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 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 and females administered 1250 ppm and females 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 females administered 1250 ppm and above.

In the spleen, deposit of hemosiderin was incresed 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-effect-level (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.

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

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 **		↓↓
Harderian gland	adenoma	2	3	4	0		
malignant tumor							
lung	bronchiolar-alveolar carcinoma	10	9	2 *	3 *		↓
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 + bronchiolar-alveolar carcinoma	16	10	5 **	9		
liver	hepatocellular adenoma + hepatocellular carcinoma	21	13	12 *	3 **		↓↓

Significant difference

*: p≦0.05		**: p≦0.01		(Fisher test)
↑: p≦0.05	increase	↑↑: p≦0.01	increase	(Peto, Cochran-Armitage test)
↓: p≦0.05	decrease	↓↓: p≦0.01	decrease	(Cochran-Armitage test)

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

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 gland	adenoma	1	0	4	3		
malignant tumor							
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	↑[a]	
mammary gland	adenocarcinoma	0	1	0	3	↑	↑
	adenosquamous carcinoma	0	1	0	1		
mammary gland	adenocarcinoma＋ adenosquamous carcinoma	0	2	0	4	↑	↑

a :Significant only in Prevalence method in Peto test.

Significant difference

*: p≦0.05		**: p≦0.01		(Fisher test)
↑: p≦0.05	increase	↑↑: p≦0.01	increase	(Peto, Cochran-Armitage test)
↓: p≦0.05	decrease	↓↓: p≦0.01	decrease	(Cochran-Armitage test)

SELECTED TABLES

SELECTED TABLES (CONTINUED)

TABLE C 1

BODY WEIGHT CHANGES AND

SURVIVAL ANIMAL NUMBERS: MALE

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

MEAN BODY WEIGHTS AND SURVIVAL

Week-Day on Study	Control Av. Wt.	Control No. of Surviv. <50>	625 ppm Av. Wt.	625 ppm % of cont. <50>	625 ppm No. of Surviv.	1250 ppm Av. Wt.	1250 ppm % of cont. <50>	1250 ppm No. of Surviv.	2500 ppm Av. Wt.	2500 ppm % of cont. <50>	2500 ppm No. of Surviv.
0-0	24.2 (50)	50/50	24.2 (50)	100	50/50	24.2 (50)	100	50/50	24.2 (50)	100	50/50
1-7	25.1 (50)	50/50	25.0 (50)	100	50/50	24.9 (50)	99	50/50	24.2 (50)	96	50/50
2-7	25.9 (50)	50/50	25.7 (50)	99	50/50	25.7 (50)	99	50/50	24.8 (50)	96	50/50
3-7	26.6 (50)	50/50	26.5 (49)	100	49/50	26.4 (50)	99	50/50	25.5 (50)	96	50/50
4-7	27.3 (50)	50/50	27.5 (49)	101	49/50	27.4 (50)	100	50/50	26.4 (50)	97	50/50
5-7	28.3 (50)	50/50	28.4 (49)	100	49/50	28.2 (50)	100	50/50	27.1 (50)	96	50/50
6-7	29.0 (50)	50/50	29.2 (49)	101	49/50	28.9 (50)	100	50/50	27.4 (50)	94	50/50
7-7	30.0 (50)	50/50	30.1 (49)	100	49/50	29.6 (50)	99	50/50	28.1 (50)	94	50/50
8-7	30.8 (50)	50/50	30.8 (49)	100	49/50	30.3 (50)	98	50/50	28.7 (50)	93	50/50
9-7	31.5 (50)	50/50	31.4 (49)	100	49/50	30.9 (50)	98	50/50	29.2 (49)	93	49/50
10-7	32.0 (50)	50/50	32.0 (49)	100	49/50	31.6 (50)	99	50/50	30.1 (49)	94	49/50
11-7	32.6 (50)	50/50	32.6 (49)	100	49/50	32.2 (50)	99	50/50	30.5 (49)	94	49/50
12-7	33.7 (50)	50/50	33.6 (49)	100	49/50	33.3 (50)	99	50/50	31.3 (49)	93	49/50
13-7	34.5 (50)	50/50	34.4 (49)	100	49/50	34.1 (50)	99	50/50	32.1 (49)	93	49/50
14-7	35.3 (50)	50/50	34.9 (49)	99	49/50	34.8 (50)	99	50/50	32.8 (49)	93	49/50
18-7	37.9 (50)	50/50	37.7 (49)	99	49/50	37.1 (50)	98	50/50	34.8 (49)	92	49/50
22-7	40.1 (50)	50/50	39.7 (49)	99	49/50	39.0 (50)	97	50/50	36.4 (49)	91	49/50
26-7	42.0 (50)	50/50	41.5 (49)	99	49/50	40.7 (50)	97	50/50	37.9 (49)	90	49/50
30-7	44.0 (50)	50/50	43.5 (48)	99	48/50	42.5 (50)	97	50/50	39.3 (49)	89	49/50
34-7	45.5 (50)	50/50	45.0 (48)	99	48/50	43.7 (50)	96	50/50	40.6 (49)	89	49/50
38-7	47.2 (50)	50/50	46.7 (48)	99	48/50	45.3 (50)	96	50/50	42.3 (49)	90	49/50
42-7	48.5 (49)	49/50	48.1 (48)	99	48/50	46.3 (50)	95	50/50	43.4 (49)	89	49/50
46-7	49.6 (49)	49/50	48.8 (48)	98	48/50	47.0 (50)	95	50/50	44.2 (49)	89	49/50
50-7	50.5 (49)	49/50	49.5 (47)	98	47/50	48.0 (50)	95	50/50	44.8 (49)	89	49/50
54-7	51.0 (49)	49/50	49.9 (47)	98	47/50	48.8 (49)	96	49/50	45.4 (49)	89	49/50
58-7	52.2 (48)	48/50	50.6 (47)	97	47/50	49.8 (49)	95	49/50	46.0 (49)	88	49/50
62-7	52.0 (48)	48/50	51.7 (45)	99	45/50	49.7 (48)	96	48/50	46.2 (49)	89	49/50
66-7	52.2 (48)	48/50	51.9 (44)	99	44/50	50.0 (47)	96	47/50	46.7 (49)	89	49/50
70-7	52.2 (47)	47/50	51.6 (44)	99	44/50	50.2 (47)	96	47/50	46.9 (48)	90	48/50
74-7	52.6 (47)	47/50	51.8 (44)	98	44/50	50.8 (45)	97	45/50	47.1 (48)	90	48/50
78-7	52.4 (45)	45/50	52.0 (43)	99	43/50	51.8 (45)	99	45/50	47.8 (48)	91	48/50
82-7	52.0 (43)	43/50	51.9 (42)	100	42/50	52.0 (44)	100	44/50	47.5 (47)	91	47/50
86-7	50.8 (41)	41/50	52.4 (41)	103	41/50	51.3 (44)	101	44/50	47.8 (46)	94	46/50
90-7	51.4 (37)	37/50	52.4 (39)	102	39/50	49.5 (43)	96	43/50	47.0 (46)	91	46/50
94-7	51.6 (32)	32/50	51.0 (38)	99	38/50	49.5 (40)	96	40/50	45.7 (45)	89	45/50
98-7	51.7 (28)	28/50	48.9 (36)	95	36/50	48.3 (38)	93	38/50	44.4 (44)	86	44/50
102-7	49.5 (27)	27/50	47.8 (35)	97	35/50	46.8 (34)	95	34/50	43.3 (40)	87	40/50
104-7	49.4 (24)	24/50	47.9 (32)	97	32/50	46.3 (31)	94	31/50	43.0 (39)	87	39/50

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

TABLE C 2

BODY WEIGHT CHANGES AND

SURVIVAL ANIMAL NUMBERS: FEMALE

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

MEAN BODY WEIGHTS AND SURVIVAL

Week-Day on Study	Control Av. Wt.	Control No. of Surviv. <50>	625 ppm Av. Wt.	625 ppm % of cont. <50>	625 ppm No. of Surviv.	1250 ppm Av. Wt.	1250 ppm % of cont. <50>	1250 ppm No. of Surviv.	2500 ppm Av. Wt.	2500 ppm % of cont. <50>	2500 ppm No. of Surviv.
0-0	20.1 (50)	50/50	20.1 (50)	100	50/50	20.1 (50)	100	50/50	20.1 (50)	100	50/50
1-7	20.5 (50)	50/50	20.2 (50)	99	50/50	20.1 (50)	98	50/50	19.9 (50)	97	50/50
2-7	21.2 (50)	50/50	20.8 (50)	98	50/50	20.8 (50)	98	50/50	20.5 (50)	97	50/50
3-7	21.7 (50)	50/50	21.6 (50)	100	50/50	21.2 (50)	98	50/50	21.0 (50)	97	50/50
4-7	22.2 (50)	50/50	21.9 (50)	99	50/50	21.8 (50)	98	50/50	21.7 (50)	98	50/50
5-7	22.7 (50)	50/50	22.5 (50)	99	50/50	22.3 (50)	98	50/50	22.1 (50)	97	50/50
6-7	23.2 (50)	50/50	23.3 (50)	100	50/50	22.7 (50)	98	50/50	22.6 (50)	97	50/50
7-7	23.8 (50)	50/50	23.6 (50)	99	50/50	23.2 (50)	97	50/50	23.1 (50)	97	50/50
8-7	24.4 (50)	50/50	24.2 (50)	99	50/50	23.8 (50)	98	50/50	23.7 (50)	97	50/50
9-7	24.6 (50)	50/50	24.4 (50)	99	50/50	24.1 (50)	98	50/50	23.9 (50)	97	50/50
10-7	24.9 (50)	50/50	24.8 (50)	100	50/50	24.5 (50)	98	50/50	24.1 (50)	97	50/50
11-7	24.8 (50)	50/50	24.7 (50)	100	50/50	24.2 (50)	98	50/50	24.2 (50)	98	50/50
12-7	25.3 (50)	50/50	25.0 (50)	99	50/50	24.6 (50)	97	50/50	24.4 (50)	96	50/50
13-7	25.8 (50)	50/50	25.4 (50)	98	50/50	25.1 (50)	97	50/50	25.0 (50)	97	50/50
14-7	26.0 (50)	50/50	25.9 (50)	100	50/50	25.8 (50)	99	50/50	25.2 (50)	97	50/50
18-7	26.6 (50)	50/50	27.2 (50)	102	50/50	26.3 (50)	99	50/50	26.0 (50)	98	50/50
22-7	28.6 (49)	49/50	28.7 (50)	100	50/50	28.1 (50)	98	50/50	27.1 (50)	95	50/50
26-7	29.3 (49)	49/50	29.6 (50)	101	50/50	28.8 (50)	98	50/50	27.5 (50)	94	50/50
30-7	30.5 (49)	49/50	30.5 (50)	100	50/50	30.1 (50)	99	50/50	28.4 (50)	93	50/50
34-7	32.1 (49)	49/50	31.7 (50)	99	50/50	31.0 (50)	97	50/50	29.3 (50)	91	50/50
38-7	33.3 (49)	49/50	33.0 (50)	99	50/50	31.7 (50)	95	50/50	30.3 (50)	91	50/50
42-7	34.0 (49)	49/50	33.9 (50)	100	50/50	32.5 (50)	96	50/50	30.9 (50)	91	50/50
46-7	34.9 (49)	49/50	34.5 (50)	99	50/50	32.9 (50)	94	50/50	31.5 (50)	90	50/50
50-7	35.4 (49)	49/50	35.5 (50)	100	50/50	33.6 (50)	95	50/50	32.1 (50)	91	50/50
54-7	36.6 (49)	49/50	36.3 (49)	99	49/50	33.9 (50)	93	50/50	32.7 (50)	89	50/50
58-7	37.3 (49)	49/50	37.1 (49)	99	49/50	34.7 (49)	93	49/50	33.0 (50)	88	50/50
62-7	37.1 (47)	47/50	36.9 (48)	99	48/50	34.3 (48)	92	48/50	32.7 (50)	88	50/50
66-7	36.8 (46)	46/50	36.6 (48)	99	48/50	34.5 (48)	94	48/50	32.4 (50)	88	50/50
70-7	37.1 (41)	41/50	36.3 (48)	98	48/50	34.3 (46)	92	46/50	32.0 (50)	86	50/50
74-7	37.6 (39)	39/50	36.8 (47)	98	47/50	35.0 (45)	93	45/50	32.1 (48)	85	48/50
78-7	38.2 (39)	39/50	37.5 (47)	98	47/50	35.4 (42)	93	42/50	32.5 (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 (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
102-7	36.3 (25)	25/50	34.8 (24)	96	24/50	33.7 (33)	93	33/50	30.8 (39)	85	39/50
104-7	37.0 (24)	24/50	34.5 (21)	93	21/50	34.4 (33)	93	33/50	30.5 (38)	82	38/50

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

TABLE C 3

BODY WEIGHT CHANGES: MALE

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

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7
Control	24.2± 0.7	25.1± 0.9	25.9± 0.9	26.6± 1.1	27.3± 1.3	28.3± 1.4	29.0± 1.5
625 ppm	24.2± 0.7	25.0± 0.7	25.7± 1.0	26.5± 1.1	27.5± 1.1	28.4± 1.2	29.2± 1.2
1250 ppm	24.2± 0.7	24.9± 0.9	25.7± 0.9	26.4± 1.0	27.4± 1.1	28.2± 1.2	28.9± 1.3
2500 ppm	24.2± 0.7	24.2± 1.0**	24.8± 1.4**	25.5± 1.3**	26.4± 1.5**	27.1± 1.5**	27.4± 1.8**

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

(HAN260)

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

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 7-7	8-7	9-7	10-7	11-7	12-7	13-7
Control	30.0± 1.6	30.8± 1.7	31.5± 1.9	32.0± 2.0	32.6± 2.1	33.7± 2.2	34.5± 2.4
625 ppm	30.1± 1.4	30.8± 1.5	31.4± 1.7	32.0± 1.7	32.6± 1.7	33.6± 1.9	34.4± 2.0
1250 ppm	29.6± 1.5	30.3± 1.6	30.9± 1.8	31.6± 2.0	32.2± 2.1	33.3± 2.3	34.1± 2.4
2500 ppm	28.1± 2.1**	28.7± 2.2**	29.2± 1.9**	30.1± 2.1**	30.5± 2.2**	31.3± 2.3**	32.1± 2.5**

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

(HAN260)

BAIS4

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

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 14-7	18-7	22-7	26-7	30-7	34-7	38-7
Control	35.3± 2.5	37.9± 2.6	40.1± 3.1	42.0± 3.4	44.0± 3.7	45.5± 3.6	47.2± 3.5
625 ppm	34.9± 2.0	37.7± 2.6	39.7± 2.8	41.5± 3.1	43.5± 3.5	45.0± 3.5	46.7± 3.5
1250 ppm	34.8± 2.4	37.1± 2.8	39.0± 3.4	40.7± 3.8	42.5± 4.1	43.7± 4.2*	45.3± 4.2*
2500 ppm	32.8± 2.5**	34.8± 2.7**	36.4± 3.0**	37.9± 3.4**	39.3± 3.6**	40.6± 3.7**	42.3± 3.9**

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

(HAN260)

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

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 42-7	46-7	50-7	54-7	58-7	62-7	66-7
Control	48.5± 3.5	49.6± 3.6	50.5± 3.7	51.0± 3.4	52.2± 3.6	52.0± 3.6	52.2± 3.9
625 ppm	48.1± 3.6	48.8± 3.6	49.5± 3.7	49.9± 4.4	50.6± 5.4	51.7± 3.5	51.9± 3.3
1250 ppm	46.3± 4.0*	47.0± 4.2**	48.0± 4.7**	48.8± 5.0*	49.8± 5.1*	49.7± 5.4*	50.0± 5.0*
2500 ppm	43.4± 4.1**	44.2± 4.2**	44.8± 4.5**	45.4± 5.5**	46.0± 5.5**	46.2± 5.5**	46.7± 5.7**

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

(HAN260)

BAIS4

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

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 70-7	74-7	78-7	82-7	86-7	90-7	94-7
Control	52.2± 4.6	52.6± 4.7	52.4± 5.5	52.0± 5.5	50.8± 7.6	51.4± 7.3	51.6± 7.7
625 ppm	51.6± 3.6	51.8± 4.2	52.0± 5.0	51.9± 5.5	52.4± 5.3	52.4± 5.1	51.0± 5.7
1250 ppm	50.2± 5.5	50.8± 6.1	51.8± 6.0	52.0± 5.9	51.3± 6.4	49.5± 7.9	49.5± 7.2
2500 ppm	46.9± 4.9**	47.1± 5.3**	47.8± 5.6**	47.5± 6.0**	47.8± 6.3	47.0± 6.5*	45.7± 6.7**

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

(HAN260)

BAIS4

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

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 98-7	102-7	104-7
Control	51.7± 6.4	49.5± 7.5	49.4± 7.6
625 ppm	48.9± 6.6	47.8± 6.4	47.9± 6.2
1250 ppm	48.3± 7.9	46.8± 8.2	46.3± 9.3
2500 ppm	44.4± 7.5**	43.3± 7.6**	43.0± 7.8**

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

(HAN260)

TABLE C 4

BODY WEIGHT CHANGES: FEMALE

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

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7
Control	20.1± 0.8	20.5± 0.8	21.2± 1.1	21.7± 1.1	22.2± 1.3	22.7± 1.4	23.2± 1.3
625 ppm	20.1± 0.8	20.2± 0.8	20.8± 1.0	21.6± 1.1	21.9± 1.1	22.5± 1.1	23.3± 1.3
1250 ppm	20.1± 0.8	20.1± 0.9*	20.8± 0.9	21.2± 1.0	21.8± 1.0	22.3± 1.1	22.7± 1.1
2500 ppm	20.1± 0.8	19.9± 0.8**	20.5± 0.8**	21.0± 0.9**	21.7± 1.0	22.1± 1.0*	22.6± 1.2

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

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

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 7-7	8-7	9-7	10-7	11-7	12-7	13-7
Control	23.8± 1.5	24.4± 1.7	24.6± 2.2	24.9± 2.0	24.8± 2.1	25.3± 2.3	25.8± 2.7
625 ppm	23.6± 1.4	24.2± 1.5	24.4± 1.5	24.8± 1.7	24.7± 1.6	25.0± 1.7	25.4± 2.0
1250 ppm	23.2± 1.2*	23.8± 1.1	24.1± 1.3	24.5± 1.3	24.2± 1.5	24.6± 1.5	25.1± 1.6
2500 ppm	23.1± 1.2*	23.7± 1.3	23.9± 1.4	24.1± 1.4*	24.2± 1.5	24.4± 1.7*	25.0± 1.7

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

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

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 14-7	18-7	22-7	26-7	30-7	34-7	38-7
Control	26.0± 2.7	26.6± 2.9	28.6± 3.8	29.3± 3.9	30.5± 4.7	32.1± 5.1	33.3± 4.9
625 ppm	25.9± 2.1	27.2± 2.1	28.7± 2.7	29.6± 3.4	30.5± 3.5	31.7± 3.9	33.0± 4.4
1250 ppm	25.8± 1.7	26.3± 2.0	28.1± 2.3	28.8± 2.8	30.1± 3.2	31.0± 3.5	31.7± 3.4
2500 ppm	25.2± 1.9	26.0± 2.1	27.1± 2.3*	27.5± 2.6*	28.4± 2.7*	29.3± 2.8**	30.3± 2.8**

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

(HAN260)

BAIS4

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

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 42-7	46-7	50-7	54-7	58-7	62-7	66-7
Control	34.0± 5.9	34.9± 5.9	35.4± 6.3	36.6± 6.5	37.3± 5.9	37.1± 4.8	36.8± 4.9
625 ppm	33.9± 4.1	34.5± 4.3	35.5± 4.6	36.3± 4.6	37.1± 4.8	36.9± 4.8	36.6± 5.2
1250 ppm	32.5± 3.6	32.9± 3.7	33.6± 4.1	33.9± 4.2	34.7± 4.8	34.3± 4.5**	34.5± 4.8
2500 ppm	30.9± 3.0**	31.5± 3.1**	32.1± 3.5**	32.7± 3.3**	33.0± 3.4**	32.7± 3.4**	32.4± 3.2**

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

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

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 70-7	74-7	78-7	82-7	86-7	90-7	94-7
Control	37.1± 5.2	37.6± 4.9	38.2± 4.9	38.0± 4.9	37.8± 4.6	37.8± 5.4	37.3± 6.2
625 ppm	36.3± 5.3	36.8± 5.0	37.5± 5.3	37.0± 5.8	37.3± 5.6	36.6± 6.3	35.7± 6.8
1250 ppm	34.3± 4.7*	35.0± 5.5*	35.4± 5.3*	35.0± 5.6*	35.2± 5.8	34.7± 5.8*	33.9± 6.0*
2500 ppm	32.0± 3.9**	32.1± 4.1**	32.5± 4.7**	32.4± 4.5**	32.7± 5.1**	32.1± 4.5**	31.2± 4.7**

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

(HAN260)

BAIS4

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

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 98-7	102-7	104-7
Control	37.1± 5.8	36.3± 6.3	37.0± 7.0
625 ppm	35.5± 6.4	34.8± 6.0	34.5± 5.7
1250 ppm	33.9± 5.9	33.7± 5.8	34.4± 7.3
2500 ppm	30.4± 4.6**	30.8± 4.3**	30.5± 4.6**

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

(HAN260)

TABLE D 1

FOOD CONSUMPTION CHANGES AND SURVIVAL ANIMAL NUMBERS: MALE

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

MEAN FOOD CONSUMPTION(FC) AND SURVIVAL

Week-Day on Study	Control Av. FC.	Control No. of Surviv. <50>	625 ppm Av. FC.	625 ppm % of cont. <50>	625 ppm No. of Surviv.	1250 ppm Av. FC.	1250 ppm % of cont. <50>	1250 ppm No. of Surviv.	2500 ppm Av. FC.	2500 ppm % of cont. <50>	2500 ppm No. of Surviv.
1-7	4.0 (50)	50/50	3.9 (50)	98	50/50	3.9 (50)	98	50/50	3.5 (50)	88	50/50
2-7	3.9 (50)	50/50	3.8 (50)	97	50/50	3.8 (50)	97	50/50	3.7 (50)	95	50/50
3-7	3.8 (50)	50/50	3.7 (49)	97	49/50	3.7 (50)	97	50/50	3.6 (50)	95	50/50
4-7	3.8 (50)	50/50	3.8 (49)	100	49/50	3.8 (50)	100	50/50	3.7 (50)	97	50/50
5-7	3.9 (50)	50/50	3.8 (49)	97	49/50	3.8 (50)	97	50/50	3.7 (50)	95	50/50
6-7	3.9 (50)	50/50	3.8 (49)	97	49/50	3.8 (50)	97	50/50	3.7 (50)	95	50/50
7-7	4.0 (50)	50/50	3.9 (49)	98	49/50	3.9 (50)	98	50/50	3.7 (50)	93	50/50
8-7	4.0 (50)	50/50	3.9 (49)	98	49/50	3.9 (50)	98	50/50	3.8 (50)	95	50/50
9-7	4.2 (50)	50/50	4.0 (49)	95	49/50	4.0 (50)	95	50/50	3.9 (49)	93	49/50
10-7	4.2 (50)	50/50	4.1 (49)	98	49/50	4.1 (50)	98	50/50	3.9 (49)	93	49/50
11-7	4.2 (50)	50/50	4.1 (49)	98	49/50	4.1 (50)	98	50/50	4.0 (49)	95	49/50
12-7	4.2 (50)	50/50	4.1 (49)	98	49/50	4.1 (50)	98	50/50	4.0 (49)	95	49/50
13-7	4.2 (50)	50/50	4.1 (49)	98	49/50	4.1 (50)	98	50/50	4.0 (49)	95	49/50
14-7	4.2 (50)	50/50	4.1 (49)	98	49/50	4.2 (50)	100	50/50	4.1 (49)	98	49/50
18-7	4.2 (50)	50/50	4.2 (49)	100	49/50	4.1 (50)	98	50/50	4.0 (49)	95	49/50
22-7	4.3 (50)	50/50	4.1 (49)	95	49/50	4.1 (50)	95	50/50	4.0 (49)	93	49/50
26-7	4.2 (50)	50/50	4.1 (49)	98	49/50	4.0 (50)	95	50/50	3.9 (49)	93	49/50
30-7	4.4 (50)	50/50	4.2 (48)	95	48/50	4.1 (50)	93	50/50	4.0 (49)	91	49/50
34-7	4.5 (50)	50/50	4.5 (48)	100	48/50	4.4 (50)	98	50/50	4.3 (49)	96	49/50
38-7	4.5 (50)	50/50	4.5 (48)	100	48/50	4.4 (50)	98	50/50	4.4 (49)	98	49/50
42-7	4.6 (49)	49/50	4.6 (48)	100	48/50	4.5 (50)	98	50/50	4.4 (49)	96	49/50
46-7	4.7 (49)	49/50	4.6 (48)	98	48/50	4.5 (50)	96	50/50	4.4 (49)	94	49/50
50-7	4.8 (49)	49/50	4.7 (47)	98	47/50	4.7 (50)	98	50/50	4.5 (49)	94	49/50
54-7	4.6 (49)	49/50	4.7 (47)	102	47/50	4.6 (49)	100	49/50	4.6 (49)	100	49/50
58-7	5.0 (48)	48/50	4.9 (47)	98	47/50	4.8 (49)	96	49/50	4.6 (49)	92	49/50
62-7	4.7 (48)	48/50	4.7 (45)	100	45/50	4.6 (48)	98	48/50	4.5 (49)	96	49/50
66-7	4.7 (48)	48/50	4.7 (44)	100	44/50	4.5 (47)	96	47/50	4.4 (49)	94	49/50
70-7	4.9 (47)	47/50	4.8 (44)	98	44/50	4.7 (47)	96	47/50	4.5 (48)	92	48/50
74-7	4.8 (47)	47/50	4.6 (44)	96	44/50	4.6 (45)	96	45/50	4.5 (48)	94	48/50
78-7	4.8 (45)	45/50	4.7 (43)	98	43/50	4.7 (45)	98	45/50	4.4 (48)	92	48/50
82-7	4.7 (43)	43/50	4.7 (42)	100	42/50	4.6 (44)	98	44/50	4.4 (47)	94	47/50
86-7	4.6 (41)	41/50	4.9 (41)	107	41/50	4.7 (44)	102	44/50	4.6 (46)	100	46/50
90-7	4.8 (37)	37/50	4.7 (39)	98	39/50	4.7 (43)	98	43/50	4.6 (46)	96	46/50
94-7	4.7 (32)	32/50	4.6 (38)	98	38/50	4.7 (40)	100	40/50	4.4 (45)	94	45/50
98-7	4.9 (28)	28/50	4.9 (36)	100	36/50	4.7 (38)	96	38/50	4.5 (44)	92	44/50
102-7	4.8 (27)	27/50	4.9 (35)	102	35/50	4.7 (34)	98	34/50	4.5 (40)	94	40/50
104-7	4.8 (24)	24/50	4.8 (32)	100	32/50	4.7 (31)	98	31/50	4.4 (39)	92	39/50

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

TABLE D 2

FOOD CONSUMPTION CHANGES AND SURVIVAL ANIMAL NUMBERS: FEMALE

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

MEAN FOOD CONSUMPTION(FC) AND SURVIVAL

Week-Day on Study	Control Av. FC.	Control No. of Surviv. <50>	625 ppm Av. FC.	625 ppm % of cont. <50>	625 ppm No. of Surviv.	1250 ppm Av. FC.	1250 ppm % of cont. <50>	1250 ppm No. of Surviv.	2500 ppm Av. FC.	2500 ppm % of cont. <50>	2500 ppm No. of Surviv.
1-7	3.6 (50)	50/50	3.5 (50)	97	50/50	3.5 (50)	97	50/50	3.3 (50)	92	50/50
2-7	3.4 (50)	50/50	3.4 (50)	100	50/50	3.4 (50)	100	50/50	3.4 (50)	100	50/50
3-7	3.4 (50)	50/50	3.4 (50)	100	50/50	3.3 (50)	97	50/50	3.3 (50)	97	50/50
4-7	3.5 (50)	50/50	3.5 (50)	100	50/50	3.4 (50)	97	50/50	3.5 (50)	100	50/50
5-7	3.5 (50)	50/50	3.5 (50)	100	50/50	3.5 (49)	100	50/50	3.5 (50)	100	50/50
6-7	3.6 (50)	50/50	3.6 (50)	100	50/50	3.5 (50)	97	50/50	3.6 (50)	100	50/50
7-7	3.7 (50)	50/50	3.6 (50)	97	50/50	3.6 (50)	97	50/50	3.7 (50)	100	50/50
8-7	3.8 (50)	50/50	3.7 (50)	97	50/50	3.8 (50)	100	50/50	3.8 (50)	100	50/50
9-7	3.9 (50)	50/50	3.8 (50)	97	50/50	3.9 (50)	100	50/50	3.8 (50)	97	50/50
10-7	3.8 (50)	50/50	3.8 (50)	100	50/50	3.8 (50)	100	50/50	3.8 (50)	100	50/50
11-7	3.9 (50)	50/50	3.8 (50)	97	50/50	3.8 (50)	97	50/50	3.9 (50)	100	50/50
12-7	3.8 (50)	50/50	3.7 (50)	97	50/50	3.7 (50)	97	50/50	3.8 (50)	100	50/50
13-7	3.9 (50)	50/50	3.8 (50)	97	50/50	3.8 (50)	97	50/50	3.9 (50)	100	50/50
14-7	3.8 (50)	50/50	3.8 (50)	100	50/50	3.8 (50)	100	50/50	3.8 (50)	100	50/50
18-7	3.8 (50)	50/50	3.7 (50)	97	50/50	3.8 (50)	100	50/50	3.8 (50)	100	50/50
22-7	3.9 (49)	49/50	3.8 (50)	97	50/50	3.8 (50)	97	50/50	3.8 (50)	97	50/50
26-7	3.7 (49)	49/50	3.7 (50)	100	50/50	3.6 (50)	97	50/50	3.5 (50)	95	50/50
30-7	3.8 (49)	49/50	3.6 (50)	95	50/50	3.7 (50)	97	50/50	3.6 (50)	95	50/50
34-7	4.1 (49)	49/50	4.0 (50)	98	50/50	4.0 (50)	98	50/50	4.0 (50)	98	50/50
38-7	4.3 (49)	49/50	4.1 (50)	95	50/50	4.1 (50)	95	50/50	4.0 (50)	93	50/50
42-7	4.2 (49)	49/50	4.2 (50)	100	50/50	4.2 (50)	100	50/50	4.2 (50)	100	50/50
46-7	4.2 (49)	49/50	4.2 (50)	100	50/50	4.1 (50)	98	50/50	4.2 (50)	100	50/50
50-7	4.2 (49)	49/50	4.4 (50)	105	50/50	4.1 (50)	98	50/50	4.1 (50)	98	50/50
54-7	4.2 (49)	49/50	4.2 (49)	100	49/50	4.1 (50)	98	50/50	4.1 (50)	98	50/50
58-7	4.1 (49)	49/50	4.2 (49)	102	49/50	4.1 (49)	100	49/50	4.1 (50)	100	50/50
62-7	4.2 (47)	47/50	4.1 (48)	98	48/50	3.9 (48)	93	48/50	4.0 (50)	95	50/50
66-7	3.9 (46)	46/50	3.8 (48)	97	48/50	3.8 (48)	97	48/50	3.8 (50)	97	50/50
70-7	4.0 (41)	41/50	3.9 (48)	98	48/50	3.8 (46)	95	46/50	3.8 (50)	95	50/50
74-7	4.1 (39)	39/50	4.0 (47)	98	47/50	3.7 (45)	90	45/50	3.7 (48)	90	48/50
78-7	4.2 (39)	39/50	4.1 (47)	98	47/50	4.0 (42)	95	42/50	3.8 (48)	90	48/50
82-7	4.2 (38)	38/50	4.3 (47)	102	47/50	4.0 (42)	95	42/50	3.9 (48)	93	48/50
86-7	4.3 (38)	38/50	4.2 (43)	98	43/50	3.9 (41)	91	41/50	3.8 (47)	88	47/50
90-7	4.2 (37)	37/50	4.2 (39)	100	39/50	3.9 (40)	93	40/50	3.9 (45)	93	45/50
94-7	4.0 (33)	33/50	4.0 (38)	100	38/50	3.9 (38)	98	38/50	3.9 (43)	98	43/50
98-7	4.4 (31)	31/50	4.4 (33)	100	33/50	4.3 (35)	98	35/50	3.9 (42)	89	42/50
102-7	4.2 (25)	25/50	4.3 (24)	102	24/50	4.1 (33)	98	33/50	4.0 (39)	95	39/50
104-7	4.3 (24)	24/50	4.5 (21)	105	21/50	4.5 (33)	105	33/50	4.1 (38)	95	38/50

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

TABLE D 3

FOOD CONSUMPTION CHANGES: MALE

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

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 1-7 (7)	2-7 (7)	3-7 (7)	4-7 (7)	5-7 (7)	6-7 (7)	7-7 (7)
Control	4.0± 0.3	3.9± 0.2	3.8± 0.3	3.8± 0.3	3.9± 0.3	3.9± 0.2	4.0± 0.3
625 ppm	3.9± 0.2	3.8± 0.4	3.7± 0.4	3.8± 0.2	3.8± 0.2	3.8± 0.3	3.9± 0.2
1250 ppm	3.9± 0.3*	3.8± 0.3	3.7± 0.3	3.8± 0.4	3.8± 0.3	3.8± 0.2	3.9± 0.3*
2500 ppm	3.5± 0.2**	3.7± 0.3*	3.6± 0.3	3.7± 0.3**	3.7± 0.3**	3.7± 0.3**	3.7± 0.3**

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

(HAN260)

BAIS4

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

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 8-7 (7)	9-7 (7)	10-7 (7)	11-7 (7)	12-7 (7)	13-7 (7)	14-7 (7)
Control	4.0± 0.3	4.2± 0.3	4.2± 0.3	4.2± 0.3	4.2± 0.3	4.2± 0.3	4.2± 0.3
625 ppm	3.9± 0.3	4.0± 0.2	4.1± 0.3	4.1± 0.3	4.1± 0.3	4.1± 0.3	4.1± 0.3
1250 ppm	3.9± 0.3	4.0± 0.3	4.1± 0.3	4.1± 0.3	4.1± 0.3*	4.1± 0.3	4.2± 0.3
2500 ppm	3.8± 0.3**	3.9± 0.2**	3.9± 0.3**	4.0± 0.3**	4.0± 0.3**	4.0± 0.3**	4.1± 0.3

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

(HAN260)

BAIS 4

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

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 18-7 (7)	22-7 (7)	26-7 (7)	30-7 (7)	34-7 (7)	38-7 (7)	42-7 (7)
Control	4.2± 0.3	4.3± 0.3	4.2± 0.3	4.4± 0.3	4.5± 0.3	4.5± 0.3	4.6± 0.3
625 ppm	4.2± 0.3	4.1± 0.3*	4.1± 0.2*	4.2± 0.3	4.5± 0.3	4.5± 0.3	4.6± 0.3
1250 ppm	4.1± 0.3	4.1± 0.3**	4.0± 0.3**	4.1± 0.4**	4.4± 0.4	4.4± 0.3	4.5± 0.4*
2500 ppm	4.0± 0.2**	4.0± 0.3**	3.9± 0.3**	4.0± 0.3**	4.3± 0.3**	4.4± 0.3*	4.4± 0.3**

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

(HAN260)

BAIS4

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

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 46-7 (7)	50-7 (7)	54-7 (7)	58-7 (7)	62-7 (7)	66-7 (7)	70-7 (7)
Control	4.7± 0.3	4.8± 0.4	4.6± 0.4	5.0± 0.3	4.7± 0.3	4.7± 0.5	4.9± 0.4
625 ppm	4.6± 0.3	4.7± 0.3	4.7± 0.3	4.9± 0.4	4.7± 0.3	4.7± 0.3	4.8± 0.3
1250 ppm	4.5± 0.4**	4.7± 0.5	4.6± 0.4	4.8± 0.4	4.6± 0.4	4.5± 0.6	4.7± 0.4*
2500 ppm	4.4± 0.3**	4.5± 0.4**	4.6± 0.4	4.6± 0.4**	4.5± 0.4**	4.4± 0.4**	4.5± 0.4**

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

(HAN260)

BAIS4

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

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 74-7 (7)	78-7 (7)	82-7 (7)	86-7 (7)	90-7 (7)	94-7 (7)	98-7 (7)
Control	4.8± 0.4	4.8± 0.7	4.7± 0.5	4.6± 1.1	4.8± 0.5	4.7± 0.9	4.9± 0.5
625 ppm	4.6± 0.4	4.7± 0.4	4.7± 0.4	4.9± 0.5	4.7± 0.7	4.6± 0.4	4.9± 0.5
1250 ppm	4.6± 0.4*	4.7± 0.4	4.6± 0.4	4.7± 0.5	4.7± 0.5	4.7± 0.7	4.7± 0.7
2500 ppm	4.5± 0.3**	4.4± 0.4**	4.4± 0.5**	4.6± 0.5	4.6± 0.5*	4.4± 0.5*	4.5± 0.6*

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

(HAN260)

BAIS4

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

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 102-7 (7)	104-7 (7)
Control	4.8± 0.5	4.8± 0.7
625 ppm	4.9± 0.8	4.8± 0.6
1250 ppm	4.7± 0.8	4.7± 0.7
2500 ppm	4.5± 0.6	4.4± 0.4**

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

(HAN260)

BAIS4

TABLE D 4

FOOD CONSUMPTION CHANGES: FEMALE

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

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 1-7 (7)	2-7 (7)	3-7 (7)	4-7 (7)	5-7 (7)	6-7 (7)	7-7 (7)
Control	3.6± 0.3	3.4± 0.3	3.4± 0.3	3.5± 0.4	3.5± 0.3	3.6± 0.3	3.7± 0.3
625 ppm	3.5± 0.2	3.4± 0.2	3.4± 0.2	3.5± 0.2	3.5± 0.2	3.6± 0.3	3.6± 0.3
1250 ppm	3.5± 0.3	3.4± 0.3	3.3± 0.2	3.4± 0.2	3.5± 0.2	3.5± 0.2	3.6± 0.3
2500 ppm	3.3± 0.3**	3.4± 0.2	3.3± 0.2	3.5± 0.2	3.5± 0.2	3.6± 0.2	3.7± 0.2

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

(HAN260)

BAIS4

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

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 8-7 (7)	9-7 (7)	10-7 (7)	11-7 (7)	12-7 (7)	13-7 (7)	14-7 (7)
Control	3.8± 0.3	3.9± 0.4	3.8± 0.3	3.9± 0.3	3.8± 0.4	3.9± 0.4	3.8± 0.4
625 ppm	3.7± 0.3	3.8± 0.3	3.8± 0.3	3.8± 0.3	3.7± 0.3	3.8± 0.3	3.8± 0.3
1250 ppm	3.8± 0.2	3.9± 0.2	3.8± 0.3	3.8± 0.3	3.7± 0.3	3.8± 0.2	3.8± 0.3
2500 ppm	3.8± 0.3	3.8± 0.3	3.8± 0.3	3.9± 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[Crj:BDF1]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 18-7(7)	22-7(7)	26-7(7)	30-7(7)	34-7(7)	38-7(7)	42-7(7)
Control	3.8± 0.3	3.9± 0.4	3.7± 0.4	3.8± 0.4	4.1± 0.5	4.3± 0.4	4.2± 0.5
625 ppm	3.7± 0.4	3.8± 0.4	3.7± 0.4	3.6± 0.5*	4.0± 0.5	4.1± 0.5	4.2± 0.4
1250 ppm	3.8± 0.3	3.8± 0.3	3.6± 0.3	3.7± 0.4	4.0± 0.4	4.1± 0.4	4.2± 0.6
2500 ppm	3.8± 0.3	3.8± 0.3	3.5± 0.3**	3.6± 0.4	4.0± 0.3	4.0± 0.4	4.2± 0.3

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

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

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 46-7 (7)	50-7 (7)	54-7 (7)	58-7 (7)	62-7 (7)	66-7 (7)	70-7 (7)
Control	4.2± 0.5	4.2± 0.6	4.2± 0.5	4.1± 0.4	4.2± 0.6	3.9± 0.5	4.0± 0.6
625 ppm	4.2± 0.4	4.4± 0.7	4.2± 0.6	4.2± 0.5	4.1± 0.5	3.8± 0.6	3.9± 0.6
1250 ppm	4.1± 0.4	4.1± 0.5	4.1± 0.6	4.1± 0.6	3.9± 0.5**	3.8± 0.5	3.8± 0.4
2500 ppm	4.2± 0.5	4.1± 0.4	4.1± 0.4	4.1± 0.5	4.0± 0.4	3.8± 0.4	3.8± 0.4

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

(HAN260)

BAIS4

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

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 74-7 (7)	78-7 (7)	82-7 (7)	86-7 (7)	90-7 (7)	94-7 (7)	98-7 (7)
Control	4.1± 0.6	4.2± 0.5	4.2± 0.5	4.3± 0.7	4.2± 0.6	4.0± 0.8	4.4± 1.0
625 ppm	4.0± 0.4	4.1± 0.7	4.3± 1.1	4.2± 0.7	4.2± 0.7	4.0± 0.8	4.4± 0.9
1250 ppm	3.7± 0.7**	4.0± 0.5	4.0± 0.6	3.9± 0.6*	3.9± 0.6	3.9± 0.6	4.3± 0.6
2500 ppm	3.7± 0.5*	3.8± 0.5**	3.9± 0.4*	3.8± 0.5**	3.9± 0.5	3.9± 0.7	3.9± 0.8**

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

(HAN260)

BAIS4

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

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 102-7 (7)	104-7 (7)
Control	4.2± 0.7	4.3± 0.6
625 ppm	4.3± 1.2	4.5± 0.7
1250 ppm	4.1± 0.6	4.5± 0.8
2500 ppm	4.0± 0.5	4.1± 0.6

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

(HAN260)

TABLE E 1

WATER CONSUMPTION CHANGES AND

SURVIVAL ANIMAL NUMBERS: MALE

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

MEAN WATER CONSUMPTION(WC) AND SURVIVAL

Week-Day on Study	Control Av. WC.	Control No. of Surviv. <50>	625 ppm Av. WC.	625 ppm % of cont. <50>	625 ppm No. of Surviv.	1250 ppm Av. WC.	1250 ppm % of cont. <50>	1250 ppm No. of Surviv.	2500 ppm Av. WC.	2500 ppm % of cont. <50>	2500 ppm No. of Surviv.
1-7	4.7 (50)	50/50	4.1 (50)	87	50/50	3.4 (50)	72	50/50	2.7 (50)	57	50/50
2-7	4.4 (49)	50/50	3.7 (50)	84	50/50	3.4 (50)	77	50/50	2.6 (50)	59	50/50
3-7	4.3 (48)	50/50	3.9 (49)	91	49/50	3.4 (50)	79	50/50	2.7 (50)	63	50/50
4-7	4.2 (48)	50/50	3.9 (49)	93	49/50	3.3 (50)	79	50/50	2.7 (50)	64	50/50
5-7	4.4 (50)	50/50	3.9 (49)	89	49/50	3.4 (50)	77	50/50	2.8 (50)	64	50/50
6-7	4.2 (50)	50/50	3.8 (49)	90	49/50	3.4 (50)	81	50/50	2.8 (50)	67	50/50
7-7	4.1 (50)	50/50	3.7 (49)	90	49/50	3.5 (50)	85	50/50	2.9 (50)	71	50/50
8-7	4.0 (50)	50/50	3.7 (49)	93	49/50	3.3 (50)	83	50/50	2.8 (50)	70	50/50
9-7	4.1 (50)	50/50	3.7 (49)	90	49/50	3.5 (50)	85	50/50	2.9 (49)	71	49/50
10-7	4.1 (50)	50/50	3.7 (49)	90	49/50	3.5 (50)	85	50/50	2.9 (49)	71	49/50
11-7	4.0 (50)	50/50	3.8 (49)	95	49/50	3.4 (50)	85	50/50	3.0 (49)	75	49/50
12-7	3.9 (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)	77	49/50
14-7	3.8 (50)	50/50	3.5 (49)	92	49/50	3.3 (50)	87	50/50	2.8 (49)	74	49/50
18-7	3.5 (50)	50/50	3.4 (49)	97	49/50	3.2 (50)	91	50/50	2.7 (49)	77	49/50
22-7	3.8 (50)	50/50	3.5 (49)	92	49/50	3.3 (50)	87	50/50	2.8 (49)	74	49/50
26-7	3.6 (50)	50/50	3.4 (49)	94	49/50	3.4 (50)	94	50/50	2.8 (49)	78	49/50
30-7	3.5 (50)	50/50	3.4 (48)	97	48/50	3.2 (50)	91	50/50	2.8 (49)	80	49/50
34-7	3.7 (50)	50/50	3.6 (48)	97	48/50	3.4 (50)	92	50/50	3.0 (49)	81	49/50
38-7	3.7 (50)	50/50	3.6 (48)	97	48/50	3.4 (50)	92	50/50	3.0 (49)	81	49/50
42-7	3.8 (49)	49/50	3.7 (48)	97	48/50	3.5 (50)	92	50/50	3.2 (49)	84	49/50
46-7	3.9 (49)	49/50	3.8 (48)	97	48/50	3.6 (50)	92	50/50	3.1 (49)	79	49/50
50-7	3.8 (49)	49/50	3.7 (47)	97	47/50	3.5 (50)	92	50/50	3.1 (49)	82	49/50
54-7	4.0 (49)	49/50	4.0 (47)	100	47/50	3.6 (49)	90	49/50	3.2 (49)	80	49/50
58-7	4.1 (48)	48/50	4.0 (46)	98	47/50	3.7 (49)	90	49/50	3.2 (49)	78	49/50
62-7	4.1 (48)	48/50	4.0 (45)	98	45/50	3.7 (48)	90	48/50	3.2 (49)	78	49/50
66-7	4.3 (48)	48/50	4.3 (44)	100	44/50	4.0 (47)	93	47/50	3.4 (49)	79	49/50
70-7	4.5 (47)	47/50	4.3 (44)	96	44/50	4.3 (47)	96	47/50	3.5 (48)	78	48/50
74-7	4.6 (47)	47/50	4.2 (44)	91	44/50	4.1 (43)	89	45/50	3.6 (48)	78	48/50
78-7	4.7 (42)	45/50	4.4 (42)	94	43/50	4.3 (43)	91	45/50	3.8 (48)	81	48/50
82-7	4.5 (41)	43/50	4.3 (39)	96	42/50	4.2 (43)	93	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
90-7	4.9 (35)	37/50	4.7 (38)	96	39/50	4.5 (41)	92	43/50	4.0 (45)	82	46/50
94-7	4.7 (31)	32/50	4.9 (38)	104	38/50	4.9 (39)	104	40/50	4.0 (44)	85	45/50
98-7	5.0 (26)	28/50	5.1 (31)	102	36/50	4.8 (36)	96	38/50	4.2 (42)	84	44/50
102-7	5.1 (25)	27/50	4.9 (29)	96	35/50	4.4 (29)	86	34/50	4.1 (37)	80	40/50
104-7	5.4 (22)	24/50	5.1 (27)	94	32/50	4.7 (28)	87	31/50	4.2 (36)	78	39/50

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

TABLE E 2

WATER CONSUMPTION CHANGES AND SURVIVAL ANIMAL NUMBERS: FEMALE

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

MEAN WATER CONSUMPTION(WC) AND SURVIVAL

Week-Day on Study	Control Av. WC.	Control No. of Surviv. <50>	625 ppm Av. WC.	625 ppm % of cont. <50>	625 ppm No. of Surviv.	1250 ppm Av. WC.	1250 ppm % of cont. <50>	1250 ppm No. of Surviv.	2500 ppm Av. WC.	2500 ppm % of cont. <50>	2500 ppm No. of Surviv.
1-7	4.3 (50)	50/50	4.0 (50)	93	50/50	3.6 (50)	84	50/50	2.7 (50)	63	50/50
2-7	4.1 (50)	50/50	3.6 (50)	88	50/50	3.4 (50)	83	50/50	2.7 (50)	66	50/50
3-7	4.1 (50)	50/50	3.7 (50)	90	50/50	3.5 (50)	85	50/50	2.8 (50)	68	50/50
4-7	4.0 (50)	50/50	3.6 (50)	90	50/50	3.6 (50)	90	50/50	2.9 (50)	73	50/50
5-7	4.2 (50)	50/50	3.7 (50)	88	50/50	3.7 (50)	88	50/50	3.0 (50)	71	50/50
6-7	4.0 (50)	50/50	3.7 (50)	93	50/50	3.6 (50)	90	50/50	3.0 (50)	75	50/50
7-7	4.1 (50)	50/50	3.7 (50)	90	50/50	3.7 (50)	90	50/50	3.1 (50)	76	50/50
8-7	4.1 (50)	50/50	3.6 (50)	88	50/50	3.6 (50)	88	50/50	3.1 (50)	76	50/50
9-7	4.2 (50)	50/50	3.7 (50)	88	50/50	3.6 (50)	86	50/50	3.1 (50)	74	50/50
10-7	4.1 (50)	50/50	3.7 (50)	90	50/50	3.7 (50)	90	50/50	3.1 (50)	76	50/50
11-7	4.1 (50)	50/50	3.7 (50)	90	50/50	3.7 (50)	90	50/50	3.1 (50)	76	50/50
12-7	4.2 (50)	50/50	3.6 (50)	86	50/50	3.5 (50)	83	50/50	3.1 (50)	74	50/50
13-7	4.2 (50)	50/50	3.7 (50)	88	50/50	3.6 (50)	86	50/50	3.1 (50)	74	50/50
14-7	4.0 (50)	50/50	3.6 (50)	90	50/50	3.6 (50)	90	50/50	3.0 (50)	75	50/50
18-7	3.8 (50)	50/50	3.4 (50)	89	50/50	3.2 (50)	84	50/50	2.9 (50)	76	50/50
22-7	4.1 (49)	49/50	3.5 (50)	85	50/50	3.3 (50)	80	50/50	3.0 (50)	73	50/50
26-7	3.9 (49)	49/50	3.3 (50)	85	50/50	3.1 (50)	79	50/50	2.8 (50)	72	50/50
30-7	3.9 (49)	49/50	3.3 (50)	85	50/50	3.2 (50)	82	50/50	2.8 (50)	72	50/50
34-7	4.1 (49)	49/50	3.4 (50)	83	50/50	3.3 (50)	80	50/50	3.0 (50)	73	50/50
38-7	4.0 (49)	49/50	3.4 (50)	85	50/50	3.3 (50)	83	50/50	2.9 (50)	73	50/50
42-7	4.1 (49)	49/50	3.6 (50)	88	50/50	3.3 (50)	80	50/50	3.0 (50)	73	50/50
46-7	4.1 (49)	49/50	3.6 (50)	88	50/50	3.4 (50)	83	50/50	3.0 (50)	73	50/50
50-7	4.1 (49)	49/50	3.6 (49)	88	50/50	3.2 (50)	78	50/50	2.8 (50)	68	50/50
54-7	4.0 (49)	49/50	3.4 (49)	85	49/50	3.3 (50)	83	50/50	2.9 (50)	73	50/50
58-7	3.9 (49)	49/50	3.5 (49)	90	49/50	3.2 (49)	82	49/50	2.8 (50)	72	50/50
62-7	3.9 (47)	47/50	3.5 (48)	90	48/50	3.2 (47)	82	48/50	2.8 (50)	72	50/50
66-7	3.9 (46)	46/50	3.7 (48)	95	48/50	3.4 (47)	87	48/50	3.0 (50)	77	50/50
70-7	4.0 (41)	41/50	3.5 (48)	88	48/50	3.4 (46)	85	46/50	3.1 (50)	78	50/50
74-7	4.1 (39)	39/50	3.7 (45)	90	47/50	3.5 (44)	85	45/50	3.3 (48)	80	48/50
78-7	4.2 (39)	39/50	3.9 (44)	93	47/50	3.8 (39)	90	42/50	3.2 (45)	76	48/50
82-7	4.2 (37)	38/50	4.1 (43)	98	47/50	4.1 (40)	98	42/50	3.4 (46)	81	48/50
86-7	4.2 (35)	38/50	4.2 (39)	100	43/50	4.2 (37)	100	41/50	3.5 (44)	83	47/50
90-7	4.3 (35)	37/50	4.1 (34)	95	39/50	4.0 (33)	93	40/50	3.8 (43)	88	45/50
94-7	4.1 (30)	33/50	4.1 (30)	100	38/50	4.6 (35)	112	38/50	3.6 (40)	88	43/50
98-7	4.4 (26)	31/50	4.3 (27)	98	33/50	4.6 (30)	105	35/50	3.8 (40)	86	42/50
102-7	4.4 (21)	25/50	4.1 (19)	93	24/50	4.2 (23)	95	33/50	4.2 (36)	95	39/50
104-7	4.5 (20)	24/50	4.0 (15)	89	21/50	4.2 (21)	93	33/50	4.2 (36)	93	38/50

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

TABLE E 3

WATER CONSUMPTION CHANGES: MALE

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

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 1-7 (3)	2-7 (3)	3-7 (3)	4-7 (3)	5-7 (3)	6-7 (3)	7-7 (3)
Control	4.7± 1.1	4.4± 0.7	4.3± 0.7	4.2± 0.7	4.4± 0.8	4.2± 0.8	4.1± 0.6
625 ppm	4.1± 0.4**	3.7± 0.5**	3.9± 0.6*	3.9± 0.8**	3.9± 0.6**	3.8± 0.6**	3.7± 0.6**
1250 ppm	3.4± 0.4**	3.4± 0.5**	3.4± 0.6**	3.3± 0.6**	3.4± 0.5**	3.4± 0.4**	3.5± 0.5**
2500 ppm	2.7± 0.3**	2.6± 0.5**	2.7± 0.5**	2.7± 0.5**	2.8± 0.5**	2.8± 0.5**	2.9± 0.5**

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

(HAN260)

BAIS4

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

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 8-7 (3)	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	4.1± 0.6	4.0± 0.7	3.9± 0.6	3.9± 0.6	3.8± 0.5
625 ppm	3.7± 0.7**	3.7± 0.6**	3.7± 0.7**	3.8± 0.6	3.6± 0.6**	3.6± 0.6*	3.5± 0.6**
1250 ppm	3.3± 0.4**	3.5± 0.5**	3.5± 0.4**	3.4± 0.4**	3.4± 0.4**	3.4± 0.4**	3.3± 0.3**
2500 ppm	2.8± 0.4**	2.9± 0.5**	2.9± 0.5**	3.0± 0.4**	2.9± 0.4**	3.0± 0.5**	2.8± 0.4**

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

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

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

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	3.5± 0.4	3.8± 0.4	3.6± 0.4	3.5± 0.4	3.7± 0.4	3.7± 0.3	3.8± 0.3
625 ppm	3.4± 0.5	3.5± 0.4**	3.4± 0.5*	3.4± 0.5	3.6± 0.5	3.6± 0.4	3.7± 0.4
1250 ppm	3.2± 0.3**	3.3± 0.3**	3.4± 0.3*	3.2± 0.3**	3.4± 0.3**	3.4± 0.3**	3.5± 0.4**
2500 ppm	2.7± 0.4**	2.8± 0.4**	2.8± 0.4**	2.8± 0.4**	3.0± 0.5**	3.0± 0.4**	3.2± 0.5**

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

(HAN260)

BAIS4

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

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 46-7 (3)	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± 0.3	4.0± 0.4	4.1± 0.5	4.1± 0.6	4.3± 0.7	4.5± 0.6
625 ppm	3.8± 0.5	3.7± 0.5	4.0± 0.8	4.0± 0.8	4.0± 0.6	4.3± 0.6	4.3± 0.6
1250 ppm	3.6± 0.4**	3.5± 0.5**	3.6± 0.4**	3.7± 0.4**	3.7± 0.5**	4.0± 1.1**	4.3± 1.2**
2500 ppm	3.1± 0.4**	3.1± 0.5**	3.2± 0.5**	3.2± 0.5**	3.2± 0.4**	3.4± 0.4**	3.5± 0.5**

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

(HAN260)

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

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 74-7 (3)	78-7 (3)	82-7 (3)	86-7 (3)	90-7 (3)	94-7 (3)	98-7 (3)
Control	4.6± 0.9	4.7± 1.0	4.5± 0.9	4.6± 1.7	4.9± 1.0	4.7± 1.5	5.0± 0.8
625 ppm	4.2± 0.8	4.4± 0.8	4.3± 0.6	4.5± 0.7	4.7± 0.9	4.9± 1.5	5.1± 1.3
1250 ppm	4.1± 0.6**	4.3± 0.6	4.2± 0.8	4.5± 1.0	4.5± 1.0	4.9± 1.5	4.8± 1.1
2500 ppm	3.6± 0.6**	3.8± 0.6**	3.8± 0.9**	4.0± 1.1**	4.0± 1.0**	4.0± 1.0**	4.2± 1.0**

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

(HAN260)

BAIS4

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

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 102-7 (3)	104-7 (3)
Control	5.1± 0.8	5.4± 1.1
625 ppm	4.9± 1.0	5.1± 1.0
1250 ppm	4.4± 1.2*	4.7± 1.2
2500 ppm	4.1± 1.0**	4.2± 1.0**

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

TABLE E 4

WATER CONSUMPTION CHANGES: FEMALE

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

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 1-7 (3)	2-7 (3)	3-7 (3)	4-7 (3)	5-7 (3)	6-7 (3)	7-7 (3)
Control	4.3± 0.4	4.1± 0.5	4.1± 0.5	4.0± 0.5	4.2± 0.5	4.0± 0.4	4.1± 0.4
625 ppm	4.0± 0.4**	3.6± 0.3**	3.7± 0.4**	3.6± 0.3**	3.7± 0.4**	3.7± 0.3**	3.7± 0.4**
1250 ppm	3.6± 0.3**	3.4± 0.4**	3.5± 0.5**	3.6± 0.5**	3.7± 0.4**	3.6± 0.5**	3.7± 0.6**
2500 ppm	2.7± 0.3**	2.7± 0.3**	2.8± 0.3**	2.9± 0.3**	3.0± 0.4**	3.0± 0.4**	3.1± 0.4**

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

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

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 8-7 (3)	9-7 (3)	10-7 (3)	11-7 (3)	12-7 (3)	13-7 (3)	14-7 (3)
Control	4.1± 0.4	4.2± 0.5	4.1± 0.5	4.1± 0.4	4.2± 0.7	4.2± 0.6	4.0± 0.4
625 ppm	3.6± 0.4**	3.7± 0.4**	3.7± 0.4**	3.7± 0.4**	3.6± 0.5**	3.7± 0.4**	3.6± 0.4**
1250 ppm	3.6± 0.3**	3.6± 0.4**	3.7± 0.4**	3.7± 0.6**	3.5± 0.4**	3.6± 0.4**	3.6± 0.6**
2500 ppm	3.1± 0.4**	3.1± 0.4**	3.1± 0.4**	3.1± 0.4**	3.1± 0.5**	3.1± 0.5**	3.0± 0.3**

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

(HAN260)

BAIS4

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

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

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	4.1± 0.6	3.9± 0.6	3.9± 0.7	4.1± 0.8	4.0± 0.7	4.1± 0.7
625 ppm	3.4± 0.3**	3.5± 0.5**	3.3± 0.4**	3.3± 0.5**	3.4± 0.6**	3.4± 0.4**	3.6± 0.4**
1250 ppm	3.2± 0.3**	3.3± 0.4**	3.1± 0.3**	3.2± 0.4**	3.3± 0.3**	3.3± 0.4**	3.3± 0.4**
2500 ppm	2.9± 0.4**	3.0± 0.4**	2.8± 0.4**	2.8± 0.3**	3.0± 0.4**	2.9± 0.4**	3.0± 0.3**

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

(HAN260)

BAIS 4

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

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 46-7 (3)	50-7 (3)	54-7 (3)	58-7 (3)	62-7 (3)	66-7 (3)	70-7 (3)
Control	4.1± 0.8	4.1± 0.8	4.0± 1.0	3.9± 0.6	3.9± 0.8	3.9± 0.8	4.0± 0.8
625 ppm	3.6± 0.5**	3.6± 0.5**	3.4± 0.5**	3.5± 0.5**	3.5± 0.6*	3.7± 0.7	3.5± 0.8*
1250 ppm	3.4± 0.7**	3.2± 0.4**	3.3± 0.7**	3.2± 0.8**	3.2± 0.5**	3.4± 0.7**	3.4± 0.9**
2500 ppm	3.0± 0.4**	2.8± 0.4**	2.9± 0.5**	2.8± 0.4**	2.8± 0.5**	3.0± 0.7**	3.1± 1.0**

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

(HAN260)

BAIS4

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

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 74-7 (3)	78-7 (3)	82-7 (3)	86-7 (3)	90-7 (3)	94-7 (3)	98-7 (3)
Control	4.1± 0.8	4.2± 0.8	4.2± 1.0	4.2± 0.9	4.3± 0.9	4.1± 1.1	4.4± 1.1
625 ppm	3.7± 0.9	3.9± 0.9	4.1± 1.2	4.2± 1.2	4.1± 1.4	4.1± 1.4	4.3± 1.5
1250 ppm	3.5± 1.0**	3.8± 1.2**	4.1± 1.5	4.2± 1.4	4.0± 1.3	4.6± 1.8	4.6± 1.6
2500 ppm	3.3± 1.4**	3.2± 1.1**	3.4± 1.5**	3.5± 1.6**	3.8± 1.7**	3.6± 1.7*	3.8± 1.8

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

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

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 102-7 (3)	104-7 (3)
Control	4.4± 1.2	4.5± 1.1
625 ppm	4.1± 1.6	4.0± 1.1
1250 ppm	4.2± 1.4	4.2± 1.4
2500 ppm	4.2± 1.7	4.2± 1.8

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

(HAN260)

TABLE F 1

CHEMICAL INTAKE CHANGES: MALE

STUDY NO. : 0712
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : mg/kg/day
REPORT TYPE : A1 104
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1		2		3		4		5		6		7	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
625 ppm	103±	10	90±	11	92±	14	88±	19	85±	15	81±	14	77±	12
1250 ppm	173±	19	167±	25	159±	29	151±	23	153±	21	147±	19	147±	21
2500 ppm	283±	32	258±	47	263±	50	256±	47	259±	45	258±	51	262±	50

STUDY NO. : 0712
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : mg／kg／day
REPORT TYPE : A1 104
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 8		9		10		11		12		13		14	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
625 ppm	74±	15	74±	13	73±	14	73±	13	67±	13	66±	12	63±	12
1250 ppm	139±	20	142±	20	138±	20	135±	19	127±	18	126±	18	119±	13
2500 ppm	245±	43	250±	46	242±	40	244±	41	232±	41	232±	43	218±	37

STUDY NO. : 0712
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : mg/kg/day
REPORT TYPE : A1 104
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 18		22		26		30		34		38		42	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
625 ppm	56±	9	56±	8	52±	9	50±	8	50±	8	49±	7	49±	7
1250 ppm	110±	14	106±	13	104±	12	96±	12	97±	13	96±	14	96±	13
2500 ppm	196±	36	195±	32	187±	30	178±	31	186±	31	179±	28	183±	34

STUDY NO. : 0712
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : mg/kg/day
REPORT TYPE : A1 104
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 46		50		54		58		62		66		70	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
625 ppm	50±	8	47±	8	51±	18	50±	17	48±	7	52±	7	52±	8
1250 ppm	95±	13	92±	13	93±	13	94±	12	95±	16	103±	42	111±	55
2500 ppm	178±	27	176±	30	177±	28	172±	26	177±	25	183±	26	189±	35

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

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 74		78		82		86		90		94		98	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
625 ppm	52±	13	53±	12	51±	10	53±	12	56±	15	62±	27	64±	22
1250 ppm	99±	16	104±	18	102±	24	110±	34	117±	39	128±	56	127±	48
2500 ppm	196±	42	202±	48	203±	74	215±	87	219±	76	227±	83	236±	72

STUDY NO. : 0712
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : mg/kg/day
REPORT TYPE : A1 104
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 102		104	
Control	0±	0	0±	0
625 ppm	64±	19	65±	19
1250 ppm	116±	37	131±	55
2500 ppm	242±	81	250±	86

TABLE F 2

CHEMICAL INTAKE CHANGES: FEMALE

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

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1		2		3		4		5		6		7	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
625 ppm	123±	11	109±	9	106±	9	102±	10	103±	11	98±	9	99±	10
1250 ppm	225±	25	202±	21	210±	30	206±	33	208±	25	199±	28	201±	34
2500 ppm	340±	32	333±	33	335±	39	333±	39	339±	46	333±	46	336±	48

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

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 8		9		10		11		12		13		14	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
625 ppm	95±	10	95±	10	94±	11	95±	9	91±	11	91±	10	86±	11
1250 ppm	192±	20	186±	23	187±	22	191±	33	180±	23	180±	25	176±	32
2500 ppm	328±	50	328±	49	322±	47	325±	45	320±	54	314±	50	301±	40

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

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 18		22		26		30		34		38		42	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
625 ppm	79±	10	78±	13	71±	10	68±	13	69±	15	66±	11	67±	12
1250 ppm	155±	20	150±	23	137±	21	134±	23	135±	21	131±	23	128±	21
2500 ppm	279±	43	274±	43	259±	44	247±	39	255±	43	244±	45	242±	33

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

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 46		50		54		58		62		66		70	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
625 ppm	67±	14	63±	12	60±	13	60±	12	61±	15	65±	16	62±	17
1250 ppm	129±	30	119±	17	124±	40	119±	48	118±	24	124±	32	130±	60
2500 ppm	239±	38	224±	39	224±	42	216±	34	220±	47	237±	69	247±	109

(HAN300)

BAIS 5

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

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 74		78		82		86		90		94		98	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
625 ppm	64±	22	66±	21	70±	27	72±	30	71±	38	72±	39	76±	35
1250 ppm	129±	52	137±	63	156±	84	156±	80	148±	72	182±	101	177±	93
2500 ppm	267±	152	256±	143	280±	178	281±	169	309±	188	307±	191	337±	209

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

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 102		104	
Control	0±	0	0±	0
625 ppm	74±	37	71±	21
1250 ppm	156±	78	152±	68
2500 ppm	356±	192	360±	200

TABLE G 1

HEMATOLOGY: MALE

STUDY NO. : 0712
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV fℓ	MCH pg	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	24	9.24± 1.47	13.1± 2.0	43.2± 6.5	46.9± 3.4	14.2± 0.9	30.2± 0.9	1921± 524
625 ppm	32	8.83± 1.00	12.7± 1.5	42.4± 4.2	48.1± 1.7	14.4± 0.5	30.0± 0.9	1850± 391
1250 ppm	31	8.63± 1.35	12.7± 1.8	42.1± 5.3	49.1± 2.9**	14.7± 0.7	30.0± 1.0	1955± 488
2500 ppm	38	8.42± 1.33	12.3± 1.9	41.2± 5.5	49.2± 2.8**	14.6± 0.7*	29.7± 1.0	1876± 490

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

(HCL070)

BAIS 5

STUDY NO. : 0712
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	RETICULOCYTE %		METHEMOGLOBIN %	
Control	24	3.7±	3.7	0.4±	0.1
625 ppm	32	3.5±	1.6	0.5±	0.2
1250 ppm	31	4.3±	4.1	0.5±	0.3
2500 ppm	38	4.8±	3.3**	0.7±	0.3**

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

(HCL070)

BAIS5

STUDY NO. : 0712
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$		Differential WBC (%) NEUTRO		LYMPHO		MONO		EOSINO		BASO		OTHER	
Control	24	7.74±	13.36	30±	14	62±	16	3±	2	3±	3	0±	0	3±	5
625 ppm	32	5.36±	3.91	28±	16	63±	19	3±	2	4±	11	0±	0	3±	4
1250 ppm	31	4.37±	2.40	34±	18	57±	20	3±	2	2±	2	0±	0	4±	6
2500 ppm	38	3.66±	1.99*	34±	18	59±	17	3±	2	1±	2	0±	0	3±	4

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

(HCL070)

BAIS5

TABLE G 2

HEMATOLOGY: FEMALE

STUDY NO. : 0712
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV fℓ	MCH pg	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	22	9.14± 1.10	13.3± 1.6	43.5± 4.1	47.9± 3.1	14.6± 0.6	30.4± 1.2	1081± 353
625 ppm	21	9.21± 0.75	13.1± 1.2	44.2± 3.5	48.1± 1.9	14.3± 0.7	29.7± 1.0	1262± 400
1250 ppm	28	8.64± 1.25	12.3± 1.9	41.8± 5.4	48.6± 3.0	14.3± 0.9	29.4± 1.2*	1150± 413
2500 ppm	38	8.31± 1.43*	11.8± 2.3*	40.2± 6.2	48.7± 4.7	14.3± 1.3	29.3± 1.5**	1232± 485

Significant difference ; * : $P \leqq 0.05$ ** : $P \leqq 0.01$ Test of Dunnett

(HCL070)

BAIS 5

STUDY NO. : 0712
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	RETICULOCYTE %		METHEMOGLOBIN %	
Control	22	3.7±	4.1	0.3±	0.1
625 ppm	21	3.5±	1.2	0.4±	0.2
1250 ppm	28	4.7±	2.0**	0.5±	0.2
2500 ppm	38	6.5±	5.3**	0.6±	0.3**

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

(HCL070)

STUDY NO. : 0712
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) NEUTRO	LYMPHO	MONO	EOSINO	BASO	OTHER
Control	22	5.36± 6.67	25± 15	61± 22	3± 2	2± 3	0± 0	10± 21
625 ppm	21	8.13± 11.97	22± 12	57± 20	3± 3	1± 1	0± 0	17± 28
1250 ppm	28	3.61± 2.06	32± 20	53± 25	2± 2	1± 1	0± 0	13± 11
2500 ppm	38	4.37± 5.71	29± 18	53± 22	3± 2	2± 2	0± 0	14± 21

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

(HCL070)

BAIS5

TABLE H 1

BIOCHEMISTRY: MALE

STUDY NO. : 0712
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	TOTAL PROTEIN g／dℓ	ALBUMIN g／dℓ	A/G RATIO	T-BILIRUBIN mg／dℓ	GLUCOSE mg／dℓ	T-CHOLESTEROL mg／dℓ	TRIGLYCERIDE mg／dℓ
Control	24	5.4± 0.7	2.6± 0.4	0.9± 0.2	0.11± 0.04	156± 37	149± 71	47± 21
625 ppm	32	5.1± 0.5*	2.4± 0.3	0.9± 0.1	0.10± 0.03	158± 37	119± 28	43± 28
1250 ppm	31	5.1± 0.5*	2.4± 0.3	1.0± 0.2	0.10± 0.02	157± 45	127± 27	48± 28
2500 ppm	38	5.0± 0.5**	2.4± 0.3	1.0± 0.1	0.12± 0.04	153± 37	129± 31	49± 35

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

(HCL074)

BAIS 5

STUDY NO. : 0712
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	PHOSPHOLIPID mg/dℓ	AST U/L	ALT U/L	LDH U/L	ALP U/L	G-GTP U/L	CK U/L
Control	24	247± 86	85± 71	44± 49	268± 134	264± 276	1± 1	51± 21
625 ppm	32	206± 48	100± 155	64± 164	314± 603	191± 66	1± 0	79± 191
1250 ppm	31	210± 52	240± 833	136± 493	516± 1557	175± 47	1± 1	59± 38
2500 ppm	38	214± 50	94± 126	43± 81	282± 344	178± 51	1± 1	73± 128

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

(HCL074)

BAIS 5

STUDY NO. : 0712
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	UREA NITROGEN mg/dℓ	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dℓ	INORGANIC PHOSPHORUS mg/dℓ
Control	24	24.8± 5.8	154± 2	4.3± 0.4	121± 3	9.2± 0.5	6.0± 0.8
625 ppm	32	26.6± 13.4	154± 2	4.3± 0.6	123± 3	8.9± 0.3	5.8± 0.9
1250 ppm	31	30.2± 16.9	154± 2	4.4± 0.8	123± 4	8.9± 0.3	6.0± 1.2
2500 ppm	38	28.5± 16.3	155± 4	4.3± 0.6	123± 5	8.9± 0.5	6.0± 0.7

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

(HCL074)

BAIS5

TABLE H 2

BIOCHEMISTRY: FEMALE

STUDY NO. : 0712
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	TOTAL PROTEIN g／dℓ	ALBUMIN g／dℓ	A/G RATIO	T-BILIRUBIN mg／dℓ	GLUCOSE mg／dℓ	T-CHOLESTEROL mg／dℓ	TRIGLYCERIDE mg／dℓ
Control	22	5.0± 0.5	2.6± 0.2	1.1± 0.2	0.10± 0.02	118± 34	83± 26	31± 15
625 ppm	21	5.2± 0.6	2.4± 0.3	0.9± 0.2	0.11± 0.05	106± 30	100± 29	40± 24
1250 ppm	28	5.1± 0.6	2.6± 0.2	1.1± 0.2	0.11± 0.02	121± 28	110± 48*	54± 75
2500 ppm	38	5.2± 0.8	2.6± 0.3	1.0± 0.2	0.13± 0.04*	119± 24	112± 39**	49± 55

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

(HCL074)

BAIS 5

STUDY NO. : 0712
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	PHOSPHOLIPID mg/dℓ	AST U/L	ALT U/L	LDH U/L	ALP U/L	G-GTP U/L	CK U/L
Control	22	151± 43	115± 79	44± 36	255± 145	412± 290	1± 1	84± 63
625 ppm	21	174± 43	114± 61	42± 28	292± 187	330± 220	1± 1	211± 458
1250 ppm	28	197± 81**	115± 95	41± 35	394± 640	319± 176	1± 1	159± 222
2500 ppm	38	188± 59*	148± 154	55± 67	631± 1182	251± 111	1± 1	97± 74

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

(HCL074)

BAIS 5

STUDY NO. : 0712
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	UREA NITROGEN mg／dℓ	SODIUM mEq／ℓ	POTASSIUM mEq／ℓ	CHLORIDE mEq／ℓ	CALCIUM mg／dℓ	INORGANIC PHOSPHORUS mg／dℓ
Control	22	23.6± 16.2	152± 3	4.1± 0.6	121± 3	9.2± 0.5	6.1± 1.3
625 ppm	21	27.9± 25.2	153± 2	4.0± 0.4	123± 3	9.6± 1.4	7.4± 2.9
1250 ppm	28	31.6± 24.7	153± 4	4.1± 0.3	123± 4	9.5± 0.7	6.9± 1.9
2500 ppm	38	28.8± 17.6	153± 2	4.1± 0.5	122± 3	9.6± 0.9	7.3± 2.5

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

(HCL074)

BAIS 5

TABLE I 1

URINALYSIS: MALE

STUDY NO. : 0712
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	±	+	2+	3+	4+	CHI	Occult blood −	±	+	2+	3+	CHI
Control	25	0	5	8	3	1	8	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 ppm	33	0	7	11	6	4	4	1		0	5	18	8	2	0		33	0	0	0	0	0		9	22	1	1	0	0		29	2	0	1	1	
1250 ppm	32	0	6	13	5	7	1	0	*	0	2	17	12	1	0	*	32	0	0	0	0	0		7	19	5	1	0	0		30	0	0	0	2	
2500 ppm	39	0	12	12	9	5	1	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 ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

(HCL101)

BAIS5

STUDY NO. : 0712
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	Urobilinogen ±	+	2+	3+	4+	CHI
Control	25	25	0	0	0	0	
625 ppm	33	33	0	0	0	0	
1250 ppm	32	32	0	0	0	0	
2500 ppm	39	39	0	0	0	0	

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

(HCL101)

BAIS 5

TABLE I 2

URINALYSIS: FEMALE

STUDY NO. : 0712
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	±	+	2+	3+	4+	CHI	Occult blood −	±	+	2+	3+	CHI
Control	25	0	6	6	1	1	7	4		2	7	10	4	2	0		25	0	0	0	0	0		12	6	7	0	0	0		23	2	0	0	0	
625 ppm	21	0	0	6	4	7	1	3	**	2	7	6	6	0	0		21	0	0	0	0	0		9	6	6	0	0	0		21	0	0	0	0	
1250 ppm	33	0	8	12	2	3	6	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	9	9	7	7	3	3		1	10	11	9	6	1		38	0	0	0	0	0		12	9	11	3	3	0		37	0	0	0	1	

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

(HCL101)

STUDY NO. : 0712
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	Urobilinogen ±	+	2+	3+	4+	CHI
Control	25	25	0	0	0	0	
625 ppm	21	21	0	0	0	0	
1250 ppm	33	33	0	0	0	0	
2500 ppm	38	38	0	0	0	0	

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

(HCL101)

TABLE K 1

ORGAN WEIGHT, ABSOLUTE: MALE

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

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

Group Name	NO. of Animals	Body Weight	ADRENALS	TESTES	HEART	LUNGS	KIDNEYS
Control	24	44.9± 7.9	0.010± 0.003	0.235± 0.047	0.215± 0.022	0.259± 0.167	0.662± 0.081
625 ppm	32	44.0± 6.2	0.010± 0.002	0.239± 0.049	0.207± 0.021	0.224± 0.075	1.087± 1.970
1250 ppm	31	42.3± 9.6	0.009± 0.002	0.248± 0.074	0.216± 0.027	0.208± 0.043	0.696± 0.252
2500 ppm	38	39.3± 7.8*	0.010± 0.002	0.232± 0.034	0.205± 0.033	0.214± 0.048	0.945± 1.196

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

(HCL040)

BAIS 5

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

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

Group Name	NO. of Animals	SPLEEN	LIVER	BRAIN
Control	24	0.139± 0.142	1.853± 0.470	0.454± 0.013
625 ppm	32	0.145± 0.114	1.679± 0.283	0.455± 0.015
1250 ppm	31	0.147± 0.231	1.777± 0.442	0.454± 0.013
2500 ppm	38	0.137± 0.149	1.584± 0.219	0.455± 0.012

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

(HCL040)

BAIS 5

TABLE K 2

ORGAN WEIGHT, ABSOLUTE: FEMALE

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

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

Group Name	NO. of Animals	Body Weight	ADRENALS	OVARIES	HEART	LUNGS	KIDNEYS
Control	22	33.1± 6.3	0.014± 0.002	0.044± 0.056	0.173± 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	0.535± 0.263
1250 ppm	30	30.9± 5.9	0.013± 0.002	0.044± 0.033	0.171± 0.022	0.210± 0.041	0.504± 0.190
2500 ppm	38	27.7± 3.9**	0.013± 0.002	0.088± 0.221	0.166± 0.022	0.203± 0.038	0.515± 0.239

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

(HCL040)

BAIS5

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

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

Group Name	NO. of Animals	SPLEEN		LIVER		BRAIN	
Control	22	0.214±	0.150	1.534±	0.427	0.476±	0.018
625 ppm	21	0.217±	0.160	1.449±	0.199	0.481±	0.017
1250 ppm	30	0.311±	0.385	1.568±	0.313	0.474±	0.016
2500 ppm	38	0.340±	0.573	1.550±	0.612	0.463±	0.016*

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

(HCL040)

TABLE L 1

ORGAN WEIGHT, RELATIVE: MALE

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

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

Group Name	NO. of Animals	Body Weight (g)	ADRENALS	TESTES	HEART	LUNGS	KIDNEYS
Control	24	44.9± 7.9	0.023± 0.006	0.534± 0.124	0.490± 0.080	0.604± 0.476	1.516± 0.323
625 ppm	32	44.0± 6.2	0.023± 0.006	0.553± 0.126	0.478± 0.062	0.529± 0.226	2.526± 4.711
1250 ppm	31	42.3± 9.6	0.024± 0.010	0.607± 0.184	0.537± 0.159	0.530± 0.220	1.707± 0.584
2500 ppm	38	39.3± 7.8*	0.026± 0.007	0.612± 0.146	0.533± 0.100	0.571± 0.187	2.587± 3.600*

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

(HCL042)

BAIS5

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

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

Group Name	NO. of Animals	SPLEEN	LIVER	BRAIN
Control	24	0.332± 0.386	4.318± 1.678	1.043± 0.189
625 ppm	32	0.341± 0.290	3.885± 0.864	1.056± 0.167
1250 ppm	31	0.353± 0.430	4.331± 1.161	1.136± 0.301
2500 ppm	38	0.358± 0.362	4.163± 1.012	1.204± 0.240*

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

(HCL042)

BAIS5

TABLE L 2

ORGAN WEIGHT, RELATIVE: FEMALE

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

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

Group Name	NO. of Animals	Body Weight (g)	ADRENALS	OVARIES	HEART	LUNGS	KIDNEYS
Control	22	33.1± 6.3	0.042± 0.008	0.135± 0.164	0.537± 0.105	0.650± 0.318	1.399± 0.343
625 ppm	21	30.9± 5.7	0.042± 0.008	0.150± 0.105	0.582± 0.129	0.837± 0.515	1.841± 1.190
1250 ppm	30	30.9± 5.9	0.043± 0.008	0.150± 0.115	0.570± 0.113	0.708± 0.202	1.715± 0.890
2500 ppm	38	27.7± 3.9**	0.047± 0.009*	0.300± 0.678	0.608± 0.087	0.757± 0.213	1.903± 0.971**

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

(HCL042)

BAIS 5

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

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

Group Name	NO. of Animals	SPLEEN	LIVER	BRAIN
Control	22	0.673± 0.523	4.684± 1.046	1.484± 0.260
625 ppm	21	0.713± 0.584	4.772± 0.735	1.606± 0.302
1250 ppm	30	0.971± 1.038	5.201± 1.219	1.587± 0.290
2500 ppm	38	1.257± 2.205	5.600± 1.938	1.701± 0.224**

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

(HCL042)

BAIS5

TABLE M 1

HISTOPATHOLOGICAL FINDINGS:

NON-NEOPLASTIC LESIONS:

MALE: ALL ANIMALS

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

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

Organ	Findings	Group Name	Control				625 ppm				1250 ppm				2500 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)
{Integumentary system/appandage}																		
skin/app			<50>				<50>				<50>				<50>			
	ulcer		1	0	0	0	0	2	0	0	1	2	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(2)	(4)	(0)	(0)	(0)	(0)	(0)	(0)
	erosion		0	0	0	0	1	2	0	0	0	2	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(2)	(4)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)
	inflammation		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)
	squamous cell hyperplasia		0	0	0	0	0	0	0	0	4	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	scab		3	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(6)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	epidermal cyst		0	0	0	0	0	2	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
subcutis			<50>				<50>				<50>				<50>			
	hematoma		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)
	inflammation		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1+ (%)	Control 50 2+ (%)	Control 50 3+ (%)	Control 50 4+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
{Integumentary system/appandage}																		
subcutis		<50>																
	xanthogranuloma		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
{Respiratory system}																		
nasal cavit		<50>																
	eosinophilic change:olfactory epithelium		16 (32)	0 (0)	0 (0)	0 (0)	13 (26)	0 (0)	0 (0)	0 (0)	13 (26)	0 (0)	0 (0)	0 (0)	14 (28)	0 (0)	0 (0)	0 (0)
	eosinophilic change:respiratory epithelium		23 (46)	0 (0)	0 (0)	0 (0)	21 (42)	0 (0)	0 (0)	0 (0)	19 (38)	0 (0)	0 (0)	0 (0)	18 (36)	0 (0)	0 (0)	0 (0)
	inflammation:foreign body		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:olfactory epithelium		9 (18)	1 (2)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)	7 (14)	0 (0)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:gland		9 (18)	1 (2)	0 (0)	0 (0)	8 (16)	0 (0)	0 (0)	0 (0)	7 (14)	1 (2)	0 (0)	0 (0)	10 (20)	0 (0)	0 (0)	0 (0)
nasopharynx		<50>																
	eosinophilic change		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 (0)	0 (0)	0 (0)	0 (0)

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

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

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1+ (%)	Control 50 2+ (%)	Control 50 3+ (%)	Control 50 4+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
{Respiratory system}																		
lung			<50>				<50>				<50>				<50>			
	congestion		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hemorrhage		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	deposit of amyloid		4 (8)	0 (0)	0 (0)	0 (0)	6 (12)	0 (0)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)	8 (16)	0 (0)	0 (0)	0 (0)
	inflammatory infiltration		2 (4)	1 (2)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	bronchiolar-alveolar cell hyperplasia		2 (4)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	eosinophilic change:bronchial epithelium		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
{Hematopoietic system}																		
bone marrow			<50>				<50>				<50>				<50>			
	congestion		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1+ (%)	Control 50 2+ (%)	Control 50 3+ (%)	Control 50 4+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
(Hematopoietic system)																		
bone marrow		<50>																
	increased hematopoiesis		12 (24)	0 (0)	0 (0)	0 (0)	11 (22)	0 (0)	0 (0)	0 (0)	10 (20)	0 (0)	0 (0)	0 (0)	9 (18)	0 (0)	0 (0)	0 (0)
	granulopoiesis:increased		2 (4)	0 (0)	0 (0)	0 (0)	6 (12)	0 (0)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)
lymph node		<50>																
	lymphadenitis		1 (2)	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 (0)	0 (0)	0 (0)
thymus		<50>																
	atrophy		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
spleen		<50>																
	deposit of hemosiderin		20 (40)	0 (0)	0 (0)	0 (0)	26 (52)	0 (0)	0 (0)	0 (0)	30 (60)	4 (8)	0 (0)	0 ** (0)	32 (64)	14 (28)	2 (4)	0 ** (0)
	deposit of melanin		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 (0)	0 (0)	0 (0)	0 (0)
	fibrosis:focal		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

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

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1+ (%)	Control 50 2+ (%)	Control 50 3+ (%)	Control 50 4+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
{Hematopoietic system}																		
spleen			<50>				<50>				<50>				<50>			
	extramedullary hematopoiesis		11 (22)	11 (22)	0 (0)	0 (0)	14 (28)	8 (16)	0 (0)	0 (0)	13 (26)	10 (20)	1 (2)	0 (0)	20 (40)	12 (24)	1 (2)	0 (0)
	follicular hyperplasia		2 (4)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
{Circulatory system}																		
heart			<50>				<50>				<50>				<50>			
	deposit of amyloid		2 (4)	0 (0)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)	7 (14)	0 (0)	0 (0)	0 (0)
	mineralization		2 (4)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	myocardial fibrosis		17 (34)	0 (0)	0 (0)	0 (0)	10 (20)	0 (0)	0 (0)	0 (0)	19 (38)	0 (0)	0 (0)	0 (0)	13 (26)	0 (0)	0 (0)	0 (0)
	arteritis		1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)
artery/aort			<50>				<50>				<50>				<50>			
	mineralization		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				625 ppm				1250 ppm				2500 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)
(Digestive system)																		
oral cavity			<50>				<50>				<50>				<50>			
	hematoma		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
tooth			<50>				<50>				<50>				<50>			
	dysplasia		0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
tongue			<50>				<50>				<50>				<50>			
	squamous cell hyperplasia		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	epidermal cyst		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	arteritis		1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
stomach			<50>				<50>				<50>				<50>			
	ulcer:forestomach		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyperplasia:forestomach		0	1	0	0	2	0	0	0	1	0	0	0	1	0	0	0
			(0)	(2)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1+ (%)	Control 50 2+ (%)	Control 50 3+ (%)	Control 50 4+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
(Digestive system)																		
stomach		<50>																
	erosion:glandular stomach		1 (2)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	hyperplasia:glandular stomach		12 (24)	0 (0)	0 (0)	0 (0)	12 (24)	0 (0)	0 (0)	0 (0)	9 (18)	0 (0)	0 (0)	0 (0)	14 (28)	0 (0)	0 (0)	0 (0)
small intes		<50>																
	ulcer		0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hemorrhage		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
liver		<50>																
	angiectasis		1 (2)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (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 (0)	0 (0)	0 (0)	0 (0)
	necrosis:focal		2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1+ (%)	Control 50 2+ (%)	Control 50 3+ (%)	Control 50 4+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
{Digestive system}																		
liver			<50>				<50>				<50>				<50>			
	necrosis:single cell		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 (2)	0 (0)	0 (0)	0 (0)
	collapse		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 (0)	0 (0)	0 (0)	0 (0)
	inflammatory infiltration		0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	inflammatory cell nest		11 (22)	0 (0)	0 (0)	0 (0)	9 (18)	0 (0)	0 (0)	0 (0)	8 (16)	0 (0)	0 (0)	0 (0)	13 (26)	1 (2)	0 (0)	0 (0)
	clear cell focus		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 (0)	0 (0)	0 (0)	0 (0)
	acidophilic cell focus		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	basophilic cell focus		1 (2)	0 (0)	0 (0)	0 (0)	6 (12)	1 (2)	0 (0)	0 (0)	3 (6)	1 (2)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)
	mixed cell focus		0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1+ (%)	Control 50 2+ (%)	Control 50 3+ (%)	Control 50 4+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
{Digestive system}																		
liver		<50>																
	biliary cyst		2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	intestinal metaplasia:bile duct		0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (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)	10 (20)	0 (0)	0 (0)	0 (0) **
pancreas		<50>																
	cyst		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
{Urinary system}																		
kidney		<50>																
	atrophy		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)
	cyst		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)	625 ppm 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)	1250 ppm 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)	2500 ppm 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)
[Urinary system]																		
kidney			<50>				<50>				<50>				<50>			
	hyaline droplet		1 (2)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)
	deposit of amyloid		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)
	hyaline cast		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	inflammatory infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	lymphocytic infiltration		0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	scar		1 (2)	1 (2)	0 (0)	0 (0)	2 (4)	3 (6)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)	1 (2)	3 (6)	0 (0)	0 (0)
	inflammatory polyp		0 (0)	2 (4)	4 (8)	0 (0)	1 (2)	3 (6)	2 (4)	0 (0)	1 (2)	4 (8)	0 (0)	0 (0)	1 (2)	1 (2)	1 (2)	0 (0)
	hydronephrosis		1 (2)	2 (4)	6 (12)	1 (2)	0 (0)	3 (6)	8 (16)	0 (0)	0 (0)	4 (8)	3 (6)	0 (0)	0 (0)	5 (10)	2 (4)	0 (0)

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)	625 ppm 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)	1250 ppm 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)	2500 ppm 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)
{Urinary system}																		
kidney																		
	pyelonephritis	<50>	0	1	0	0	0	0	1	0	1	2	0	0	0	0	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(2)	(0)	(2)	(4)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:papilla		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:cortex		2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	regeneration:proximal tubule		19	1	0	0	17	2	0	0	17	1	0	0	21	0	0	0
			(38)	(2)	(0)	(0)	(34)	(4)	(0)	(0)	(34)	(2)	(0)	(0)	(42)	(0)	(0)	(0)
	urothelial hyperplasia:pelvis		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
urin bladd																		
	dilatation	<50>	0	1	0	0	0	7	0	0	1	4	0	0	0	2	0	0
			(0)	(2)	(0)	(0)	(0)	(14)	(0)	(0)	(2)	(8)	(0)	(0)	(0)	(4)	(0)	(0)
	ulcer		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)
	simple tubule hyperplasia		1	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0
			(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1+ (%)	Control 50 2+ (%)	Control 50 3+ (%)	Control 50 4+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
(Urinary system)																		
urin bladd			<50>				<50>				<50>				<50>			
	xanthogranuloma		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
(Endocrine system)																		
pituitary			<50>				<50>				<50>				<49>			
	Rathke pouch		2 (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)
thyroid			<50>				<50>				<50>				<50>			
	cystic thyroid follicle		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 (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)	1 (2)	0 (0)	0 (0)	0 (0)	10 (20)	0 (0)	0 (0)	0 ** (0)
adrenal			<50>				<50>				<50>				<50>			
	hyperplasia:medulla		0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
(Reproductive system)																		
testis			<50>				<50>				<50>				<50>			
	mineralization		2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)	625 ppm 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)	1250 ppm 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)	2500 ppm 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)
(Reproductive system)																		
testis		<50>	0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0
	xanthogranuloma		(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)
epididymis		<50>	4	2	0	0	0	1	0	0	3	2	0	0	1	0	0	0
	spermatogenic granuloma		(8)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(6)	(4)	(0)	(0)	(2)	(0)	(0)	(0)
prostate		<50>	0	1	0	0	0	1	0	0	0	2	0	0	0	0	0	0
	inflammation		(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)
prep/cli gl		<50>	1	0	0	0	2	0	0	0	1	0	0	0	1	0	0	0
	duct ectasia		(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
(Nervous system)																		
brain		<50>	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	hemorrhage		(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization		18	0	0	0	11	0	0	0	16	0	0	0	11	0	0	0
			(36)	(0)	(0)	(0)	(22)	(0)	(0)	(0)	(32)	(0)	(0)	(0)	(22)	(0)	(0)	(0)

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1+ (%)	Control 50 2+ (%)	Control 50 3+ (%)	Control 50 4+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
(Special sense organs/appendage)																		
eye		<50>																
	cataract		2 (4)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)
	keratitis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Harder gl		<50>																
	lymphocytic infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)
	hyperplasia		1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
(Musculoskeletal system)																		
muscle		<50>																
	mineralization		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
bone		<50>																
	osteosclerosis		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

TABLE M 4

HISTOPATHOLOGICAL FINDINGS:

NON-NEOPLASTIC LESIONS:

FEMALE: ALL ANIMALS

Organ	Findings	Group Name	Control				625 ppm				1250 ppm				2500 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)
{Integumentary system/appandage}																		
skin/app			<50>				<50>				<50>				<50>			
	epidermal cyst		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
{Respiratory system}																		
nasal cavit			<50>				<50>				<50>				<50>			
	eosinophilic change:olfactory epithelium		4 (8)	0 (0)	0 (0)	0 (0)	3 (6)	1 (2)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	6 (12)	1 (2)	0 (0)	0 (0)
	eosinophilic change:respiratory epithelium		28 (56)	8 (16)	0 (0)	0 (0)	26 (52)	2 (4)	0 (0)	0 (0)	28 (56)	3 (6)	0 (0)	0 (0)	33 (66)	5 (10)	1 (2)	0 (0)
	inflammation:respiratory epithelium		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 (0)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:olfactory epithelium		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:gland		9 (18)	0 (0)	0 (0)	0 (0)	11 (22)	0 (0)	0 (0)	0 (0)	10 (20)	0 (0)	0 (0)	0 (0)	9 (18)	0 (0)	0 (0)	0 (0)
nasopharynx			<50>				<50>				<50>				<50>			
	eosinophilic change		3 (6)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1+ (%)	Control 50 2+ (%)	Control 50 3+ (%)	Control 50 4+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
{Respiratory system}																		
lung			<50>				<50>				<50>				<50>			
	congestion		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 (2)	0 (0)	0 (0)	0 (0)
	deposit of amyloid		3 (6)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	7 (14)	0 (0)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)
	inflammatory infiltration		3 (6)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)
	lymphocytic infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)
	bronchiolar-alveolar cell hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
{Hematopoietic system}																		
bone marrow			<50>				<50>				<50>				<50>			
	granulation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)
	increased hematopoiesis		10 (20)	0 (0)	0 (0)	0 (0)	13 (26)	0 (0)	0 (0)	0 (0)	11 (22)	0 (0)	0 (0)	0 (0)	8 (16)	0 (0)	0 (0)	0 (0)

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1+ (%)	Control 50 2+ (%)	Control 50 3+ (%)	Control 50 4+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
{Hematopoietic system}																		
bone marrow		<50>																
	granulopoiesis:increased		5 (10)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)
lymph node		<50>																
	lymphadenitis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)
spleen		<50>																
	deposit of hemosiderin		30 (60)	0 (0)	0 (0)	0 (0)	34 (68)	3 (6)	0 (0)	0 (0)	38 (76)	6 (12)	0 (0)	0 ** (0)	30 (60)	12 (24)	5 (10)	0 ** (0)
	deposit of melanin		1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	extramedullary hematopoiesis		7 (14)	11 (22)	1 (2)	0 (0)	13 (26)	13 (26)	2 (4)	0 (0)	13 (26)	10 (20)	0 (0)	0 (0)	19 (38)	12 (24)	0 (0)	0 * (0)
	follicular hyperplasia		1 (2)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	2 (4)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
{Circulatory system}																		
heart		<50>																
	thrombus		0 (0)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
{ c } c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1+ (%)	Control 50 2+ (%)	Control 50 3+ (%)	Control 50 4+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
(Circulatory system)																		
heart			<50>				<50>				<50>				<50>			
	deposit of amyloid		2 (4)	0 (0)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)	6 (12)	1 (2)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)
	mineralization		2 (4)	0 (0)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	inflammatory infiltration		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	myocardial fibrosis		13 (26)	0 (0)	0 (0)	0 (0)	13 (26)	0 (0)	0 (0)	0 (0)	20 (40)	0 (0)	0 (0)	0 (0)	17 (34)	0 (0)	0 (0)	0 (0)
	arteritis		1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
(Digestive system)																		
tongue			<50>				<50>				<50>				<50>			
	inflammatory infiltration		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	arteritis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1+ (%)	Control 50 2+ (%)	Control 50 3+ (%)	Control 50 4+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
(Digestive system)																		
stomach		<50>																
	hyperplasia:forestomach		1 (2)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)
	erosion:glandular stomach		2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)
	hyperplasia:glandular stomach		8 (16)	0 (0)	0 (0)	0 (0)	11 (22)	0 (0)	0 (0)	0 (0)	12 (24)	0 (0)	0 (0)	0 (0)	12 (24)	0 (0)	0 (0)	0 (0)
small intes		<50>																
	adhesion		0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
liver		<50>																
	angiectasis		1 (2)	3 (6)	0 (0)	0 (0)	1 (2)	3 (6)	0 (0)	0 (0)	1 (2)	2 (4)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)
	necrosis:central		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	necrosis:focal		0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)	625 ppm 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)	1250 ppm 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)	2500 ppm 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)
(Digestive system)																		
liver																		
	inflammatory infiltration	<50>	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	lymphocytic infiltration		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	inflammatory cell nest		14	0	0	0	14	0	0	0	12	0	0	0	17	1	0	0
			(28)	(0)	(0)	(0)	(28)	(0)	(0)	(0)	(24)	(0)	(0)	(0)	(34)	(2)	(0)	(0)
	acidophilic cell focus		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	biliary cyst		0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	deposit of brown pigment		0	0	0	0	0	0	0	0	0	0	0	0	10	0	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
(Urinary system)																		
kidney																		
	cyst	<50>	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

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

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)	625 ppm 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)	1250 ppm 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)	2500 ppm 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)
(Urinary system)																		
kidney			<50>				<50>				<50>				<50>			
	hyaline droplet		14 (28)	0 (0)	0 (0)	0 (0)	9 (18)	0 (0)	0 (0)	0 (0)	10 (20)	0 (0)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 * (0)
	hyaline cast		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)
	inflammatory infiltration		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 (0)	0 (0)	0 (0)	0 (0)
	lymphocytic infiltration		4 (8)	1 (2)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)
	osseous metaplasia		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	scar		3 (6)	5 (10)	0 (0)	0 (0)	4 (8)	5 (10)	0 (0)	0 (0)	2 (4)	9 (18)	1 (2)	0 (0)	6 (12)	5 (10)	0 (0)	0 (0)
	inflammatory polyp		1 (2)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)
	hydronephrosis		0 (0)	3 (6)	1 (2)	0 (0)	0 (0)	5 (10)	1 (2)	0 (0)	1 (2)	4 (8)	2 (4)	0 (0)	1 (2)	6 (12)	1 (2)	0 (0)

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1+ (%)	Control 50 2+ (%)	Control 50 3+ (%)	Control 50 4+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
{Urinary system}																		
kidney																		
	tubular necrosis	<50>	0 (0)	1 (2)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	papillary necrosis		3 (6)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	7 (14)	1 (2)	0 (0)	0 (0)	6 (12)	1 (2)	0 (0)	0 (0)
	mineralization:papilla		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 (2)	0 (0)	0 (0)	0 (0)
	glomerulosclerosis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)
	regeneration:proximal tubule		2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4 (8)	1 (2)	0 (0)	0 (0)
	desquamation:pelvis		0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	urothelial hyperplasia:pelvis		2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)
ureter																		
	dilatation	<50>	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 (0)	0 (0)	0 (0)	0 (0)

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1+ (%)	Control 50 2+ (%)	Control 50 3+ (%)	Control 50 4+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
{Urinary system}																		
urin bladd		<50>																
	dilatation		1 (2)	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 (0)	0 (0)	0 (0)
	lymphocytic infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)
	xanthogranuloma		0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
{Endocrine system}																		
pituitary		<50>																
	angiectasis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	cyst		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	hyperplasia		3 (6)	0 (0)	0 (0)	0 (0)	3 (6)	2 (4)	0 (0)	0 (0)	4 (8)	1 (2)	0 (0)	0 (0)	4 (8)	1 (2)	0 (0)	0 (0)
	Rathke pouch		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1+ (%)	Control 50 2+ (%)	Control 50 3+ (%)	Control 50 4+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
{Endocrine system}																		
thyroid																		
	arteritis	<50>	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	deposit of brown pigment		0	0	0	0	0	0	0	0	0	0	0	0	7	0	0	0 *
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(14)	(0)	(0)	(0)
adrenal																		
	spindle-cell hyperplasia	<50>	4	0	0	0	2	0	0	0	2	0	0	0	1	0	0	0
			(8)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	fatty change:corticomedullary junction		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)
{Reproductive system}																		
ovary																		
	thrombus	<50>	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	cyst		3	0	0	0	8	0	0	0	5	0	0	0	7	0	0	0
			(6)	(0)	(0)	(0)	(16)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(14)	(0)	(0)	(0)

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1+ (%)	Control 50 2+ (%)	Control 50 3+ (%)	Control 50 4+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
(Reproductive system)																		
uterus		<50>	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0
	dilatation		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)
	cystic endometrial hyperplasia		9	4	0	0	8	0	0	0	11	1	0	0	11	2	0	0
			(18)	(8)	(0)	(0)	(16)	(0)	(0)	(0)	(22)	(2)	(0)	(0)	(22)	(4)	(0)	(0)
(Nervous system)																		
brain		<50>	12	0	0	0	11	0	0	0	13	0	0	0	10	0	0	0
	mineralization		(24)	(0)	(0)	(0)	(22)	(0)	(0)	(0)	(26)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
spinal cord		<50>	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
	gliosis		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
(Special sense organs/appendage)																		
eye		<50>	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
	keratitis		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1+ (%)	Control 50 2+ (%)	Control 50 3+ (%)	Control 50 4+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
{Special sense organs/appendage}																		
Harder gl		<50>																
	lymphocytic infiltration		0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)
	hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
{Musculoskeletal system}																		
muscle		<50>																
	hematoma		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	mineralization		1 (2)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
bone		<50>																
	osteosclerosis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
{Body cavities}																		
pleura		<50>																
	inflammation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

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

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

Organ	Findings	Group Name	Control				625 ppm				1250 ppm				2500 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)
{Body cavities}																		
mediastinum			<50>				<50>				<50>				<50>			
	inflammatory infiltration		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
peritoneum			<50>				<50>				<50>				<50>			
	inflammation		0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

TABLE P 1

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS: MALE

Group Name	Control	625 ppm	1250 ppm	2500 ppm
	SITE : lung TUMOR : bronchiolar-alveolar adenoma			
Tumor rate				
Overall rates(a)	6/50(12.0)	2/50(4.0)	3/50(6.0)	6/50(12.0)
Adjusted rates(b)	19.23	6.25	7.32	13.04
Terminal rates(c)	4/24(16.7)	2/32(6.3)	2/31(6.5)	4/39(10.3)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.4977			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.6997			
Fisher Exact test(e)		P = 0.1343	P = 0.2435	P = 0.6202
	SITE : lung TUMOR : bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	10/50(20.0)	9/50(18.0)	2/50(4.0)	3/50(6.0)
Adjusted rates(b)	20.83	25.71	6.45	5.13
Terminal rates(c)	5/24(20.8)	8/32(25.0)	2/31(6.5)	2/39(5.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8551			
Prevalence method(d)	P = 0.9978			
Combined analysis(d)	P = 0.9989			
Cochran-Armitage test(e)	P = 0.0124*			
Fisher Exact test(e)		P = 0.5000	P = 0.0139*	P = 0.0357*
	SITE : lung TUMOR : bronchiolar-alveolar adenoma, bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	16/50(32.0)	10/50(20.0)	5/50(10.0)	9/50(18.0)
Adjusted rates(b)	38.46	28.57	12.90	17.39
Terminal rates(c)	9/24(37.5)	9/32(28.1)	4/31(12.9)	6/39(15.4)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8551			
Prevalence method(d)	P = 0.9753			
Combined analysis(d)	P = 0.9872			
Cochran-Armitage test(e)	P = 0.0943			
Fisher Exact test(e)		P = 0.1271	P = 0.0064**	P = 0.0826

Group Name	Control	625 ppm	1250 ppm	2500 ppm
	SITE : lymph node TUMOR : malignant lymphoma			
Tumor rate				
Overall rates(a)	7/50(14.0)	4/50(8.0)	9/50(18.0)	6/50(12.0)
Adjusted rates(b)	16.67	9.38	16.13	12.82
Terminal rates(c)	4/24(16.7)	3/32(9.4)	5/31(16.1)	5/39(12.8)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8199			
Prevalence method(d)	P = 0.5467			
Combined analysis(d)	P = 0.7459			
Cochran-Armitage test(e)	P = 0.9433			
Fisher Exact test(e)		P = 0.2623	P = 0.3929	P = 0.5000
	SITE : spleen TUMOR : hemangioma			
Tumor rate				
Overall rates(a)	1/50(2.0)	3/50(6.0)	1/50(2.0)	1/50(2.0)
Adjusted rates(b)	3.33	9.38	3.23	2.56
Terminal rates(c)	0/24(0.0)	3/32(9.4)	1/31(3.2)	1/39(2.6)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.7576			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.6742			
Fisher Exact test(e)		P = 0.3087	P = 0.7525	P = 0.7525
	SITE : spleen TUMOR : hemangioma, hemangiosarcoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	4/50(8.0)	1/50(2.0)	1/50(2.0)
Adjusted rates(b)	3.33	12.50	3.23	2.56
Terminal rates(c)	0/24(0.0)	4/32(12.5)	1/31(3.2)	1/39(2.6)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.8184			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.5583			
Fisher Exact test(e)		P = 0.1811	P = 0.7525	P = 0.7525

Group Name	Control	625 ppm	1250 ppm	2500 ppm
	SITE : liver TUMOR : hemangioma			
Tumor rate				
Overall rates(a)	2/50(4.0)	3/50(6.0)	3/50(6.0)	1/50(2.0)
Adjusted rates(b)	4.17	9.38	9.68	2.56
Terminal rates(c)	1/24(4.2)	3/32(9.4)	3/31(9.7)	1/39(2.6)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.9629 ?			
Prevalence method(d)	P = 0.7503			
Combined analysis(d)	P = 0.8614			
Cochran-Armitage test(e)	P = 0.5259			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.5000
	SITE : liver TUMOR : hepatocellular adenoma			
Tumor rate				
Overall rates(a)	16/50(32.0)	8/50(16.0)	9/50(18.0)	1/50(2.0)
Adjusted rates(b)	50.00	21.21	29.03	2.13
Terminal rates(c)	12/24(50.0)	6/32(18.8)	9/31(29.0)	0/39(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 1.0000			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.0002**			
Fisher Exact test(e)		P = 0.0500	P = 0.0826	P < 0.0001**
	SITE : liver TUMOR : histiocytic sarcoma			
Tumor rate				
Overall rates(a)	6/50(12.0)	2/50(4.0)	4/50(8.0)	1/50(2.0)
Adjusted rates(b)	0.0	0.0	0.0	2.56
Terminal rates(c)	0/24(0.0)	0/32(0.0)	0/31(0.0)	1/39(2.6)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.9956			
Prevalence method(d)	P = 0.1404			
Combined analysis(d)	P = 0.9804			
Cochran-Armitage test(e)	P = 0.0897			
Fisher Exact test(e)		P = 0.1343	P = 0.3703	P = 0.0559

Group Name	Control	625 ppm	1250 ppm	2500 ppm
	SITE : liver TUMOR : hepatocellular carcinoma			
Tumor rate				
Overall rates(a)	7/50(14.0)	6/50(12.0)	5/50(10.0)	2/50(4.0)
Adjusted rates(b)	16.67	18.75	12.90	2.56
Terminal rates(c)	4/24(16.7)	6/32(18.8)	4/31(12.9)	1/39(2.6)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.6956			
Prevalence method(d)	P = 0.9914			
Combined analysis(d)	P = 0.9910			
Cochran-Armitage test(e)	P = 0.0796			
Fisher Exact test(e)		P = 0.5000	P = 0.3798	P = 0.0798
	SITE : liver TUMOR : hemangioma, hemangiosarcoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	4/50(8.0)	3/50(6.0)	2/50(4.0)
Adjusted rates(b)	4.17	12.50	9.68	2.56
Terminal rates(c)	1/24(4.2)	4/32(12.5)	3/31(9.7)	1/39(2.6)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.4556			
Prevalence method(d)	P = 0.8076			
Combined analysis(d)	P = 0.7729			
Cochran-Armitage test(e)	P = 0.7932			
Fisher Exact test(e)		P = 0.3389	P = 0.5000	P = 0.6913
	SITE : liver TUMOR : hepatocellular adenoma, hepatocellular carcinoma			
Tumor rate				
Overall rates(a)	21/50(42.0)	13/50(26.0)	12/50(24.0)	3/50(6.0)
Adjusted rates(b)	58.33	36.36	35.48	4.35
Terminal rates(c)	14/24(58.3)	11/32(34.4)	11/31(35.5)	1/39(2.6)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.6956			
Prevalence method(d)	P = 1.0000			
Combined analysis(d)	P = 1.0000			
Cochran-Armitage test(e)	P < 0.0001**			
Fisher Exact test(e)		P = 0.0695	P = 0.0441*	P < 0.0001**

Group Name	Control	625 ppm	1250 ppm	2500 ppm
	SITE : Harderian gland TUMOR : adenoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	3/50(6.0)	4/50(8.0)	0/50(0.0)
Adjusted rates(b)	8.33	9.38	12.90	0.0
Terminal rates(c)	2/24(8.3)	3/32(9.4)	4/31(12.9)	0/39(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.9440			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.2733			
Fisher Exact test(e)		P = 0.5000	P = 0.3389	P = 0.2475
	SITE : Harderian gland TUMOR : adenoma, adenocarcinoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	3/50(6.0)	4/50(8.0)	0/50(0.0)
Adjusted rates(b)	8.33	9.38	12.90	0.0
Terminal rates(c)	2/24(8.3)	3/32(9.4)	4/31(12.9)	0/39(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.9682			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.1539			
Fisher Exact test(e)		P = 0.6611	P = 0.5000	P = 0.1212

(HPT360A)

BAIS5

(a) : Number of tumor-bearing animals/number of animals examined at the site.
(b) : Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.
(c) : Observed tumor incidence at terminal kill.
(d) : Beneath the control incidence are the P-values associated with the trend test.
Standard method : Death analysis
Prevalence method : Incidental tumor test
Combined analysis : Death analysis + Incidental tumor test
(e) : The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.
? : The conditional probabilities of the largest and smallest possible out comes can not estimated or this P-value is beyond the estimated P-value.
------ : There is no data which should be statistical analysis.
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01
N.C. :Statistical value cannot be calculated and was not significant.

Group Name	Control	625 ppm	1250 ppm	2500 ppm
	SITE : ALL SITE TUMOR : hemangioma			
Tumor rate				
Overall rates(a)	3/50(6.0)	5/50(10.0)	3/50(6.0)	2/50(4.0)
Adjusted rates(b)	6.90	15.63	9.68	5.13
Terminal rates(c)	1/24(4.2)	5/32(15.6)	3/31(9.7)	2/39(5.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.9629 ?			
Prevalence method(d)	P = 0.8186			
Combined analysis(d)	P = 0.8953			
Cochran-Armitage test(e)	P = 0.4671			
Fisher Exact test(e)		P = 0.3575	P = 0.6611	P = 0.5000
	SITE : ALL SITE TUMOR : histiocytic sarcoma			
Tumor rate				
Overall rates(a)	7/50(14.0)	5/50(10.0)	6/50(12.0)	4/50(8.0)
Adjusted rates(b)	0.0	4.88	0.0	7.69
Terminal rates(c)	0/24(0.0)	1/32(3.1)	0/31(0.0)	3/39(7.7)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.9879			
Prevalence method(d)	P = 0.0861			
Combined analysis(d)	P = 0.8952			
Cochran-Armitage test(e)	P = 0.4007			
Fisher Exact test(e)		P = 0.3798	P = 0.5000	P = 0.2623

Group Name	Control	625 ppm	1250 ppm	2500 ppm
	SITE : ALL SITE TUMOR : malignant lymphoma			
Tumor rate				
Overall rates(a)	7/50(14.0)	4/50(8.0)	10/50(20.0)	7/50(14.0)
Adjusted rates(b)	16.67	9.38	19.35	15.38
Terminal rates(c)	4/24(16.7)	3/32(9.4)	6/31(19.4)	6/39(15.4)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8199			
Prevalence method(d)	P = 0.4130			
Combined analysis(d)	P = 0.6450			
Cochran-Armitage test(e)	P = 0.6793			
Fisher Exact test(e)		P = 0.2623	P = 0.2977	P = 0.6129

(HPT360A)

BAIS5

(a) : Number of tumor-bearing animals/number of animals examined at the site.
(b) : Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.
(c) : Observed tumor incidence at terminal kill.
(d) : Beneath the control incidence are the P-values associated with the trend test.
Standard method : Death analysis
Prevalence method : Incidental tumor test
Combined analysis : Death analysis + Incidental tumor test
(e) : The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.
? : The conditional probabilities of the largest and smallest possible out comes can not estimated or this P-value is beyond the estimated P-value.
------ : There is no data which should be statistical analysis.
Significant difference ; * : $P \leqq 0.05$ ** : $P \leqq 0.01$
N.C. :Statistical value cannot be calculated and was not significant.

TABLE P 2

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS: FEMALE

Group Name	Control	625 ppm	1250 ppm	2500 ppm
	SITE : lung TUMOR : bronchiolar-alveolar adenoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	3/50(6.0)	1/50(2.0)	1/50(2.0)
Adjusted rates(b)	8.33	9.52	3.03	2.63
Terminal rates(c)	2/24(8.3)	2/21(9.5)	1/33(3.0)	1/38(2.6)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.8884			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.3979			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.5000
	SITE : lung TUMOR : bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	4/50(8.0)	1/50(2.0)	2/50(4.0)
Adjusted rates(b)	0.0	14.29	3.03	2.63
Terminal rates(c)	0/24(0.0)	3/21(14.3)	1/33(3.0)	1/38(2.6)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.4490			
Prevalence method(d)	P = 0.6716			
Combined analysis(d)	P = 0.6326			
Cochran-Armitage test(e)	P = 1.0000			
Fisher Exact test(e)		P = 0.1811	P = 0.7525	P = 0.5000
	SITE : lung TUMOR : bronchiolar-alveolar adenoma, bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	7/50(14.0)	2/50(4.0)	3/50(6.0)
Adjusted rates(b)	8.33	23.81	6.06	5.26
Terminal rates(c)	2/24(8.3)	5/21(23.8)	2/33(6.1)	2/38(5.3)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.4490			
Prevalence method(d)	P = 0.8831			
Combined analysis(d)	P = 0.8556			
Cochran-Armitage test(e)	P = 0.5552			
Fisher Exact test(e)		P = 0.1589	P = 0.5000	P = 0.6611

Group Name	Control	625 ppm	1250 ppm	2500 ppm
	SITE : lymph node TUMOR : malignant lymphoma			
Tumor rate				
Overall rates(a)	18/50(36.0)	17/50(34.0)	21/50(42.0)	10/50(20.0)
Adjusted rates(b)	41.67	33.33	45.45	15.79
Terminal rates(c)	10/24(41.7)	7/21(33.3)	15/33(45.5)	6/38(15.8)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.9682			
Prevalence method(d)	P = 0.9890			
Combined analysis(d)	P = 0.9984			
Cochran-Armitage test(e)	P = 0.0934			
Fisher Exact test(e)		P = 0.5000	P = 0.3410	P = 0.0591
	SITE : liver TUMOR : hemangioma			
Tumor rate				
Overall rates(a)	1/50(2.0)	1/50(2.0)	1/50(2.0)	3/50(6.0)
Adjusted rates(b)	4.17	2.27	2.94	7.89
Terminal rates(c)	1/24(4.2)	0/21(0.0)	0/33(0.0)	3/38(7.9)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.1578			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.2072			
Fisher Exact test(e)		P = 0.7525	P = 0.7525	P = 0.3087
	SITE : liver TUMOR : hepatocellular adenoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	6/50(12.0)	4/50(8.0)	5/50(10.0)
Adjusted rates(b)	12.00	17.86	12.12	13.16
Terminal rates(c)	2/24(8.3)	2/21(9.5)	4/33(12.1)	5/38(13.2)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.6464			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.9027			
Fisher Exact test(e)		P = 0.3703	P = 0.6425	P = 0.5000

Group Name	Control	625 ppm	1250 ppm	2500 ppm
	SITE : liver TUMOR : histiocytic sarcoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	3/50(6.0)	0/50(0.0)	1/50(2.0)
Adjusted rates(b)	0.0	3.13	0.0	0.0
Terminal rates(c)	0/24(0.0)	0/21(0.0)	0/33(0.0)	0/38(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8579			
Prevalence method(d)	P = 0.6376			
Combined analysis(d)	P = 0.8942			
Cochran-Armitage test(e)	P = 0.3266			
Fisher Exact test(e)		P = 0.5000	P = 0.2475	P = 0.5000
	SITE : liver TUMOR : hemangioma, hemangiosarcoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	2/50(4.0)	1/50(2.0)	3/50(6.0)
Adjusted rates(b)	4.17	4.76	2.94	7.89
Terminal rates(c)	1/24(4.2)	1/21(4.8)	0/33(0.0)	3/38(7.9)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.2414			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.3293			
Fisher Exact test(e)		P = 0.5000	P = 0.7525	P = 0.3087
	SITE : liver TUMOR : hepatocellular adenoma, hepatocellular carcinoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	6/50(12.0)	5/50(10.0)	5/50(10.0)
Adjusted rates(b)	12.00	17.86	15.15	13.16
Terminal rates(c)	2/24(8.3)	2/21(9.5)	5/33(15.2)	5/38(13.2)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.6407			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.8734			
Fisher Exact test(e)		P = 0.3703	P = 0.5000	P = 0.5000

Group Name	Control	625 ppm	1250 ppm	2500 ppm
	SITE : pituitary gland TUMOR : adenoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	9/50(18.0)	6/50(12.0)	7/50(14.0)
Adjusted rates(b)	16.67	23.81	15.38	13.16
Terminal rates(c)	4/24(16.7)	5/21(23.8)	5/33(15.2)	5/38(13.2)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.2302			
Prevalence method(d)	P = 0.7216			
Combined analysis(d)	P = 0.5825			
Cochran-Armitage test(e)	P = 0.6188			
Fisher Exact test(e)		P = 0.1168	P = 0.3703	P = 0.2623
	SITE : ovary TUMOR : papillary adenoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	0/50(0.0)	4/50(8.0)	1/50(2.0)
Adjusted rates(b)	3.23	0.0	12.12	2.27
Terminal rates(c)	0/24(0.0)	0/21(0.0)	4/33(12.1)	0/38(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.3991			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.6742			
Fisher Exact test(e)		P = 0.5000	P = 0.1811	P = 0.7525
	SITE : uterus TUMOR : endometrial stromal polyp			
Tumor rate				
Overall rates(a)	3/50(6.0)	2/50(4.0)	2/50(4.0)	2/50(4.0)
Adjusted rates(b)	11.11	6.25	5.13	5.26
Terminal rates(c)	2/24(8.3)	0/21(0.0)	1/33(3.0)	2/38(5.3)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.7312			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.6865			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.5000

Group Name	Control	625 ppm	1250 ppm	2500 ppm
	SITE : uterus TUMOR : histiocytic sarcoma			
Tumor rate				
Overall rates(a)	16/50(32.0)	14/50(28.0)	12/50(24.0)	12/50(24.0)
Adjusted rates(b)	18.52	13.04	21.21	27.27
Terminal rates(c)	4/24(16.7)	2/21(9.5)	7/33(21.2)	9/38(23.7)
Statistical analysis				
Peto test				
Standard method(d)	P = 1.0000			
Prevalence method(d)	P = 0.0444*			
Combined analysis(d)	P = 0.9459			
Cochran-Armitage test(e)	P = 0.3600			
Fisher Exact test(e)		P = 0.4138	P = 0.2522	P = 0.2522
	SITE : mammary gland TUMOR : adenocarcinoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	1/50(2.0)	0/50(0.0)	3/50(6.0)
Adjusted rates(b)	0.0	4.76	0.0	4.88
Terminal rates(c)	0/24(0.0)	1/21(4.8)	0/33(0.0)	1/38(2.6)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1467			
Prevalence method(d)	P = 0.1237			
Combined analysis(d)	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 : adenocarcinoma, adenosquamous carcinoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	2/50(4.0)	0/50(0.0)	4/50(8.0)
Adjusted rates(b)	0.0	4.76	0.0	7.32
Terminal rates(c)	0/24(0.0)	1/21(4.8)	0/33(0.0)	1/38(2.6)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3193			
Prevalence method(d)	P = 0.0446*			
Combined analysis(d)	P = 0.0469*			
Cochran-Armitage test(e)	P = 0.0356*			
Fisher Exact test(e)		P = 0.2475	P = N.C.	P = 0.0587

Group Name	Control	625 ppm	1250 ppm	2500 ppm
	SITE : Harderian gland TUMOR : adenoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	0/50(0.0)	4/50(8.0)	3/50(6.0)
Adjusted rates(b)	3.70	0.0	12.12	7.32
Terminal rates(c)	0/24(0.0)	0/21(0.0)	4/33(12.1)	2/38(5.3)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.1492			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.1432			
Fisher Exact test(e)		P = 0.5000	P = 0.1811	P = 0.3087
	SITE : Harderian gland TUMOR : adenoma, adenocarcinoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	0/50(0.0)	4/50(8.0)	3/50(6.0)
Adjusted rates(b)	3.85	0.0	12.12	7.32
Terminal rates(c)	0/24(0.0)	0/21(0.0)	4/33(12.1)	2/38(5.3)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.9209 ?			
Prevalence method(d)	P = 0.1549			
Combined analysis(d)	P = 0.3059			
Cochran-Armitage test(e)	P = 0.3270			
Fisher Exact test(e)		P = 0.2475	P = 0.3389	P = 0.5000

(HPT360A)

BAIS5

(a) : Number of tumor-bearing animals/number of animals examined at the site.
(b) : Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.
(c) : Observed tumor incidence at terminal kill.
(d) : Beneath the control incidence are the P-values associated with the trend test.
Standard method : Death analysis
Prevalence method : Incidental tumor test
Combined analysis : Death analysis + Incidental tumor test
(e) : The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.
? : The conditional probabilities of the largest and smallest possible out comes can not estimated or this P-value is beyond the estimated P-value.
------ : There is no data which should be statistical analysis.
Significant difference ; * : $P \leqq 0.05$ ** : $P \leqq 0.01$
N.C. :Statistical value cannot be calculated and was not significant.

Group Name	Control	625 ppm	1250 ppm	2500 ppm
	SITE : ALL SITE TUMOR : hemangioma			
Tumor rate				
Overall rates(a)	1/50(2.0)	4/50(8.0)	4/50(8.0)	4/50(8.0)
Adjusted rates(b)	4.17	8.70	11.76	10.53
Terminal rates(c)	1/24(4.2)	1/21(4.8)	3/33(9.1)	4/38(10.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.6336			
Prevalence method(d)	P = 0.2193			
Combined analysis(d)	P = 0.2863			
Cochran-Armitage test(e)	P = 0.3086			
Fisher Exact test(e)		P = 0.1811	P = 0.1811	P = 0.1811
	SITE : ALL SITE TUMOR : histiocytic sarcoma			
Tumor rate				
Overall rates(a)	18/50(36.0)	17/50(34.0)	13/50(26.0)	13/50(26.0)
Adjusted rates(b)	18.52	13.79	21.21	27.91
Terminal rates(c)	4/24(16.7)	2/21(9.5)	7/33(21.2)	9/38(23.7)
Statistical analysis				
Peto test				
Standard method(d)	P = 1.0000			
Prevalence method(d)	P = 0.0586			
Combined analysis(d)	P = 0.9717			
Cochran-Armitage test(e)	P = 0.2224			
Fisher Exact test(e)		P = 0.5000	P = 0.1937	P = 0.1937

Group Name	Control	625 ppm	1250 ppm	2500 ppm
	SITE : ALL SITE TUMOR : malignant lymphoma			
Tumor rate				
Overall rates(a)	18/50(36.0)	17/50(34.0)	21/50(42.0)	10/50(20.0)
Adjusted rates(b)	41.67	33.33	45.45	15.79
Terminal rates(c)	10/24(41.7)	7/21(33.3)	15/33(45.5)	6/38(15.8)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.9682			
Prevalence method(d)	P = 0.9890			
Combined analysis(d)	P = 0.9984			
Cochran-Armitage test(e)	P = 0.0934			
Fisher Exact test(e)		P = 0.5000	P = 0.3410	P = 0.0591

(HPT360A)

BAIS5

(a) : Number of tumor-bearing animals/number of animals examined at the site.
(b) : Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.
(c) : Observed tumor incidence at terminal kill.
(d) : Beneath the control incidence are the P-values associated with the trend test.
Standard method : Death analysis
Prevalence method : Incidental tumor test
Combined analysis : Death analysis + Incidental tumor test
(e) : The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.
? : The conditional probabilities of the largest and smallest possible out comes can not estimated or this P-value is beyond the estimated P-value.
------ : There is no data which should be statistical analysis.
Significant difference ; * : $P \leqq 0.05$ ** : $P \leqq 0.01$
N.C. :Statistical value cannot be calculated and was not significant.

TABLE R

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

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[1)]		40	1.7	0 - 8
adenosquamous carcinoma[2)]		0	0.0	0 - 0
1) + 2)		40	1.7	0 - 8
Uterus	2345			
Histiocytic sarcoma		483	20.6	10 - 34

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/Crlj[Crj:BDF1]
SEX : MALE

COUSE OF DEATH (SUMMARY)
(0-105W)

Group Name	Control	625 ppm	1250 ppm	2500 ppm
Number of Dead and Moribund Animal	26	18	19	11
no microscop confirm	2	1	0	1
renal lesion	0	1	1	1
urinary retention	0	6	3	2
hydronephrosis	7	6	3	2
tumor d:leukemia	3	1	4	1
tumor d:subcutis	0	0	1	0
tumor d:lung	2	0	0	1
tumor d:lymph node	1	0	0	0
tumor d:liver	9	2	5	2
tumor d:urin bladd	1	0	0	0
tumor d:epididymis	0	1	1	1
tumor d:muscle	0	0	1	0
tumor d:peritoneum	1	0	0	0

(BIO120)

BAIS5

TABLE S 2

CAUSE OF DEATH: FEMALE

STUDY NO. : 0712
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
SEX : FEMALE

COUSE OF DEATH (SUMMARY)
(0-105W)

Group Name	Control	625 ppm	1250 ppm	2500 ppm
Number of Dead and Moribund Animal	26	29	17	12
no microscop confirm	0	1	3	1
renal lesion	1	0	0	0
hydronephrosis	0	0	1	1
peritonitis	1	0	0	0
tumor d:leukemia	8	9	6	4
tumor d:subcutis	0	2	0	1
tumor d:lung	1	1	0	1
tumor d:liver	2	2	0	1
tumor d:pituitary	0	2	0	2
tumor d:uterus	11	11	5	0
tumor d:mammary gl	0	1	0	1
tumor d:Harder gl	1	0	0	0
tumor d:muscle	1	0	0	0
tumor d:mediastinum	0	0	1	0
tumor d:retroperit	0	0	1	0

FIGURES

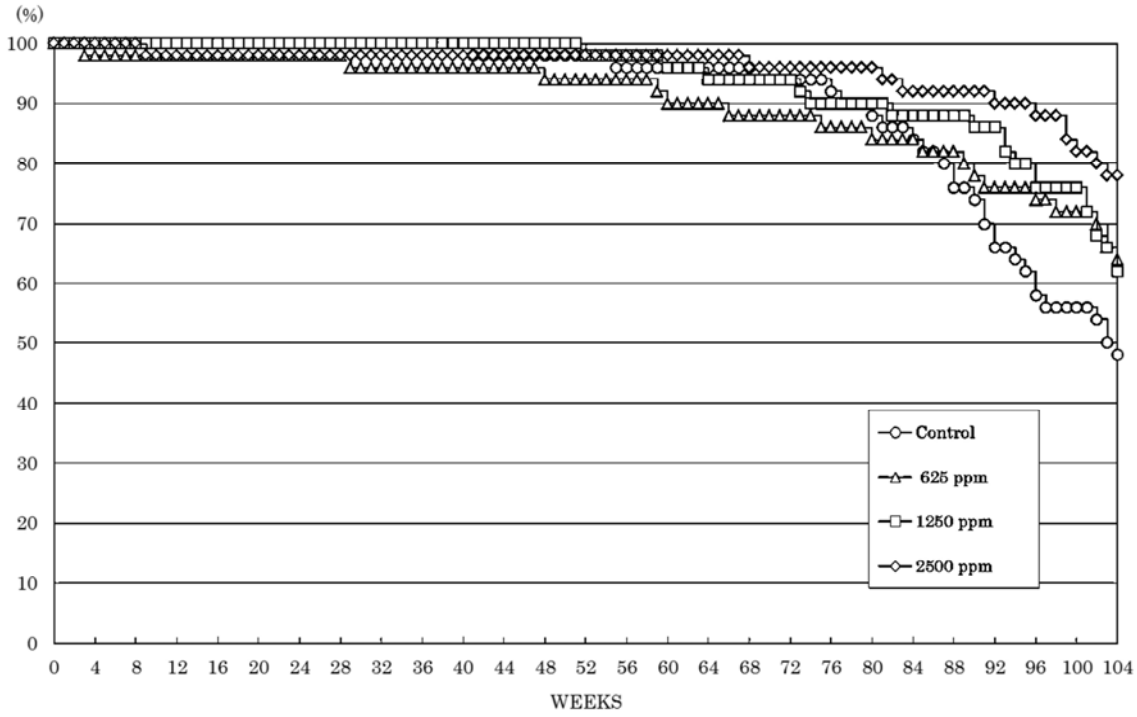


FIGURE 1　SURVIVAL ANIMAL RATE OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 3-AMINOPHENOL

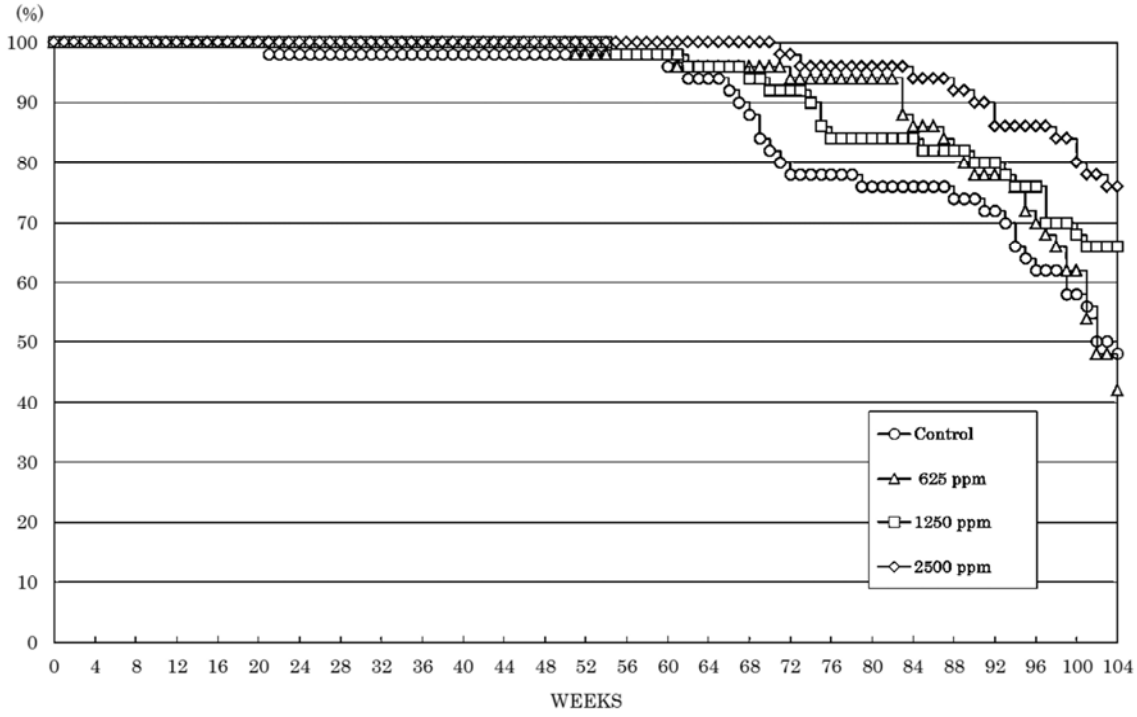


FIGURE 2　SURVIVAL ANIMAL RATE OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 3-AMINOPHENOL

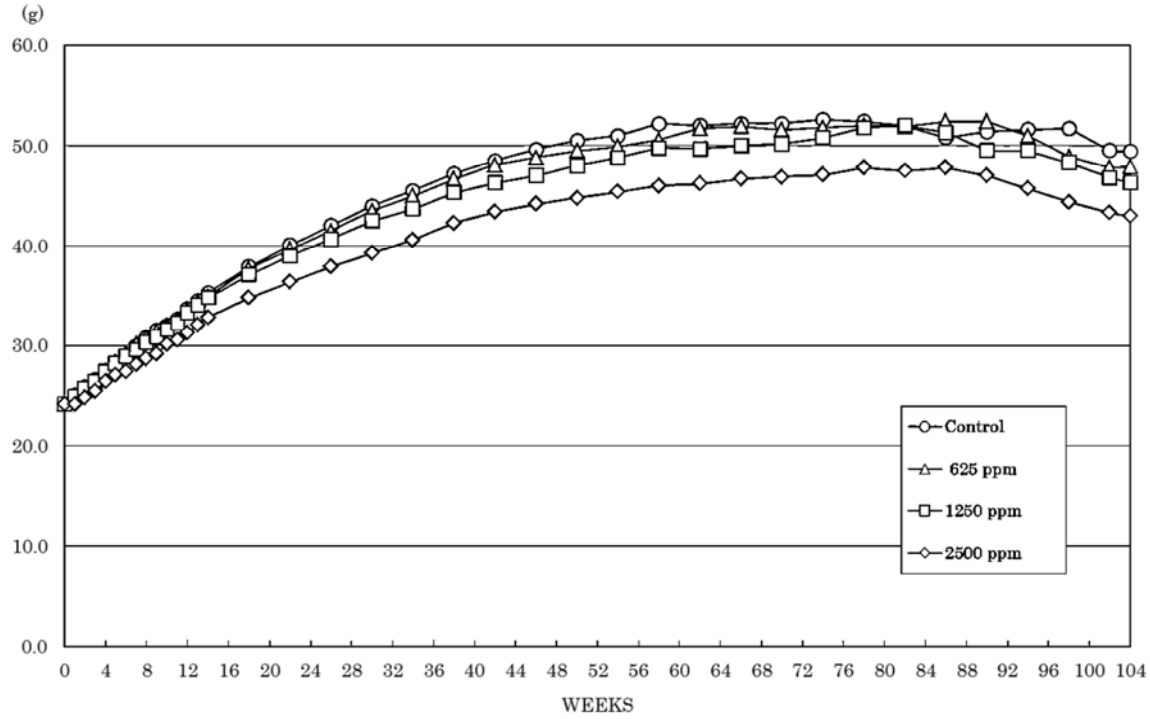


FIGURE 3 BODY WEIGHT CHANGES OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 3-AMINOPHENOL

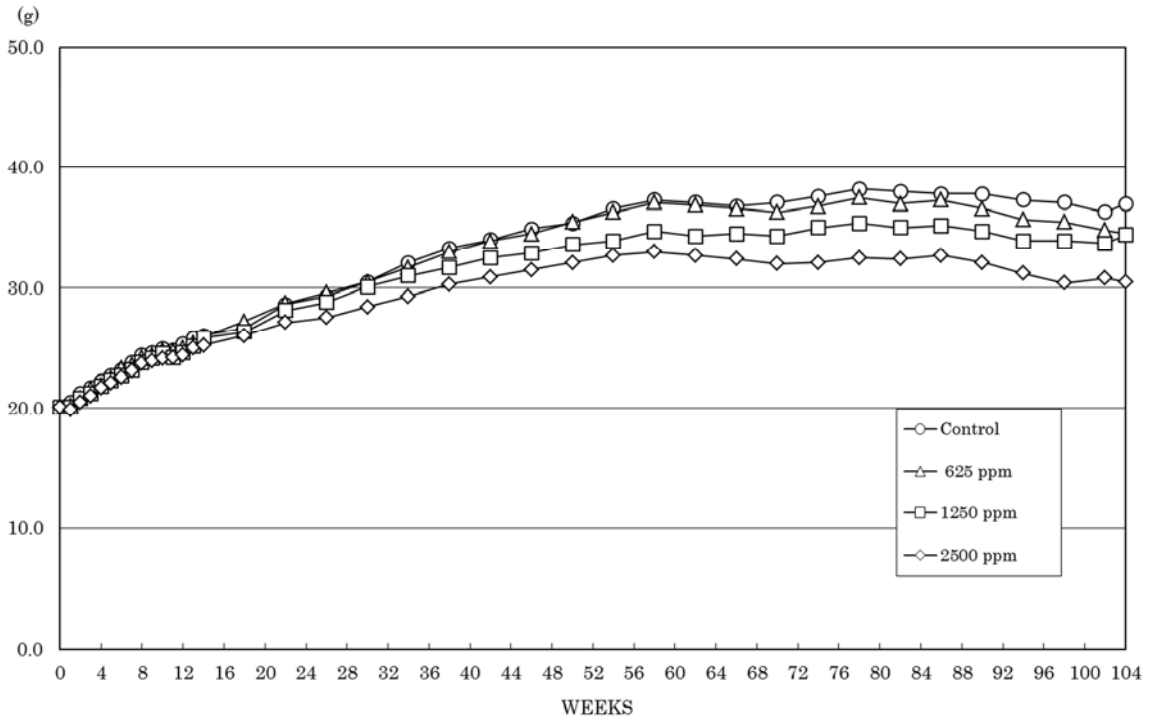


FIGURE 4 BODY WEIGHT CHANGES OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 3-AMINOPHENOL

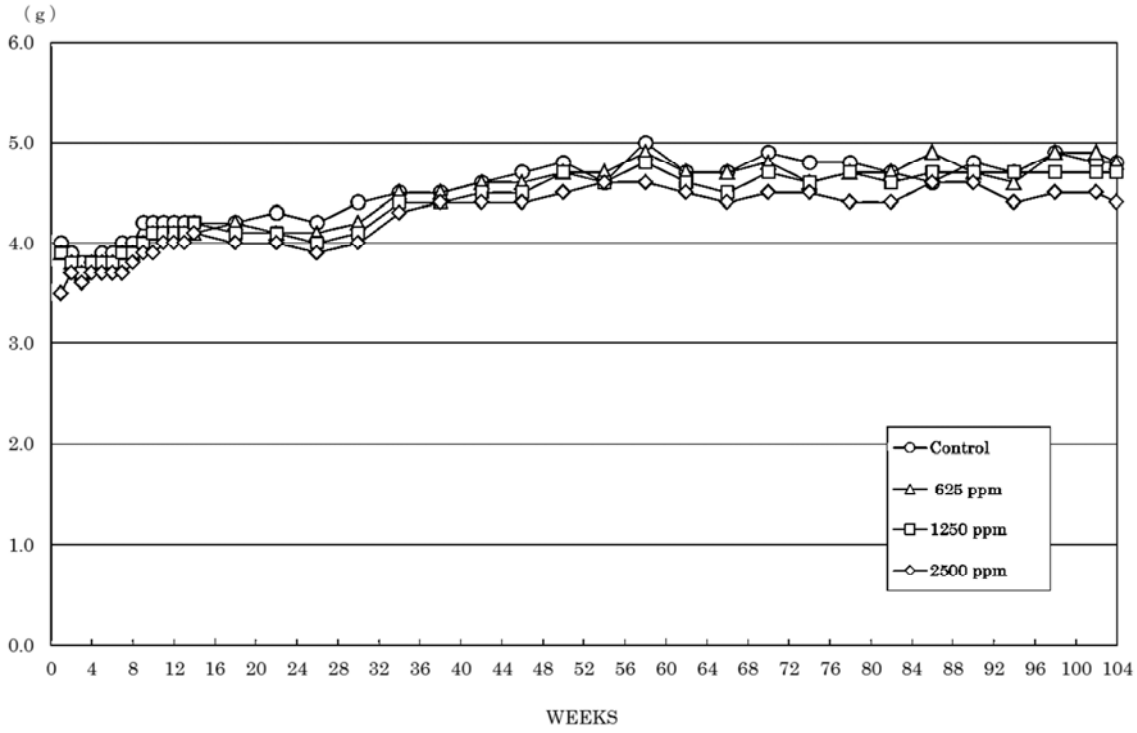


FIGURE 5 FOOD CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 3-AMINOPHENOL

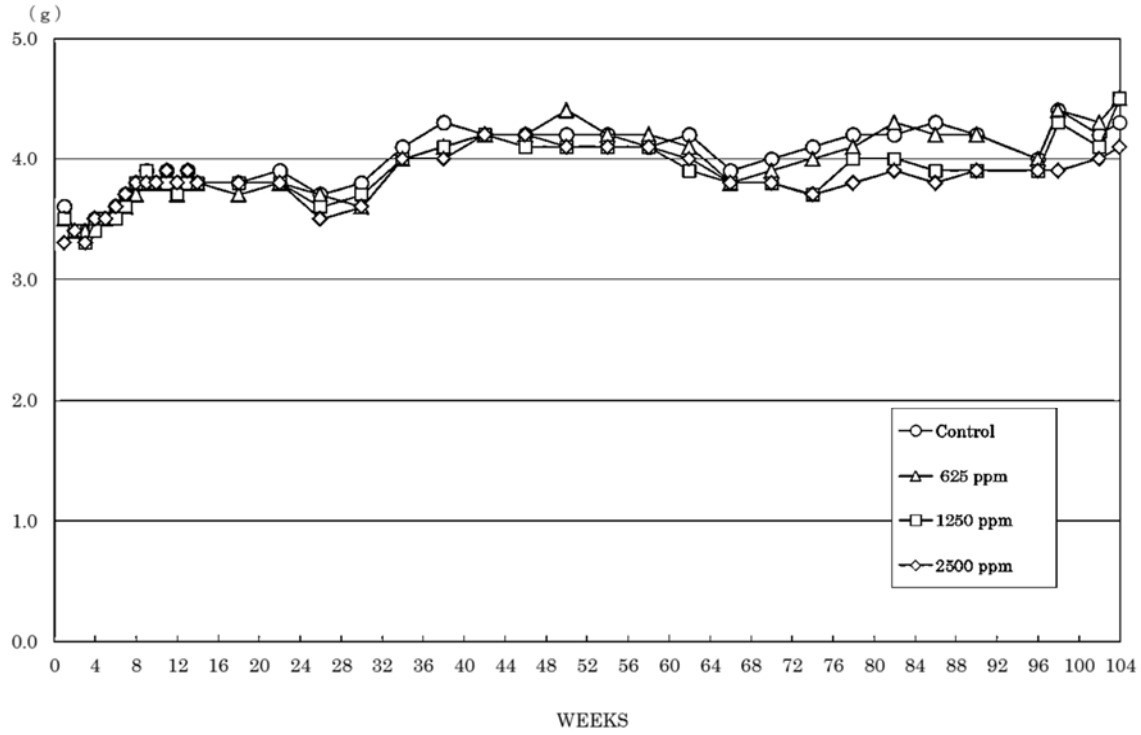


FIGURE 6 FOOD CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 3-AMINOPHENOL

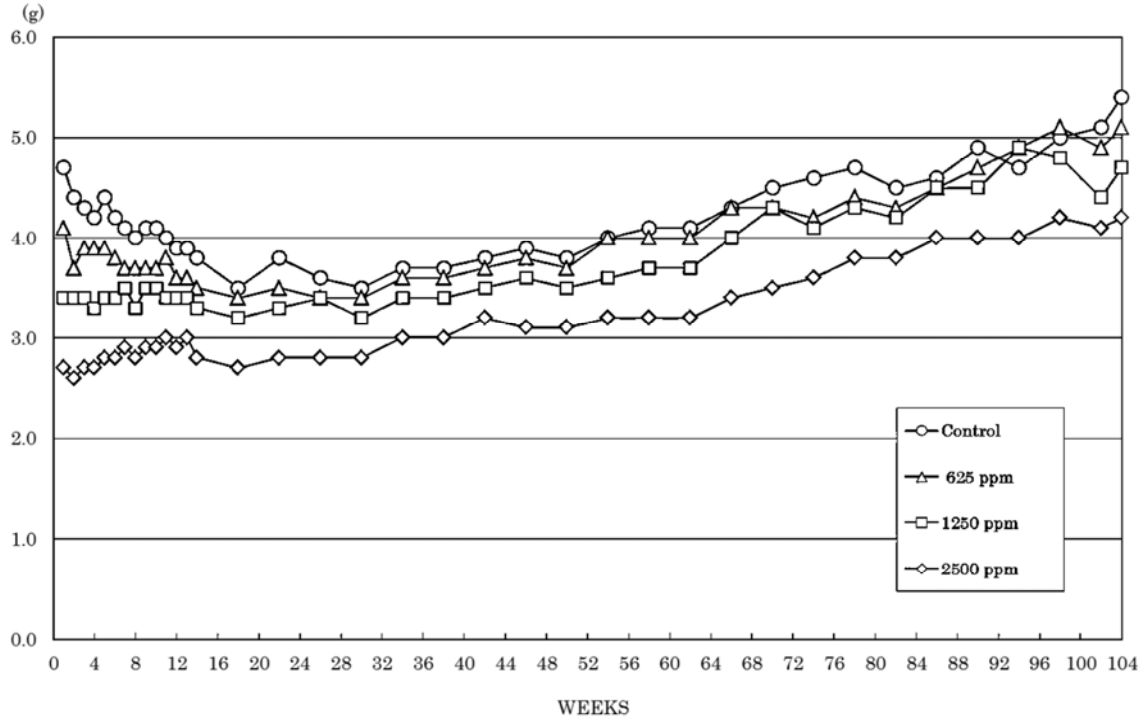


FIGURE 7 WATER CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 3-AMINOPHENOL

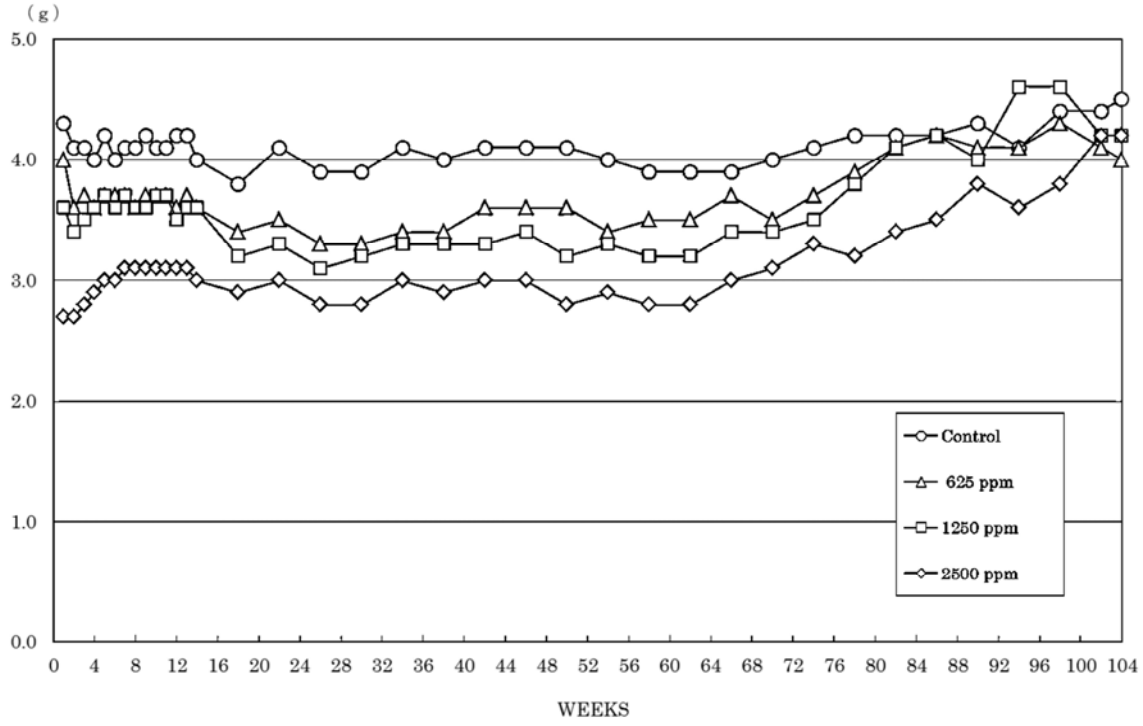
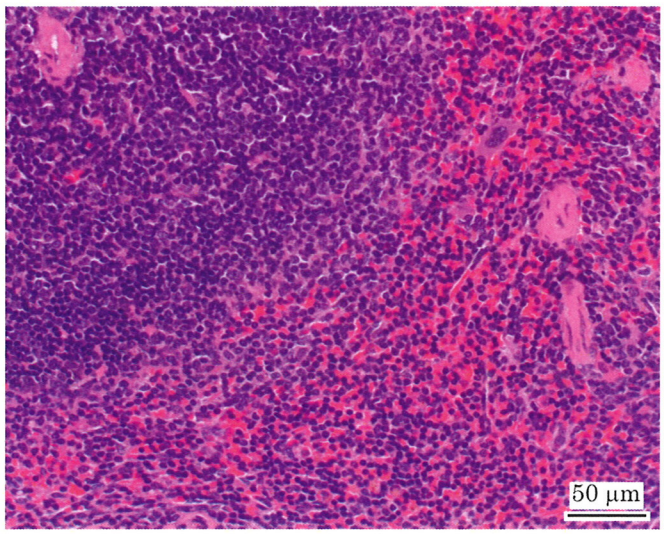
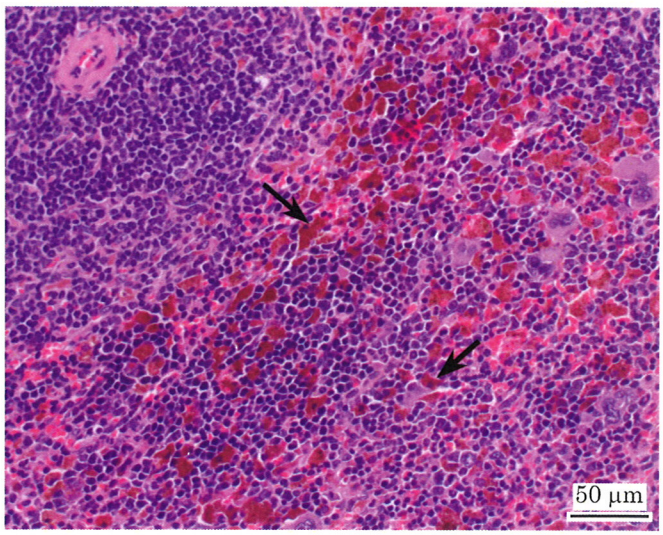


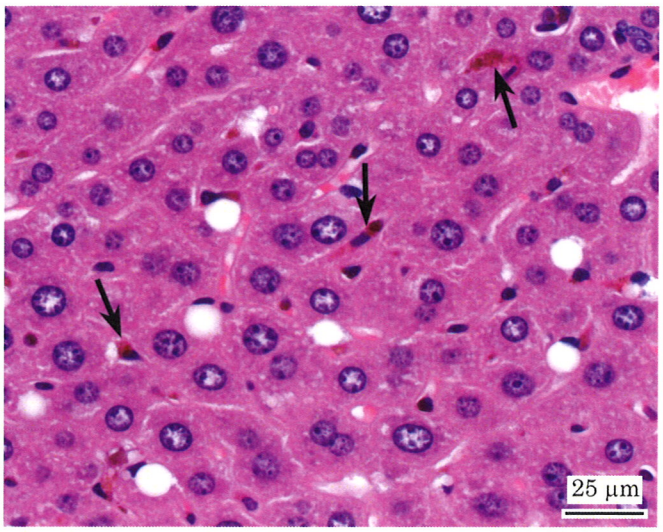
FIGURE 8 WATER CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 3-AMINOPHENOL



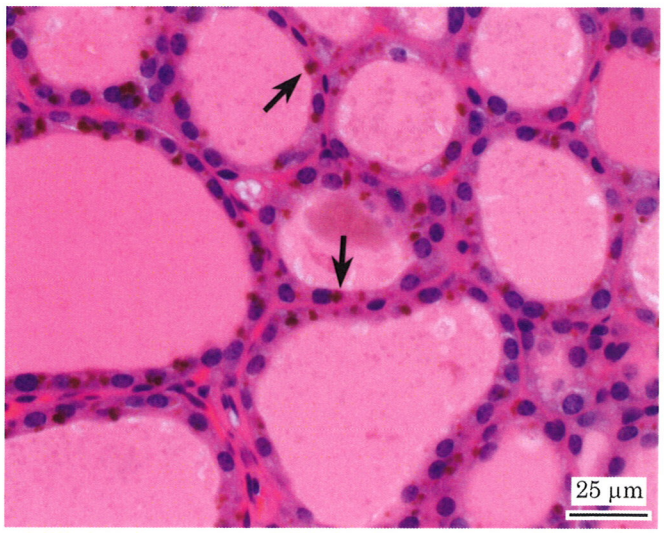
Photograph 1
Spleen: Normal
Mouse, Male, Control, Animal No. 0712-1001 (H&E)



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)