (%) (%) (%) (%) (%)	1+ 2+ 3+ 4+ (%) (%) (%) (%)		50 1+ 2+ 3+ 4+ (%) (%) (%) (%)
{Body cavities}				
mediastinum inflammatory infiltration	$\langle 50 \rangle$ $\begin{pmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 &$	<pre></pre>	$\begin{array}{cccc} \langle 50\rangle & & \\ 0 & 0 & 0 & \\ ( 0) & ( 0) & ( 0) & ( 0) \end{array}$	$\begin{array}{cccc} \langle 50 \rangle \\ 1 & 0 & 0 \\ ( 2 ) & ( 0 ) & ( 0 ) \\ \end{array}$
peritoneum inflammation	(20)> (50)> 0 0 1 0	6 (50) 10 0 0	(50)> 	20) (20)
Grade 1+:Slight 2+:Moderat < a > a :Number of animals examine h h :Mumber of animals examine	e 3+:Marked 4+:Severe d at the site			
Significant difference; $*: P \leq 0.05$	aron ★* : P ≦ 0.01 Test of Chi Square			

(HPT150)

# TABLE P 1

# NEOPLASTIC LESIONS-INCIDENCE AND

# STATISTICAL ANALYSIS: MALE

STUDY No. : 0712 Animal : Mouse B6d2F1/C Sex : Male	NEOPI (Crj:BDF1]	LASTIC LESIONS-INCIDENCE AND STATISTICAL	L ANALYSIS	<b>_</b>	PAGE : 1
Group Name	Control	625 ррт	1250 ppm	2500 ppm	
	SITE : lung TUMOR : bronchiolar-alveolar adenor	Ë			
lumor rate Overall rates(a) Adiustad rates(b)	6/50 (12.0) 10.32	2/50 (4,0)	3/50 ( 6. 0)	6/50 (12.0)	
Terminal rates (c) Statistical analysis	4/24 (16.7)	6. 25 2/32 ( 6. 3)	7.32 2/31(6.5)	13.04 4/39(10.3)	
Peto test Standard method(d)					
Prevalence method (d) Combined analysis (d)	P = 0.4977 P =				
Goonran-Armitage test(e) Fisher Exact test(e)	P = 0. 6997	P = 0.1343	P = 0. 2435	P = 0. 6202	
Tumor vato	SITE : lung TUMOR : bronchiolar-alveolar carcir	noma			
Overall rates (a)	10/50 ( 20.0)	9/50 ( 18. 0)	2/50 ( 4.0)	3/50 ( 6.0)	
Terminal rates (c) Statistical analysis	5/24 (20.8)	25. /1 8/32 (25. 0)	6.45 2/31(6.5)	5.13 2/39(5.1)	
Peto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armizae test(d)	P = 0.8551 P = 0.9978 P = 0.9989 P = 0.124*				
Fisher Exact test (e)		P = 0. 5000	P = 0.0139*	P = 0.0357*	
Tumor roto	SITE : lung TUMOR : bronchiolar-alveolar adenom	ma, bronchiolar-alveolar carcinoma			
overall rates (a) Addinsted rates (b)	16/50 (32.0) 38 46	10/50 ( 20. 0)	5/50 ( 10. 0)	9/50 ( 18. 0)	
Terminal rates (c) Statistical analysis	9/24 ( 37.5)	9/32 ( 28. 1)	12. 90 4/31 (12. 9)	17.39 6/39 (15.4)	
reto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armisze est(d)	P = 0.8551 P = 0.9753 P = 0.9872 D = 0.0072				
Fisher Exact test (e)	6470 m - L	P = 0.1271	P = 0.0064**	P = 0.0826	
(HPT360A)					DATO

BA I S5

SEX : MALE	r1J LUTJ: BUF1J			PAGE :	2
Group Name	Control	625 ррт	1250 ррт	2500 ppm	
Timor	SITE : Iymph node TUMOR : malignant lymphoma				
lumor rate Overall rates(a) Adjucted rates(b)	7/50 (14.0)	4/50 ( 8. 0)	9/50 (18.0)	6/50 (12.0)	
Terminal rates (c) Statistical analysis	10. b/ 4/24 (16. 7)	9.38 3/32 (9.4)	16. 13 5/31 (16. 1)	12 82 5/39 (12 8)	
Peto test Standard method(d) Prevalence method(d)	P = 0.8199 P = 0.5467				
Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e)	P = 0. 7459 P = 0. 9433	P = 0. 2623	P = 0.3929	P = 0.5000	
	SITE : spleen TUMOR : hemangioma				
lumor rate Overall rates(a) Adiusted rates(b)	1/50(2.0)	3/50 ( 6. 0)	1/50 ( 2.0)	1/50 ( 2.0)	
Terminal rates (c) Statistical analysis	5:33 0/24 ( 0.0)	9.38 3/32 ( 9.4)	3. 23 1/31 ( 3. 2)	2.56 1/39(2.6)	
Peto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Amitaze test(a)	P = P = 0.7576 P = 0.6742 P = 0.6742				
Fisher Exact test (e)		P = 0.3087	P = 0.7525	P = 0.7525	
Tumor roto	SITE : spleen TUMOR : hemangioma,hemangiosarcom	11.3			
umor rate Overall rates(a) Adiusted rates(h)	1/50(2.0) 3.33	4/50 ( 8. 0) 12 E0	1/50 ( 2.0)	1/50 ( 2.0)	
Terminal rates (c) Statistical analysis	0/24 ( 0.0)	4/32 (12.5)	3. 23 1/31(3.2)	2. 36 1/39 (2. 6)	
Peto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitzee test(a)	P = P = 0.8184 P = 0.6503				
Fisher Exact test (e)		P = 0. 1811	P = 0.7525	P = 0.7525	
(HPT360A)					10140

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

STUDY No. : 0712

BA I S5

STUDY No. : 0712 ANIMAL : MOUSE B6D2F1/C	rij [Crj:BDF1]	EOPLASTIC LESIONS-INCIDENCE AND STATIS	TICAL ANALYSIS		
Sex : male					AGE : 3
Group Name	Control	625 ррт	1250 ррт	2500 ррт	
	SITE : liver TUMOR : hemangioma				
lumor rate Overall rates(a) Adiucted rates(b)	2/50 ( 4.0)	3/50 ( 6. 0)	3/50 ( 6.0)	1/50 ( 2.0)	
Terminal rates (1) Terminal rates (c) Statistical analysis	4. 17 1/24 ( 4. 2)	9.38 3/32 ( 9.4)	9.68 3/31 (9.7)	2.56 1/39 (2.6)	
Peto test Standard method(d) Prevalence method(d)	P = 0.9629 P = 0.7503 P = 0.7503				
compined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.553	P = 0.5000	P = 0.5000	P = 0.5000	
T	SITE : liver TUMOR : hepatocellular adenoma				
lumur rate Overall rates(a) Adiusted rates(b)	16/50 (32.0) 50.00	8/50 (16.0)	9/50 ( 18. 0)	1/50 ( 2.0)	
Terminal rates (c) Statistical analysis	12/24 ( 50. 0)	21. 21 6/32 (18.8)	29, 03 9/31 (29.0)	2. 13 0/39 ( 0. 0)	
Peto test Standard method(d) Prevalence method(d) Comhined analysis(d)	P = 1.0000 P = 1.0000				
Cochran-Armitage test (e) Fisher Exact test (e)	P = 0.0002**	P = 0.0500	P = 0. 0826	P < 0.0001**	
T	SITE : liver TUMOR : histiocytic sarcoma				
lumor rate Overall rates(a) Adiusted rates(h)	6/50 ( 12. 0) 0.0	2/50 ( 4. 0)	4/50 ( 8.0)	1/50 ( 2.0)	
Terminal rates (c) Statistical analysis	0/24 ( 0.0)	0/32 ( 0.0)	0.0 0/31 ( 0.0)	2.56 1/39 (2.6)	
Peto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.9956 P = 0.1404 P = 0.9804 P = 0.0897	P = 0. 1343	P = 0. 3703	P = 0.0559	

(HPT360A)
STUDY No. : 0712 ANIMAL : MOUSE B6D2F1/C SEX : MALE	rlj [Crj:B0F1]	NEOPLASTIC LESIONS-INCIDENCE AND STATIS	TICAL ANALYSIS	, P∆AG	~
Group Name	Control	625 ppm	1250 ppm	2500 ppm	-
	SITE : liver TUMOR : hepatocellular carcin	una A			
Tumor rate Overall rates(a)	7/50 ( 14. 0)	6/50 ( 12. 0)	5/50(10.0)	2750 4 0)	
Adjusted rates(b) Terminal rates(c)	16.67 4/24 (16.7)	18.75 6/32 (18.8)	12.90		
Statistical analysis Peto test Standard method(d)	P = 0.6956				
Frevarence method (d) Combined analysis (d) Cochran-Armitage test(e)	P = 0.9914 P = 0.9910 P = 0.706				
Fisher Exact test (e)	-	P = 0.5000	P = 0.3798	P = 0. 0798	
	SITE : Liver TUMOR : hemangioma,hemangios	rcoma			1
Overall rates (a) Adjucted rates (b)	2/50 ( 4 0)	4/50 ( 8. 0)	3/50(6.0)	2/50 ( 4. 0)	
Terminal rates (c)	4. 17 1/24 ( 4. 2)	12.50 4/32 (12.5)	9.68 3/31(9.7)	2.56 1/39 (2.6)	
statistical analysis Peto test					
Standard method(d) Prevalence method(d) Combined analysis(d)	P = 0.4556 P = 0.8076 P = 0.7729				
Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.7932	P = 0. 3389	P = 0. 5000	P = 0.6913	
Timor sata	SITE : liver TUMOR : hepatocellular adenom	a, hepatocellular carcinoma			1
overall rates (a) Adjusted rates (b)	21/50 (42.0) 5833	13/50 ( 26. 0) 36. 36	12/50 (24.0)	3/50 ( 9. 0)	
Terminal rates (C) Statistical analysis	14/24 (58.3)	30, 30 11/32 ( 34, 4)	35. 48 11/31 (35. 5)	4. 35 1/39 (2.6)	
reto test Standard method (d) Prevalence method (d) Combined analysis (d) Cochran-Armitage test (e) Eichor Evert test (e)	P = 0.6956 P = 1.0000 P = 1.0000 P < 0.0001**				
רואופי באמנו ובאו וכי		P = 0.0695	P = 0.0441*	P < 0. 0001**	

(HPT360A)

STUDY No. : 0712 ANIMAL : MOUSE B6D2F1/C SEX : MALE	rlj[Crj:BDF1]	NEOPLASTIC LESIONS-INCIDENCE AND STATI	ISTICAL ANALYSIS		
					PAGE : 5
Group Name	Control	625 ррт	1250 ppm	2500 ppm	
	SITE : Harderian gland TIMOP : donoma				
Tumor rate					
Overall rates (a)	2/50 (4.0)	3/50 ( 6.0)	4/50 ( 8.0)	0/20(00)	
Adjusted rates (b)	8.33	9.38	12.90		
lerminal rates(c) Statistical analysis	2/24 (8.3)	3/32 (9.4)	4/31 (12.9)	0/39 ( 0.0)	
Peto test Standard method(d)					
Prevalence method (d)	P = 0.9440				
Combined analysis (d)	P = = 9				
Cochran-Armitage test(e) Fisher Evect test(e)	P = 0.2733				
I I SIIGI EXAUL LEST (E/		P = 0.5000	P = 0.3389	P = 0.2475	
	SITE : Harderian gland				
Tumor rate	IUMUK : AUERIOMA, AUERIOCATCINO	13			
Overall rates (a)	3/50 ( 6.0)	3/50 ( 6. 0)	4/2U( 8 D)	0 (50 ( 0 0)	
Adjusted rates(b)	8.33	9.38	12 00		
Terminal rates(c) Statistical analysis	2/24 (8.3)	3/32 (9.4)	4/31 (12.9)	0/39 ( 0. 0)	
Peto test					
Standard method (d)					
Prevalence method (d)	P = 0.9682				
Combined analysis (d)					
Cochran-Armitage test(e)	P = 0.1539				
Fisher Exact test(e)		P = 0.6611	P = 0.5000	P = 0.1212	
(HPT360A)					RAICE
<ul> <li>(a): Number of tumor-bearin</li> <li>(b): Kaplan-Meier estimated</li> <li>(c): Observed tumor incider</li> </ul>	ng animals/number of animals exa d tumor incidence at the end of ore at terminal vill	nined at the site. the study after adjusting for intercurre	ent mortality.		00 I M0
(d) : Beneath the control ir Standard method : Do	ncidence are the P-values associ eath analysis	ated with the trend test.			
Prevalence method : lr Combined analysis : De	ıcidental tumor test eath analysis + Incidental tum	or test			
<ul> <li>(e): The Cochran-Armitage a</li> <li>? The conditional probat</li> <li> : There is no data</li> </ul>	and Fisher exact test compare di Dilities of the largest and smal which should be statistical ana	ectly the overall incidence rates. lest possible out comes can not estimate vsis.	ed or this P-value is beyond the estima	ated P-value.	
Significant difference ; N.C.:Statistical value cann	* : $P \leq 0.05$ ** : $P \leq 0.101$	li smificant.			

STUDY No. : 0712 ANIMAL : MOUSE B6D2F1/C SEX : MALE	crij (Crj:BDF1)	NEOPLASTIC LESIONS-INCIDENCE AND STATIS	STICAL ANALYSIS	PA	AGE : 1
Group Name	Control	625 ppm	1250 ppm	2500 ром	
Times and	SITE : ALL SITE TUMOR : hemangioma				
lumor rate Overall rates(a) Adiusted rates(h)	3/50 ( 6. 0) 6. an	5/50 ( 10. 0) 15 52	3/50( 6.0)	2/50 ( 4, 0)	
Terminal rates (c) Statistical analysis Pern test	1/24 ( 4.2)	5/32 (15.6)	9. b8 3/31 ( 9. 7)	5.13 2/39(5.1)	
Standard method(d) Prevalence method(d) Combined analysis(d)	P = 0.9629 ? P = 0.8186 P = 0.8953				
Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.4671	P = 0.3575	P = 0.6611	P = 0.5000	
Turner	SITE : ALL SITE TUMOR : histiocytic sarcoma				
lumor rate Overall rates(a) Adiusted rates(h)	7/50 (14.0)	5/50 ( 10. 0)	6/50 ( 12. 0)	4/50 ( 8.0)	
Terminal rates (c) Statistical analysis	0/24 ( 0.0)	4, 60 1/32(3,1)	0.0 0/31 ( 0.0)	7. 69 3/39 (7. 7)	
Feto test Standard method (d) Prevalence method (d) Combined analysis (d) Cochran-Arnitzee test(d)	P = 0.9879 P = 0.0861 P = 0.8952 P = 0.4007				
Fisher Exact test (e)		P = 0.3798	P = 0.5000	P = 0.2623	
(HPT360A)					BAI S5

STUDY No. : 0712 ANIMAL : MOUSE B6D2F1/C. SEX : MALE	r lj [Crj:BDF1]	NEOPLASTIC LESIONS-INCIDENCE AND STATIS'	ICAL ANALYSIS		PAGE : 2
Group Name	Control	625 ppm	1250 ppm	2500 ррт	
Tumor voto	SITE : ALL SITE TUMOR : malignant lymphoma				
umor rate Overall rates (a) Adjusted rates (b) Terminal rates (c) Statistical analysis	7/50 (14.0) 16.67 4/24 (16.7)	4/50 ( 8 0) 9.38 3/32 ( 9.4)	10/50 { 20. 0) 19. 35 6/31 ( 19. 4)	7/50 (14.0) 15.38 6/39 (15.4)	
Standard method(d) Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.8139 P = 0.4130 P = 0.6450 P = 0.6793	P = 0. 2623	P = 0. 2977	P = 0. 6129	
(HPT360A)					BAIS5
<ul> <li>(a): Number of tumor-bearir</li> <li>(b): Kaplan-Meier estimate(</li> <li>(c): Observed tumor incider</li> <li>(d): Beneath the control ir Standard method : Df Prevalence method : Ir Combined analysis : Df</li> <li>(e): The Cochran-Armitage a ?: The conditional probab</li> <li></li></ul>	Mg animals/number of animals exa d tumor incidence at the end of the eat terminal kill. The eat terminal kill. The eath analysis ath analysis the P-values associ eath analysis the exact ath exact test compare di silities of the largest and smal which should be statistical ana the should be statistical ana the calculated and was not signot be calculated and was not signot the exact at and should be statistical ana the calculated and was not signot	mined at the site. the study after adjusting for intercurrent ated with the trend test. or test rectly the overall incidence rates. lest possible out comes can not estimated lysis. 01 gnificant.	mortality. or this P-value is beyond the estimat	ed P-value.	

#### TABLE P 2

# NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS: FEMALE

STUDY No. : 0712 ANIMAL : MOUSE B6D2F1/C	rlj [Crj:BDF1]	NEOPLASTIC LESIONS-INCIDENCE AND STATISTICA	NL ANALYSIS		
SEX : FEMALE				PAGE :	9
Group Name	Control	625 ppm	1250 ppm	2500 ppm	
	SITE : lung TUMOR : bronchiolar-alveolar a	denoma			
lumor rate Overall rates(a)	2/50 ( 4.0)	3/50 ( 6. 0)	1/50 ( 2.0)	1/50/ 2.01	
Adjusted rates (b) Terminal rates (c)	8. 33 2/24 ( 8. 3)	9.52 2/21(9.5)	3.03 1/33 (3.0)	2. 63 1/38 ( 2. 6)	
statistical analysis Peto test					
Standard method(d) Prevalence method(d)	P = P =8884				
Combined analysis (d)					
uudan-Armitage test(e) Fisher Exact test(e)	P = U. 3979	P = 0.5000	P = 0.5000	P = 0.5000	
	SITE : lung TUMOR : bronchiolar-alveolar c	arcinoma			
Tumor rate	1 /LO / 0 01				
Adjusted rates (b)	() .C .D .C	4/50 (8.0)	1/50 ( 2.0)	2/50 ( 4, 0)	
Terminal rates (c) Statictical analysis	0/24 ( 0.0)	3/21 (14.3)	3. 03 1/33 ( 3. 0)	2. 63 1/38 (2. 6)	
Peto test					
Standard method(d) Prevalence method(d)	P = 0.4490 P = 0.6716				
Combined analysis (d)	P = 0.6326				
coonran-Armitage test(e) Fisher Exact test(e)	P = 1. 0000	P = 0.1811	P = 0.7525	P = 0.5000	
	SITE : lung TUMOR : bronchiolar-alveolar a	denoma bronchiolar-alveolar carcinoma			
overall rates (a) Adjusted rates (b)	3/50 ( 6. 0)	7/50 (14.0)	2/50 ( 4.0)	3/50 ( 6.0)	
Terminal rates (c) Statistical analysis	2/24 (8.3)	5/21 (23.8)	6. U6 2/33 ( 6. 1)	5.26 2/38 ( 5.3)	
Peto test Standard method(d) Prevalence method(d) Combined analysis(d)	P = 0.4490 P = 0.8831 P = 0.8556				
Cochran-Armitage test(e) Fisher Exact test(e)	P = 0. 5552	P = 0.1589	P = 0.5000	P = 0.6611	

(HPT360A)

STUDY No. : 0712 ANIMAL : MOUSE B6D2F1/C	rlj [Crj:BDF1]	NEOPLASTIC LESIONS-INCIDENCE AND STATI	ISTICAL ANALYSIS		
SEX : FEMALE				PAG	(GE : 7
Group Name	Control	625 ррт	1250 ррт	2500 ррт	
	SITE : Iymph node TUMOR : malignant lymphoma				
lumor rate Overall rates (a)	18/50 (36.0)	17/50 (34.0)	21/50 (42.0)	10/50 ( 20 0)	
Adjusted rates(b) Terminal rates(c)	41.67 10/24(41.7)	33. 33 7721 (333)	45.45 15/33 / AE EV		
Statistical analysis Peto test			10.00 × 10.00	0/38 ( 13. 8)	
Standard method (d)	P = 0.9682				
Prevalence method(d) Combined analysis(d)	P = 0.9890 P = 0.9984				
Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.0934	P = 0.5000	P = 0.3410	P = 0.0591	
	SITE : liver TUMOR : hemangioma				
lumor rate Overall rates(a)	1/50(2,0)	1 /50 ( 2 0)	1 /50 / 0 01		
Adjusted rates (b)	4.17	7 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	(0.7) NC/I	3/50 ( b. U) 7 00	
Terminal rates(c) Ctatictical analysis	1/24 ( 4.2)	0/21 ( 0.0)	0/33 ( 0.0)	3/38 ( 7.9)	
Peto test	,				
Standard method(d) Prevalence method(d)	P = 0 1578				
Combined analysis (d)					
uochran-Armitage test(e) Fisher Exact test(e)	P = 0. 2072	P = 0.7525	P = 0.7525	P = 0.3087	
	SITE : liver TUMOR : hepatocellular adenom				
lumor rate Overall rates (a)	4/50 ( 8.0)	6/50 (12.0)	4/50 ( 8.0)	5/50 ( 10. 0)	
Adjusted rates(b) Terminal rates(c) Statistical andlysis	12.00 2/24 ( 8.3)	17. 86 2/21(9. 5)	12. 12 4/33 (12. 1)	13.16 5/38 (13.2)	
Peto test					
Standard method(d) Prevalence method(d)	P = P = 0.6464				
Cochran-Armitage test(e)	P = P = 0.9027				
Fisher Exact test(e)		P = 0.3703	P = 0.6425	P = 0.5000	

(HPT360A)

STUDY No. : 0712 ANIMAL : MOUSE B6D2F1/C	rlj [Crj:BDF1]	JEOPLASTIC LESIONS-INCIDENCE AND STATISTICA	L ANALYSIS		
SEX : FEMALE				PAGE : 1	8
Group Name	Control	625 ppm	1250 ррт	2500 ррт	
Tunner .	SITE : liver TUMOR : histiocytic sarcoma				1
overali rates (a) Adjusted rates (b)	2/50 ( 4. 0)	3/50 ( 6. 0)	0/50 ( 0.0)	1/50 ( 2.0)	
Aujusteu rates(D) Terminal rates(c) Statistical analysis	u.u 0/24(0.0)	3. 13 0/21 ( 0. 0)	0. 0 0/33 ( 0. 0)	0.0 0/38 ( 0.0)	
Peto test Standard method(d) Prevalence method(d)	P = 0.8579 P = 0.6376				
Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.8942 P = 0.3266	P = 0.5000	P = 0. 2475	P = 0.5000	
	SITE : liver TIMOR : hemanoioma hemanoiocar	0.0.2			1
Tumor rate		CE A			
Uverall rates (a) Adjusted rates (b)	1/50 ( 2.0)	2/50 (4,0)	1/50 (2.0)	3/50 ( 6. 0)	
Terminal rates(C) Statistical analysis	1/24 ( 4. 2)	1/21 ( 4.8)	2. 34 0/33 ( 0. 0)	a/38 (7.9)	
Peto test					
Prevalence method(d)	P = 0.2414				
Combined analysis(d) Cochran-Armitage test(e)	P = P = 0.3293				
Fisher Exact test (e)		P = 0.5000	P = 0.7525	P = 0.3087	
Timor	SITE : liver TUMOR : hepatocellular adenoma.	hepatocellular carcinoma			reason
overall rates (a) Adjusted rates (b)	4/50 ( 8.0) 12.00	6/50 (12.0) 17 86	5/50(10.0)	5/50 ( 10. 0)	
Terminal rates (c) Statistical analysis	2/24(8.3)	2/21 ( 9.5)	5/33 (15.2)	5/38 (13.2)	
Peto test Standard method(d) Prevalence method(d) Combined analysis(d)	P = P = 0.6407 P =				
Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.8734	P = 0.3703	P = 0.5000	P = 0.5000	

(HPT360A)

STUDY No. : 0712 ANIMAL : MOUSE B6D2F1//	Crtj [Crj:BDF1]	NEOPLASTIC LESIONS-INCIDENCE AND STAT	'ISTICAL ANALYSIS		
SEA : FEMALE					PAGE : 9
Group Name	Control	625 ррт	1250 ppm	2500 ррт	
	SITE : pituitary gland TIMOR : adanoma				
Tumor rate					
Overall rates(a) Adiusted rates(b)	4/50 ( 8.0) 16.67	9/50 (18.0)	6/50 ( 12. 0)	7/50 (14.0)	
Terminal rates (c) Statistical analysis	4/24 (16.7)	5/21 (23.8)	15.38 5/33(15.2)	13. 16 5/38 ( 13. 2)	
Peto test					
Standard method (d)	P = 0.2302				
Combined analysis (d)	P = 0.5825				
Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.6188	P = 0.1168	P = 0.3703	D - 0 9693	
				r = 0. 2023	
Tumor rato	SITE : ovary TUMOR : papillary adenoma				
Overall rates (a)	1/50 (2.0)	0/20 ( 0.0)	4/50(8,0)	1/50 ( 2 0)	
Adjusted rates(b) Terminal rates(c)	3.23	0.0	12.12	2. 27	
Statistical analysis Peto test	0/ 24 1 0. 0/	U/ 21 ( D. U)	4/33 (12.1)	0/38 ( 0.0)	
Standard method (d)	P =				
Prevalence method(d) Combined analysis(d)	P = 0. 3991 P =				
Cochran-Armitage test(e)	P = 0.6742				
FISNER EXACT TEST (E)		P = 0.5000	P = 0.1811	P = 0.7525	
	SITE : uterus				
Tumor rata	TUMOR : endometrial stromal po	lyp			
Overall rates (a)	3/50 ( 6.0)	2/50 ( 4, 0)	2/50 ( 4.0)	2/50 (4,0)	
Aujusteo rates(b) Terminal rates(c)	11. 11 2/24 ( 8. 3)	6.25 0/21 ( 0 0)	5.13 1/33/ 3.0)		
Statistical analysis				2/30/ 3.3/	
Standard method (d)	P =				
Prevalence method(d) Combined analysis(d)	P = 0. 7312 P =				
Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.6865	P = 0.5000	P = 0.5000	P = 0.5000	
(HPT360A)					10140

STUDY No. : 0712 ANIMAL : MOUSE B6D2F1/C	rlj [Crj:BDF1]	NEOPLASTIC LESIONS-INCIDENCE AND STATIS	STICAL ANALYSIS		
SEK : FEMALE				PAGE : 11	10
Group Name	Control	625 ррт	1250 ppm	2500 ррт	1
	SITE : uterus TUMOR : histiocytic sarcoma				1
Tumor rate Overall rates(a)	16/50 ( 32 0)	1.4 /En ( 28 n)	10 /E0 / 01 01		
Adjusted rates (b)	18. 52	14/30/2000	(0.742) 00 /21 10 /21	12/50 ( 24. 0) 27 27	
Terminal rates(c) Statistical analysis	4/24 (16.7)	2/21 (9.5)	7/33 ( 21. 2)	9/38 ( 23. 7)	
Peto test Standard mothod (d)					
Prevalence method (d)	F = 1.0000 P = 0.0444*				
Combined analysis (d)	P = 0.9459				
Fisher Exact test (e)	r - u. 3000	P = 0.4138	P = 0. 2522	P = 0.2522	
	SITE · mammarvaland				I
·	TUMOR : adenocarcinoma				
lumor rate Overall rates(a)	0/50( 0.0)				
Adjusted rates (b)	0.0	1/30 ( 2. U) 4. 76	0/50 ( 0.0) 0.0	3/50 ( 6. 0)	
Terminal rates(c) Statistical analysis	0/24 ( 0.0)	1/21 ( 4 8)	0/33 ( 0.0)		
Peto test					
Standard method (d)	P = 0.1467				
Combined analysis (d)	P = 0.123t P = 0.0483*				
Cochran-Armitage test(e)	P = 0.0405*				
Fisher Exact test(e)		P = 0.5000	P = N. C.	P = 0.1212	
	SITE : mammary gland				
Tumor rate	IUMUK : adenocarcinoma, adenos	quamous carcinoma			
Overal I rates (a)	0/50 ( 0.0)	2/50 ( 4.0)	0/20(0.0)	4/50 ( 8.0)	
Adjusted rates (b)	0.0	4, 76	0.0	7. 32	
Statistical analysis	U/ 24 (	1/21 ( 4.8)	0/33 ( 0.0)	1/38 ( 2.6)	
retu test Standard method(d) Prevalence method(d)	P = 0.3193 P = 0.0446*				
Combined analysis (d)	$P = 0.0469 \times D = 0.0266 \times D$				
Fisher Exact test (e)	- c. c	P = 0.2475	P = N. C.	P = 0.0587	

(HPT360A)

STUDY No. : 0712 ANIMAL : MOUSE B6D2F1/C SEX : FEMALE	rlj [Crj:BDF1]	NEOPLASTIC LESIONS-INCIDENCE AND STAT	ristical analysis	PAGE :	=
Group Name	Control	625 ррт	1250 ррт	2500 ррт	
-	SITE : Harderian gland TUMOR : adenoma				
lumor rate Overali rates(a) Adinated cates(b)	1/50 ( 2.0)	0/20 ( 0.0)	4/50 ( 8.0)	3/50 ( 6. 0)	
Terminal rates (c) Statistical analysis	3. / U 0/24 ( 0. 0)	0.0 0/21 ( 0.0)	12. 12 4/33 (12. 1)	7.32 2/38 (5.3)	
Peto test Standard method(d) Prevalence method(d) Combined analysis(d) Contromed analysis(d)	P = P = 0.1492 P =				
Fisher Exact test (e)	P = 0.1432	P = 0.5000	P = 0.1811	P = 0.3087	
	SITE : Harderian gland TUMOR : adenoma,adenocarcinc	ma			
Tumor rate Overall rates(a)	2/50 ( 4. 0)	0/20(0.0)	4/50 (8.0)	3/50 ( 6.0)	
Adjusted rates(b) Terminal rates(c) Statistical analysis	3.85 0/24( 0.0)	0.0 0/21 ( 0.0)	12.12 4/33 (12.1)	7.32 2/38 (5.3)	
Peto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e)	P = 0.9209 ? P = 0.1549 P = 0.3059 P = 0.3270	P = 0. 2475	P = 0.3389	P = 0.5000	
(HPT360A)					BA I S5
<ul> <li>(a): Number of tumor-beari</li> <li>(b): Kaplan-Meier estimate</li> <li>(c): Observed tumor incide</li> <li>(d): Beneath the control i</li> <li>Standard method : D</li> </ul>	ng animals/number of animals exa d tumor incidence at the end of nce at terminal kill. ncidence are the P-values associ eath analysis	mined at the site. the study after adjusting for intercurre ated with the trend test.	ent mortality.		

Prevalence method : Incidental tumor test Combined analysis : Death analysis + 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 :  $*: P \leq 0.05$   $**: P \leq 0.01$ M.C.:Statistical value cannot be calculated and was not significant.

STUDY No. : 0712 ANIMAL : MOUSE B6D2F1/C SEX : FEMALE	rlj [Crj:BDF1]	NEOPLASTIC LESIONS-INCIDENCE AND STATIS	STICAL ANALYSIS	đ	AGE : 3
Group Name	Control	625 ррт	1250 ppm	2500 ppm	
Tumor rate	SITE : ALL SITE TUMOR : hemangioma				
overall rate Overall rates (a) Adjusted rates (b) Terminal rates (c) Statistical analysis	1/50 ( 2.0) 4.17 1/24 ( 4.2)	4/50 ( 8.0) 8.70 1/21 ( 4.8)	4/50 ( 8. 0) 11. 76 3/33 ( 9. 1)	4/50 ( 8. 0) 10. 53 4/38 ( 10. 5)	
Figure 1 (1) Standard method (d) Prevalence method (d) Combined analysis (d) Cochran-Armitage test (e) Fisher Exact test (e)	P = 0.6336 P = 0.2193 P = 0.2863 P = 0.3086	P = 0. 1811	P = 0. 1811	P = 0. 1811	
Tumor rate	SITE : ALL SITE TUMOR : histiocytic sarcoma				
Overal Lates (a) Overal Lates (a) Adjusted rates (b) Terminal rates (c) Statistical analysis	18/50 (36.0) 18.52 4/24 (16.7)	17/50 (34,0) 13.79 2/21 (9.5)	13/50(26.0) 21.21 7/33(21.2)	13/50 (2.6.0) 27.91 9/38 (23.7)	
Peto test Standard method(d) Prevalence method(d) Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e)	P = 1.0000 P = 0.0586 P = 0.9717 P = 0.2224	P = 0.5000	P = 0. 1937	P = 0. 1937	
(HPT360A)					BA I S5

STUDY No. : 0712 ANIMAL : MOUSE B6D2F1/C SEX : FEMALE	rlj (Crj: BDF1)	NEOPLASTIC LESIONS-INCIDENCE AND STATI	ISTICAL ANALYSIS		PAGE : 4
Group Name	Control	625 ррт	1250 ppm	2500 ppm	
Tumor rate Overall rates (a) Adjusted rates (b) Terminal rates (c) Statistical analysis Peto test method (d) Prevalence method (d) Prevalence method (d) Combined analysis (d) Cochran-Armitage test (e) (HPT360A) (HPT3	SITE : ALL SITE TUMOR : malignant lymphoma 18/50 (36.0) 10/24 (41.7) 10/24 (41.7) 10/24 (41.7) = 0.9880 P = 0.9880 P = 0.9984 P = 0.99844 P = 0.99844 P = 0.99844 P = 0.998444 P = 0.99844444444444444444444444444444444444	17/50 (34.0) $33.33$ $7/21 (33.3)$ $P = 0.5000$ $P = 0.5000$ The study after adjusting for intercurre the study after adjusting for intercurre inted with the trend test. The overall incidence rates. The possible out comes can not estimate of isonificant.	21/50(42.0) 45.45 15/33(45.5) P = 0.3410 ant mortality.	10/50 ( 20. 0) 15. 79 6/38 ( 15. 8) F = 0. 0591 ated P-value.	BALS5

#### TABLE R

# HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER: B6D2F1/Crlj FEMALE MICE

Organs Tumors	No. of animals examined	No. of animals bearing tumor	Incidence (%)	Min Max. (%)
Mammary gland	2347			
adenocarcinoma"		40	1.7	0 - 8
adenosquamous carcinoma <sup>2)</sup>		0	0.0	0 - 0
1) + 2)		40	1.7	0 - 8
Uterus	2345			
Histiocytic sarcoma		483	20.6	10 - 34

## TABLE RHISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONSIN JAPAN BIOASSAY RESEARCH CENTER :B6D2F1/Crlj FEMALE MICE

47 carcinogenicity studies examined in Japan Bioassay Research Center were used.

Study No. : 0044, 0060, 0062, 0064, 0066, 0068, 0096, 0105, 0116, 0140, 0159, 0163, 0190, 0206, 0211, 0225, 0243, 0268, 0270, 0279, 0285, 0297, 0319, 0329, 0343, 0348, 0366, 0372, 0402, 0406, 0418, 0422, 0438, 0449, 0458, 0462, 0498, 0515, 0561, 0580, 0611, 0613, 0642, 0676, 0685, 0705, 0732

## TABLE S 1

#### CAUSE OF DEATH: MALE

STUDY NO. : 0712 ANIMAL : MOUSE	B6D2F1/Cr1j [Cr.	j:B0F1]		COUSE OF DEATH (SUMMARY) (0-105W)	
JEA . MALE					PAGE : 1
Group Name	Control	625 ppm	1250 ppm	2500 ррт	
Number of Dead and Moribund Animal	26	18	19		
no microscop confirm	1 2		0		
renal lesion	0	-	,		
urinary retention	0	9			
hydronephros i s	7	9	, co		
tumor d:leukemia	33	-	4		
tumor d:subcutis	0	0			
tumor d:lung	2	0	0		
tumor d:İymph node		0	0		
tumor d:liver	6	2			
tumor d:urin bladd	-	0	0		
tumor d:epididymis	0				
tumor d:muscle	0	0			
tumor d:peritoneum	****	0	0		
(B10120)					BAIS5

### TABLE S 2

### CAUSE OF DEATH: FEMALE

STUDY NO. : 0712 ANIMAL : MOUSE SEX : FEMALE	B6D2F1/Cr1j[Crj	:BDF1]		COUSE OF DEATH (SUMMARY) (0-105W)	PAGE : 2	~
Group Name	Control	625 ppm	1250 ppm	2500 ррт		r
Number of Dead and Moribund Animal	26	29	17	12		1
no microscop confirm	0	-	3			ſ
renal lesion	-	0	0	. 0		
hydronephrosis	0	0	-	·		
peritonitis	-	0	. 0			
tumor d:leukemia	8	6	9	4		
tumor d:subcutis	0	2	0			
tumor d:lung		-	0			
tumor d:liver	2	2	. 0			
tumor d:pituitary	0	2	0	6		
tumor d:uterus	=	=	5			
tumor d:mammary gl	0			<b>,</b>		
tumor d:Harder gl		0	. 0			
tumor d:muscle	-	0				
tumor d:mediastinum	0	0	,			
tumor d:retroperit	0	0		. 0		
(B10120)					BAIS5	

#### FIGURES

- FIGURE 1 SURVIVAL ANIMAL RATE OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 3-AMINOPHENOL
- FIGURE 2 SURVIVAL ANIMAL RATE OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 3-AMINOPHENOL
- FIGURE 3 BODY WEIGHT CHANGES OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 3-AMINOPHENOL
- FIGURE 4 BODY WEIGHT CHANGES OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 3-AMINOPHENOL
- FIGURE 5 FOOD CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 3-AMINOPHENOL
- FIGURE 6 FOOD CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 3-AMINOPHENOL
- FIGURE 7 WATER CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 3-AMINOPHENOL
- FIGURE 8 WATER CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 3-AMINOPHENOL



FIGURE 1 SURVIVAL ANIMAL RATE OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 3-AMINOPHENOL



FIGURE 2 SURVIVAL ANIMAL RATE OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 3-AMINOPHENOL



FIGURE 3 BODY WEIGHT CHANGES OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 3-AMINOPHENOL



FIGURE 4 BODY WEIGHT CHANGES OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 3-AMINOPHENOL



FIGURE 5 FOOD CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 3-AMINOPHENOL



FIGURE 6 FOOD CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 3-AMINOPHENOL



FIGURE 7 WATER CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 3-AMINOPHENOL



FIGURE 8 WATER CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 3-AMINOPHENOL



Photograph 1 Spleen: Normal Mouse, Male, Control, Animal No. 0712-1001 (H&E)



Photograph 2 Spleen: Deposit of hemosiderin (Arrows) and extramedullary hematopoiesis Mouse, Male, 2500 ppm, Animal No. 0712-1301 (H&E)



Photograph 3 Liver: Deposit of brown pigment (Arrows) Mouse, Male, 2500 ppm, Animal No. 0712-1301 (H&E)



Photograph 4 Thyroid: Deposit of brown pigment (Arrows) Mouse, Female, 2500 ppm, Animal No. 0712-2336 (H&E)