Summary of Drinking Water Carcinogenicity Study of 2-Methyl-1-Propanol in B6D2F1 Mice

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Japan Bioassay Research Center

Japan Industrial Safety and Health Association

PREFACE

The tests were contracted and supported by the Ministry of Health, Labour and Welfare of Japan. The tests were conducted by Japan Bioassay Research Center (JBRC) and the report was prepared by JBRC and peer reviewed by outside expert pathologist. Complete report was submitted to Ministry of Health, Labour and Welfare of Japan on September 30, 2009.

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

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Purpose, materials and methods

2-Methyl-1-propanol (CAS No. 78-83-1) is a colorless clear liquid with a melting point of -108°C and a boiling point of 107.9°C. It is soluble in water (8.7 wt%), alcohol, and ether.

The carcinogenicity and chronic toxicity of 2-methyl-1-propanol were examined in B6D2F1/Crlj mice. Groups of test animals were administered 2-methyl-1-propanol in their drinking water for 2 years (104 weeks). Each group consisted of either 50 male or 50 female mice. The drinking water concentrations of 2-methyl-1-propanol were 0, 5000, 10000 or 20000 ppm (w/w) for males, and 0, 2500, 5000 or 10000 ppm for females. 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. 2-Methyl-1-propanol was analyzed for purity and stability by both infrared spectrometry and gas chromatography before and after its use. The concentrations of 2-methyl-1-propanol in the drinking water were determined by gas 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. For hematology and blood biochemistry at the terminal necropsy, surviving animals were fasted overnight and bled under deep ether anesthesia. Organs and tissues were removed, weighed and examined for macroscopic lesions at necropsy. The organs and tissues were then fixed and embedded in paraffin. Five μm thick tissue sections were prepared and stained with hematoxylin and eosin and examined microscopically. Incidences of neoplastic lesions were statistically analyzed by Fisher's exact test. Any positive dose-response trends of 2-methyl-1-propanol induction of neoplastic lesions were analyzed by Peto's test. Incidences of non-neoplastic lesions and urinalysis were analyzed by the Chi-square test. Changes in body weight, food consumption, hematological and blood biochemical parameters, and organ weights were analyzed by Dunnett's test. The present studies were conducted in accordance with the Organisation for Economic Co-operation and Development (OECD) Good Laboratory Practice and with reference to the OECD Guideline for

Testing of Chemicals 451 “Carcinogenicity Studies”.

Results

No significant differences in survival rates were found between any of the groups administered 2-methyl-1-propanol and their respective controls. The growth rates of the females administered 10000 ppm were slightly suppressed toward the end of the administration periods, and body weights at 104 weeks were 88% of the control. Food consumption in the 5000 ppm- and 10000 ppm-administered females showed temporary decreases. Food consumption in the 5000 ppm-administered males also showed temporary decreases. Food consumption in the 10000-administered males decreased substantially, and consumption in the 20000-administered males was decreased for most of the 2-year administration period. Water consumption was decreased through the most of the 2-year administration period in males administered 2500 ppm or above and in females administered 5000 ppm or above. No other clinical signs were observed.

No significant increases in the incidence of neoplastic or tumor-related lesions was found in any of the 2-methyl-1-propanol-administered groups of either sex compared with their respective controls; nor was there a change in any other parameter in any of the groups.

The no-observed-adverse-effect-level (NOAEL) of 2-methyl-1-propanol in the drinking water was 20000 ppm (1796 mg/kg body weight per day) in males and 5000 ppm (664 mg/kg body weight per day) for the endpoint of body weight in females.

Conclusions

There was no evidence of carcinogenic activity of 2-methyl-1-propanol in male or female mice.

Incidences of selected neoplastic lesions of male mice in the 2-year drinking water carcinogenicity study of 2-Methyl-1-propanol

Dose (ppm)		0	5000	10000	20000	Peto test	Cochran-Armitage test
Number of examined animals		50	50	50	50		
benign tumor							
lung	bronchiolar-alveolar adenoma	7	4	4	3		
liver	hepatocellular adenoma	12	7	14	7		
malignant tumor							
lung	bronchiolar-alveolar carcinoma	4	10	7	5		
lymph node	malignant lymphoma	13	6	6	6		
liver	hepatocellular carcinoma	6	9	6	6		
	histiocytic sarcoma	3	3	1	4		
	hemangiosarcoma	1	2	3	1		

Incidences of selected neoplastic lesions of female mice in the 2-year drinking water carcinogenicity study of 2-Methyl-1-propanol

Dose (ppm)		0	2500	5000	10000	Peto test	Cochran-Armitage test
Number of examined animals		50	50	50	50		
benign tumor							
liver	hepatocellular adenoma	3	1	4	1		
	hemangioma	3	3	3	1		
pituitary	adenoma	12	9	5	6		
ovary	cystadenoma	0	0	3	1		
	hemangioma	0	1	4	0		
Harderian gland	adenoma	3	2	0	4		
malignant tumor							
lung	bronchiolar-alveolar carcinoma	2	2	1	3		
lymph node	malignant lymphoma	12	18	19	16		
uterus	histiocytic sarcoma	8	14	7	14		

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)

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TABLE C 1

BODY WEIGHT CHANGES AND

SURVIVAL ANIMAL NUMBERS: MALE

STUDY NO. : 0613
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>	5000 ppm Av.Wt.	5000 ppm % of cont. <50>	5000 ppm No. of Surviv.	10000 ppm Av.Wt.	10000 ppm % of cont. <50>	10000 ppm No. of Surviv.	20000 ppm Av.Wt.	20000 ppm % of cont. <50>	20000 ppm No. of Surviv.
0-0	23.9 (50)	50/50	23.9 (50)	100	50/50	23.9 (50)	100	50/50	23.9 (50)	100	50/50
1-7	24.5 (50)	50/50	24.3 (50)	99	50/50	24.5 (50)	100	50/50	24.4 (50)	100	50/50
2-7	25.4 (50)	50/50	25.2 (50)	99	50/50	25.4 (50)	100	50/50	25.3 (50)	100	50/50
3-7	26.4 (50)	50/50	26.2 (50)	99	50/50	26.4 (50)	100	50/50	26.2 (50)	99	50/50
4-7	27.0 (50)	50/50	26.8 (50)	99	50/50	27.2 (50)	101	50/50	26.9 (50)	100	50/50
5-7	27.4 (50)	50/50	27.7 (50)	101	50/50	27.8 (50)	101	50/50	27.6 (50)	101	50/50
6-7	28.0 (50)	50/50	28.3 (50)	101	50/50	28.4 (50)	101	50/50	28.1 (50)	100	50/50
7-7	28.5 (50)	50/50	28.7 (50)	101	50/50	28.9 (50)	101	50/50	28.4 (50)	100	50/50
8-7	29.0 (50)	50/50	29.3 (50)	101	50/50	29.5 (50)	102	50/50	29.1 (50)	100	50/50
9-7	30.0 (50)	50/50	30.3 (50)	101	50/50	30.6 (50)	102	50/50	30.0 (50)	100	50/50
10-7	30.6 (50)	50/50	31.0 (50)	101	50/50	31.2 (50)	102	50/50	30.5 (50)	100	50/50
11-7	30.9 (50)	50/50	31.4 (50)	102	50/50	31.7 (50)	103	50/50	31.0 (50)	100	50/50
12-7	31.9 (50)	50/50	32.4 (50)	102	50/50	32.5 (50)	102	50/50	31.8 (50)	100	50/50
13-7	32.9 (50)	50/50	33.2 (50)	101	50/50	33.3 (50)	101	50/50	32.5 (50)	99	50/50
14-7	32.9 (50)	50/50	33.6 (50)	102	50/50	33.8 (50)	103	50/50	33.0 (50)	100	50/50
18-7	35.2 (50)	50/50	35.8 (50)	102	50/50	36.0 (50)	102	50/50	34.9 (50)	99	50/50
22-7	37.2 (50)	50/50	37.9 (50)	102	50/50	37.8 (50)	102	50/50	36.6 (50)	98	50/50
26-7	39.2 (50)	50/50	39.6 (50)	101	50/50	39.6 (50)	101	50/50	38.0 (50)	97	50/50
30-7	41.3 (50)	50/50	41.6 (49)	101	49/50	41.5 (50)	100	50/50	39.9 (50)	97	50/50
34-7	42.4 (50)	50/50	42.8 (49)	101	49/50	42.6 (50)	100	50/50	40.9 (50)	96	50/50
38-7	43.9 (50)	50/50	44.2 (49)	101	49/50	43.9 (50)	100	50/50	42.1 (50)	96	50/50
42-7	44.9 (50)	50/50	45.2 (49)	101	49/50	44.7 (50)	100	50/50	43.1 (50)	96	50/50
46-7	46.3 (50)	50/50	46.3 (49)	100	49/50	45.8 (50)	99	50/50	44.2 (50)	95	50/50
50-7	47.5 (50)	50/50	47.6 (49)	100	49/50	47.1 (50)	99	50/50	45.4 (50)	96	50/50
54-7	48.6 (50)	50/50	48.5 (49)	100	49/50	48.1 (50)	99	50/50	46.4 (50)	95	50/50
58-7	49.2 (50)	50/50	49.1 (49)	100	49/50	48.6 (49)	99	49/50	47.1 (49)	96	49/50
62-7	49.6 (50)	50/50	49.1 (49)	99	49/50	48.9 (49)	99	49/50	47.5 (49)	96	49/50
66-7	49.3 (50)	50/50	49.3 (49)	100	49/50	49.4 (49)	100	49/50	47.9 (49)	97	49/50
70-7	49.9 (49)	49/50	50.2 (47)	101	47/50	49.8 (49)	100	49/50	48.4 (49)	97	49/50
74-7	50.6 (47)	47/50	50.4 (47)	100	47/50	50.0 (48)	99	48/50	48.6 (49)	96	49/50
78-7	50.2 (47)	47/50	49.4 (46)	98	46/50	49.3 (48)	98	48/50	47.9 (49)	95	49/50
82-7	50.5 (46)	46/50	50.1 (43)	99	43/50	49.6 (46)	98	46/50	48.4 (48)	96	48/50
86-7	51.1 (44)	44/50	49.9 (41)	98	41/50	49.8 (45)	97	45/50	48.1 (48)	94	48/50
90-7	49.6 (41)	41/50	49.4 (40)	100	40/50	50.1 (43)	101	43/50	49.5 (45)	100	45/50
94-7	48.0 (40)	40/50	49.1 (38)	102	38/50	49.0 (41)	102	41/50	48.9 (45)	102	45/50
98-7	47.8 (38)	38/50	49.1 (36)	103	36/50	49.6 (36)	104	36/50	48.6 (45)	102	45/50
102-7	46.2 (35)	35/50	47.5 (35)	103	35/50	48.2 (36)	104	36/50	47.5 (41)	103	41/50
104-7	45.5 (35)	35/50	47.8 (33)	105	33/50	47.5 (36)	104	36/50	46.8 (41)	103	41/50

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

TABLE C 2

BODY WEIGHT CHANGES AND

SURVIVAL ANIMAL NUMBERS: FEMALE

STUDY NO. : 0613
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>	2500 ppm Av. Wt.	2500 ppm % of cont. <50>	2500 ppm No. of Surviv.	5000 ppm Av. Wt.	5000 ppm % of cont. <50>	5000 ppm No. of Surviv.	10000 ppm Av. Wt.	10000 ppm % of cont. <50>	10000 ppm No. of Surviv.
0-0	19.5 (50)	50/50	19.5 (50)	100	50/50	19.5 (50)	100	50/50	19.5 (50)	100	50/50
1-7	19.8 (50)	50/50	19.5 (50)	98	50/50	19.8 (50)	100	50/50	19.7 (50)	99	50/50
2-7	20.4 (50)	50/50	20.3 (50)	100	50/50	20.3 (50)	100	50/50	20.4 (50)	100	50/50
3-7	21.0 (50)	50/50	21.0 (50)	100	50/50	21.0 (50)	100	50/50	21.1 (50)	100	50/50
4-7	21.5 (50)	50/50	21.5 (50)	100	50/50	21.4 (50)	100	50/50	21.6 (50)	100	50/50
5-7	22.1 (50)	50/50	22.0 (50)	100	50/50	22.0 (50)	100	50/50	22.0 (50)	100	50/50
6-7	22.4 (50)	50/50	22.4 (50)	100	50/50	22.3 (50)	100	50/50	22.4 (50)	100	50/50
7-7	22.8 (50)	50/50	22.8 (50)	100	50/50	22.8 (50)	100	50/50	22.7 (50)	100	50/50
8-7	23.2 (50)	50/50	23.5 (50)	101	50/50	23.1 (50)	100	50/50	23.3 (50)	100	50/50
9-7	23.6 (50)	50/50	23.8 (50)	101	50/50	23.4 (50)	99	50/50	23.7 (50)	100	50/50
10-7	24.2 (50)	50/50	24.0 (50)	99	50/50	23.9 (50)	99	50/50	23.9 (50)	99	50/50
11-7	24.0 (50)	50/50	24.2 (50)	101	50/50	23.8 (50)	99	50/50	23.9 (50)	100	50/50
12-7	24.6 (50)	50/50	24.3 (50)	99	50/50	24.2 (50)	98	50/50	24.3 (50)	99	50/50
13-7	24.8 (50)	50/50	24.8 (50)	100	50/50	24.3 (50)	98	50/50	24.5 (50)	99	50/50
14-7	25.0 (50)	50/50	25.1 (50)	100	50/50	24.8 (50)	99	50/50	24.6 (50)	98	50/50
18-7	26.0 (50)	50/50	26.3 (50)	101	50/50	25.6 (50)	98	50/50	26.1 (50)	100	50/50
22-7	27.0 (50)	50/50	27.3 (50)	101	50/50	26.6 (50)	99	50/50	26.8 (50)	99	50/50
26-7	27.6 (50)	50/50	27.9 (50)	101	50/50	27.3 (50)	99	50/50	27.9 (50)	101	50/50
30-7	29.0 (50)	50/50	28.9 (50)	100	50/50	28.0 (50)	97	50/50	28.7 (49)	99	49/50
34-7	29.5 (50)	50/50	29.5 (50)	100	50/50	28.8 (50)	98	50/50	29.1 (49)	99	49/50
38-7	30.8 (50)	50/50	30.6 (50)	99	50/50	30.2 (50)	98	50/50	30.1 (49)	98	49/50
42-7	31.1 (50)	50/50	31.0 (50)	100	50/50	30.1 (50)	97	50/50	30.3 (49)	97	49/50
46-7	32.2 (50)	50/50	31.8 (50)	99	50/50	31.2 (50)	97	50/50	31.3 (49)	97	49/50
50-7	33.2 (50)	50/50	32.7 (49)	98	49/50	32.1 (49)	97	49/50	32.3 (49)	97	49/50
54-7	33.9 (50)	50/50	33.3 (48)	98	48/50	32.6 (48)	96	48/50	33.0 (49)	97	49/50
58-7	34.3 (50)	50/50	34.4 (47)	100	47/50	32.7 (48)	95	48/50	33.2 (49)	97	49/50
62-7	34.8 (50)	50/50	34.6 (46)	99	46/50	32.7 (47)	94	47/50	33.3 (49)	96	49/50
66-7	35.5 (49)	49/50	34.7 (45)	98	45/50	33.3 (46)	94	46/50	33.7 (48)	95	48/50
70-7	35.7 (49)	49/50	34.9 (41)	98	41/50	33.5 (46)	94	46/50	34.2 (48)	96	48/50
74-7	35.9 (47)	47/50	34.7 (40)	97	40/50	34.0 (44)	95	44/50	33.7 (48)	94	48/50
78-7	35.4 (44)	44/50	34.7 (39)	98	39/50	33.9 (44)	96	44/50	33.4 (46)	94	46/50
82-7	36.2 (44)	44/50	35.4 (36)	98	36/50	34.1 (41)	94	41/50	34.3 (42)	95	42/50
86-7	36.9 (41)	41/50	35.5 (34)	96	34/50	34.1 (40)	92	40/50	34.5 (39)	93	39/50
90-7	36.8 (40)	40/50	35.9 (34)	98	34/50	34.5 (38)	94	38/50	33.7 (36)	92	36/50
94-7	36.3 (39)	39/50	35.3 (33)	97	33/50	34.3 (36)	94	36/50	33.6 (32)	93	32/50
98-7	36.2 (34)	34/50	35.9 (30)	99	30/50	34.5 (34)	95	34/50	33.2 (30)	92	30/50
102-7	35.8 (32)	32/50	34.8 (28)	97	28/50	34.5 (32)	96	32/50	33.8 (24)	94	24/50
104-7	35.6 (29)	29/50	33.4 (26)	94	26/50	34.2 (31)	96	31/50	31.4 (20)	88	20/50

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

TABLE C 3

BODY WEIGHT CHANGES: MALE

STUDY NO. : 0613
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	23.9± 0.9	24.5± 0.9	25.4± 1.0	26.4± 1.1	27.0± 1.2	27.4± 1.3	28.0± 1.4
5000 ppm	23.9± 0.9	24.3± 1.6	25.2± 1.4	26.2± 1.1	26.8± 1.2	27.7± 1.4	28.3± 1.3
10000 ppm	23.9± 0.9	24.5± 1.0	25.4± 1.2	26.4± 1.2	27.2± 1.2	27.8± 1.3	28.4± 1.5
20000 ppm	23.9± 0.9	24.4± 0.8	25.3± 0.8	26.2± 0.9	26.9± 1.1	27.6± 1.2	28.1± 1.4

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

STUDY NO. : 0613
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	28.5± 1.5	29.0± 1.6	30.0± 1.9	30.6± 2.0	30.9± 2.1	31.9± 2.2	32.9± 2.3
5000 ppm	28.7± 1.6	29.3± 1.6	30.3± 1.9	31.0± 2.0	31.4± 2.2	32.4± 2.2	33.2± 2.3
10000 ppm	28.9± 1.5	29.5± 1.8	30.6± 2.0	31.2± 2.1	31.7± 2.2	32.5± 2.4	33.3± 2.6
20000 ppm	28.4± 1.5	29.1± 1.5	30.0± 1.8	30.5± 2.3	31.0± 2.1	31.8± 2.3	32.5± 2.3

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

STUDY NO. : 0613
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	32.9± 2.4	35.2± 2.9	37.2± 3.2	39.2± 3.9	41.3± 4.2	42.4± 4.5	43.9± 4.7
5000 ppm	33.6± 2.4	35.8± 2.8	37.9± 3.1	39.6± 3.5	41.6± 3.7	42.8± 3.7	44.2± 4.1
10000 ppm	33.8± 2.7	36.0± 3.0	37.8± 3.3	39.6± 3.7	41.5± 4.0	42.6± 4.2	43.9± 4.3
20000 ppm	33.0± 2.4	34.9± 2.7	36.6± 3.2	38.0± 3.5	39.9± 3.9	40.9± 4.1	42.1± 4.3

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

STUDY NO. : 0613
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	44.9± 4.7	46.3± 4.7	47.5± 4.6	48.6± 4.5	49.2± 4.4	49.6± 4.3	49.3± 4.6
5000 ppm	45.2± 4.0	46.3± 3.8	47.6± 3.8	48.5± 3.7	49.1± 3.7	49.1± 3.9	49.3± 4.9
10000 ppm	44.7± 4.5	45.8± 4.5	47.1± 4.6	48.1± 4.5	48.6± 3.9	48.9± 4.1	49.4± 4.2
20000 ppm	43.1± 4.2	44.2± 4.3*	45.4± 4.5	46.4± 4.6*	47.1± 4.4*	47.5± 4.5	47.9± 4.4

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

(HAN260)

BAIS 4

STUDY NO. : 0613
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	49.9± 5.7	50.6± 5.2	50.2± 6.1	50.5± 5.9	51.1± 6.0	49.6± 6.6	48.0± 7.6
5000 ppm	50.2± 4.6	50.4± 4.9	49.4± 6.2	50.1± 6.0	49.9± 5.4	49.4± 6.9	49.1± 5.9
10000 ppm	49.8± 4.4	50.0± 4.8	49.3± 5.1	49.6± 5.1	49.8± 5.5	50.1± 6.0	49.0± 5.6
20000 ppm	48.4± 4.5	48.6± 5.1	47.9± 5.2	48.4± 5.6	48.1± 6.9	49.5± 6.1	48.9± 6.4

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

STUDY NO. : 0613
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	47.8± 7.5	46.2± 7.3	45.5± 7.6
5000 ppm	49.1± 6.0	47.5± 7.6	47.8± 7.3
10000 ppm	49.6± 5.3	48.2± 5.3	47.5± 5.1
20000 ppm	48.6± 6.7	47.5± 7.1	46.8± 7.7

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

TABLE C 4

BODY WEIGHT CHANGES: FEMALE

STUDY NO. : 0613
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	19.5± 0.9	19.8± 1.0	20.4± 0.9	21.0± 1.1	21.5± 1.1	22.1± 1.1	22.4± 1.0
2500 ppm	19.5± 0.9	19.5± 1.2	20.3± 1.0	21.0± 1.0	21.5± 1.1	22.0± 1.0	22.4± 1.1
5000 ppm	19.5± 0.9	19.8± 0.9	20.3± 0.8	21.0± 0.9	21.4± 0.9	22.0± 1.1	22.3± 1.2
10000 ppm	19.5± 0.9	19.7± 0.9	20.4± 1.0	21.1± 1.0	21.6± 1.1	22.0± 1.1	22.4± 1.1

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

STUDY NO. : 0613
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	22.8± 1.1	23.2± 1.2	23.6± 1.2	24.2± 1.6	24.0± 1.2	24.6± 1.4	24.8± 1.5
2500 ppm	22.8± 1.2	23.5± 1.1	23.8± 1.3	24.0± 1.4	24.2± 1.6	24.3± 1.4	24.8± 1.6
5000 ppm	22.8± 1.1	23.1± 1.3	23.4± 1.4	23.9± 1.5	23.8± 1.5	24.2± 1.6	24.3± 1.7
10000 ppm	22.7± 1.2	23.3± 1.2	23.7± 1.3	23.9± 1.3	23.9± 1.5	24.3± 1.5	24.5± 1.6

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

STUDY NO. : 0613
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	25.0± 1.4	26.0± 1.6	27.0± 1.7	27.6± 2.0	29.0± 2.5	29.5± 2.9	30.8± 2.9
2500 ppm	25.1± 1.5	26.3± 1.7	27.3± 2.3	27.9± 2.6	28.9± 3.0	29.5± 2.8	30.6± 3.3
5000 ppm	24.8± 1.7	25.6± 1.8	26.6± 1.9	27.3± 2.2	28.0± 2.8	28.8± 2.6	30.2± 3.3
10000 ppm	24.6± 1.6	26.1± 2.3	26.8± 2.1	27.9± 2.4	28.7± 2.6	29.1± 3.0	30.1± 3.4

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

STUDY NO. : 0613
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	31.1± 2.9	32.2± 3.3	33.2± 3.5	33.9± 4.4	34.3± 4.6	34.8± 4.3	35.5± 4.1
2500 ppm	31.0± 3.3	31.8± 3.9	32.7± 3.9	33.3± 4.5	34.4± 4.5	34.6± 4.4	34.7± 4.3
5000 ppm	30.1± 3.5	31.2± 4.0	32.1± 4.3	32.6± 4.6	32.7± 4.8	32.7± 4.8	33.3± 4.8
10000 ppm	30.3± 3.6	31.3± 3.9	32.3± 4.2	33.0± 4.0	33.2± 4.6	33.3± 4.5	33.7± 4.4

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

STUDY NO. : 0613
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	35.7± 4.7	35.9± 4.9	35.4± 4.5	36.2± 4.7	36.9± 5.2	36.8± 5.1	36.3± 6.1
2500 ppm	34.9± 4.0	34.7± 4.0	34.7± 4.1	35.4± 4.5	35.5± 4.6	35.9± 5.0	35.3± 4.6
5000 ppm	33.5± 4.9	34.0± 4.3	33.9± 4.3	34.1± 4.5	34.1± 4.5*	34.5± 4.7	34.3± 4.7
10000 ppm	34.2± 4.2	33.7± 4.7	33.4± 4.4	34.3± 4.4	34.5± 4.2	33.7± 4.1*	33.6± 3.8

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

STUDY NO. : 0613
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	36.2± 5.8	35.8± 6.1	35.6± 6.3
2500 ppm	35.9± 4.8	34.8± 3.8	33.4± 4.0
5000 ppm	34.5± 4.6	34.5± 4.9	34.2± 5.0
10000 ppm	33.2± 4.9	33.8± 6.3	31.4± 3.8**

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

(HAN260)

BAIS 4

TABLE D 1

FOOD CONSUMPTION CHANGES AND

SURVIVAL ANIMAL NUMBERS: MALE

STUDY NO. : 0613
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>	5000 ppm Av. FC.	5000 ppm % of cont. <50>	5000 ppm No. of Surviv.	10000 ppm Av. FC.	10000 ppm % of cont. <50>	10000 ppm No. of Surviv.	20000 ppm Av. FC.	20000 ppm % of cont. <50>	20000 ppm No. of Surviv.
1-7	3.8 (50)	50/50	3.8 (49)	100	50/50	3.8 (50)	100	50/50	3.6 (50)	95	50/50
2-7	3.8 (50)	50/50	3.7 (50)	97	50/50	3.7 (50)	97	50/50	3.7 (49)	97	50/50
3-7	3.8 (50)	50/50	3.7 (50)	97	50/50	3.7 (50)	97	50/50	3.7 (50)	97	50/50
4-7	3.9 (50)	50/50	3.8 (50)	97	50/50	3.8 (50)	97	50/50	3.8 (50)	97	50/50
5-7	3.9 (50)	50/50	3.9 (50)	100	50/50	3.8 (50)	97	50/50	3.7 (50)	95	50/50
6-7	3.9 (50)	50/50	3.8 (50)	97	50/50	3.8 (50)	97	50/50	3.8 (50)	97	50/50
7-7	4.0 (50)	50/50	3.9 (50)	98	50/50	3.9 (50)	98	50/50	3.8 (50)	95	50/50
8-7	4.1 (50)	50/50	4.0 (50)	98	50/50	4.0 (50)	98	50/50	4.0 (50)	98	50/50
9-7	4.2 (50)	50/50	4.2 (50)	100	50/50	4.1 (50)	98	50/50	4.1 (50)	98	50/50
10-7	4.2 (50)	50/50	4.1 (50)	98	50/50	4.1 (50)	98	50/50	4.0 (50)	95	50/50
11-7	4.2 (50)	50/50	4.1 (50)	98	50/50	4.1 (50)	98	50/50	4.0 (50)	95	50/50
12-7	4.2 (50)	50/50	4.0 (50)	95	50/50	4.0 (50)	95	50/50	4.0 (50)	95	50/50
13-7	4.3 (50)	50/50	4.1 (50)	95	50/50	4.1 (50)	95	50/50	4.0 (50)	93	50/50
14-7	3.9 (50)	50/50	3.9 (50)	100	50/50	3.9 (50)	100	50/50	3.9 (50)	100	50/50
18-7	4.1 (50)	50/50	4.0 (50)	98	50/50	3.9 (50)	95	50/50	3.9 (50)	95	50/50
22-7	4.2 (50)	50/50	4.1 (50)	98	50/50	4.0 (49)	95	50/50	4.0 (50)	95	50/50
26-7	4.4 (50)	50/50	4.2 (50)	95	50/50	4.2 (50)	95	50/50	4.1 (50)	93	50/50
30-7	4.3 (50)	50/50	4.2 (49)	98	49/50	4.1 (50)	95	50/50	4.2 (50)	98	50/50
34-7	4.3 (50)	50/50	4.2 (49)	98	49/50	4.2 (50)	98	50/50	4.1 (50)	95	50/50
38-7	4.4 (50)	50/50	4.3 (49)	98	49/50	4.2 (50)	95	50/50	4.2 (50)	95	50/50
42-7	4.5 (50)	50/50	4.4 (49)	98	49/50	4.3 (50)	96	50/50	4.3 (50)	96	50/50
46-7	4.4 (50)	50/50	4.3 (49)	98	49/50	4.2 (50)	95	50/50	4.2 (50)	95	50/50
50-7	4.4 (50)	50/50	4.3 (49)	98	49/50	4.2 (50)	95	50/50	4.2 (50)	95	50/50
54-7	4.4 (50)	50/50	4.2 (49)	95	49/50	4.1 (50)	93	50/50	4.0 (50)	91	50/50
58-7	4.4 (50)	50/50	4.2 (49)	95	49/50	4.1 (49)	93	49/50	4.2 (49)	95	49/50
62-7	4.7 (50)	50/50	4.5 (49)	96	49/50	4.3 (49)	91	49/50	4.3 (49)	91	49/50
66-7	4.6 (50)	50/50	4.6 (49)	100	49/50	4.5 (49)	98	49/50	4.3 (49)	93	49/50
70-7	4.8 (49)	49/50	4.8 (47)	100	47/50	4.6 (49)	96	49/50	4.5 (49)	94	49/50
74-7	5.0 (47)	47/50	4.8 (47)	96	47/50	4.7 (48)	94	48/50	4.6 (49)	92	49/50
78-7	4.9 (47)	47/50	4.7 (46)	96	46/50	4.6 (48)	94	48/50	4.6 (49)	94	49/50
82-7	4.9 (46)	46/50	4.9 (43)	100	43/50	4.8 (46)	98	46/50	4.6 (48)	94	48/50
86-7	5.1 (44)	44/50	4.9 (41)	96	41/50	4.9 (45)	96	45/50	4.6 (48)	90	48/50
90-7	4.8 (41)	41/50	4.8 (40)	100	40/50	4.8 (43)	100	43/50	4.7 (45)	98	45/50
94-7	4.8 (40)	40/50	4.8 (38)	100	38/50	4.7 (41)	98	41/50	4.5 (45)	94	45/50
98-7	5.2 (38)	38/50	5.0 (36)	96	36/50	4.9 (36)	94	36/50	4.6 (45)	88	45/50
102-7	5.0 (35)	35/50	4.8 (35)	96	35/50	4.6 (36)	92	36/50	4.5 (41)	90	41/50
104-7	4.9 (35)	35/50	4.8 (33)	98	33/50	4.6 (36)	94	36/50	4.4 (41)	90	41/50

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

TABLE D 2

FOOD CONSUMPTION CHANGES AND

SURVIVAL ANIMAL NUMBERS: FEMALE

STUDY NO. : 0613
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>	2500 ppm Av. FC.	2500 ppm % of cont. <50>	2500 ppm No. of Surviv.	5000 ppm Av. FC.	5000 ppm % of cont. <50>	5000 ppm No. of Surviv.	10000 ppm Av. FC.	10000 ppm % of cont. <50>	10000 ppm No. of Surviv.
1-7	3.4 (50)	50/50	3.3 (50)	97	50/50	3.4 (50)	100	50/50	3.4 (50)	100	50/50
2-7	3.4 (50)	50/50	3.3 (50)	97	50/50	3.3 (50)	97	50/50	3.3 (50)	97	50/50
3-7	3.5 (50)	50/50	3.4 (50)	97	50/50	3.3 (50)	94	50/50	3.4 (50)	97	50/50
4-7	3.4 (50)	50/50	3.4 (50)	100	50/50	3.3 (50)	97	50/50	3.3 (50)	97	50/50
5-7	3.5 (50)	50/50	3.5 (50)	100	50/50	3.5 (50)	100	50/50	3.4 (50)	97	50/50
6-7	3.6 (50)	50/50	3.5 (50)	97	50/50	3.4 (50)	94	50/50	3.4 (50)	94	50/50
7-7	3.7 (50)	50/50	3.7 (50)	100	50/50	3.6 (50)	97	50/50	3.5 (50)	95	50/50
8-7	3.8 (50)	50/50	3.8 (50)	100	50/50	3.7 (50)	97	50/50	3.8 (50)	100	50/50
9-7	3.8 (50)	50/50	3.8 (50)	100	50/50	3.7 (50)	97	50/50	3.8 (50)	100	50/50
10-7	3.9 (50)	50/50	3.8 (50)	97	50/50	3.7 (50)	95	50/50	3.7 (50)	95	50/50
11-7	3.8 (50)	50/50	3.8 (50)	100	50/50	3.7 (50)	97	50/50	3.8 (50)	100	50/50
12-7	3.8 (50)	50/50	3.7 (50)	97	50/50	3.7 (50)	97	50/50	3.7 (50)	97	50/50
13-7	3.8 (50)	50/50	3.8 (50)	100	50/50	3.7 (50)	97	50/50	3.7 (50)	97	50/50
14-7	3.6 (50)	50/50	3.7 (50)	103	50/50	3.6 (50)	100	50/50	3.5 (49)	97	50/50
18-7	3.6 (50)	50/50	3.7 (50)	103	50/50	3.5 (50)	97	50/50	3.6 (50)	100	50/50
22-7	3.8 (50)	50/50	3.8 (50)	100	50/50	3.7 (50)	97	50/50	3.7 (50)	97	50/50
26-7	3.9 (50)	50/50	4.0 (50)	103	50/50	3.9 (50)	100	50/50	4.0 (50)	103	50/50
30-7	3.8 (50)	50/50	3.8 (50)	100	50/50	3.7 (50)	97	50/50	3.9 (49)	103	49/50
34-7	3.8 (50)	50/50	3.8 (50)	100	50/50	3.7 (50)	97	50/50	3.8 (49)	100	49/50
38-7	4.0 (50)	50/50	3.9 (50)	98	50/50	3.9 (50)	98	50/50	3.8 (49)	95	49/50
42-7	4.1 (50)	50/50	4.0 (50)	98	50/50	3.9 (50)	95	50/50	3.8 (49)	93	49/50
46-7	3.9 (50)	50/50	3.9 (50)	100	50/50	3.9 (50)	100	50/50	3.8 (49)	97	49/50
50-7	4.1 (50)	50/50	3.9 (49)	95	49/50	3.9 (49)	95	49/50	3.9 (49)	95	49/50
54-7	4.0 (50)	50/50	3.8 (48)	95	48/50	3.8 (48)	95	48/50	3.9 (49)	98	49/50
58-7	3.8 (50)	50/50	3.9 (47)	103	47/50	3.6 (48)	95	48/50	3.7 (49)	97	49/50
62-7	4.1 (50)	50/50	4.0 (46)	98	46/50	3.8 (47)	93	47/50	3.9 (49)	95	49/50
66-7	4.2 (49)	49/50	4.0 (45)	95	45/50	4.0 (46)	95	46/50	3.9 (48)	93	48/50
70-7	4.1 (49)	49/50	4.1 (41)	100	41/50	4.0 (46)	98	46/50	4.0 (48)	98	48/50
74-7	4.0 (47)	47/50	4.1 (40)	103	40/50	3.9 (44)	98	44/50	3.7 (48)	93	48/50
78-7	4.0 (44)	44/50	4.0 (39)	100	39/50	3.8 (44)	95	44/50	3.8 (46)	95	46/50
82-7	4.1 (44)	44/50	4.3 (36)	105	36/50	4.1 (41)	100	41/50	4.0 (42)	98	42/50
86-7	4.4 (41)	41/50	4.2 (34)	95	34/50	4.3 (40)	98	40/50	4.1 (39)	93	39/50
90-7	4.5 (40)	40/50	4.2 (34)	93	34/50	4.1 (38)	91	38/50	4.0 (36)	89	36/50
94-7	4.3 (39)	39/50	4.4 (33)	102	33/50	4.3 (36)	100	36/50	3.8 (32)	88	32/50
98-7	4.6 (34)	34/50	4.4 (30)	96	30/50	4.4 (34)	96	34/50	3.9 (30)	85	30/50
102-7	4.2 (32)	32/50	4.2 (28)	100	28/50	4.2 (32)	100	32/50	4.0 (24)	95	24/50
104-7	4.3 (29)	29/50	4.2 (26)	98	26/50	4.2 (31)	98	31/50	3.9 (20)	91	20/50

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

TABLE D 3

FOOD CONSUMPTION CHANGES: MALE

STUDY NO. : 0613
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	3.8± 0.3	3.8± 0.3	3.8± 0.3	3.9± 0.2	3.9± 0.3	3.9± 0.3	4.0± 0.3
5000 ppm	3.8± 0.4	3.7± 0.3	3.7± 0.3	3.8± 0.3	3.9± 0.3	3.8± 0.2	3.9± 0.3
10000 ppm	3.8± 0.3	3.7± 0.2	3.7± 0.2	3.8± 0.2*	3.8± 0.3	3.8± 0.2	3.9± 0.3**
20000 ppm	3.6± 0.2**	3.7± 0.2**	3.7± 0.2**	3.8± 0.2*	3.7± 0.2*	3.8± 0.4**	3.8± 0.2**

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

STUDY NO. : 0613
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	4.1± 0.3	4.2± 0.3	4.2± 0.3	4.2± 0.3	4.2± 0.3	4.3± 0.3	3.9± 0.3
5000 ppm	4.0± 0.2	4.2± 0.3	4.1± 0.3	4.1± 0.2	4.0± 0.2	4.1± 0.3*	3.9± 0.3
10000 ppm	4.0± 0.2**	4.1± 0.3	4.1± 0.2*	4.1± 0.3	4.0± 0.3*	4.1± 0.3**	3.9± 0.3
20000 ppm	4.0± 0.3*	4.1± 0.3*	4.0± 0.3**	4.0± 0.3**	4.0± 0.3**	4.0± 0.2**	3.9± 0.2

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

STUDY NO. : 0613
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	4.1± 0.3	4.2± 0.2	4.4± 0.3	4.3± 0.3	4.3± 0.3	4.4± 0.3	4.5± 0.3
5000 ppm	4.0± 0.2*	4.1± 0.3	4.2± 0.3*	4.2± 0.3	4.2± 0.3	4.3± 0.3*	4.4± 0.3
10000 ppm	3.9± 0.3**	4.0± 0.3**	4.2± 0.3*	4.1± 0.3**	4.2± 0.3	4.2± 0.3**	4.3± 0.3**
20000 ppm	3.9± 0.3**	4.0± 0.3**	4.1± 0.3**	4.2± 0.3	4.1± 0.3*	4.2± 0.3**	4.3± 0.3**

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

STUDY NO. : 0613
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	4.4± 0.3	4.4± 0.3	4.4± 0.3	4.4± 0.3	4.7± 0.3	4.6± 0.6	4.8± 0.5
5000 ppm	4.3± 0.3	4.3± 0.3	4.2± 0.3**	4.2± 0.3**	4.5± 0.3**	4.6± 0.5	4.8± 0.3
10000 ppm	4.2± 0.3*	4.2± 0.3	4.1± 0.3**	4.1± 0.3**	4.3± 0.3**	4.5± 0.3**	4.6± 0.4**
20000 ppm	4.2± 0.3**	4.2± 0.3**	4.0± 0.3**	4.2± 0.3**	4.3± 0.3**	4.3± 0.3**	4.5± 0.3**

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

STUDY NO. : 0613
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	5.0± 0.4	4.9± 0.4	4.9± 0.8	5.1± 0.4	4.8± 0.6	4.8± 0.6	5.2± 0.7
5000 ppm	4.8± 0.4	4.7± 0.8	4.9± 0.5	4.9± 0.7	4.8± 0.5	4.8± 0.4	5.0± 0.6
10000 ppm	4.7± 0.5**	4.6± 0.4**	4.8± 0.3	4.9± 0.3*	4.8± 0.4	4.7± 0.5	4.9± 0.3*
20000 ppm	4.6± 0.3**	4.6± 0.3**	4.6± 0.4**	4.6± 0.5**	4.7± 0.4	4.5± 0.4*	4.6± 0.4**

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

(HAN260)

STUDY NO. : 0613
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	5.0± 0.5	4.9± 0.5
5000 ppm	4.8± 0.8	4.8± 0.7
10000 ppm	4.6± 0.4**	4.6± 0.4*
20000 ppm	4.5± 0.6**	4.4± 0.5**

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

TABLE D 4

FOOD CONSUMPTION CHANGES: FEMALE

STUDY NO. : 0613
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	3.4± 0.3	3.4± 0.2	3.5± 0.2	3.4± 0.2	3.5± 0.2	3.6± 0.2	3.7± 0.2
2500 ppm	3.3± 0.3	3.3± 0.2	3.4± 0.2	3.4± 0.2	3.5± 0.2	3.5± 0.2	3.7± 0.2
5000 ppm	3.4± 0.3	3.3± 0.2	3.3± 0.2	3.3± 0.2*	3.5± 0.2	3.4± 0.2**	3.6± 0.2*
10000 ppm	3.4± 0.3	3.3± 0.2	3.4± 0.2	3.3± 0.2*	3.4± 0.2**	3.4± 0.2*	3.5± 0.2**

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

(HAN260)

BAIS 4

STUDY NO. : 0613
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± 0.2	3.8± 0.2	3.9± 0.3	3.8± 0.3	3.8± 0.2	3.8± 0.3	3.6± 0.2
2500 ppm	3.8± 0.2	3.8± 0.2	3.8± 0.2	3.8± 0.3	3.7± 0.2	3.8± 0.2	3.7± 0.3
5000 ppm	3.7± 0.3	3.7± 0.2	3.7± 0.3**	3.7± 0.2	3.7± 0.3	3.7± 0.2	3.6± 0.3
10000 ppm	3.8± 0.3	3.8± 0.2	3.7± 0.3**	3.8± 0.2	3.7± 0.3	3.7± 0.3	3.5± 0.2

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

STUDY NO. : 0613
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	3.6± 0.6	3.8± 0.3	3.9± 0.4	3.8± 0.4	3.8± 0.4	4.0± 0.4	4.1± 0.4
2500 ppm	3.7± 0.3	3.8± 0.3	4.0± 0.3	3.8± 0.3	3.8± 0.4	3.9± 0.5	4.0± 0.4
5000 ppm	3.5± 0.3	3.7± 0.3	3.9± 0.3	3.7± 0.4	3.7± 0.3	3.9± 0.4	3.9± 0.4
10000 ppm	3.6± 0.4	3.7± 0.3	4.0± 0.3	3.9± 0.4	3.8± 0.4	3.8± 0.4	3.8± 0.4**

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

(HAN260)

BAIS 4

STUDY NO. : 0613
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	3.9± 0.4	4.1± 0.6	4.0± 0.5	3.8± 0.5	4.1± 0.6	4.2± 0.5	4.1± 0.6
2500 ppm	3.9± 0.4	3.9± 0.5	3.8± 0.4	3.9± 0.4	4.0± 0.5	4.0± 0.7*	4.1± 0.4
5000 ppm	3.9± 0.4	3.9± 0.4	3.8± 0.4	3.6± 0.4	3.8± 0.5*	4.0± 0.4*	4.0± 0.4
10000 ppm	3.8± 0.4	3.9± 0.4	3.9± 0.4	3.7± 0.5	3.9± 0.5	3.9± 0.4**	4.0± 0.5

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

(HAN260)

BAIS 4

STUDY NO. : 0613
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	4.0± 0.6	4.0± 0.5	4.1± 0.6	4.4± 0.5	4.5± 0.6	4.3± 0.9	4.6± 0.7
2500 ppm	4.1± 0.5	4.0± 0.6	4.3± 0.6	4.2± 0.7	4.2± 0.6	4.4± 0.9	4.4± 0.7
5000 ppm	3.9± 0.5	3.8± 0.5	4.1± 0.5	4.3± 0.9	4.1± 0.5*	4.3± 0.5	4.4± 0.4
10000 ppm	3.7± 0.4	3.8± 0.4	4.0± 0.5	4.1± 0.5*	4.0± 0.8**	3.8± 0.5**	3.9± 0.7**

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

STUDY NO. : 0613
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± 0.6	4.3± 0.8
2500 ppm	4.2± 0.7	4.2± 0.7
5000 ppm	4.2± 0.6	4.2± 0.6
10000 ppm	4.0± 0.5	3.9± 0.5

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. : 0613
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>	5000 ppm Av. WC.	5000 ppm % of cont. <50>	5000 ppm No. of Surviv.	10000 ppm Av. WC.	10000 ppm % of cont. <50>	10000 ppm No. of Surviv.	20000 ppm Av. WC.	20000 ppm % of cont. <50>	20000 ppm No. of Surviv.
1-7	4.5 (50)	50/50	4.0 (50)	89	50/50	4.0 (49)	89	50/50	3.7 (49)	82	50/50
2-7	4.3 (48)	50/50	4.0 (50)	93	50/50	3.9 (50)	91	50/50	3.7 (50)	86	50/50
3-7	4.3 (49)	50/50	4.0 (50)	93	50/50	3.8 (49)	88	50/50	3.6 (49)	84	50/50
4-7	4.2 (49)	50/50	3.8 (50)	90	50/50	3.7 (50)	88	50/50	3.4 (50)	81	50/50
5-7	4.5 (50)	50/50	3.8 (50)	84	50/50	3.6 (49)	80	50/50	3.5 (50)	78	50/50
6-7	4.2 (50)	50/50	3.7 (50)	88	50/50	3.5 (49)	83	50/50	3.3 (50)	79	50/50
7-7	4.3 (50)	50/50	3.8 (50)	88	50/50	3.6 (50)	84	50/50	3.3 (50)	77	50/50
8-7	4.2 (50)	50/50	3.7 (50)	88	50/50	3.5 (50)	83	50/50	3.2 (50)	76	50/50
9-7	4.1 (50)	50/50	3.6 (50)	88	50/50	3.3 (50)	80	50/50	3.1 (50)	76	50/50
10-7	4.0 (50)	50/50	3.4 (50)	85	50/50	3.2 (50)	80	50/50	3.0 (49)	75	50/50
11-7	3.8 (50)	50/50	3.4 (50)	89	50/50	3.2 (50)	84	50/50	3.0 (50)	79	50/50
12-7	3.9 (50)	50/50	3.4 (50)	87	50/50	3.2 (50)	82	50/50	3.0 (50)	77	50/50
13-7	3.8 (50)	50/50	3.3 (50)	87	50/50	3.1 (50)	82	50/50	2.9 (50)	76	50/50
14-7	3.9 (50)	50/50	3.4 (50)	87	50/50	3.2 (50)	82	50/50	3.1 (50)	79	50/50
18-7	3.8 (50)	50/50	3.3 (49)	87	50/50	3.3 (50)	87	50/50	2.9 (49)	76	50/50
22-7	3.8 (50)	50/50	3.3 (50)	87	50/50	3.1 (49)	82	50/50	2.8 (50)	74	50/50
26-7	3.7 (49)	50/50	3.3 (50)	89	50/50	3.2 (49)	86	50/50	3.0 (48)	81	50/50
30-7	3.7 (50)	50/50	3.3 (49)	89	49/50	3.1 (50)	84	50/50	2.9 (50)	78	50/50
34-7	3.8 (50)	50/50	3.3 (49)	87	49/50	3.1 (50)	82	50/50	2.9 (50)	76	50/50
38-7	3.8 (50)	50/50	3.3 (49)	87	49/50	3.2 (50)	84	50/50	3.0 (50)	79	50/50
42-7	3.8 (49)	50/50	3.4 (49)	89	49/50	3.2 (50)	84	50/50	3.0 (50)	79	50/50
46-7	3.9 (50)	50/50	3.3 (49)	85	49/50	3.2 (50)	82	50/50	3.0 (50)	77	50/50
50-7	3.8 (50)	50/50	3.3 (49)	87	49/50	3.3 (50)	87	50/50	2.9 (50)	76	50/50
54-7	3.9 (50)	50/50	3.3 (49)	85	49/50	3.3 (50)	85	50/50	3.1 (50)	79	50/50
58-7	3.8 (49)	50/50	3.3 (49)	87	49/50	3.2 (49)	84	49/50	3.1 (49)	82	49/50
62-7	4.1 (50)	50/50	3.5 (49)	85	49/50	3.5 (49)	85	49/50	3.3 (49)	80	49/50
66-7	4.2 (50)	50/50	3.7 (49)	88	49/50	3.6 (49)	86	49/50	3.3 (49)	79	49/50
70-7	4.3 (49)	49/50	3.7 (47)	86	47/50	3.6 (49)	84	49/50	3.4 (49)	79	49/50
74-7	4.3 (46)	47/50	3.8 (47)	88	47/50	3.7 (48)	86	48/50	3.5 (49)	81	49/50
78-7	4.6 (46)	47/50	3.9 (45)	85	46/50	3.9 (48)	85	48/50	3.7 (49)	80	49/50
82-7	4.4 (45)	46/50	4.0 (43)	91	43/50	3.9 (46)	89	46/50	3.6 (48)	82	48/50
86-7	4.4 (43)	44/50	3.7 (41)	84	41/50	3.9 (44)	89	45/50	3.4 (48)	77	48/50
90-7	4.5 (39)	41/50	4.0 (40)	89	40/50	3.8 (42)	84	43/50	3.7 (45)	82	45/50
94-7	4.7 (35)	40/50	4.1 (38)	87	38/50	4.0 (40)	85	41/50	3.8 (45)	81	45/50
98-7	4.9 (35)	38/50	4.4 (36)	90	36/50	4.2 (36)	86	36/50	3.8 (45)	78	45/50
102-7	4.9 (32)	35/50	4.1 (34)	84	35/50	4.2 (36)	86	36/50	3.9 (41)	80	41/50
104-7	4.9 (29)	35/50	4.1 (32)	84	33/50	4.1 (35)	84	36/50	3.9 (40)	80	41/50

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

TABLE E 2

WATER CONSUMPTION CHANGES AND

SURVIVAL ANIMAL NUMBERS: FEMALE

STUDY NO. : 0613
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>	2500 ppm Av. WC.	2500 ppm % of cont. <50>	2500 ppm No. of Surviv.	5000 ppm Av. WC.	5000 ppm % of cont. <50>	5000 ppm No. of Surviv.	10000 ppm Av. WC.	10000 ppm % of cont. <50>	10000 ppm No. of Surviv.
1-7	4.3 (50)	50/50	3.8 (50)	88	50/50	3.8 (50)	88	50/50	3.8 (50)	88	50/50
2-7	4.1 (50)	50/50	3.9 (50)	95	50/50	3.7 (50)	90	50/50	3.7 (50)	90	50/50
3-7	4.1 (50)	50/50	3.9 (50)	95	50/50	3.8 (50)	93	50/50	3.8 (50)	93	50/50
4-7	4.0 (50)	50/50	3.9 (50)	98	50/50	3.7 (50)	93	50/50	3.6 (50)	90	50/50
5-7	4.1 (50)	50/50	3.8 (49)	93	50/50	3.7 (50)	90	50/50	3.6 (50)	88	50/50
6-7	4.1 (50)	50/50	3.9 (50)	95	50/50	3.6 (50)	88	50/50	3.7 (50)	90	50/50
7-7	4.3 (50)	50/50	4.2 (50)	98	50/50	4.0 (50)	93	50/50	3.9 (50)	91	50/50
8-7	4.0 (50)	50/50	3.9 (49)	98	50/50	3.9 (50)	98	50/50	3.8 (50)	95	50/50
9-7	4.0 (50)	50/50	3.9 (50)	98	50/50	3.7 (50)	93	50/50	3.6 (50)	90	50/50
10-7	4.0 (50)	50/50	3.8 (50)	95	50/50	3.6 (50)	90	50/50	3.7 (50)	93	50/50
11-7	3.8 (50)	50/50	3.8 (50)	100	50/50	3.5 (50)	92	50/50	3.7 (50)	97	50/50
12-7	3.8 (50)	50/50	3.7 (50)	97	50/50	3.7 (50)	97	50/50	3.6 (50)	95	50/50
13-7	3.9 (50)	50/50	3.7 (50)	95	50/50	3.5 (50)	90	50/50	3.5 (50)	90	50/50
14-7	3.8 (50)	50/50	3.7 (50)	97	50/50	3.6 (50)	95	50/50	3.4 (50)	89	50/50
18-7	4.2 (50)	50/50	3.8 (48)	90	50/50	3.6 (50)	86	50/50	3.6 (50)	86	50/50
22-7	4.1 (49)	50/50	3.7 (49)	90	50/50	3.7 (50)	90	50/50	3.5 (50)	85	50/50
26-7	4.0 (50)	50/50	3.7 (49)	93	50/50	3.6 (50)	90	50/50	3.7 (50)	93	50/50
30-7	4.0 (50)	50/50	3.6 (48)	90	50/50	3.4 (50)	85	50/50	3.4 (49)	85	49/50
34-7	4.0 (49)	50/50	3.6 (49)	90	50/50	3.6 (49)	90	50/50	3.4 (48)	85	49/50
38-7	3.8 (49)	50/50	3.6 (49)	95	50/50	3.7 (50)	97	50/50	3.4 (48)	89	49/50
42-7	3.9 (50)	50/50	3.5 (49)	90	50/50	3.6 (50)	92	50/50	3.3 (49)	85	49/50
46-7	3.9 (50)	50/50	3.5 (50)	90	50/50	3.4 (49)	87	50/50	3.3 (49)	85	49/50
50-7	3.9 (50)	50/50	3.4 (48)	87	49/50	3.4 (49)	87	49/50	3.2 (49)	82	49/50
54-7	3.8 (50)	50/50	3.5 (48)	92	48/50	3.4 (48)	89	48/50	3.4 (49)	89	49/50
58-7	3.7 (50)	50/50	3.5 (47)	95	47/50	3.2 (48)	86	48/50	3.2 (49)	86	49/50
62-7	3.9 (49)	50/50	3.6 (46)	92	46/50	3.5 (47)	90	47/50	3.3 (49)	85	49/50
66-7	4.1 (48)	49/50	3.7 (43)	90	45/50	3.4 (46)	83	46/50	3.3 (48)	80	48/50
70-7	4.0 (47)	49/50	3.7 (40)	93	41/50	3.5 (46)	88	46/50	3.1 (48)	78	48/50
74-7	4.3 (46)	47/50	3.9 (40)	91	40/50	3.5 (44)	81	44/50	3.3 (48)	77	48/50
78-7	4.2 (44)	44/50	3.8 (37)	90	39/50	3.5 (44)	83	44/50	3.4 (46)	81	46/50
82-7	4.1 (43)	44/50	3.9 (35)	95	36/50	3.6 (41)	88	41/50	3.4 (42)	83	42/50
86-7	4.2 (40)	41/50	3.5 (34)	83	34/50	3.5 (40)	83	40/50	3.4 (39)	81	39/50
90-7	4.3 (39)	40/50	3.7 (34)	86	34/50	3.6 (38)	84	38/50	3.3 (35)	77	36/50
94-7	4.3 (38)	39/50	3.9 (33)	91	33/50	3.7 (36)	86	36/50	3.5 (32)	81	32/50
98-7	4.3 (32)	34/50	4.1 (30)	95	30/50	3.8 (34)	88	34/50	3.5 (30)	81	30/50
102-7	4.3 (32)	32/50	3.9 (28)	91	28/50	3.7 (32)	86	32/50	3.8 (24)	88	24/50
104-7	4.2 (29)	29/50	3.7 (26)	88	26/50	3.7 (31)	88	31/50	3.8 (20)	90	20/50

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

TABLE E 3

WATER CONSUMPTION CHANGES: MALE

STUDY NO. : 0613
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	4.5± 0.7	4.3± 0.8	4.3± 0.8	4.2± 0.7	4.5± 0.9	4.2± 0.9	4.3± 0.7
5000 ppm	4.0± 0.9**	4.0± 0.7	4.0± 0.7	3.8± 0.7*	3.8± 0.6**	3.7± 0.7**	3.8± 0.7**
10000 ppm	4.0± 0.8**	3.9± 0.8*	3.8± 0.6**	3.7± 0.8**	3.6± 0.6**	3.5± 0.5**	3.6± 0.7**
20000 ppm	3.7± 0.5**	3.7± 0.8**	3.6± 0.4**	3.4± 0.6**	3.5± 0.5**	3.3± 0.5**	3.3± 0.4**

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

STUDY NO. : 0613
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	4.2± 0.7	4.1± 0.6	4.0± 0.7	3.8± 0.6	3.9± 0.6	3.8± 0.5	3.9± 0.5
5000 ppm	3.7± 0.7**	3.6± 0.6**	3.4± 0.6**	3.4± 0.5**	3.4± 0.5**	3.3± 0.5**	3.4± 0.5**
10000 ppm	3.5± 0.6**	3.3± 0.5**	3.2± 0.5**	3.2± 0.4**	3.2± 0.4**	3.1± 0.4**	3.2± 0.4**
20000 ppm	3.2± 0.6**	3.1± 0.4**	3.0± 0.4**	3.0± 0.4**	3.0± 0.5**	2.9± 0.4**	3.1± 0.4**

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

STUDY NO. : 0613
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	3.8± 0.5	3.8± 0.4	3.7± 0.3	3.7± 0.3	3.8± 0.5	3.8± 0.4	3.8± 0.4
5000 ppm	3.3± 0.4**	3.3± 0.3**	3.3± 0.3**	3.3± 0.5**	3.3± 0.3**	3.3± 0.3**	3.4± 0.3**
10000 ppm	3.3± 0.6**	3.1± 0.4**	3.2± 0.6**	3.1± 0.4**	3.1± 0.4**	3.2± 0.4**	3.2± 0.4**
20000 ppm	2.9± 0.4**	2.8± 0.3**	3.0± 0.5**	2.9± 0.3**	2.9± 0.3**	3.0± 0.3**	3.0± 0.3**

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

(HAN260)

BAIS 4

STUDY NO. : 0613
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± 0.6	3.8± 0.5	3.9± 0.4	3.8± 0.5	4.1± 0.4	4.2± 0.8	4.3± 0.8
5000 ppm	3.3± 0.3**	3.3± 0.3**	3.3± 0.3**	3.3± 0.3**	3.5± 0.3**	3.7± 0.4**	3.7± 0.4**
10000 ppm	3.2± 0.4**	3.3± 0.4**	3.3± 0.4**	3.2± 0.3**	3.5± 0.3**	3.6± 0.4**	3.6± 0.5**
20000 ppm	3.0± 0.3**	2.9± 0.3**	3.1± 0.3**	3.1± 0.3**	3.3± 0.3**	3.3± 0.3**	3.4± 0.3**

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

STUDY NO. : 0613
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	4.3± 0.5	4.6± 0.5	4.4± 0.7	4.4± 0.7	4.5± 1.0	4.7± 0.6	4.9± 0.8
5000 ppm	3.8± 0.5**	3.9± 0.7**	4.0± 0.5**	3.7± 0.7**	4.0± 0.6**	4.1± 0.7**	4.4± 0.8*
10000 ppm	3.7± 0.7**	3.9± 0.6**	3.9± 0.5**	3.9± 0.7**	3.8± 0.5**	4.0± 0.7**	4.2± 0.6**
20000 ppm	3.5± 0.3**	3.7± 0.3**	3.6± 0.4**	3.4± 0.6**	3.7± 0.3**	3.8± 0.6**	3.8± 0.5**

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

STUDY NO. : 0613
ANIMAL : MOUSE B6D2F1/Crlj[Cr;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	4.9± 1.0	4.9± 0.8
5000 ppm	4.1± 0.8**	4.1± 0.8**
10000 ppm	4.2± 0.8**	4.1± 0.5**
20000 ppm	3.9± 0.6**	3.9± 0.8**

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

TABLE E 4

WATER CONSUMPTION CHANGES: FEMALE

STUDY NO. : 0613
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± 0.4	4.1± 0.4	4.0± 0.3	4.1± 0.4	4.1± 0.4	4.3± 0.4
2500 ppm	3.8± 0.6**	3.9± 0.5**	3.9± 0.4	3.9± 0.4	3.8± 0.3**	3.9± 0.4	4.2± 0.6
5000 ppm	3.8± 0.4**	3.7± 0.3**	3.8± 0.3**	3.7± 0.4**	3.7± 0.3**	3.6± 0.4**	4.0± 0.4**
10000 ppm	3.8± 0.4**	3.7± 0.5**	3.8± 0.5**	3.6± 0.4**	3.6± 0.4**	3.7± 0.4**	3.9± 0.4**

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

STUDY NO. : 0613
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	4.0± 0.4	4.0± 0.4	4.0± 0.4	3.8± 0.4	3.8± 0.4	3.9± 0.5	3.8± 0.4
2500 ppm	3.9± 0.4	3.9± 0.6*	3.8± 0.4*	3.8± 0.4	3.7± 0.6	3.7± 0.4*	3.7± 0.5
5000 ppm	3.9± 0.5	3.7± 0.6**	3.6± 0.3**	3.5± 0.4**	3.7± 0.4	3.5± 0.4**	3.6± 0.5*
10000 ppm	3.8± 0.4*	3.6± 0.4**	3.7± 0.4**	3.7± 0.4	3.6± 0.3*	3.5± 0.4**	3.4± 0.3**

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

STUDY NO. : 0613
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	4.2± 0.7	4.1± 0.7	4.0± 0.8	4.0± 0.8	4.0± 0.8	3.8± 0.7	3.9± 0.6
2500 ppm	3.8± 0.5**	3.7± 0.3**	3.7± 0.5	3.6± 0.4	3.6± 0.7**	3.6± 0.4	3.5± 0.5**
5000 ppm	3.6± 0.5**	3.7± 0.4**	3.6± 0.4	3.4± 0.5**	3.6± 0.4*	3.7± 0.4	3.6± 0.8**
10000 ppm	3.6± 0.3**	3.5± 0.4**	3.7± 0.9**	3.4± 0.5**	3.4± 0.6**	3.4± 0.5**	3.3± 0.4**

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

STUDY NO. : 0613
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	3.9± 0.7	3.9± 0.5	3.8± 0.6	3.7± 0.4	3.9± 0.6	4.1± 0.5	4.0± 0.7
2500 ppm	3.5± 0.6**	3.4± 0.7**	3.5± 0.6*	3.5± 0.8**	3.6± 0.7**	3.7± 0.8**	3.7± 0.6
5000 ppm	3.4± 0.8**	3.4± 0.4**	3.4± 0.5**	3.2± 0.5**	3.5± 0.5**	3.4± 0.5**	3.5± 0.7**
10000 ppm	3.3± 0.5**	3.2± 0.5**	3.4± 0.4**	3.2± 0.4**	3.3± 0.5**	3.3± 0.5**	3.1± 0.4**

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

STUDY NO. : 0613
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	4.3± 0.7	4.2± 0.8	4.1± 0.7	4.2± 0.6	4.3± 0.6	4.3± 1.0	4.3± 0.7
2500 ppm	3.9± 1.0**	3.8± 1.1**	3.9± 0.9	3.5± 0.8**	3.7± 0.8**	3.9± 1.0	4.1± 0.7
5000 ppm	3.5± 0.5**	3.5± 0.6**	3.6± 0.6**	3.5± 0.6**	3.6± 0.9**	3.7± 0.7**	3.8± 0.7*
10000 ppm	3.3± 0.6**	3.4± 0.7**	3.4± 0.5**	3.4± 0.8**	3.3± 0.9**	3.5± 0.7**	3.5± 0.9**

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

STUDY NO. : 0613
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	4.3± 0.7	4.2± 0.8
2500 ppm	3.9± 0.8	3.7± 1.1
5000 ppm	3.7± 0.8**	3.7± 1.0
10000 ppm	3.8± 0.8*	3.8± 0.8

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

TABLE F 1

CHEMICAL INTAKE CHANGES: MALE

STUDY NO. : 0613
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) 1		2		3		4		5		6		7	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
5000 ppm	809±	165	800±	124	767±	131	716±	134	683±	105	648±	124	660±	141
10000 ppm	1621±	322	1554±	328	1452±	224	1362±	325	1300±	218	1241±	179	1267±	282
20000 ppm	3077±	482	2970±	670	2716±	347	2537±	474	2525±	384	2376±	415	2361±	354

STUDY NO. : 0613
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
5000 ppm	636±	128	590±	112	559±	116	538±	100	526±	106	505±	95	514±	97
10000 ppm	1181±	238	1100±	191	1045±	198	1007±	179	999±	158	934±	149	968±	171
20000 ppm	2227±	411	2101±	341	1982±	324	1944±	360	1897±	352	1776±	289	1898±	326

STUDY NO. : 0613
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) 18		22		26		30		34		38		42	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
5000 ppm	469±	86	434±	60	421±	57	401±	73	386±	57	371±	50	376±	49
10000 ppm	911±	198	816±	138	809±	198	764±	121	723±	117	735±	125	729±	98
20000 ppm	1703±	292	1565±	204	1576±	318	1481±	195	1449±	172	1421±	187	1424±	177

STUDY NO. : 0613
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
5000 ppm	361±	48	345±	46	339±	39	342±	37	360±	44	375±	50	375±	53
10000 ppm	707±	104	696±	103	686±	122	662±	79	709±	81	728±	97	725±	105
20000 ppm	1358±	167	1298±	151	1348±	153	1327±	156	1403±	152	1388±	171	1422±	163

STUDY NO. : 0613
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
5000 ppm	381±	64	401±	80	406±	72	374±	90	413±	94	430±	107	454±	123
10000 ppm	733±	147	793±	129	796±	143	793±	174	768±	125	814±	133	864±	148
20000 ppm	1446±	158	1544±	210	1507±	205	1410±	239	1512±	231	1596±	400	1589±	293

STUDY NO. : 0613
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
5000 ppm	432±	111	434±	123
10000 ppm	872±	175	874±	173
20000 ppm	1654±	342	1665±	388

TABLE F 2

CHEMICAL INTAKE CHANGES: FEMALE

STUDY NO. : 0613
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
2500 ppm	484±	70	487±	69	471±	37	451±	47	436±	39	441±	48	459±	73
5000 ppm	948±	97	917±	90	909±	83	865±	70	833±	68	815±	79	879±	87
10000 ppm	1925±	207	1830±	236	1809±	225	1679±	216	1635±	182	1639±	181	1718±	200

(HAN300)

STUDY NO. : 0613
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) 8		9		10		11		12		13		14	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
2500 ppm	419±	41	408±	70	395±	50	394±	45	387±	69	374±	56	368±	64
5000 ppm	835±	98	785±	140	763±	75	746±	77	763±	81	713±	83	732±	105
10000 ppm	1649±	173	1538±	187	1561±	193	1540±	187	1494±	162	1444±	194	1399±	155

STUDY NO. : 0613
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) 18		22		26		30		34		38		42	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
2500 ppm	360±	57	341±	42	335±	60	316±	48	308±	74	300±	48	288±	57
5000 ppm	697±	88	697±	87	672±	85	606±	93	629±	97	611±	88	610±	143
10000 ppm	1386±	154	1311±	174	1332±	365	1183±	222	1191±	265	1135±	195	1121±	213

STUDY NO. : 0613
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) 46		50		54		58		62		66		70	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
2500 ppm	283±	61	269±	78	271±	79	261±	67	265±	61	269±	75	267±	47
5000 ppm	551±	122	535±	95	532±	99	504±	89	536±	93	516±	99	534±	150
10000 ppm	1060±	210	1020±	213	1041±	192	994±	176	997±	189	1006±	200	936±	176

STUDY NO. : 0613
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) 74		78		82		86		90		94		98	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
2500 ppm	286±	73	275±	78	276±	78	247±	53	259±	61	275±	64	288±	58
5000 ppm	523±	104	520±	117	543±	117	524±	126	526±	151	545±	128	561±	133
10000 ppm	1008±	200	1048±	259	1004±	177	1006±	248	978±	286	1046±	196	1049±	242

STUDY NO. : 0613
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) 102		104	
Control	0±	0	0±	0
2500 ppm	281±	64	281±	104
5000 ppm	548±	131	548±	152
10000 ppm	1145±	225	1220±	353

TABLE G 1

HEMATOLOGY: MALE

STUDY NO. : 0613
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	35	9.25± 1.98	13.5± 2.7	42.2± 7.2	46.4± 4.9	14.6± 0.8	31.7± 1.8	1653± 373
5000 ppm	32	9.06± 1.71	13.3± 2.4	41.6± 6.6	46.6± 3.7	14.7± 0.6	31.7± 1.7	1577± 416
10000 ppm	36	9.45± 1.03	13.8± 1.4	43.1± 3.8	45.8± 2.3	14.7± 0.8	32.0± 0.7	1579± 391
20000 ppm	39	9.56± 0.54	14.1± 0.9	43.9± 2.4	46.0± 1.1	14.8± 0.4	32.2± 0.7	1548± 334

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

(HCL070)

BAIS 4

STUDY NO. : 0613
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 %
Control	35	3.5± 3.7
5000 ppm	32	3.6± 3.9
10000 ppm	36	2.7± 1.0
20000 ppm	39	2.5± 0.9

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

(HCL070)

STUDY NO. : 0613
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 (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHER
Control	35	4.62± 2.54	2± 5	29± 13	2± 1	0± 0	4± 2	62± 17	1± 4
5000 ppm	32	4.31± 2.26	1± 3	25± 12	2± 1	0± 0	4± 2	68± 14	1± 2
10000 ppm	36	4.60± 2.66	1± 1	24± 10	3± 3	0± 0	5± 2	66± 11	1± 4
20000 ppm	39	4.07± 2.05	1± 1	28± 16	2± 1	0± 0	4± 2	65± 16	0± 1

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

(HCL070)

TABLE G 2

HEMATOLOGY: FEMALE

STUDY NO. : 0613
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	27	9.44± 1.16	14.0± 1.8	43.8± 4.9	46.5± 1.5	14.8± 0.5	32.0± 1.1	967± 313
2500 ppm	25	8.76± 1.67	13.2± 2.2	41.8± 5.2	48.8± 6.8	15.2± 0.9	31.4± 2.1	1012± 423
5000 ppm	30	9.46± 0.93	13.9± 1.5	43.3± 3.8	45.9± 1.8	14.7± 0.6	32.1± 1.0	980± 339
10000 ppm	18	9.25± 1.07	13.7± 1.9	42.5± 4.6	46.1± 2.2	14.8± 0.8	32.2± 1.1	1049± 250

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

(HCL070)

BAIS 4

STUDY NO. : 0613
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 %
Control	27	3.6± 2.6
2500 ppm	25	6.7± 10.8
5000 ppm	30	4.1± 4.2
10000 ppm	18	4.0± 3.8

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

STUDY NO. : 0613
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 (%) N-BAND		N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHER	
Control	27	11.42±	36.08	1±	1	19±	8	3±	4	0±	0	4±	2	67±	17	7±	21
2500 ppm	25	22.16±	96.11	2±	3	28±	14	3±	4	0±	0	4±	2	56±	20	6±	19
5000 ppm	30	4.17±	2.97	1±	1	21±	10	1±	1	0±	0	4±	2	68±	13	5±	9
10000 ppm	18	3.46±	2.90	1±	1	27±	16	2±	1	0±	0	5±	2	62±	18	4±	6

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

(HCL070)

TABLE H 1

BIOCHEMISTRY: MALE

STUDY NO. : 0613
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	35	5.0± 0.8	2.3± 0.4	0.9± 0.1	0.13± 0.03	156± 52	112± 41	46± 27
5000 ppm	32	5.0± 0.8	2.4± 0.4	1.0± 0.2	0.13± 0.03	175± 38	110± 45	45± 22
10000 ppm	36	5.4± 0.9	2.6± 0.4	0.9± 0.1	0.13± 0.02	194± 26**	127± 52	45± 18
20000 ppm	40	5.0± 0.5	2.4± 0.3	1.0± 0.1*	0.13± 0.03	190± 41**	105± 30	44± 24

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

(HCL074)

STUDY NO. : 0613
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 IU／ℓ	ALT IU／ℓ	LDH IU／ℓ	ALP IU／ℓ	G-GTP IU／ℓ	CK IU／ℓ
Control	35	186± 61	174± 292	97± 169	571± 667	136± 48	1± 1	91± 115
5000 ppm	32	194± 72	74± 47	44± 73	424± 393	139± 131	1± 1	60± 33
10000 ppm	36	219± 67	98± 140	73± 132	452± 277	133± 43	1± 1	55± 23
20000 ppm	40	185± 40	79± 103	32± 44*	409± 192	135± 35	1± 1	59± 30

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

(HCL074)

STUDY NO. : 0613
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	35	28.6± 21.1	154± 2	4.6± 0.9	122± 5	8.7± 0.5	6.1± 0.9
5000 ppm	32	24.4± 9.9	153± 3	4.2± 0.3*	121± 4	8.7± 0.4	5.8± 0.8
10000 ppm	36	22.5± 3.4	153± 2	4.2± 0.3	120± 3	8.9± 0.6	5.7± 0.6
20000 ppm	40	22.7± 10.1*	153± 2	4.3± 0.3	121± 2	8.6± 0.3	5.8± 0.8

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

TABLE H 2

BIOCHEMISTRY: FEMALE

STUDY NO. : 0613
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	28	5.0± 0.6	2.5± 0.3	1.0± 0.2	0.14± 0.05	134± 31	82± 28	52± 38
2500 ppm	25	5.2± 0.9	2.5± 0.3	1.0± 0.3	0.18± 0.17	136± 30	86± 36	37± 21
5000 ppm	31	4.9± 0.4	2.5± 0.2	1.0± 0.2	0.14± 0.05	138± 37	74± 25	36± 20
10000 ppm	19	5.1± 0.5	2.5± 0.2	1.0± 0.2	0.13± 0.03	147± 20	82± 24	38± 25

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

(HCL074)

BAIS4

STUDY NO. : 0613
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 IU/l	ALT IU/l	LDH IU/l	ALP IU/l	G-GTP IU/l	CK IU/l
Control	28	145± 42	141± 156	53± 40	467± 266	234± 159	1± 1	82± 45
2500 ppm	25	151± 65	127± 99	60± 63	719± 872	173± 70	1± 1	118± 153
5000 ppm	31	138± 39	142± 142	52± 60	602± 648	194± 79	1± 1	97± 91
10000 ppm	19	149± 36	100± 45	29± 9	573± 631	170± 67	1± 0	104± 60

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

(HCL074)

STUDY NO. : 0613
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	28	16.8± 5.9	152± 2	4.2± 0.4	121± 3	9.0± 0.4	6.1± 1.1
2500 ppm	25	20.7± 11.6	152± 2	4.3± 0.5	121± 3	9.0± 0.5	6.3± 1.5
5000 ppm	31	19.0± 10.0	152± 2	4.3± 0.6	121± 2	8.9± 0.4	6.3± 1.3
10000 ppm	19	18.0± 4.4	151± 2	4.1± 0.4	120± 3	8.8± 0.5	5.9± 1.0

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

TABLE I 1

URINALYSIS: MALE

STUDY NO. : 0613
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	33	0	3	9	8	12	1	0		0	17	14	1	1	0		33	0	0	0	0	0		15	9	9	0	0	0		27	0	1	1	4	
5000 ppm	33	0	1	11	17	4	0	0		0	10	16	6	1	0		33	0	0	0	0	0		8	12	12	1	0	0		29	0	0	0	4	
10000 ppm	36	0	3	16	15	2	0	0	*	0	4	18	14	0	0	**	36	0	0	0	0	0		8	12	14	2	0	0		32	0	0	0	4	
20000 ppm	40	0	4	25	9	2	0	0	**	0	10	26	4	0	0		40	0	0	0	0	0		12	12	16	0	0	0		38	0	0	0	2	

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

(HCL101)

STUDY NO. : 0613
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	33	33	0	0	0	0	
5000 ppm	33	33	0	0	0	0	
10000 ppm	36	36	0	0	0	0	
20000 ppm	40	40	0	0	0	0	

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

(HCL101)

TABLE I 2

URINALYSIS: FEMALE

STUDY NO. : 0613
ANIMAL : MOUSE B6D2F1/Crlj[Cr.j: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	30	0	2	4	0	9	11	4		0	4	15	9	2	0		30	0	0	0	0	0		6	18	3	3	0	0		25	0	0	4	1	
2500 ppm	26	0	3	6	6	5	5	1	*	0	1	7	17	1	0		26	0	0	0	0	0		1	15	6	4	0	0		17	1	4	1	3	
5000 ppm	32	0	2	4	5	11	9	1		0	1	18	12	1	0		32	0	0	0	0	0		0	18	10	4	0	0	*	28	0	1	0	3	
10000 ppm	21	0	1	2	6	10	1	1	**	0	1	10	8	2	0		21	0	0	0	0	0		2	12	4	3	0	0		20	0	0	0	1	

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

(HCL101)

STUDY NO. : 0613
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	30	30	0	0	0	0	
2500 ppm	26	26	0	0	0	0	
5000 ppm	32	32	0	0	0	0	
10000 ppm	21	21	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. : 0613
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	35	41.4± 8.0	0.011± 0.002	0.200± 0.035	0.224± 0.018	0.212± 0.069	0.648± 0.047
5000 ppm	32	44.4± 7.4	0.010± 0.002	0.223± 0.033	0.221± 0.022	0.199± 0.057	0.695± 0.175
10000 ppm	36	44.0± 5.1	0.010± 0.002	0.216± 0.037	0.221± 0.025	0.202± 0.030	0.786± 0.576
20000 ppm	40	44.0± 6.8	0.010± 0.002	0.209± 0.042	0.219± 0.019	0.216± 0.141	0.665± 0.061

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

STUDY NO. : 0613
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	35	0.162±	0.255	1.688±	0.721	0.452±	0.017
5000 ppm	32	0.114±	0.079	1.806±	1.050	0.455±	0.017
10000 ppm	36	0.120±	0.092	1.812±	0.562	0.454±	0.015
20000 ppm	40	0.095±	0.078	1.585±	0.279	0.452±	0.022

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

TABLE K 2

ORGAN WEIGHT, ABSOLUTE: FEMALE

STUDY NO. : 0613
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	28	32.9± 5.9	0.014± 0.003	0.049± 0.094	0.182± 0.032	0.205± 0.057	0.470± 0.169
2500 ppm	25	30.6± 3.4	0.015± 0.003	0.041± 0.044	0.178± 0.031	0.215± 0.067	0.562± 0.269
5000 ppm	31	31.4± 4.8	0.014± 0.003	0.200± 0.659	0.176± 0.022	0.193± 0.023	0.552± 0.514
10000 ppm	19	28.9± 3.9	0.013± 0.001	0.105± 0.243	0.164± 0.014	0.198± 0.040	0.475± 0.145

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

STUDY NO. : 0613
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	28	0.307±	0.648	1.642±	0.607	0.473±	0.018
2500 ppm	25	0.296±	0.363	1.577±	0.406	0.481±	0.018
5000 ppm	31	0.223±	0.159	1.430±	0.200	0.470±	0.018
10000 ppm	19	0.172±	0.116	1.367±	0.254	0.472±	0.021

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

TABLE L 1

ORGAN WEIGHT, RELATIVE: MALE

STUDY NO. : 0613
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	35	41.4± 8.0	0.027± 0.009	0.499± 0.127	0.563± 0.128	0.535± 0.207	1.630± 0.374
5000 ppm	32	44.4± 7.4	0.024± 0.008	0.514± 0.104	0.513± 0.107	0.464± 0.181	1.638± 0.651
10000 ppm	36	44.0± 5.1	0.022± 0.005	0.495± 0.092	0.510± 0.080	0.466± 0.094	1.851± 1.554
20000 ppm	40	44.0± 6.8	0.024± 0.008	0.483± 0.101	0.508± 0.075	0.534± 0.569	1.538± 0.201

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

STUDY NO. : 0613
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	35	0.448± 0.789	4.195± 1.960	1.138± 0.262
5000 ppm	32	0.270± 0.229	4.160± 2.405	1.057± 0.218
10000 ppm	36	0.286± 0.247	4.204± 1.523	1.047± 0.132
20000 ppm	40	0.214± 0.158	3.662± 0.809	1.053± 0.182

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

TABLE L 2

ORGAN WEIGHT, RELATIVE: FEMALE

STUDY NO. : 0613
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	28	32.9± 5.9	0.044± 0.010	0.156± 0.316	0.565± 0.123	0.646± 0.227	1.465± 0.605
2500 ppm	25	30.6± 3.4	0.048± 0.012	0.136± 0.139	0.591± 0.140	0.714± 0.260	1.901± 1.133*
5000 ppm	31	31.4± 4.8	0.045± 0.011	0.662± 2.166	0.567± 0.085	0.622± 0.095	1.797± 1.713
10000 ppm	19	28.9± 3.9	0.047± 0.007	0.401± 0.994	0.572± 0.062	0.699± 0.173	1.669± 0.562*

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

(HCL042)

STUDY NO. : 0613
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	28	0.965± 1.956	5.051± 1.810	1.481± 0.255
2500 ppm	25	1.001± 1.315	5.179± 1.269	1.588± 0.179
5000 ppm	31	0.727± 0.535	4.618± 0.762	1.525± 0.214
10000 ppm	19	0.609± 0.437	4.755± 0.821	1.652± 0.172*

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

TABLE M 1

HISTOPATHOLOGICAL FINDINGS:

NON-NEOPLASTIC LESIONS:

MALE: ALL ANIMALS

STUDY NO. : 0613
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				5000 ppm				10000 ppm				20000 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		0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(2)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis		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)
	scab		2	1	0	0	1	2	0	0	0	1	0	0	1	0	0	0
			(4)	(2)	(0)	(0)	(2)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(2)	(0)	(0)	(0)
{Respiratory system}																		
nasal cavit			<50>				<50>				<50>				<50>			
	eosinophilic change:olfactory epithelium		16	1	0	0	23	0	1	0	18	1	0	0	15	0	0	0
			(32)	(2)	(0)	(0)	(46)	(0)	(2)	(0)	(36)	(2)	(0)	(0)	(30)	(0)	(0)	(0)
	eosinophilic change:respiratory epithelium		16	3	0	0	9	0	1	0	10	0	0	0	12	0	0	0
			(32)	(6)	(0)	(0)	(18)	(0)	(2)	(0)	(20)	(0)	(0)	(0)	(24)	(0)	(0)	(0)
	respiratory metaplasia		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)
	inflammation:foreign body		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)

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				5000 ppm				10000 ppm				20000 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
{Respiratory system}																		
nasal cavit			<50>				<50>				<50>				<50>			
	inflammation:respiratory epithelium		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)	(0)	(0)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		21	0	0	0	8	0	0	0 **	11	0	0	0	11	0	0	0
			(42)	(0)	(0)	(0)	(16)	(0)	(0)	(0)	(22)	(0)	(0)	(0)	(22)	(0)	(0)	(0)
	respiratory metaplasia:gland		24	0	0	0	13	1	0	0	19	1	0	0	19	1	0	0
			(48)	(0)	(0)	(0)	(26)	(2)	(0)	(0)	(38)	(2)	(0)	(0)	(38)	(2)	(0)	(0)
	squamous cell metaplasia:respiratory epithelium		0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
nasopharynx			<50>				<50>				<50>				<50>			
	eosinophilic change		1	1	0	0	1	0	1	0	1	0	0	0	1	0	0	0
			(2)	(2)	(0)	(0)	(2)	(0)	(2)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
lung			<50>				<50>				<50>				<50>			
	hemorrhage		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)	(0)	(0)	(0)	(0)
	edema		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)

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				5000 ppm				10000 ppm				20000 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}																		
lung			<50>				<50>				<50>				<50>			
	inflammatory infiltration		0	0	0	0	1	0	0	0	2	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(4)	(2)	(0)	(0)	(0)	(0)	(0)	(0)
	accumulation of foamy cells		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)	(0)	(0)	(0)	(0)
	bronchiolar-alveolar cell hyperplasia		0	0	0	0	0	0	0	0	2	0	0	0	2	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(2)	(0)	(0)
{Hematopoietic system}																		
bone marrow			<50>				<50>				<50>				<50>			
	congestion		1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	increased hematopoiesis		6	0	0	0	6	0	0	0	7	0	0	0	6	0	0	0
			(12)	(0)	(0)	(0)	(12)	(0)	(0)	(0)	(14)	(0)	(0)	(0)	(12)	(0)	(0)	(0)
	myelofibrosis		0	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
	megakaryocyte:increased		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)

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				5000 ppm				10000 ppm				20000 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}																		
bone marrow			<50>				<50>				<50>				<50>			
	granulopoiesis:increased		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)
lymph node			<50>				<50>				<50>				<50>			
	lymphadenitis		0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(2)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen			<50>				<50>				<50>				<50>			
	angiectasis		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)
	deposit of melanin		1	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	extramedullary hematopoiesis		10	6	0	0	12	10	0	0	15	6	0	0	10	5	0	0
			(20)	(12)	(0)	(0)	(24)	(20)	(0)	(0)	(30)	(12)	(0)	(0)	(20)	(10)	(0)	(0)
	follicular hyperplasia		0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)
{Circulatory system}																		
heart			<50>				<50>				<50>				<50>			
	mineralization		2	0	0	0	2	1	0	0	0	0	0	0	0	0	0	0
			(4)	(0)	(0)	(0)	(4)	(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	2	3	4	5000 ppm 50 1	2	3	4	10000 ppm 50 1	2	3	4	20000 ppm 50 1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Circulatory system}																		
heart				<50>				<50>				<50>				<50>		
	arteritis		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)
artery/aort				<50>				<50>				<50>				<50>		
	arteritis		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)
{Digestive system}																		
tooth				<50>				<50>				<50>				<50>		
	dysplasia		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)	(0)	(0)	(0)	(0)
tongue				<50>				<50>				<50>				<50>		
	arteritis		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)
salivary gl				<50>				<50>				<50>				<50>		
	abscess		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)	(0)	(0)	(0)	(0)
stomach				<50>				<50>				<50>				<50>		
	hyperplasia:forestomach		0	1	1	0	1	1	0	0	1	0	0	0	0	0	0	0
			(0)	(2)	(2)	(0)	(2)	(2)	(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

Organ	Findings	Group Name	Control				5000 ppm				10000 ppm				20000 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}																		
stomach			<50>				<50>				<50>				<50>			
	erosion:glandular stomach		3	1	0	0	8	0	0	0	8	0	0	0	7	0	0	0
			(6)	(2)	(0)	(0)	(16)	(0)	(0)	(0)	(16)	(0)	(0)	(0)	(14)	(0)	(0)	(0)
	hyperplasia:glandular stomach		17	0	0	0	16	0	0	0	19	0	0	0	13	0	0	0
			(34)	(0)	(0)	(0)	(32)	(0)	(0)	(0)	(38)	(0)	(0)	(0)	(26)	(0)	(0)	(0)
large intes			<50>				<50>				<50>				<50>			
	lymphoid hyperplasia		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)	(0)	(0)	(0)
liver			<50>				<50>				<50>				<50>			
	necrosis:focal		1	1	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(2)	(2)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	fatty change:central		0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	inflammatory infiltration		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)
	inflammatory cell nest		6	0	0	0	3	0	0	0	1	0	0	0	1	0	0	0
			(12)	(0)	(0)	(0)	(6)	(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	Control				5000 ppm				10000 ppm				20000 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}																		
liver			<50>				<50>				<50>				<50>			
	clear cell focus		0	0	0	0	0	2	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	acidophilic cell focus		1	1	0	0	0	2	0	0	2	0	1	0	2	1	0	0
			(2)	(2)	(0)	(0)	(0)	(4)	(0)	(0)	(4)	(0)	(2)	(0)	(4)	(2)	(0)	(0)
	basophilic cell focus		1	0	0	0	2	0	0	0	0	1	0	0	3	0	0	0
			(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(6)	(0)	(0)	(0)
	bile duct hyperplasia		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)	(0)	(0)	(0)	(0)
	biliary cyst		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)
gall bladd			<50>				<50>				<49>				<49>			
	cyst		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)
	hyperplasia		2	0	0	0	1	0	0	0	2	0	0	0	2	0	0	0
			(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
{Urinary system}																		
kidney			<50>				<50>				<50>				<50>			
	cyst		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)

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				5000 ppm				10000 ppm				20000 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}																		
kidney			<50>				<50>				<50>				<50>			
	hyaline droplet		2	0	0	0	3	0	0	0	1	0	0	0	5	0	0	0
			(4)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	inflammatory infiltration		1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	lymphocytic infiltration		2	1	0	0	1	0	0	0	4	0	0	0	2	0	0	0
			(4)	(2)	(0)	(0)	(2)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	osseous metaplasia		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)	(0)	(0)	(0)	(0)
	scar		2	1	0	0	3	1	0	0	1	0	0	0	1	0	0	0
			(4)	(2)	(0)	(0)	(6)	(2)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	inflammatory polyp		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)	(0)	(0)	(0)
	hydronephrosis		0	0	0	1	1	0	4	0	0	2	2	0	0	0	0	0
			(0)	(0)	(0)	(2)	(2)	(0)	(8)	(0)	(0)	(4)	(4)	(0)	(0)	(0)	(0)	(0)
	mineralization:cortex		3	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(6)	(0)	(0)	(0)	(2)	(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

Organ	Findings	Group Name	Control				5000 ppm				10000 ppm				20000 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}																		
kidney			<50>				<50>				<50>				<50>			
	regeneration:proximal tubule		2	1	0	0	2	0	0	0	2	0	0	0	3	0	0	0
			(4)	(2)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
urin bladd			<50>				<50>				<50>				<50>			
	dilatation		0	2	1	0	0	0	1	0	1	0	0	0	0	0	0	0
			(0)	(4)	(2)	(0)	(0)	(0)	(2)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	lymphocytic infiltration		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)
urethra			<50>				<50>				<50>				<50>			
	inflammation		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)	(0)	(0)	(0)
{Endocrine system}																		
pituitary			<50>				<50>				<50>				<50>			
	hyperplasia		0	2	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	Rathke pouch		0	0	0	0	4	0	0	0	3	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(6)	(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

Organ	Findings	Group Name	Control				5000 ppm				10000 ppm				20000 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Endocrine system}																		
thyroid			<50>				<50>				<50>				<50>			
	cyst		0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	follicular hyperplasia		1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)
	C-cell hyperplasia		2	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
parathyroid			<50>				<50>				<50>				<50>			
	cyst		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)
adrenal			<50>				<50>				<50>				<50>			
	spindle-cell hyperplasia		3	0	0	0	1	0	0	0	2	0	0	0	0	0	0	0
			(6)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyperplasia:cortical cell		0	0	0	0	1	0	0	0	0	0	1	0	0	1	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(2)	(0)	(0)
{Reproductive system}																		
testis			<50>				<50>				<50>				<50>			
	atrophy		0	0	0	0	0	0	0	0	2	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(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	Control				5000 ppm				10000 ppm				20000 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Reproductive system)																		
testis			<50>				<50>				<50>				<50>			
	xanthogranuloma		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)	(0)	(0)
epididymis			<50>				<50>				<50>				<50>			
	inflammatory infiltration		0	1	0	0	0	0	0	0	0	0	0	0	2	0	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	spermatogenic granuloma		0	0	0	0	1	0	0	0	1	1	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(2)	(0)	(0)	(2)	(0)	(0)	(0)
	xanthogranuloma		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)	(0)	(0)
semin ves			<50>				<50>				<50>				<50>			
	inflammation		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)
prostate			<50>				<50>				<50>				<50>			
	lymphocytic infiltration		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)
	hyperplasia		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(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. : 0613
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 (%)	5000 ppm 50 1 (%)	5000 ppm 50 2 (%)	5000 ppm 50 3 (%)	5000 ppm 50 4 (%)	10000 ppm 50 1 (%)	10000 ppm 50 2 (%)	10000 ppm 50 3 (%)	10000 ppm 50 4 (%)	20000 ppm 50 1 (%)	20000 ppm 50 2 (%)	20000 ppm 50 3 (%)	20000 ppm 50 4 (%)
{Reproductive system}																		
prep/cli gl			<50>				<50>				<50>				<50>			
	cyst		0 (0)	0 (0)	1 (2)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
{Nervous system}																		
brain			<50>				<50>				<50>				<50>			
	hemorrhage		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)
	mineralization		16 (32)	0 (0)	0 (0)	0 (0)	15 (30)	0 (0)	0 (0)	0 (0)	9 (18)	0 (0)	0 (0)	0 (0)	17 (34)	0 (0)	0 (0)	0 (0)
	epidermal cyst		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)	1 (2)	0 (0)	0 (0)
spinal cord			<50>				<50>				<50>				<50>			
	hemorrhage		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	necrosis:focal		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				5000 ppm 50				10000 ppm 50				20000 ppm 50			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Special sense organs/appendage}																		
Harder gl			<50>				<50>				<50>				<50>			
	hyperplasia		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)
{Musculoskeletal system}																		
muscle			<50>				<50>				<50>				<50>			
	necrosis		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)
	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)
{Body cavities}																		
pleura			<50>				<50>				<50>				<50>			
	pleuritis		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)	0 (0)	0 (0)
retroperit			<50>				<50>				<50>				<50>			
	hemorrhage		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

TABLE M 4

HISTOPATHOLOGICAL FINDINGS:

NON-NEOPLASTIC LESIONS:

FEMALE: ALL ANIMALS

Organ	Findings	Group Name	Control				2500 ppm				5000 ppm				10000 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	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)
	scab		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)
	sebaceous hyperplasia		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)	(0)	(0)	(0)	(0)
subcutis			<50>				<50>				<50>				<50>			
	hemorrhage		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)
	inflammation		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)	(0)	(0)
{Respiratory system}																		
nasal cavit			<50>				<50>				<50>				<50>			
	exudate		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)

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 (%)	2500 ppm 50 1 (%)	2500 ppm 50 2 (%)	2500 ppm 50 3 (%)	2500 ppm 50 4 (%)	5000 ppm 50 1 (%)	5000 ppm 50 2 (%)	5000 ppm 50 3 (%)	5000 ppm 50 4 (%)	10000 ppm 50 1 (%)	10000 ppm 50 2 (%)	10000 ppm 50 3 (%)	10000 ppm 50 4 (%)
{Respiratory system}																		
nasal cavit			<50>				<50>				<50>				<50>			
	inflammatory infiltration		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)
	eosinophilic change:olfactory epithelium		15 (30)	1 (2)	0 (0)	0 (0)	10 (20)	1 (2)	0 (0)	0 (0)	9 (18)	0 (0)	0 (0)	0 (0)	9 (18)	0 (0)	0 (0)	0 (0)
	eosinophilic change:respiratory epithelium		26 (52)	8 (16)	0 (0)	0 (0)	28 (56)	3 (6)	0 (0)	0 (0)	35 (70)	2 (4)	0 (0)	0 (0)	33 (66)	1 (2)	0 (0)	0 * (0)
	inflammation:respiratory epithelium		2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	6 (12)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:olfactory epithelium		15 (30)	0 (0)	0 (0)	0 (0)	6 (12)	0 (0)	0 (0)	0 * (0)	11 (22)	0 (0)	0 (0)	0 (0)	10 (20)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:gland		22 (44)	1 (2)	0 (0)	0 (0)	22 (44)	0 (0)	0 (0)	0 (0)	18 (36)	2 (4)	0 (0)	0 (0)	21 (42)	0 (0)	0 (0)	0 (0)
	squamous cell metaplasia:respiratory epithelium		1 (2)	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)
nasopharynx			<50>				<50>				<50>				<50>			
	eosinophilic change		9 (18)	2 (4)	0 (0)	0 (0)	4 (8)	1 (2)	0 (0)	0 (0)	3 (6)	1 (2)	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	Control				2500 ppm				5000 ppm				10000 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}																		
lung			<50>				<50>				<50>				<50>			
	inflammatory infiltration		1	0	0	0	2	0	0	0	1	0	0	0	2	0	0	0
			(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	lymphocytic infiltration		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)
	bronchiolar-alveolar 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)
	arteritis		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)
{Hematopoietic system}																		
bone marrow			<50>				<50>				<50>				<50>			
	increased hematopoiesis		5	0	0	0	9	0	0	0	6	0	0	0	5	0	0	0
			(10)	(0)	(0)	(0)	(18)	(0)	(0)	(0)	(12)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	myelofibrosis		1	0	0	0	0	1	0	0	2	0	0	0	2	0	0	0
			(2)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	megakaryocyte:increased		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)

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				2500 ppm				5000 ppm				10000 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}																		
spleen			<50>				<50>				<50>				<50>			
	fibrosis:focal		0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)
	extramedullary hematopoiesis		12	4	2	0	10	10	1	0	11	7	0	0	8	5	0	0
			(24)	(8)	(4)	(0)	(20)	(20)	(2)	(0)	(22)	(14)	(0)	(0)	(16)	(10)	(0)	(0)
	follicular hyperplasia		1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Circulatory system}																		
heart			<50>				<50>				<50>				<50>			
	thrombus		0	0	1	0	0	0	1	0	0	1	0	0	0	0	0	0
			(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization		1	0	0	0	1	0	0	0	0	0	0	0	5	0	0	0
			(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	inflammatory cell nest		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)	(0)	(0)	(0)	(0)
	myocardial fibrosis		1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(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 (%)	2500 ppm 50 1 (%)	2500 ppm 50 2 (%)	2500 ppm 50 3 (%)	2500 ppm 50 4 (%)	5000 ppm 50 1 (%)	5000 ppm 50 2 (%)	5000 ppm 50 3 (%)	5000 ppm 50 4 (%)	10000 ppm 50 1 (%)	10000 ppm 50 2 (%)	10000 ppm 50 3 (%)	10000 ppm 50 4 (%)
{Circulatory system}																		
heart			<50>				<50>				<50>				<50>			
	arteritis		0 (0)	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>			
	arteritis		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)	0 (0)	0 (0)
{Digestive system}																		
tongue			<50>				<50>				<50>				<50>			
	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)	2 (4)	0 (0)	0 (0)	0 (0)
salivary gl			<50>				<49>				<50>				<50>			
	lymphocytic infiltration		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
stomach			<50>				<50>				<50>				<50>			
	ulcer:forestomach		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)
	hyperplasia:forestomach		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)

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

Organ	Findings	Group Name	Control				2500 ppm				5000 ppm				10000 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)																		
stomach			<50>				<50>				<50>				<50>			
	erosion:glandular stomach		5	2	0	0	1	0	0	0	7	0	0	0	2	0	0	0
			(10)	(4)	(0)	(0)	(2)	(0)	(0)	(0)	(14)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	ulcer:glandular stomach		1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyperplasia:glandular stomach		15	0	0	0	16	0	0	0	12	0	0	0	8	0	0	0
			(30)	(0)	(0)	(0)	(32)	(0)	(0)	(0)	(24)	(0)	(0)	(0)	(16)	(0)	(0)	(0)
liver			<50>				<50>				<50>				<50>			
	angiectasis		0	1	1	0	0	0	0	0	4	0	0	0	1	0	0	0
			(0)	(2)	(2)	(0)	(0)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	necrosis:central		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)	(0)	(0)	(0)
	necrosis:focal		1	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	inflammatory infiltration		1	0	0	0	2	0	0	0	1	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	inflammatory cell nest		11	0	0	0	7	0	0	0	12	0	0	0	8	0	0	0
			(22)	(0)	(0)	(0)	(14)	(0)	(0)	(0)	(24)	(0)	(0)	(0)	(16)	(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				2500 ppm				5000 ppm				10000 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}																		
liver			<50>				<50>				<50>				<50>			
	extramedullary hematopoiesis		0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	clear cell focus		0	0	0	0	0	0	0	0	0	1	0	0	1	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(2)	(2)	(0)	(0)
	acidophilic cell focus		0	2	0	0	0	0	0	0	3	0	0	0	1	1	0	0
			(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(2)	(2)	(0)	(0)
	basophilic cell focus		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)
	biliary 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)
gall bladd			<49>				<48>				<50>				<50>			
	hyperplasia		1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
pancreas			<50>				<50>				<50>				<50>			
	fibrosis:focal		0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(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				2500 ppm				5000 ppm				10000 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
{Urinary system}																		
kidney			<50>				<50>				<50>				<50>			
	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)
	hyaline droplet		7	0	0	0	14	0	0	0	5	0	0	0	14	0	0	0
			(14)	(0)	(0)	(0)	(28)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(28)	(0)	(0)	(0)
	deposit of hemosiderin		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)
	inflammatory infiltration		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)	(0)
	lymphocytic infiltration		4	0	0	0	3	0	0	0	3	0	0	0	2	0	0	0
			(8)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	scar		1	0	0	0	0	0	0	0	1	0	0	0	2	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	inflammatory polyp		0	2	0	0	2	1	0	0	1	0	0	0	0	2	0	0
			(0)	(4)	(0)	(0)	(4)	(2)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(4)	(0)	(0)
	hydronephrosis		0	0	2	2	1	1	2	0	0	0	2	0	1	3	1	0
			(0)	(0)	(4)	(4)	(2)	(2)	(4)	(0)	(0)	(0)	(4)	(0)	(2)	(6)	(2)	(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				2500 ppm				5000 ppm				10000 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}																		
kidney			<50>				<50>				<50>				<50>			
	pyelonephritis		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)	(0)	(0)
	arthritis		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)
	hyaline droplet:glomerulus		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)
urin bladd			<50>				<50>				<50>				<50>			
	dilatation		0	1	1	0	1	2	0	0	0	0	0	0	0	1	0	0
			(0)	(2)	(2)	(0)	(2)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)
	inflammatory infiltration		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	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)
{Endocrine system}																		
pituitary			<50>				<50>				<50>				<50>			
	angiectasis		0	0	0	0	1	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(2)	(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	Control				2500 ppm				5000 ppm				10000 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Endocrine system}																		
pituitary			<50>				<50>				<50>				<50>			
	cyst		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)	(0)	(0)	(0)	(0)
	hyperplasia		7	2	1	0	4	5	3	0	9	2	3	0	5	2	4	0
			(14)	(4)	(2)	(0)	(8)	(10)	(6)	(0)	(18)	(4)	(6)	(0)	(10)	(4)	(8)	(0)
	Rathke pouch		1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
thyroid			<50>				<50>				<50>				<50>			
	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)
	C-cell hyperplasia		3	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
parathyroid			<50>				<50>				<50>				<50>			
	hyperplasia		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)	(0)	(0)	(0)	(0)
adrenal			<50>				<50>				<50>				<50>			
	degeneration		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				2500 ppm 50				5000 ppm 50				10000 ppm 50			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Endocrine system}																		
adrenal			<50>				<50>				<50>				<50>			
	spindle-cell hyperplasia		32 (64)	2 (4)	0 (0)	0 (0)	32 (64)	1 (2)	0 (0)	0 (0)	30 (60)	1 (2)	0 (0)	0 (0)	25 (50)	2 (4)	0 (0)	0 (0)
	focal fatty change:cortex		0 (0)	3 (6)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
{Reproductive system}																		
ovary			<50>				<50>				<50>				<50>			
	angiectasis		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)
	cyst		5 (10)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)	2 (4)	3 (6)	0 (0)	0 (0)
	hyperplasia		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)
uterus			<50>				<50>				<50>				<50>			
	dilatation		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				2500 ppm				5000 ppm				10000 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Reproductive system}																		
uterus			<50>				<50>				<50>				<50>			
	thrombus		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)	(0)	(0)	(0)
	inflammatory infiltration		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)
	stromal hyperplasia		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)	(0)	(0)	(0)	(0)
	cystic endometrial hyperplasia		26	0	0	0	16	1	0	0	22	1	0	0	16	1	0	0
			(52)	(0)	(0)	(0)	(32)	(2)	(0)	(0)	(44)	(2)	(0)	(0)	(32)	(2)	(0)	(0)
vagina			<50>				<50>				<50>				<50>			
	polyp		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)
mammary gl			<50>				<50>				<50>				<50>			
	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)
prep/cli gl			<50>				<50>				<50>				<50>			
	cyst		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)

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 (%)	2500 ppm 50 1 (%)	2500 ppm 50 2 (%)	2500 ppm 50 3 (%)	2500 ppm 50 4 (%)	5000 ppm 50 1 (%)	5000 ppm 50 2 (%)	5000 ppm 50 3 (%)	5000 ppm 50 4 (%)	10000 ppm 50 1 (%)	10000 ppm 50 2 (%)	10000 ppm 50 3 (%)	10000 ppm 50 4 (%)
{Nervous system}																		
brain		<50>																
	hemorrhage		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	mineralization		5 (10)	0 (0)	0 (0)	0 (0)	7 (14)	0 (0)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)	7 (14)	0 (0)	0 (0)	0 (0)
{Special sense organs/appendage}																		
eye		<50>																
	inflammatory infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)
	cataract		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)
	retinal atrophy		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)	0 (0)	0 (0)
	keratitis		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)	1 (2)	0 (0)
Harder gl		<50>																
	degeneration		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)

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				2500 ppm				5000 ppm				10000 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Special sense organs/appendage}																		
Harder gl			<50>				<50>				<50>				<50>			
	hyperplasia		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Musculoskeletal system}																		
muscle			<50>				<50>				<50>				<50>			
	mineralization		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)	(4)	(0)	(0)	(0)
bone			<50>				<50>				<50>				<50>			
	osteosclerosis		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)	(0)	(0)	(0)	(0)
{Body cavities}																		
mediastinum			<50>				<50>				<50>				<50>			
	inflammation		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)
peritoneum			<50>				<50>				<50>				<50>			
	peritonitis		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)	(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	5000 ppm	10000 ppm	20000 ppm
	SITE : lung			
	TUMOR : bronchiolar-alveolar adenoma			
Tumor rate				
Overall rates(a)	7/50(14.0)	4/50(8.0)	4/50(8.0)	3/50(6.0)
Adjusted rates(b)	20.00	12.12	11.11	7.32
Terminal rates(c)	7/35(20.0)	4/33(12.1)	4/36(11.1)	3/41(7.3)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.9414			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.2102			
Fisher Exact test(e)		P = 0.2623	P = 0.2623	P = 0.1589
	SITE : lung			
	TUMOR : bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	10/50(20.0)	7/50(14.0)	5/50(10.0)
Adjusted rates(b)	9.76	24.24	13.16	10.64
Terminal rates(c)	3/35(8.6)	8/33(24.2)	4/36(11.1)	3/41(7.3)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5791			
Prevalence method(d)	P = 0.6094			
Combined analysis(d)	P = 0.6373			
Cochran-Armitage test(e)	P = 0.8311			
Fisher Exact test(e)		P = 0.0739	P = 0.2623	P = 0.5000
	SITE : lung			
	TUMOR : bronchiolar-alveolar adenoma, bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	11/50(22.0)	14/50(28.0)	11/50(22.0)	8/50(16.0)
Adjusted rates(b)	28.57	36.36	23.68	17.02
Terminal rates(c)	10/35(28.6)	12/33(36.4)	8/36(22.2)	6/41(14.6)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5791			
Prevalence method(d)	P = 0.9016			
Combined analysis(d)	P = 0.9071			
Cochran-Armitage test(e)	P = 0.2989			
Fisher Exact test(e)		P = 0.3224	P = 0.5952	P = 0.3055

Group Name	Control	5000 ppm	10000 ppm	20000 ppm
	SITE : lymph node			
	TUMOR : malignant lymphoma			
Tumor rate				
Overall rates(a)	13/50(26.0)	6/50(12.0)	6/50(12.0)	6/50(12.0)
Adjusted rates(b)	17.14	12.12	8.33	14.63
Terminal rates(c)	6/35(17.1)	4/33(12.1)	3/36(8.3)	6/41(14.6)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.9976			
Prevalence method(d)	P = 0.5755			
Combined analysis(d)	P = 0.9697			
Cochran-Armitage test(e)	P = 0.1056			
Fisher Exact test(e)		P = 0.0624	P = 0.0624	P = 0.0624
	SITE : liver			
	TUMOR : hepatocellular adenoma			
Tumor rate				
Overall rates(a)	12/50(24.0)	7/50(14.0)	14/50(28.0)	7/50(14.0)
Adjusted rates(b)	25.71	16.22	33.33	14.63
Terminal rates(c)	9/35(25.7)	5/33(15.2)	12/36(33.3)	6/41(14.6)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8050			
Prevalence method(d)	P = 0.7987			
Combined analysis(d)	P = 0.8594			
Cochran-Armitage test(e)	P = 0.4028			
Fisher Exact test(e)		P = 0.1540	P = 0.4100	P = 0.1540
	SITE : liver			
	TUMOR : histiocytic sarcoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	3/50(6.0)	1/50(2.0)	4/50(8.0)
Adjusted rates(b)	2.86	3.03	2.78	0.0
Terminal rates(c)	1/35(2.9)	1/33(3.0)	1/36(2.8)	0/41(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.2212			
Prevalence method(d)	P = 0.8247			
Combined analysis(d)	P = 0.4353			
Cochran-Armitage test(e)	P = 0.7136			
Fisher Exact test(e)		P = 0.6611	P = 0.3087	P = 0.5000

Group Name	Control	5000 ppm	10000 ppm	20000 ppm
	SITE : liver			
	TUMOR : hemangiosarcoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	2/50(4.0)	3/50(6.0)	1/50(2.0)
Adjusted rates(b)	2.86	6.06	2.78	0.0
Terminal rates(c)	1/35(2.9)	2/33(6.1)	1/36(2.8)	0/41(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1735			
Prevalence method(d)	P = 0.8679			
Combined analysis(d)	P = 0.5743			
Cochran-Armitage test(e)	P = 0.9481			
Fisher Exact test(e)		P = 0.5000	P = 0.3087	P = 0.7525
	SITE : liver			
	TUMOR : hepatocellular carcinoma			
Tumor rate				
Overall rates(a)	6/50(12.0)	9/50(18.0)	6/50(12.0)	6/50(12.0)
Adjusted rates(b)	15.79	14.29	13.89	9.09
Terminal rates(c)	5/35(14.3)	4/33(12.1)	5/36(13.9)	2/41(4.9)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3664			
Prevalence method(d)	P = 0.8232			
Combined analysis(d)	P = 0.7299			
Cochran-Armitage test(e)	P = 0.7529			
Fisher Exact test(e)		P = 0.2883	P = 0.6202	P = 0.6202

Group Name	Control	5000 ppm	10000 ppm	20000 ppm
	SITE : liver			
	TUMOR : hepatocellular adenoma, hepatocellular carcinoma			
Tumor rate				
Overall rates(a)	16/50(32.0)	16/50(32.0)	18/50(36.0)	13/50(26.0)
Adjusted rates(b)	34.29	30.56	41.67	22.92
Terminal rates(c)	12/35(34.3)	9/33(27.3)	15/36(41.7)	8/41(19.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5794			
Prevalence method(d)	P = 0.8183			
Combined analysis(d)	P = 0.8187			
Cochran-Armitage test(e)	P = 0.5201			
Fisher Exact test(e)		P = 0.5848	P = 0.4165	P = 0.3299

(HPT360A)

BAIS4

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

STUDY No. : 0613
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

Group Name	Control	5000 ppm	10000 ppm	20000 ppm
	SITE : ALL SITE			
	TUMOR : histiocytic sarcoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	7/50(14.0)	6/50(12.0)	6/50(12.0)
Adjusted rates(b)	2.86	15.15	11.11	4.88
Terminal rates(c)	1/35(2.9)	5/33(15.2)	4/36(11.1)	2/41(4.9)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3428			
Prevalence method(d)	P = 0.5921			
Combined analysis(d)	P = 0.4560			
Cochran-Armitage test(e)	P = 0.6803			
Fisher Exact test(e)		P = 0.2623	P = 0.3703	P = 0.3703
	SITE : ALL SITE			
	TUMOR : malignant lymphoma			
Tumor rate				
Overall rates(a)	13/50(26.0)	6/50(12.0)	6/50(12.0)	8/50(16.0)
Adjusted rates(b)	17.14	12.12	8.33	19.51
Terminal rates(c)	6/35(17.1)	4/33(12.1)	3/36(8.3)	8/41(19.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.9976			
Prevalence method(d)	P = 0.3175			
Combined analysis(d)	P = 0.9017			
Cochran-Armitage test(e)	P = 0.3182			
Fisher Exact test(e)		P = 0.0624	P = 0.0624	P = 0.1631

Group Name	Control	5000 ppm	10000 ppm	20000 ppm
	SITE : ALL SITE TUMOR : hemangiosarcoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	3/50(6.0)	4/50(8.0)	2/50(4.0)
Adjusted rates(b)	8.57	9.09	2.78	2.44
Terminal rates(c)	3/35(8.6)	3/33(9.1)	1/36(2.8)	1/41(2.4)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1846			
Prevalence method(d)	P = 0.9198			
Combined analysis(d)	P = 0.7177			
Cochran-Armitage test(e)	P = 0.6872			
Fisher Exact test(e)		P = 0.6611	P = 0.5000	P = 0.5000

(HPT360A)

BAIS4

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

TABLE P 2

NEOPLASTIC LESIONS-INCIDENCE AND

STATISTICAL ANALYSIS: FEMALE

Group Name	Control	2500 ppm	5000 ppm	10000 ppm
	SITE : lung			
	TUMOR : bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	2/50(4.0)	1/50(2.0)	3/50(6.0)
Adjusted rates(b)	5.26	7.69	3.23	6.90
Terminal rates(c)	1/29(3.4)	2/26(7.7)	1/31(3.2)	1/20(5.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1155			
Prevalence method(d)	P = 0.4665			
Combined analysis(d)	P = 0.2751			
Cochran-Armitage test(e)	P = 0.6256			
Fisher Exact test(e)		P = 0.6913	P = 0.5000	P = 0.5000
	SITE : lung			
	TUMOR : bronchiolar-alveolar adenoma,bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	3/50(6.0)	1/50(2.0)	3/50(6.0)
Adjusted rates(b)	10.53	8.82	3.23	6.90
Terminal rates(c)	2/29(6.9)	2/26(7.7)	1/31(3.2)	1/20(5.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1155			
Prevalence method(d)	P = 0.7930			
Combined analysis(d)	P = 0.6173			
Cochran-Armitage test(e)	P = 0.6370			
Fisher Exact test(e)		P = 0.5000	P = 0.1811	P = 0.5000
	SITE : lymph node			
	TUMOR : malignant lymphoma			
Tumor rate				
Overall rates(a)	12/50(24.0)	18/50(36.0)	19/50(38.0)	16/50(32.0)
Adjusted rates(b)	20.69	30.77	32.26	20.00
Terminal rates(c)	6/29(20.7)	8/26(30.8)	10/31(32.3)	4/20(20.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.0718			
Prevalence method(d)	P = 0.5195			
Combined analysis(d)	P = 0.1217			
Cochran-Armitage test(e)	P = 0.5235			
Fisher Exact test(e)		P = 0.1376	P = 0.0971	P = 0.2522

Group Name	Control	2500 ppm	5000 ppm	10000 ppm
	SITE : liver			
	TUMOR : hemangioma			
Tumor rate				
Overall rates(a)	3/50(6.0)	3/50(6.0)	3/50(6.0)	1/50(2.0)
Adjusted rates(b)	8.33	11.11	9.68	2.50
Terminal rates(c)	2/29(6.9)	2/26(7.7)	3/31(9.7)	0/20(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.8274			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.3236			
Fisher Exact test(e)		P = 0.6611	P = 0.6611	P = 0.3087
	SITE : liver			
	TUMOR : hepatocellular adenoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	1/50(2.0)	4/50(8.0)	1/50(2.0)
Adjusted rates(b)	10.34	3.70	11.43	5.00
Terminal rates(c)	3/29(10.3)	0/26(0.0)	3/31(9.7)	1/20(5.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.6815			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.5259			
Fisher Exact test(e)		P = 0.3087	P = 0.5000	P = 0.3087
	SITE : liver			
	TUMOR : hepatocellular adenoma, hepatocellular carcinoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	2/50(4.0)	4/50(8.0)	3/50(6.0)
Adjusted rates(b)	10.34	7.41	9.68	5.88
Terminal rates(c)	3/29(10.3)	1/26(3.8)	3/31(9.7)	1/20(5.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3485			
Prevalence method(d)	P = 0.5490			
Combined analysis(d)	P = 0.4708			
Cochran-Armitage test(e)	P = 0.8844			
Fisher Exact test(e)		P = 0.3389	P = 0.6425	P = 0.5000

Group Name	Control	2500 ppm	5000 ppm	10000 ppm
	SITE : pituitary gland TUMOR : adenoma			
Tumor rate				
Overall rates(a)	12/50(24.0)	9/50(18.0)	5/50(10.0)	6/50(12.0)
Adjusted rates(b)	30.56	25.71	15.15	25.00
Terminal rates(c)	8/29(27.6)	6/26(23.1)	4/31(12.9)	5/20(25.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8917 ?			
Prevalence method(d)	P = 0.9072			
Combined analysis(d)	P = 0.9362			
Cochran-Armitage test(e)	P = 0.0900			
Fisher Exact test(e)		P = 0.3121	P = 0.0542	P = 0.0961
	SITE : pituitary gland TUMOR : adenoma, adenocarcinoma			
Tumor rate				
Overall rates(a)	12/50(24.0)	9/50(18.0)	5/50(10.0)	7/50(14.0)
Adjusted rates(b)	30.56	25.71	15.15	25.00
Terminal rates(c)	8/29(27.6)	6/26(23.1)	4/31(12.9)	5/20(25.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3751			
Prevalence method(d)	P = 0.9072			
Combined analysis(d)	P = 0.8835			
Cochran-Armitage test(e)	P = 0.1662			
Fisher Exact test(e)		P = 0.3121	P = 0.0542	P = 0.1540
	SITE : ovary TUMOR : cystadenoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	0/50(0.0)	3/50(6.0)	1/50(2.0)
Adjusted rates(b)	0.0	0.0	9.68	2.13
Terminal rates(c)	0/29(0.0)	0/26(0.0)	3/31(9.7)	0/20(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.1470			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.3056			
Fisher Exact test(e)		P = N.C.	P = 0.1212	P = 0.5000

Group Name	Control	2500 ppm	5000 ppm	10000 ppm
	SITE : ovary			
	TUMOR : hemangioma			
Tumor rate				
Overall rates(a)	0/50(0.0)	1/50(2.0)	4/50(8.0)	0/50(0.0)
Adjusted rates(b)	0.0	3.85	8.57	0.0
Terminal rates(c)	0/29(0.0)	1/26(3.8)	2/31(6.5)	0/20(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.4037			
Prevalence method(d)	P = 0.4525			
Combined analysis(d)	P = 0.4291			
Cochran-Armitage test(e)	P = 0.9390			
Fisher Exact test(e)		P = 0.5000	P = 0.0587	P = N.C.
	SITE : uterus			
	TUMOR : histiocytic sarcoma			
Tumor rate				
Overall rates(a)	8/50(16.0)	14/50(28.0)	7/50(14.0)	14/50(28.0)
Adjusted rates(b)	6.90	15.38	6.45	15.00
Terminal rates(c)	2/29(6.9)	4/26(15.4)	2/31(6.5)	3/20(15.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.2268			
Prevalence method(d)	P = 0.1735			
Combined analysis(d)	P = 0.1331			
Cochran-Armitage test(e)	P = 0.3085			
Fisher Exact test(e)		P = 0.1135	P = 0.5000	P = 0.1135

Group Name	Control	2500 ppm	5000 ppm	10000 ppm
	SITE : Harderian gland			
	TUMOR : adenoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	2/50(4.0)	0/50(0.0)	4/50(8.0)
Adjusted rates(b)	8.33	7.69	0.0	10.00
Terminal rates(c)	2/29(6.9)	2/26(7.7)	0/31(0.0)	2/20(10.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.3053			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.6038			
Fisher Exact test(e)		P = 0.5000	P = 0.1212	P = 0.5000

(HPT360A)

BAIS4

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

Group Name	Control	2500 ppm	5000 ppm	10000 ppm
	SITE : ALL SITE TUMOR : hemangioma			
Tumor rate				
Overall rates(a)	3/50(6.0)	4/50(8.0)	7/50(14.0)	2/50(4.0)
Adjusted rates(b)	8.33	14.81	17.14	5.00
Terminal rates(c)	2/29(6.9)	3/26(11.5)	5/31(16.1)	1/20(5.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.4037			
Prevalence method(d)	P = 0.6299			
Combined analysis(d)	P = 0.6085			
Cochran-Armitage test(e)	P = 0.7245			
Fisher Exact test(e)		P = 0.5000	P = 0.1589	P = 0.5000
	SITE : ALL SITE TUMOR : histiocytic sarcoma			
Tumor rate				
Overall rates(a)	11/50(22.0)	14/50(28.0)	7/50(14.0)	15/50(30.0)
Adjusted rates(b)	17.24	15.38	6.45	15.00
Terminal rates(c)	5/29(17.2)	4/26(15.4)	2/31(6.5)	3/20(15.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1595			
Prevalence method(d)	P = 0.5142			
Combined analysis(d)	P = 0.2043			
Cochran-Armitage test(e)	P = 0.5168			
Fisher Exact test(e)		P = 0.3224	P = 0.2178	P = 0.2472

Group Name	Control	2500 ppm	5000 ppm	10000 ppm
	SITE : ALL SITE			
	TUMOR : malignant lymphoma			
Tumor rate				
Overall rates(a)	13/50(26.0)	18/50(36.0)	20/50(40.0)	17/50(34.0)
Adjusted rates(b)	24.14	30.77	35.48	25.00
Terminal rates(c)	7/29(24.1)	8/26(30.8)	11/31(35.5)	5/20(25.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.0718			
Prevalence method(d)	P = 0.4440			
Combined analysis(d)	P = 0.1029			
Cochran-Armitage test(e)	P = 0.4799			
Fisher Exact test(e)		P = 0.1937	P = 0.1008	P = 0.2565

(HPT360A)

BAIS4

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

TABLE R 1

CAUSE OF DEATH: MALE

STUDY NO. : 0613
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
SEX : MALE

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

Group Name	Control	5000 ppm	10000 ppm	20000 ppm
Number of Dead and Moribund Animal	15	17	14	9
no microscop confirm	1	0	3	0
hepatic lesion	0	1	0	0
body cavity lesion	1	0	0	0
central nervo lesion	0	0	0	1
urinary retention	2	1	0	0
arteritis	0	1	0	0
hydronephrosis	0	1	0	0
tumor d:leukemia	7	2	3	0
tumor d:subcutis	0	1	0	1
tumor d:lung	0	1	1	0
tumor d:spleen	1	0	1	0
tumor d:liver	3	7	4	7
tumor d:urin bladd	0	0	1	0
tumor d:periph nerv	0	0	1	0
tumor d:bone	0	1	0	0
tumor d:pleura	0	1	0	0

TABLE R 2

CAUSE OF DEATH: FEMALE

STUDY NO. : 0613
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
SEX : FEMALE

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

Group Name	Control	2500 ppm	5000 ppm	10000 ppm
Number of Dead and Moribund Animal	21	24	19	30
cardiovascular les	0	1	0	0
reproductive sy les	0	0	0	1
body cavity lesion	0	0	0	1
urinary retention	2	1	0	0
arteritis	0	0	1	0
hydronephrosis	3	0	1	1
peritonitis	1	0	0	0
tumor d:leukemia	6	10	9	12
tumor d:subcutis	0	1	0	0
tumor d:lung	0	0	0	1
tumor d:liver	1	0	1	2
tumor d:pituitary	1	0	0	1
tumor d:thyroid	0	0	0	1
tumor d:ovary	0	0	1	0
tumor d:uterus	6	10	6	10
tumor d:brain	1	0	0	0
tumor d:muscle	0	1	0	0

FIGURES

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

FIGURE 2 SURVIVAL ANIMAL RATE OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-METHYL-1-PROPANOL

FIGURE 3 BODY WEIGHT CHANGES OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-METHYL-1-PROPANOL

FIGURE 4 BODY WEIGHT CHANGES OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-METHYL-1-PROPANOL

FIGURE 5 FOOD CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-METHYL-1-PROPANOL

FIGURE 6 FOOD CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-METHYL-1-PROPANOL

FIGURE 7 WATER CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-METHYL-1-PROPANOL

FIGURE 8 WATER CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-METHYL-1-PROPANOL

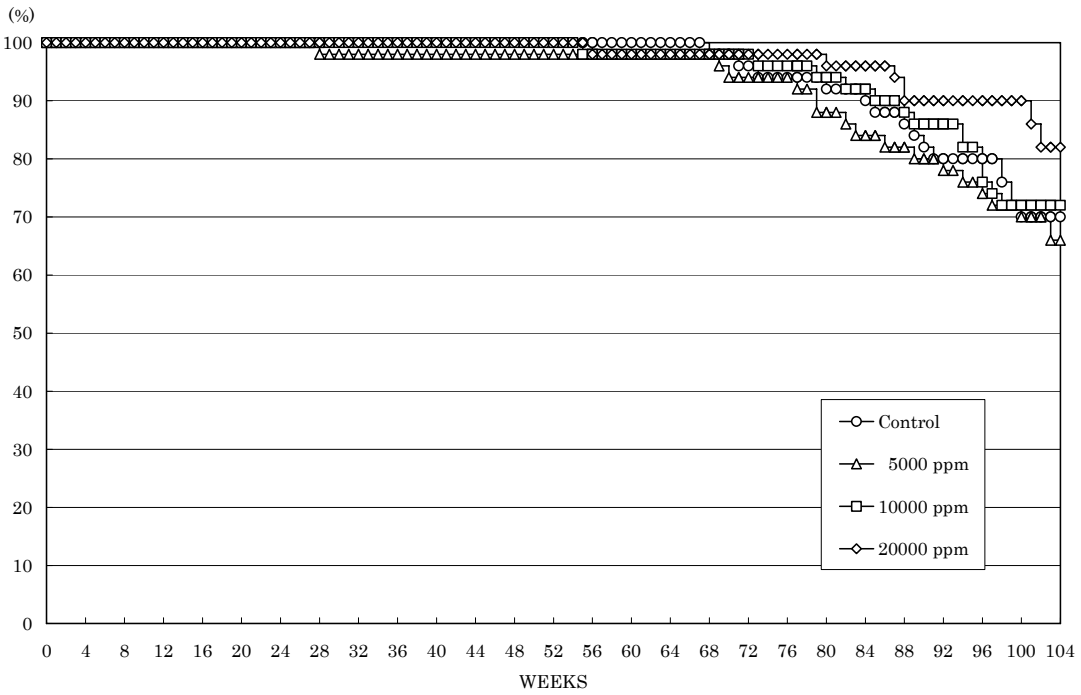

FIGURE 1　SURVIVAL ANIMAL RATE OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-METHYL-1-PROPANOL

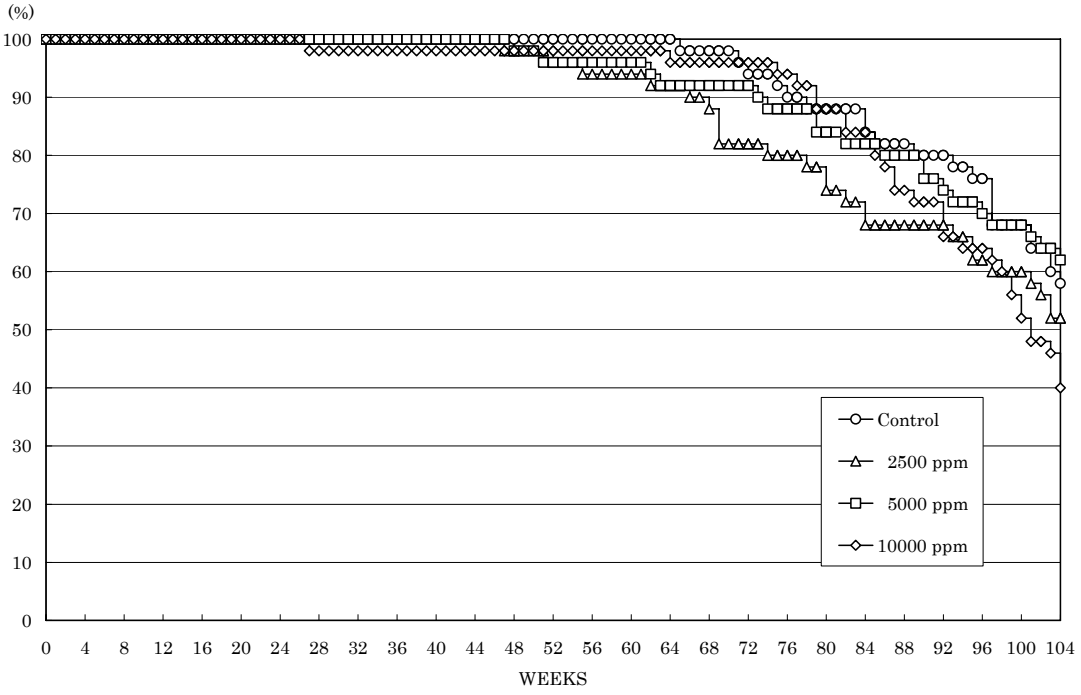

FIGURE 2　SURVIVAL ANIMAL RATE OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-METHYL-1-PROPANOL

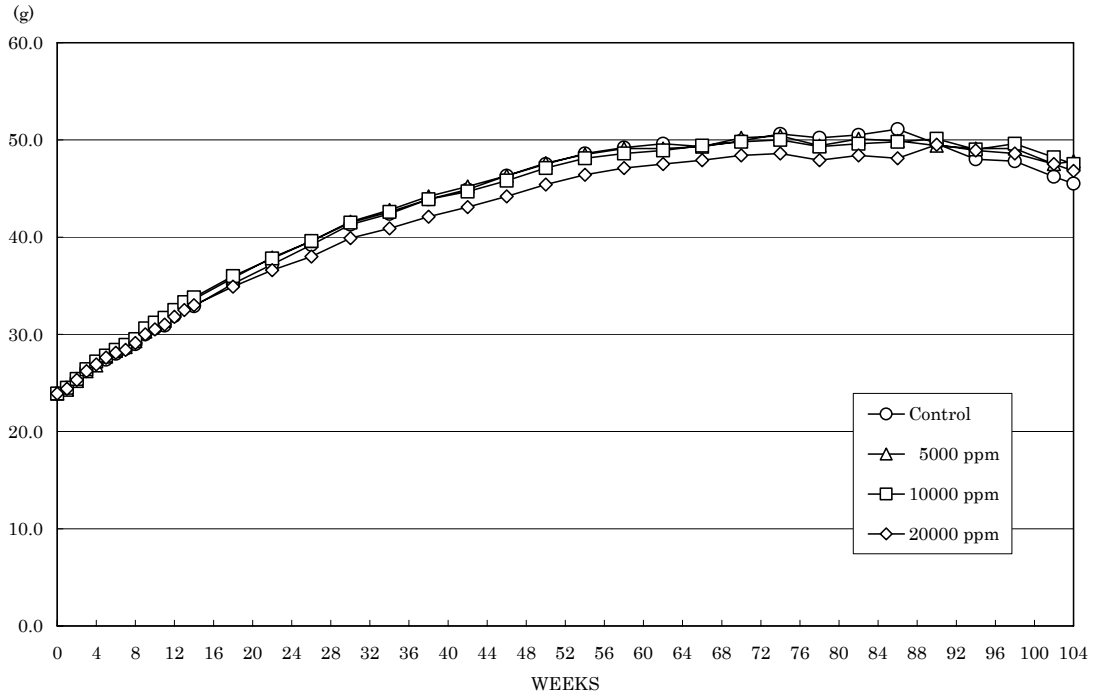

FIGURE 3 BODY WEIGHT CHANGES OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-METHYL-1-PROPANOL

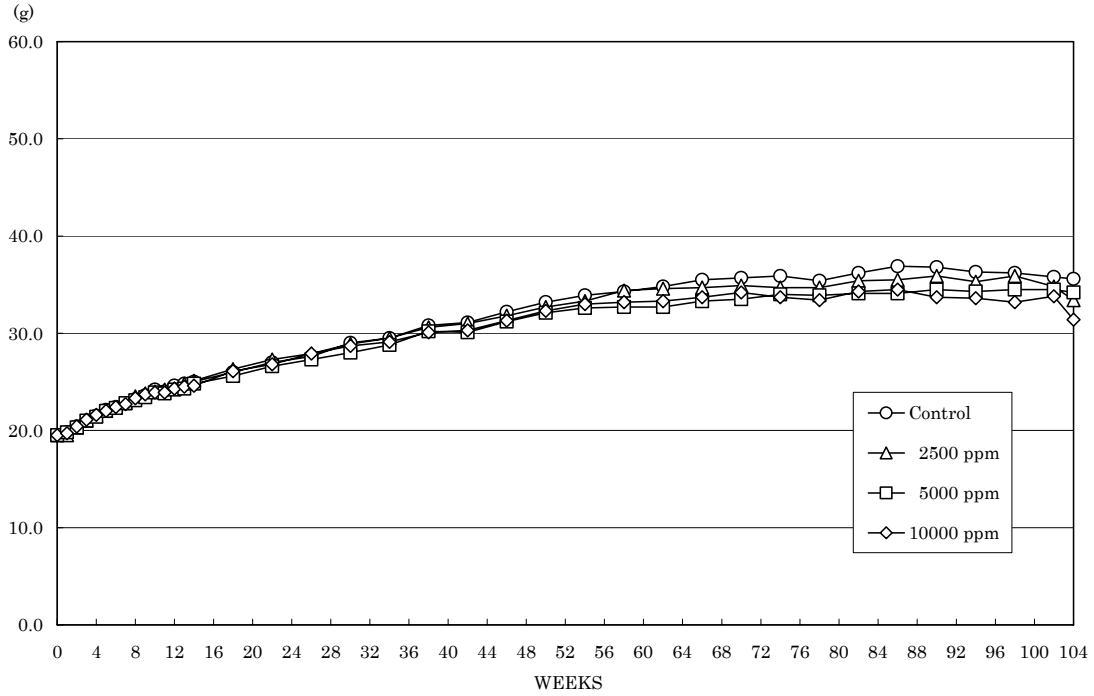

FIGURE 4 BODY WEIGHT CHANGES OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-METHYL-1-PROPANOL

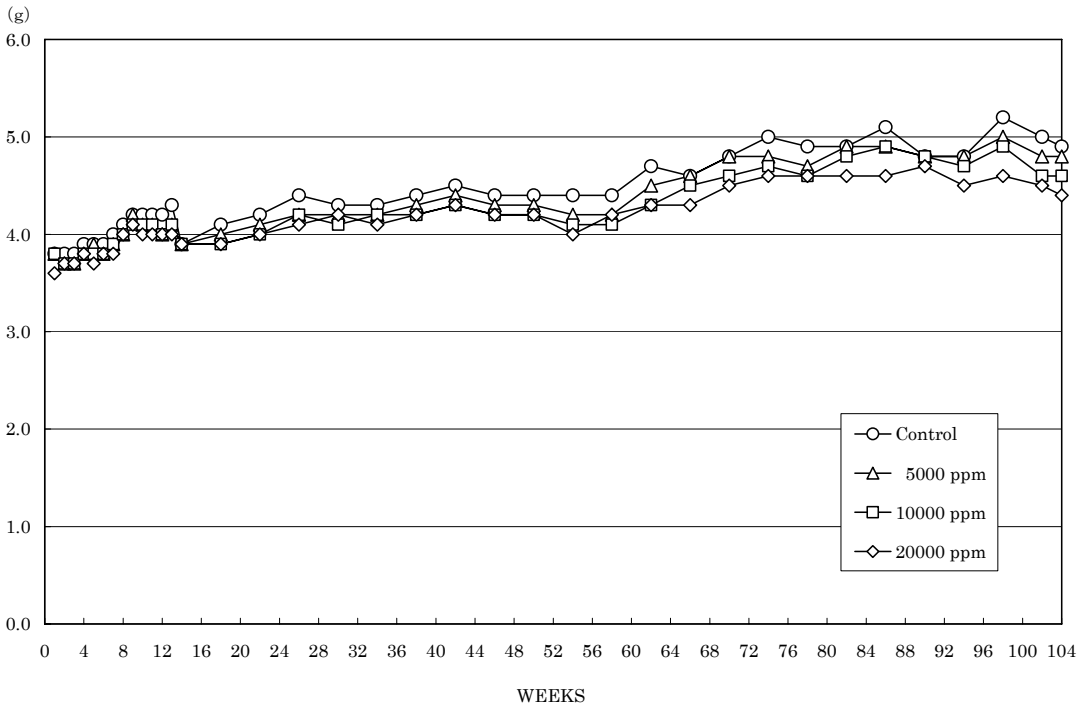

FIGURE 5 FOOD CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-METHYL-1-PROPANOL

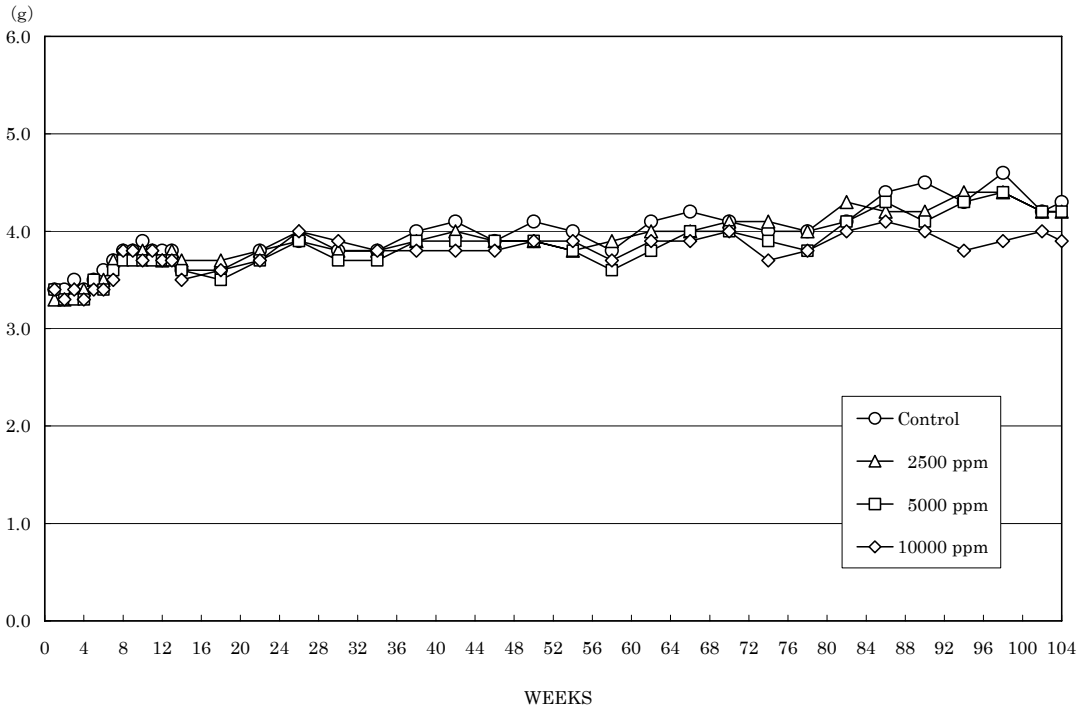

FIGURE 6 FOOD CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-METHYL-1-PROPANOL

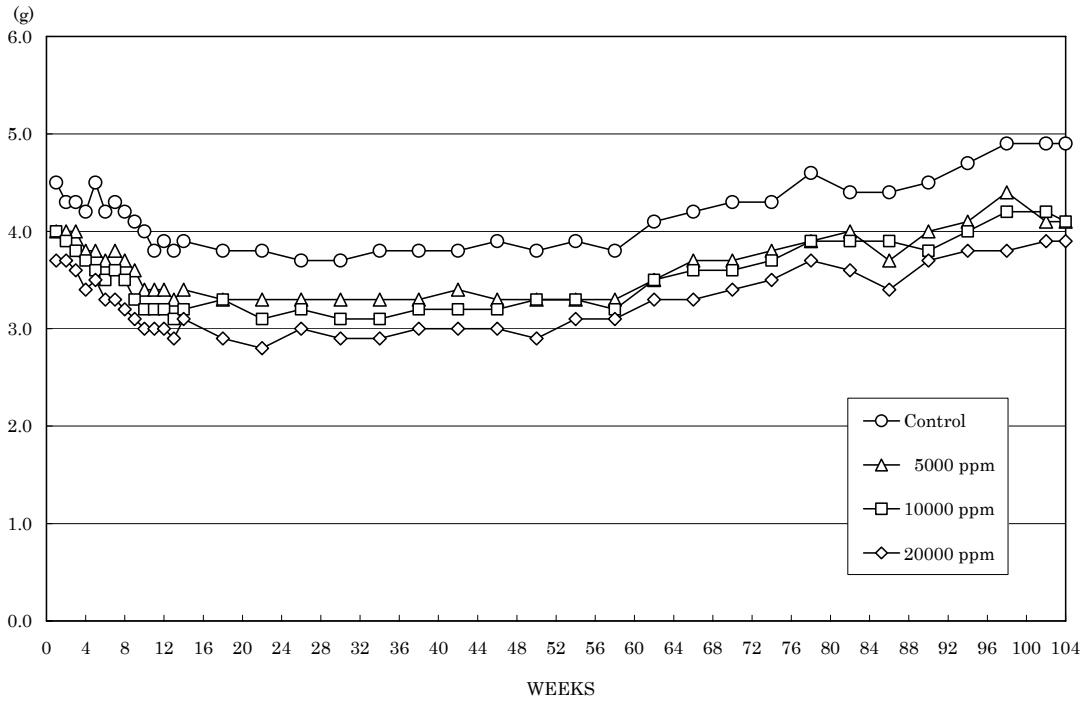

FIGURE 7 WATER CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-METHYL-1-PROPANOL

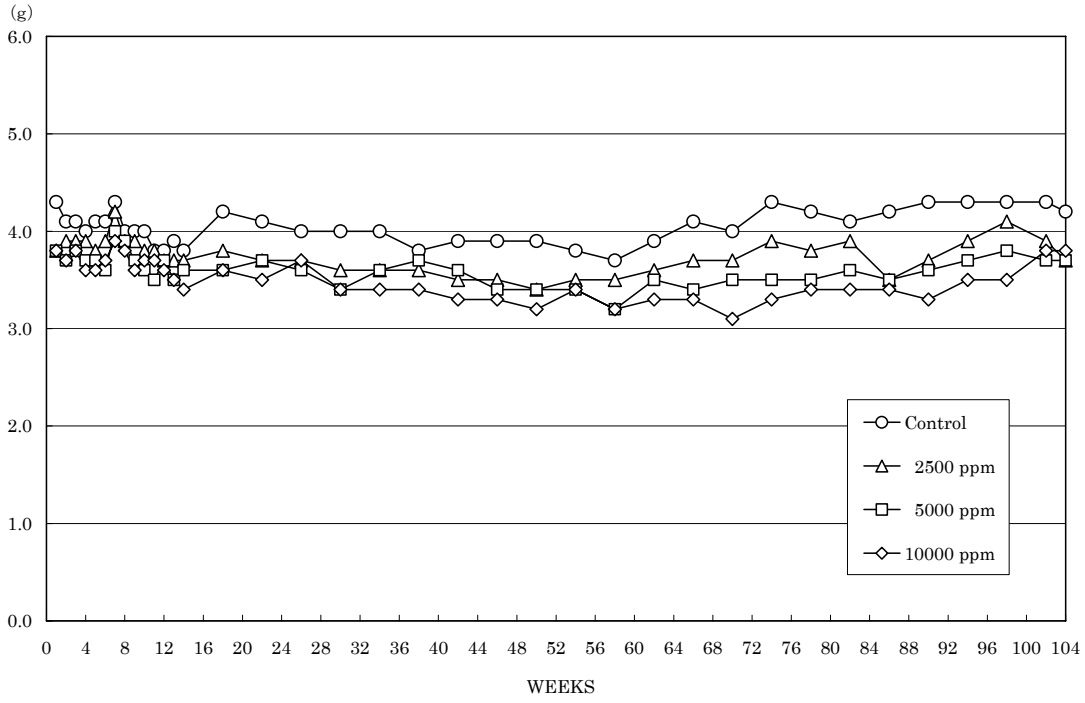

FIGURE 8 WATER CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-METHYL-1-PROPANOL