Summary of Feed Carcinogenicity Study of 2-Amino-4-Chlorophenol 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, 2008.

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

Summary of Feed Carcinogenicity Study of 2-Amino-4-chlorophenol in B6D2F1 MICE

Purpose, materials and methods

2-Amino-4-chlorophenol (ACP, CAS No. 95-85-2) is a crystalline solid with a melting point of 137°C. It is insoluble in water.

The carcinogenicity and chronic toxicity of ACP (greater than 99.1% pure) were examined by feeding groups of B6D2F1/Crlj mice ACP-containing diets for 2 years (104 weeks). Each group of test animals consisted of either 50 male or 50 female mice. The dietary concentration of ACP was 0, 512, 1280, or 3200 ppm (w/w). Both sexes were exposed to each concentration of ACP. The highest dose level was chosen so as not to exceed the maximum tolerated dose (MTD), based on both growth rate and toxicity in a previous 13-week toxicity study. The identity of the ACP used in these experiments was confirmed by both infrared spectrometry and mass spectrometry, and it was analyzed by gas chromatography before and after its use to affirm its stability. To ensure that the concentration of ACP in the diet remained constant, the concentration of APC in the diet was determined by high performance liquid chromatography at the time of preparation and on the 4th day after preparation; ACP-containing food was stored at room temperature. The animals were observed daily for clinical signs and mortality. Body weight and food consumption were measured once a week for the first 14 weeks and every 4 weeks thereafter. All animals, including those found dead or in a moribund state as well as those surviving to the end of the 2-year exposure period, underwent complete necropsy. Urinalysis was performed near the end of the 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 ACP 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

There was no significant difference in survival rate, body weight or food consumption between any ACP-fed group of either sex and their respective controls.

The incidence of squamous cell papillomas in the forestomach was increased in the 3200 ppm-fed male group compared to their control group. Also, the incidences of squamous cell papillomas in the forestomach in all ACP-fed male groups were higher than the historical control data of the Japan Bioassay Research Center (JBRC). Therefore, the increased incidences of squamous cell papillomas in the forestomach in males is related to ACP administration. A slight increase in the incidence of squamous cell papillomas in the forestomach was also observed in the ACP-fed females, but those incidences were within the range of historical JBRC control data.

Conclusions

In mice, there was some evidence of carcinogenic activity of 2-amino-4-chlorophenol in males, based on an increased incidences of squamous cell papillomas in the forestomach. There was no evidence of carcinogenic activity of 2-amino-4-chlorophenol in females.

SELECTED TABLES

TABLE C 1

BODY WEIGHT CHANGES AND

SURVIVAL ANIMAL NUMBERS: MALE

STUDY NO. : 0580
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>	512 ppm Av. Wt.	512 ppm % of cont. <50>	512 ppm No. of Surviv.	1280 ppm Av. Wt.	1280 ppm % of cont. <50>	1280 ppm No. of Surviv.	3200 ppm Av. Wt.	3200 ppm % of cont. <50>	3200 ppm No. of Surviv.
0-0	24.0 (50)	50/50	24.0 (50)	100	50/50	24.0 (50)	100	50/50	24.0 (50)	100	50/50
1-7	25.4 (50)	50/50	25.1 (50)	99	50/50	25.1 (50)	99	50/50	24.7 (50)	97	50/50
2-7	26.4 (50)	50/50	26.1 (50)	99	50/50	25.8 (50)	98	50/50	25.8 (50)	98	50/50
3-7	27.3 (50)	50/50	27.0 (50)	99	50/50	27.0 (50)	99	50/50	26.6 (50)	97	50/50
4-7	28.2 (50)	50/50	27.7 (50)	98	50/50	27.9 (50)	99	50/50	27.3 (50)	97	50/50
5-7	29.1 (50)	50/50	28.7 (50)	99	50/50	28.8 (50)	99	50/50	28.4 (50)	98	50/50
6-7	29.7 (50)	50/50	29.4 (50)	99	50/50	29.5 (50)	99	50/50	29.1 (50)	98	50/50
7-7	30.6 (50)	50/50	30.0 (50)	98	50/50	30.2 (50)	99	50/50	29.8 (50)	97	50/50
8-7	31.2 (50)	50/50	30.9 (50)	99	50/50	30.7 (50)	98	50/50	30.2 (50)	97	50/50
9-7	31.9 (50)	50/50	31.6 (50)	99	50/50	31.5 (50)	99	50/50	31.1 (49)	97	49/50
10-7	32.3 (50)	50/50	32.0 (50)	99	50/50	32.1 (50)	99	50/50	32.0 (49)	99	49/50
11-7	33.0 (50)	50/50	32.0 (50)	97	50/50	32.4 (50)	98	50/50	32.1 (49)	97	49/50
12-7	34.3 (50)	50/50	33.4 (50)	97	50/50	33.6 (50)	98	50/50	33.4 (49)	97	49/50
13-7	35.0 (50)	50/50	34.6 (50)	99	50/50	34.5 (50)	99	50/50	34.1 (49)	97	49/50
14-7	35.4 (50)	50/50	35.2 (50)	99	50/50	35.1 (50)	99	50/50	34.8 (49)	98	49/50
18-7	37.8 (50)	50/50	37.9 (50)	100	50/50	37.7 (50)	100	50/50	37.6 (49)	99	49/50
22-7	40.0 (50)	50/50	39.4 (50)	99	50/50	39.4 (50)	99	50/50	39.1 (49)	98	49/50
26-7	42.9 (50)	50/50	42.5 (49)	99	49/50	42.0 (50)	98	50/50	41.4 (49)	97	49/50
30-7	44.5 (50)	50/50	44.1 (49)	99	49/50	43.7 (50)	98	50/50	43.0 (49)	97	49/50
34-7	46.3 (49)	49/50	46.1 (49)	100	49/50	44.8 (50)	97	50/50	44.2 (49)	95	49/50
38-7	47.5 (49)	49/50	47.5 (49)	100	49/50	46.2 (50)	97	50/50	46.2 (49)	97	49/50
42-7	49.2 (49)	49/50	48.4 (49)	98	49/50	47.7 (50)	97	50/50	47.6 (48)	97	48/50
46-7	50.7 (48)	48/50	49.9 (49)	98	49/50	49.3 (50)	97	50/50	48.9 (48)	96	48/50
50-7	51.4 (48)	48/50	49.5 (49)	96	49/50	49.3 (50)	96	50/50	49.3 (48)	96	48/50
54-7	52.1 (48)	48/50	51.2 (49)	98	49/50	50.6 (50)	97	50/50	50.9 (47)	98	47/50
58-7	52.1 (47)	47/50	50.9 (49)	98	49/50	51.1 (49)	98	49/50	50.6 (47)	97	47/50
62-7	52.8 (47)	47/50	51.6 (49)	98	49/50	52.1 (48)	99	48/50	51.2 (47)	97	47/50
66-7	53.3 (45)	45/50	52.1 (48)	98	48/50	52.2 (47)	98	47/50	51.7 (47)	97	47/50
70-7	53.4 (43)	43/50	52.9 (48)	99	48/50	52.6 (46)	99	46/50	52.4 (47)	98	47/50
74-7	54.4 (43)	43/50	53.8 (46)	99	46/50	52.9 (45)	97	45/50	53.1 (47)	98	47/50
78-7	55.0 (43)	43/50	54.4 (45)	99	45/50	52.9 (45)	96	45/50	53.4 (47)	97	47/50
82-7	53.8 (43)	43/50	53.6 (45)	100	45/50	52.8 (44)	98	44/50	53.2 (45)	99	45/50
86-7	53.3 (40)	40/50	53.4 (45)	100	45/50	52.5 (43)	98	43/50	53.0 (45)	99	45/50
90-7	54.4 (37)	37/50	55.7 (43)	102	43/50	54.0 (41)	99	41/50	53.9 (42)	99	42/50
94-7	51.8 (37)	37/50	56.4 (40)	109	40/50	51.9 (40)	100	40/50	52.5 (40)	101	40/50
98-7	51.5 (34)	34/50	54.9 (38)	107	38/50	50.4 (38)	98	38/50	52.5 (38)	102	38/50
102-7	50.5 (33)	33/50	55.1 (35)	109	35/50	49.4 (38)	98	38/50	52.6 (36)	104	36/50
104-7	48.8 (33)	33/50	53.0 (34)	109	34/50	49.3 (36)	101	36/50	51.7 (35)	106	35/50

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

TABLE C 2

BODY WEIGHT CHANGES AND

SURVIVAL ANIMAL NUMBERS: FEMALE

STUDY NO. : 0580
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>	512 ppm Av. Wt.	512 ppm % of cont. <50>	512 ppm No. of Surviv.	1280 ppm Av. Wt.	1280 ppm % of cont. <50>	1280 ppm No. of Surviv.	3200 ppm Av. Wt.	3200 ppm % of cont. <50>	3200 ppm No. of Surviv.
0-0	19.2 (50)	50/50	19.2 (50)	100	50/50	19.2 (50)	100	50/50	19.2 (50)	100	50/50
1-7	20.1 (50)	50/50	20.1 (50)	100	50/50	19.8 (50)	99	50/50	19.7 (50)	98	50/50
2-7	20.3 (50)	50/50	20.5 (50)	101	50/50	20.2 (50)	100	50/50	20.2 (50)	100	50/50
3-7	20.9 (50)	50/50	20.9 (50)	100	50/50	20.9 (50)	100	50/50	20.6 (50)	99	50/50
4-7	21.3 (50)	50/50	21.3 (50)	100	50/50	21.2 (50)	100	50/50	21.2 (50)	100	50/50
5-7	22.1 (50)	50/50	22.1 (50)	100	50/50	22.0 (50)	100	50/50	21.9 (50)	99	50/50
6-7	22.5 (50)	50/50	22.3 (50)	99	50/50	22.4 (50)	100	50/50	22.4 (50)	100	50/50
7-7	22.7 (50)	50/50	23.0 (50)	101	50/50	22.8 (50)	100	50/50	22.8 (50)	100	50/50
8-7	23.6 (50)	50/50	23.7 (50)	100	50/50	23.2 (50)	98	50/50	23.6 (50)	100	50/50
9-7	24.0 (50)	50/50	24.2 (50)	101	50/50	23.6 (50)	98	50/50	23.7 (50)	99	50/50
10-7	24.2 (50)	50/50	24.7 (50)	102	50/50	24.0 (50)	99	50/50	24.1 (50)	100	50/50
11-7	24.7 (50)	50/50	24.8 (50)	100	50/50	24.0 (50)	97	50/50	24.2 (50)	98	50/50
12-7	24.8 (50)	50/50	25.1 (50)	101	50/50	24.6 (50)	99	50/50	24.7 (50)	100	50/50
13-7	25.8 (50)	50/50	25.8 (50)	100	50/50	25.1 (50)	97	50/50	25.3 (50)	98	50/50
14-7	26.3 (50)	50/50	26.2 (50)	100	50/50	25.6 (50)	97	50/50	25.8 (50)	98	50/50
18-7	27.5 (50)	50/50	27.9 (50)	101	50/50	27.0 (50)	98	50/50	27.2 (50)	99	50/50
22-7	29.0 (50)	50/50	29.2 (50)	101	50/50	28.7 (50)	99	50/50	28.9 (49)	100	49/50
26-7	31.2 (50)	50/50	31.4 (50)	101	50/50	30.5 (50)	98	50/50	30.3 (49)	97	49/50
30-7	32.0 (50)	50/50	32.7 (50)	102	50/50	31.7 (50)	99	50/50	31.4 (49)	98	49/50
34-7	33.4 (50)	50/50	33.9 (50)	101	50/50	32.6 (50)	98	50/50	32.4 (49)	97	49/50
38-7	34.7 (50)	50/50	35.3 (50)	102	50/50	34.4 (50)	99	50/50	34.6 (49)	100	49/50
42-7	35.9 (50)	50/50	36.8 (50)	103	50/50	35.4 (50)	99	50/50	36.3 (48)	101	48/50
46-7	37.0 (50)	50/50	37.7 (50)	102	50/50	36.3 (50)	98	50/50	37.6 (48)	102	48/50
50-7	37.4 (50)	50/50	38.8 (50)	104	50/50	36.9 (50)	99	50/50	38.1 (48)	102	48/50
54-7	39.0 (50)	50/50	40.1 (50)	103	50/50	38.6 (50)	99	50/50	39.5 (48)	101	48/50
58-7	38.8 (50)	50/50	39.8 (49)	103	49/50	38.6 (50)	99	50/50	39.2 (48)	101	48/50
62-7	39.1 (50)	50/50	40.0 (48)	102	48/50	38.9 (49)	99	49/50	39.8 (48)	102	48/50
66-7	39.7 (49)	49/50	41.1 (47)	104	47/50	39.5 (49)	99	49/50	40.6 (48)	102	48/50
70-7	39.5 (49)	49/50	41.3 (47)	105	47/50	39.7 (49)	101	49/50	40.6 (47)	103	47/50
74-7	40.0 (49)	49/50	41.7 (47)	104	47/50	40.2 (48)	101	48/50	40.6 (47)	102	47/50
78-7	41.3 (48)	48/50	42.3 (46)	102	46/50	40.6 (47)	98	47/50	41.2 (46)	100	46/50
82-7	40.1 (48)	48/50	42.5 (44)	106	44/50	39.9 (47)	100	47/50	40.8 (44)	102	44/50
86-7	39.8 (47)	47/50	42.8 (43)	108	43/50	40.8 (44)	103	44/50	40.7 (41)	102	41/50
90-7	39.9 (45)	45/50	43.3 (41)	109	41/50	41.3 (40)	104	40/50	41.0 (38)	103	38/50
94-7	39.0 (41)	41/50	41.7 (39)	107	39/50	41.4 (36)	106	36/50	40.3 (36)	103	36/50
98-7	40.8 (36)	36/50	41.6 (34)	102	34/50	41.0 (33)	100	33/50	40.1 (34)	98	34/50
102-7	40.5 (34)	34/50	41.3 (29)	102	29/50	41.5 (30)	102	30/50	38.8 (30)	96	30/50
104-7	39.6 (34)	34/50	39.1 (28)	99	28/50	40.6 (28)	103	28/50	38.1 (30)	96	30/50

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

TABLE C 3

BODY WEIGHT CHANGES: MALE

STUDY NO. : 0580
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7
Control	24.0± 0.8	25.4± 1.2	26.4± 1.3	27.3± 1.4	28.2± 1.5	29.1± 1.6	29.7± 1.6
512 ppm	24.0± 0.8	25.1± 1.0	26.1± 0.9	27.0± 1.1	27.7± 1.3	28.7± 1.4	29.4± 1.4
1280 ppm	24.0± 0.8	25.1± 1.0	25.8± 1.3*	27.0± 1.4	27.9± 1.5	28.8± 1.8	29.5± 1.8
3200 ppm	24.0± 0.8	24.7± 1.2**	25.8± 1.2*	26.6± 1.6	27.3± 1.9**	28.4± 1.7	29.1± 2.0

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

STUDY NO. : 0580
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 7-7	8-7	9-7	10-7	11-7	12-7	13-7
Control	30.6± 1.7	31.2± 1.7	31.9± 2.0	32.3± 2.3	33.0± 2.4	34.3± 2.3	35.0± 2.6
512 ppm	30.0± 1.7	30.9± 1.7	31.6± 1.8	32.0± 2.1	32.0± 2.1	33.4± 1.9	34.6± 2.0
1280 ppm	30.2± 1.9	30.7± 2.1	31.5± 2.2	32.1± 2.2	32.4± 2.3	33.6± 2.6	34.5± 2.8
3200 ppm	29.8± 2.1	30.2± 2.4	31.1± 1.9	32.0± 2.1	32.1± 2.1	33.4± 2.3	34.1± 2.4

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

STUDY NO. : 0580
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 14-7	18-7	22-7	26-7	30-7	34-7	38-7
Control	35.4± 2.7	37.8± 3.8	40.0± 4.3	42.9± 4.9	44.5± 4.9	46.3± 4.5	47.5± 4.5
512 ppm	35.2± 2.2	37.9± 2.5	39.4± 3.9	42.5± 3.2	44.1± 3.3	46.1± 3.4	47.5± 3.5
1280 ppm	35.1± 2.8	37.7± 3.4	39.4± 4.0	42.0± 4.1	43.7± 4.3	44.8± 4.2	46.2± 4.2
3200 ppm	34.8± 2.4	37.6± 2.8	39.1± 3.3	41.4± 4.1	43.0± 4.0	44.2± 4.3*	46.2± 4.5

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

STUDY NO. : 0580
ANIMAL : MOUSE BGD2F1/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	49.2± 4.0	50.7± 3.8	51.4± 3.3	52.1± 3.1	52.1± 3.9	52.8± 4.1	53.3± 4.0
512 ppm	48.4± 3.5	49.9± 3.2	49.5± 3.7*	51.2± 3.3	50.9± 4.0	51.6± 4.4	52.1± 5.6
1280 ppm	47.7± 3.9	49.3± 3.7	49.3± 4.3*	50.6± 4.5	51.1± 4.3	52.1± 4.4	52.2± 4.5
3200 ppm	47.6± 3.9	48.9± 4.1	49.3± 3.9*	50.9± 3.8	50.6± 4.3	51.2± 5.0	51.7± 4.6

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

(HAN260)

STUDY NO. : 0580
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	53.4± 3.8	54.4± 4.0	55.0± 4.6	53.8± 5.9	53.3± 5.9	54.4± 6.2	51.8± 7.0
512 ppm	52.9± 5.9	53.8± 6.2	54.4± 6.6	53.6± 6.7	53.4± 8.4	55.7± 6.7	56.4± 5.1*
1280 ppm	52.6± 4.7	52.9± 5.2	52.9± 6.1	52.8± 6.1	52.5± 7.7	54.0± 6.9	51.9± 8.1
3200 ppm	52.4± 5.3	53.1± 5.3	53.4± 6.8	53.2± 4.8	53.0± 6.0	53.9± 6.4	52.5± 6.2

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

(HAN260)

BAIS 4

STUDY NO. : 0580
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 98-7	102-7	104-7
Control	51.5± 7.5	50.5± 7.9	48.8± 8.5
512 ppm	54.9± 6.1	55.1± 6.5*	53.0± 6.9
1280 ppm	50.4± 7.9	49.4± 9.7	49.3± 8.4
3200 ppm	52.5± 6.3	52.6± 7.3	51.7± 7.2

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

TABLE C 4

BODY WEIGHT CHANGES: FEMALE

STUDY NO. : 0580
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	19.2± 0.8	20.1± 1.0	20.3± 1.2	20.9± 1.2	21.3± 1.2	22.1± 1.3	22.5± 1.3
512 ppm	19.2± 0.8	20.1± 1.0	20.5± 1.0	20.9± 1.0	21.3± 1.1	22.1± 1.2	22.3± 1.3
1280 ppm	19.2± 0.8	19.8± 1.0	20.2± 1.2	20.9± 1.4	21.2± 1.4	22.0± 1.4	22.4± 1.4
3200 ppm	19.2± 0.8	19.7± 1.1	20.2± 1.1	20.6± 1.1	21.2± 1.3	21.9± 1.3	22.4± 1.5

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

STUDY NO. : 0580
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	22.7± 1.2	23.6± 1.5	24.0± 1.7	24.2± 1.9	24.7± 1.9	24.8± 2.1	25.8± 2.3
512 ppm	23.0± 1.5	23.7± 1.5	24.2± 1.6	24.7± 1.9	24.8± 2.2	25.1± 2.3	25.8± 2.2
1280 ppm	22.8± 1.7	23.2± 1.6	23.6± 1.9	24.0± 1.8	24.0± 2.0	24.6± 2.1	25.1± 2.2
3200 ppm	22.8± 1.5	23.6± 1.5	23.7± 1.5	24.1± 1.8	24.2± 1.9	24.7± 1.7	25.3± 1.9

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

STUDY NO. : 0580
ANIMAL : MOUSE BGD2F1/Crlj[Crj:BDF1]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 14-7	18-7	22-7	26-7	30-7	34-7	38-7
Control	26.3± 2.4	27.5± 2.9	29.0± 3.4	31.2± 3.6	32.0± 4.1	33.4± 4.4	34.7± 4.3
512 ppm	26.2± 2.3	27.9± 2.8	29.2± 3.0	31.4± 3.9	32.7± 3.9	33.9± 4.3	35.3± 4.4
1280 ppm	25.6± 2.3	27.0± 2.9	28.7± 3.5	30.5± 3.8	31.7± 4.3	32.6± 4.3	34.4± 4.8
3200 ppm	25.8± 2.3	27.2± 2.9	28.9± 3.6	30.3± 3.6	31.4± 3.8	32.4± 4.0	34.6± 4.8

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

STUDY NO. : 0580
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	35.9± 4.6	37.0± 5.0	37.4± 5.4	39.0± 5.5	38.8± 5.6	39.1± 5.6	39.7± 5.2
512 ppm	36.8± 4.4	37.7± 4.9	38.8± 5.1	40.1± 5.1	39.8± 5.5	40.0± 5.7	41.1± 5.7
1280 ppm	35.4± 4.8	36.3± 5.0	36.9± 4.8	38.6± 5.0	38.6± 5.4	38.9± 5.6	39.5± 5.4
3200 ppm	36.3± 3.9	37.6± 4.1	38.1± 4.2	39.5± 4.1	39.2± 4.5	39.8± 4.2	40.6± 4.2

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

STUDY NO. : 0580
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	39.5± 5.7	40.0± 6.5	41.3± 6.1	40.1± 6.6	39.8± 6.2	39.9± 7.3	39.0± 7.6
512 ppm	41.3± 6.0	41.7± 5.9	42.3± 6.1	42.5± 6.0	42.8± 5.8	43.3± 5.8	41.7± 6.4
1280 ppm	39.7± 5.5	40.2± 5.2	40.6± 5.8	39.9± 6.0	40.8± 5.3	41.3± 6.0	41.4± 5.4
3200 ppm	40.6± 4.1	40.6± 4.3	41.2± 4.7	40.8± 4.8	40.7± 5.1	41.0± 5.3	40.3± 5.6

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

STUDY NO. : 0580
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	40.8± 5.9	40.5± 6.1	39.6± 6.1
512 ppm	41.6± 5.6	41.3± 5.9	39.1± 5.6
1280 ppm	41.0± 5.2	41.5± 5.1	40.6± 4.8
3200 ppm	40.1± 6.0	38.8± 7.2	38.1± 7.0

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

TABLE D 1

FOOD CONSUMPTION CHANGES AND

SURVIVAL ANIMAL NUMBERS: MALE

STUDY NO. : 0580
ANIMAL : MOUSE B6D2F1/Cr1j[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>	512 ppm Av. FC.	512 ppm % of cont. <50>	512 ppm No. of Surviv.	1280 ppm Av. FC.	1280 ppm % of cont. <50>	1280 ppm No. of Surviv.	3200 ppm Av. FC.	3200 ppm % of cont. <50>	3200 ppm No. of Surviv.
1-7	4.2 (50)	50/50	4.1 (50)	98	50/50	4.0 (50)	95	50/50	4.0 (50)	95	50/50
2-7	3.8 (50)	50/50	4.0 (50)	105	50/50	3.8 (50)	100	50/50	4.0 (50)	105	50/50
3-7	3.9 (50)	50/50	3.9 (50)	100	50/50	4.0 (50)	103	50/50	4.1 (50)	105	50/50
4-7	4.0 (50)	50/50	3.9 (50)	98	50/50	4.0 (50)	100	50/50	3.9 (50)	98	50/50
5-7	4.0 (50)	50/50	3.9 (50)	98	50/50	4.0 (50)	100	50/50	4.1 (50)	103	50/50
6-7	3.9 (50)	50/50	4.0 (50)	103	50/50	3.9 (49)	100	50/50	4.1 (50)	105	50/50
7-7	4.0 (50)	50/50	4.0 (50)	100	50/50	4.0 (50)	100	50/50	4.1 (50)	103	50/50
8-7	4.0 (50)	50/50	4.0 (50)	100	50/50	3.9 (50)	98	50/50	3.9 (50)	98	50/50
9-7	4.0 (50)	50/50	4.1 (50)	103	50/50	4.2 (50)	105	50/50	4.1 (49)	103	49/50
10-7	4.0 (50)	50/50	4.0 (50)	100	50/50	4.1 (50)	103	50/50	4.2 (49)	105	49/50
11-7	4.1 (50)	50/50	3.9 (50)	95	50/50	3.9 (50)	95	50/50	4.1 (49)	100	49/50
12-7	4.1 (50)	50/50	4.3 (50)	105	50/50	4.3 (50)	105	50/50	4.4 (49)	107	49/50
13-7	4.1 (50)	50/50	4.3 (50)	105	50/50	4.1 (50)	100	50/50	4.2 (49)	102	49/50
14-7	3.8 (50)	50/50	4.1 (50)	108	50/50	4.0 (50)	105	50/50	3.9 (49)	103	49/50
18-7	4.4 (50)	50/50	4.3 (50)	98	50/50	4.5 (50)	102	50/50	4.6 (49)	105	49/50
22-7	4.3 (50)	50/50	4.1 (50)	95	50/50	4.1 (50)	95	50/50	4.1 (49)	95	49/50
26-7	4.5 (50)	50/50	4.5 (49)	100	49/50	4.3 (50)	96	50/50	4.3 (49)	96	49/50
30-7	4.6 (50)	50/50	4.6 (49)	100	49/50	4.6 (50)	100	50/50	4.6 (49)	100	49/50
34-7	4.3 (49)	49/50	4.5 (49)	105	49/50	4.4 (50)	102	50/50	4.4 (49)	102	49/50
38-7	4.2 (49)	49/50	4.4 (49)	105	49/50	4.2 (50)	100	50/50	4.4 (49)	105	49/50
42-7	4.6 (49)	49/50	4.6 (49)	100	49/50	4.7 (50)	102	50/50	4.8 (48)	104	48/50
46-7	4.5 (48)	48/50	4.5 (49)	100	49/50	4.5 (50)	100	50/50	4.3 (48)	96	48/50
50-7	4.7 (48)	48/50	4.5 (49)	96	49/50	4.3 (50)	91	50/50	4.6 (48)	98	48/50
54-7	5.0 (48)	48/50	5.0 (49)	100	49/50	4.8 (50)	96	50/50	4.9 (47)	98	47/50
58-7	4.6 (47)	47/50	4.6 (49)	100	49/50	4.8 (49)	104	49/50	4.6 (47)	100	47/50
62-7	4.7 (47)	47/50	4.5 (49)	96	49/50	4.9 (48)	104	48/50	4.7 (47)	100	47/50
66-7	4.9 (45)	45/50	4.9 (47)	100	48/50	4.9 (47)	100	47/50	5.2 (47)	106	47/50
70-7	5.0 (43)	43/50	5.0 (46)	100	48/50	5.0 (46)	100	46/50	5.0 (46)	100	47/50
74-7	4.9 (43)	43/50	4.9 (46)	100	46/50	5.0 (45)	102	45/50	4.9 (44)	100	47/50
78-7	5.4 (43)	43/50	5.1 (45)	94	45/50	5.0 (44)	93	45/50	5.3 (47)	98	47/50
82-7	5.0 (43)	43/50	5.0 (44)	100	45/50	4.8 (44)	96	44/50	5.0 (44)	100	45/50
86-7	4.8 (40)	40/50	4.8 (44)	100	45/50	4.9 (42)	102	43/50	5.1 (43)	106	45/50
90-7	5.6 (37)	37/50	5.3 (43)	95	43/50	5.4 (41)	96	41/50	5.6 (41)	100	42/50
94-7	5.1 (37)	37/50	5.0 (40)	98	40/50	4.6 (38)	90	40/50	4.6 (38)	90	40/50
98-7	4.9 (34)	34/50	5.0 (37)	102	38/50	4.6 (37)	94	38/50	4.7 (35)	96	38/50
102-7	5.3 (33)	33/50	5.4 (35)	102	35/50	5.2 (37)	98	38/50	5.3 (36)	100	36/50
104-7	4.7 (32)	33/50	4.7 (34)	100	34/50	5.1 (35)	109	36/50	5.0 (34)	106	35/50

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

TABLE D 2

FOOD CONSUMPTION CHANGES AND

SURVIVAL ANIMAL NUMBERS: FEMALE

STUDY NO. : 0580
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>	512 ppm Av. FC.	512 ppm % of cont. <50>	512 ppm No. of Surviv.	1280 ppm Av. FC.	1280 ppm % of cont. <50>	1280 ppm No. of Surviv.	3200 ppm Av. FC.	3200 ppm % of cont. <50>	3200 ppm No. of Surviv.
1-7	3.8 (50)	50/50	3.8 (50)	100	50/50	3.7 (50)	97	50/50	3.8 (50)	100	50/50
2-7	3.5 (50)	50/50	3.6 (50)	103	50/50	3.4 (50)	97	50/50	3.5 (50)	100	50/50
3-7	3.6 (50)	50/50	3.6 (50)	100	50/50	3.7 (50)	103	50/50	3.5 (50)	97	50/50
4-7	3.4 (50)	50/50	3.5 (50)	103	50/50	3.4 (50)	100	50/50	3.4 (50)	100	50/50
5-7	3.6 (50)	50/50	3.5 (50)	97	50/50	3.5 (50)	97	50/50	3.5 (50)	97	50/50
6-7	3.7 (50)	50/50	3.8 (50)	103	50/50	3.7 (50)	100	50/50	3.7 (50)	100	50/50
7-7	3.5 (50)	50/50	3.7 (50)	106	50/50	3.7 (50)	106	50/50	3.6 (50)	103	50/50
8-7	3.8 (50)	50/50	3.8 (50)	100	50/50	3.8 (50)	100	50/50	3.9 (50)	103	50/50
9-7	3.9 (50)	50/50	4.1 (50)	105	50/50	4.0 (50)	103	50/50	3.8 (50)	97	50/50
10-7	3.7 (50)	50/50	4.0 (50)	108	50/50	3.8 (50)	103	50/50	3.8 (50)	103	50/50
11-7	3.9 (50)	50/50	3.9 (49)	100	50/50	3.8 (50)	97	50/50	3.8 (50)	97	50/50
12-7	4.0 (50)	50/50	4.1 (50)	103	50/50	4.1 (50)	103	50/50	4.0 (50)	100	50/50
13-7	4.1 (50)	50/50	4.1 (50)	100	50/50	4.3 (50)	105	50/50	4.0 (50)	98	50/50
14-7	4.0 (50)	50/50	4.0 (50)	100	50/50	4.0 (50)	100	50/50	3.8 (50)	95	50/50
18-7	4.3 (50)	50/50	4.3 (50)	100	50/50	4.5 (50)	105	50/50	4.3 (50)	100	50/50
22-7	4.4 (50)	50/50	4.5 (50)	102	50/50	4.6 (50)	105	50/50	4.5 (49)	102	49/50
26-7	4.6 (50)	50/50	4.5 (50)	98	50/50	4.5 (50)	98	50/50	4.3 (49)	93	49/50
30-7	4.9 (50)	50/50	4.9 (50)	100	50/50	5.1 (50)	104	50/50	4.8 (49)	98	49/50
34-7	4.5 (49)	50/50	4.8 (50)	107	50/50	4.9 (50)	109	50/50	4.3 (49)	96	49/50
38-7	4.5 (50)	50/50	4.3 (50)	96	50/50	4.6 (50)	102	50/50	4.7 (49)	104	49/50
42-7	5.2 (50)	50/50	5.4 (50)	104	50/50	5.3 (50)	102	50/50	5.2 (48)	100	48/50
46-7	4.8 (49)	50/50	4.7 (50)	98	50/50	4.6 (50)	96	50/50	4.9 (48)	102	48/50
50-7	4.8 (49)	50/50	4.8 (49)	100	50/50	4.6 (47)	96	50/50	4.8 (46)	100	48/50
54-7	5.3 (50)	50/50	5.4 (50)	102	50/50	5.5 (50)	104	50/50	5.3 (48)	100	48/50
58-7	5.3 (50)	50/50	5.1 (49)	96	49/50	5.0 (50)	94	50/50	4.8 (48)	91	48/50
62-7	4.7 (49)	50/50	4.7 (48)	100	48/50	4.7 (49)	100	49/50	5.2 (48)	111	48/50
66-7	5.2 (48)	49/50	5.4 (47)	104	47/50	5.2 (48)	100	49/50	5.3 (47)	102	48/50
70-7	4.9 (48)	49/50	4.8 (47)	98	47/50	4.8 (48)	98	49/50	5.2 (47)	106	47/50
74-7	5.2 (48)	49/50	5.5 (47)	106	47/50	5.2 (48)	100	48/50	5.2 (45)	100	47/50
78-7	5.2 (47)	48/50	5.6 (45)	108	46/50	5.4 (47)	104	47/50	5.3 (46)	102	46/50
82-7	5.2 (47)	48/50	5.8 (44)	112	44/50	4.9 (46)	94	47/50	5.2 (43)	100	44/50
86-7	4.5 (46)	47/50	5.2 (42)	116	43/50	4.8 (43)	107	44/50	5.1 (40)	113	41/50
90-7	5.3 (44)	45/50	5.6 (37)	106	41/50	5.5 (38)	104	40/50	5.8 (36)	109	38/50
94-7	4.9 (39)	41/50	5.1 (39)	104	39/50	5.5 (34)	112	36/50	5.4 (34)	110	36/50
98-7	5.3 (36)	36/50	5.3 (34)	100	34/50	5.3 (32)	100	33/50	5.5 (34)	104	34/50
102-7	5.6 (34)	34/50	6.2 (28)	111	29/50	5.9 (28)	105	30/50	6.0 (29)	107	30/50
104-7	4.6 (32)	34/50	4.8 (27)	104	28/50	5.4 (26)	117	28/50	5.4 (28)	117	30/50

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

TABLE D 3

FOOD CONSUMPTION CHANGES: MALE

STUDY NO. : 0580
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(4)	2-7(4)	3-7(4)	4-7(4)	5-7(4)	6-7(4)	7-7(4)
Control	4.2± 0.5	3.8± 0.5	3.9± 0.5	4.0± 0.5	4.0± 0.5	3.9± 0.4	4.0± 0.5
512 ppm	4.1± 0.4	4.0± 0.5	3.9± 0.5	3.9± 0.6	3.9± 0.5	4.0± 0.5	4.0± 0.6
1280 ppm	4.0± 0.5	3.8± 0.6	4.0± 0.5	4.0± 0.5	4.0± 0.5	3.9± 0.4	4.0± 0.6
3200 ppm	4.0± 0.7	4.0± 0.7	4.1± 0.6	3.9± 0.7	4.1± 0.6	4.1± 0.6	4.1± 0.6

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

STUDY NO. : 0580
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(4)	9-7(4)	10-7(4)	11-7(4)	12-7(4)	13-7(4)	14-7(4)
Control	4.0± 0.4	4.0± 0.4	4.0± 0.6	4.1± 0.6	4.1± 0.4	4.1± 0.4	3.8± 0.6
512 ppm	4.0± 0.5	4.1± 0.4	4.0± 0.6	3.9± 0.7	4.3± 0.4	4.3± 0.5	4.1± 0.6
1280 ppm	3.9± 0.7	4.2± 0.4	4.1± 0.4	3.9± 0.5	4.3± 0.5	4.1± 0.5	4.0± 0.6
3200 ppm	3.9± 0.8	4.1± 0.5	4.2± 0.6	4.1± 0.6	4.4± 0.6	4.2± 0.4	3.9± 0.7

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

STUDY NO. : 0580
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(4)	22-7(4)	26-7(4)	30-7(4)	34-7(4)	38-7(4)	42-7(4)
Control	4.4± 0.5	4.3± 0.7	4.5± 0.6	4.6± 0.5	4.3± 0.8	4.2± 0.7	4.6± 0.4
512 ppm	4.3± 0.4	4.1± 0.6	4.5± 0.5	4.6± 0.6	4.5± 0.5	4.4± 0.5	4.6± 0.5
1280 ppm	4.5± 0.5	4.1± 0.7	4.3± 0.5	4.6± 0.4	4.4± 0.7	4.2± 0.8	4.7± 0.5
3200 ppm	4.6± 0.4	4.1± 0.7	4.3± 0.6	4.6± 0.5	4.4± 0.8	4.4± 0.7	4.8± 0.5

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

STUDY NO. : 0580
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(4)	50-7(4)	54-7(4)	58-7(4)	62-7(4)	66-7(4)	70-7(4)
Control	4.5± 0.7	4.7± 0.6	5.0± 0.7	4.6± 0.9	4.7± 1.0	4.9± 0.7	5.0± 1.0
512 ppm	4.5± 0.5	4.5± 0.9	5.0± 0.7	4.6± 0.7	4.5± 1.0	4.9± 0.9	5.0± 0.6
1280 ppm	4.5± 0.6	4.3± 0.9*	4.8± 0.9	4.8± 0.7	4.9± 0.8	4.9± 0.8	5.0± 0.9
3200 ppm	4.3± 0.8	4.6± 0.8	4.9± 0.5	4.6± 1.0	4.7± 1.1	5.2± 1.0	5.0± 0.8

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

(HAN260)

STUDY NO. : 0580
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(4)	78-7(4)	82-7(4)	86-7(4)	90-7(4)	94-7(4)	98-7(4)
Control	4.9± 0.7	5.4± 0.7	5.0± 1.0	4.8± 1.4	5.6± 0.9	5.1± 1.0	4.9± 1.4
512 ppm	4.9± 0.8	5.1± 0.8	5.0± 1.3	4.8± 1.2	5.3± 1.0	5.0± 1.0	5.0± 0.9
1280 ppm	5.0± 1.1	5.0± 0.8	4.8± 1.0	4.9± 1.0	5.4± 1.1	4.6± 1.2	4.6± 1.1
3200 ppm	4.9± 1.1	5.3± 0.9	5.0± 1.1	5.1± 1.3	5.6± 1.1	4.6± 1.3	4.7± 1.2

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

STUDY NO. : 0580
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(4)	104-7(4)
Control	5.3± 1.2	4.7± 1.6
512 ppm	5.4± 1.2	4.7± 1.5
1280 ppm	5.2± 1.2	5.1± 1.3
3200 ppm	5.3± 1.4	5.0± 1.2

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

TABLE D 4

FOOD CONSUMPTION CHANGES: FEMALE

STUDY NO. : 0580
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(4)	2-7(4)	3-7(4)	4-7(4)	5-7(4)	6-7(4)	7-7(4)
Control	3.8± 0.6	3.5± 0.5	3.6± 0.6	3.4± 0.6	3.6± 0.6	3.7± 0.6	3.5± 0.5
512 ppm	3.8± 0.6	3.6± 0.5	3.6± 0.6	3.5± 0.5	3.5± 0.4	3.8± 0.5	3.7± 0.6
1280 ppm	3.7± 0.5	3.4± 0.6	3.7± 0.6	3.4± 0.5	3.5± 0.6	3.7± 0.5	3.7± 0.5
3200 ppm	3.8± 0.6	3.5± 0.6	3.5± 0.6	3.4± 0.5	3.5± 0.4	3.7± 0.5	3.6± 0.5

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

(HAN260)

STUDY NO. : 0580
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(4)	9-7(4)	10-7(4)	11-7(4)	12-7(4)	13-7(4)	14-7(4)
Control	3.8± 0.7	3.9± 0.6	3.7± 0.7	3.9± 0.6	4.0± 0.6	4.1± 0.7	4.0± 0.8
512 ppm	3.8± 0.5	4.1± 0.5	4.0± 0.6	3.9± 0.6	4.1± 0.7	4.1± 0.7	4.0± 0.6
1280 ppm	3.8± 0.7	4.0± 0.7	3.8± 0.6	3.8± 0.7	4.1± 0.8	4.3± 1.0	4.0± 0.9
3200 ppm	3.9± 0.5	3.8± 0.4	3.8± 0.6	3.8± 0.5	4.0± 0.6	4.0± 0.6	3.8± 0.6

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

STUDY NO. : 0580
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(4)	22-7(4)	26-7(4)	30-7(4)	34-7(4)	38-7(4)	42-7(4)
Control	4.3± 0.7	4.4± 1.0	4.6± 1.0	4.9± 0.9	4.5± 1.0	4.5± 1.1	5.2± 1.0
512 ppm	4.3± 0.7	4.5± 0.7	4.5± 1.0	4.9± 1.0	4.8± 1.0	4.3± 0.9	5.4± 1.0
1280 ppm	4.5± 1.0	4.6± 1.1	4.5± 1.2	5.1± 1.1	4.9± 1.2	4.6± 1.3	5.3± 1.2
3200 ppm	4.3± 0.9	4.5± 0.9	4.3± 0.8	4.8± 0.9	4.3± 0.8	4.7± 1.1	5.2± 1.1

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

(HAN260)

BAIS 4

STUDY NO. : 0580
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(4)	50-7(4)	54-7(4)	58-7(4)	62-7(4)	66-7(4)	70-7(4)
Control	4.8± 1.2	4.8± 1.2	5.3± 1.2	5.3± 1.5	4.7± 1.2	5.2± 1.1	4.9± 1.3
512 ppm	4.7± 1.1	4.8± 1.0	5.4± 0.9	5.1± 1.3	4.7± 1.0	5.4± 1.1	4.8± 1.3
1280 ppm	4.6± 1.2	4.6± 1.3	5.5± 1.3	5.0± 1.4	4.7± 1.3	5.2± 1.2	4.8± 1.4
3200 ppm	4.9± 1.1	4.8± 1.0	5.3± 1.0	4.8± 1.3	5.2± 1.0	5.3± 1.1	5.2± 1.1

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

STUDY NO. : 0580
ANIMAL : MOUSE BGD2F1/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(4)	78-7(4)	82-7(4)	86-7(4)	90-7(4)	94-7(4)	98-7(4)
Control	5.2± 1.4	5.2± 1.2	5.2± 1.3	4.5± 1.6	5.3± 1.5	4.9± 1.8	5.3± 1.5
512 ppm	5.5± 1.4	5.6± 1.0	5.8± 1.3	5.2± 1.2	5.6± 1.1	5.1± 1.6	5.3± 1.1
1280 ppm	5.2± 1.3	5.4± 1.2	4.9± 1.4	4.8± 1.4	5.5± 1.4	5.5± 1.5	5.3± 1.5
3200 ppm	5.2± 1.4	5.3± 1.2	5.2± 1.3	5.1± 1.7	5.8± 1.2	5.4± 1.4	5.5± 1.6

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

STUDY NO. : 0580
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(4)	104-7(4)
Control	5.6± 1.6	4.6± 1.0
512 ppm	6.2± 1.2	4.8± 1.3
1280 ppm	5.9± 1.5	5.4± 1.2
3200 ppm	6.0± 1.5	5.4± 1.3*

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

TABLE E 1

CHEMICAL INTAKE CHANGES: MALE

STUDY NO. : 0580
ANIMAL : MOUSE BGD2F1/Crlj[Crj:BDF1]
UNIT : g／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	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
512 ppm	0.083± 0.008	0.079± 0.009	0.074± 0.008	0.071± 0.009	0.070± 0.007	0.069± 0.008	0.068± 0.010
1280 ppm	0.204± 0.023	0.189± 0.027	0.189± 0.025	0.182± 0.025	0.179± 0.023	0.171± 0.017	0.171± 0.024
3200 ppm	0.515± 0.076	0.495± 0.082	0.490± 0.070	0.459± 0.069	0.457± 0.066	0.453± 0.061	0.437± 0.066

STUDY NO. : 0580
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g／kg／d a y
REPORT TYPE : A1 104
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 8	9	10	11	12	13	14
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
512 ppm	0.067± 0.008	0.066± 0.007	0.064± 0.009	0.062± 0.010	0.065± 0.007	0.064± 0.008	0.059± 0.008
1280 ppm	0.163± 0.027	0.169± 0.018	0.164± 0.017	0.153± 0.021	0.162± 0.017	0.153± 0.019	0.145± 0.021
3200 ppm	0.413± 0.070	0.425± 0.053	0.420± 0.056	0.410± 0.059	0.423± 0.058	0.395± 0.039	0.362± 0.065

STUDY NO. : 0580
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g／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	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
512 ppm	0.059± 0.006	0.053± 0.007	0.055± 0.007	0.053± 0.007	0.050± 0.006	0.048± 0.006	0.049± 0.007
1280 ppm	0.152± 0.017	0.134± 0.022	0.133± 0.017	0.135± 0.014	0.126± 0.020	0.117± 0.022	0.127± 0.015
3200 ppm	0.390± 0.042	0.338± 0.052	0.332± 0.045	0.348± 0.057	0.321± 0.055	0.309± 0.048	0.323± 0.050

STUDY NO. : 0580
ANIMAL : MOUSE B6D2F1/CrlJ[Crj:BDF1]
UNIT : g／kg／d a y
REPORT TYPE : A1 104
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 46	50	54	58	62	66	70
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
512 ppm	0.046± 0.005	0.047± 0.009	0.050± 0.008	0.046± 0.008	0.045± 0.009	0.048± 0.007	0.048± 0.006
1280 ppm	0.118± 0.019	0.112± 0.020	0.122± 0.023	0.120± 0.018	0.120± 0.021	0.122± 0.021	0.122± 0.024
3200 ppm	0.285± 0.051	0.300± 0.049	0.308± 0.043	0.293± 0.058	0.296± 0.072	0.323± 0.078	0.306± 0.060

STUDY NO. : 0580
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g／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	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
512 ppm	0.047± 0.007	0.048± 0.007	0.048± 0.012	0.047± 0.012	0.048± 0.008	0.046± 0.009	0.046± 0.009
1280 ppm	0.122± 0.025	0.122± 0.022	0.117± 0.025	0.122± 0.027	0.130± 0.039	0.113± 0.031	0.117± 0.034
3200 ppm	0.295± 0.068	0.322± 0.053	0.298± 0.068	0.305± 0.079	0.334± 0.071	0.278± 0.079	0.288± 0.079

STUDY NO. : 0580
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g／kg／d a y
REPORT TYPE : A1 104
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 102	104
Control	0.000± 0.000	0.000± 0.000
512 ppm	0.051± 0.012	0.046± 0.016
1280 ppm	0.141± 0.047	0.138± 0.050
3200 ppm	0.328± 0.092	0.320± 0.118

TABLE E 2

CHEMICAL INTAKE CHANGES: FEMALE

STUDY NO. : 0580
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g／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	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
512 ppm	0.096± 0.015	0.090± 0.013	0.089± 0.014	0.083± 0.012	0.082± 0.010	0.088± 0.011	0.083± 0.012
1280 ppm	0.238± 0.024	0.213± 0.030	0.224± 0.037	0.204± 0.031	0.204± 0.033	0.214± 0.031	0.209± 0.027
3200 ppm	0.624± 0.094	0.554± 0.090	0.547± 0.081	0.514± 0.071	0.505± 0.058	0.534± 0.059	0.500± 0.066

STUDY NO. : 0580
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g／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	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
512 ppm	0.082± 0.011	0.086± 0.011	0.084± 0.011	0.081± 0.011	0.083± 0.011	0.082± 0.014	0.079± 0.012
1280 ppm	0.212± 0.038	0.215± 0.037	0.205± 0.032	0.204± 0.040	0.212± 0.039	0.218± 0.050	0.199± 0.043
3200 ppm	0.529± 0.060	0.510± 0.050	0.508± 0.059	0.501± 0.059	0.520± 0.065	0.512± 0.068	0.476± 0.065

STUDY NO. : 0580
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g／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	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
512 ppm	0.079± 0.013	0.079± 0.013	0.073± 0.013	0.077± 0.014	0.072± 0.012	0.063± 0.013	0.076± 0.013
1280 ppm	0.213± 0.046	0.204± 0.045	0.191± 0.045	0.209± 0.049	0.192± 0.044	0.170± 0.041	0.194± 0.041
3200 ppm	0.503± 0.082	0.499± 0.083	0.452± 0.080	0.492± 0.073	0.431± 0.094	0.433± 0.080	0.459± 0.081

STUDY NO. : 0580
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g／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	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
512 ppm	0.063± 0.013	0.064± 0.013	0.069± 0.013	0.066± 0.015	0.060± 0.012	0.068± 0.013	0.060± 0.016
1280 ppm	0.163± 0.040	0.162± 0.044	0.182± 0.045	0.167± 0.041	0.157± 0.037	0.172± 0.039	0.157± 0.042
3200 ppm	0.421± 0.087	0.411± 0.078	0.429± 0.061	0.389± 0.084	0.415± 0.067	0.419± 0.069	0.413± 0.080

STUDY NO. : 0580
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g／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	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
512 ppm	0.068± 0.016	0.069± 0.015	0.071± 0.019	0.062± 0.014	0.068± 0.016	0.064± 0.020	0.065± 0.016
1280 ppm	0.167± 0.036	0.173± 0.037	0.159± 0.042	0.152± 0.041	0.171± 0.040	0.175± 0.050	0.166± 0.043
3200 ppm	0.411± 0.100	0.411± 0.094	0.407± 0.093	0.404± 0.125	0.457± 0.097	0.433± 0.101	0.441± 0.111

STUDY NO. : 0580
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g／kg／d a y
REPORT TYPE : A1 104
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 102	104
Control	0.000± 0.000	0.000± 0.000
512 ppm	0.078± 0.017	0.064± 0.020
1280 ppm	0.183± 0.050	0.173± 0.040
3200 ppm	0.498± 0.103	0.464± 0.115

TABLE F 1

HEMATOLOGY: MALE

STUDY NO. : 0580
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	33	9.73± 1.52	13.8± 1.9	40.8± 4.9	42.2± 2.5	14.3± 0.8	33.9± 1.1	1530± 441
512 ppm	34	9.57± 0.96	14.0± 1.3	41.0± 3.8	42.9± 2.2	14.6± 0.8	34.1± 0.9	1660± 341
1280 ppm	35	9.23± 1.44	13.4± 2.0	39.3± 5.3	42.9± 3.5	14.5± 1.0	33.9± 1.3	1601± 429
3200 ppm	35	9.39± 1.56	13.6± 2.1	40.1± 5.1	43.3± 4.0	14.5± 0.7	33.7± 1.9	1667± 348

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

STUDY NO. : 0580
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	33	3.3±	3.5
512 ppm	34	2.5±	1.0
1280 ppm	35	3.5±	3.5
3200 ppm	35	4.2±	7.6

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

STUDY NO. : 0580
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	33	3.84± 3.68	1± 1	27± 10	2± 1	0± 0	4± 2	63± 12	2± 5
512 ppm	34	4.19± 3.97	1± 1	25± 12	2± 1	0± 0	4± 2	65± 16	3± 13
1280 ppm	35	5.26± 10.39	1± 2	29± 15	3± 2	0± 0	3± 2	60± 18	4± 16
3200 ppm	35	3.70± 1.74	1± 1	25± 13	2± 1	0± 0	3± 2	68± 15	1± 2

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

(HCL070)

BAIS 4

TABLE F 2

HEMATOLOGY: FEMALE

STUDY NO. : 0580
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	34	9.11± 1.50	13.5± 2.0	39.9± 4.4	44.3± 4.2	14.9± 0.8	33.9± 1.6	1051± 351
512 ppm	28	9.66± 0.88	14.1± 1.2	41.5± 2.7	43.1± 2.1	14.9± 0.5	34.6± 0.9	1030± 302
1280 ppm	28	9.66± 0.76	14.3± 1.1	41.1± 2.7	42.7± 1.4	14.8± 0.4	34.8± 0.8**	1173± 156
3200 ppm	29	9.44± 0.64	14.0± 1.0	40.8± 2.3	43.2± 1.4	14.9± 0.4	34.4± 0.8	1138± 298

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

(HCL070)

BAIS 4

STUDY NO. : 0580
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	34	5.2±	6.3
512 ppm	28	3.2±	2.8
1280 ppm	28	2.6±	1.0
3200 ppm	29	3.6±	1.8

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

STUDY NO. : 0580
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	34	5.11± 6.94	1± 1	25± 15	1± 1	0± 0	4± 2	63± 19	6± 14
512 ppm	28	27.20± 127.52	1± 1	21± 10	2± 1	0± 0	4± 2	68± 17	4± 19
1280 ppm	28	3.55± 2.29	1± 1	22± 7	2± 2	0± 0	4± 2	69± 10	2± 7
3200 ppm	29	2.83± 1.41	2± 1	30± 18	2± 1	0± 0	4± 2	59± 20	3± 6

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

TABLE G 1

BIOCHEMISTRY: MALE

STUDY NO. : 0580
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	33	5.6± 0.8	2.7± 0.5	1.0± 0.2	0.14± 0.05	178± 49	125± 57	37± 23
512 ppm	34	5.4± 0.8	2.7± 0.4	1.0± 0.1	0.13± 0.03	199± 36	128± 65	50± 22*
1280 ppm	35	5.7± 1.2	2.7± 0.4	1.0± 0.2	0.15± 0.07	177± 57	125± 110	38± 20
3200 ppm	35	5.5± 0.9	2.8± 0.5	1.0± 0.2	0.15± 0.08	188± 47	140± 82	49± 19

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

(HCL074)

BA1S4

STUDY NO. : 0580
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	33	208± 83	699± 3131	271± 1033	1891± 8012	167± 119	1± 1	56± 35
512 ppm	34	218± 91	115± 209	65± 106*	495± 335	153± 122	1± 1	50± 13
1280 ppm	35	206± 144	97± 99	62± 96	473± 291	129± 33	1± 1	63± 49
3200 ppm	35	229± 96	102± 254**	114± 443*	1578± 7106	151± 100	0± 1	80± 184

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

(HCL074)

BA1S4

STUDY NO. : 0580
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	33	20.0± 3.7	153± 1	4.2± 0.4	120± 2	9.3± 0.6	6.4± 1.1
512 ppm	34	23.1± 11.4	153± 2	4.3± 0.5	121± 2	9.1± 0.6	6.5± 1.0
1280 ppm	35	26.4± 15.0**	153± 3	4.4± 0.6	120± 4	9.2± 0.8	6.6± 1.3
3200 ppm	35	26.2± 19.9*	153± 2	4.4± 0.6	120± 4	9.1± 0.6	6.4± 1.0

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

(HCL074)

BA1S4

TABLE G 2

BIOCHEMISTRY: FEMALE

STUDY NO. : 0580
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	34	4.9± 0.6	2.5± 0.3	1.1± 0.2	0.14± 0.05	137± 40	73± 23	31± 14
512 ppm	28	4.9± 0.4	2.6± 0.2	1.1± 0.1	0.14± 0.05	144± 29	71± 18	31± 16
1280 ppm	28	5.0± 0.6	2.6± 0.4	1.1± 0.2	0.13± 0.02	142± 29	80± 34	30± 14
3200 ppm	30	5.2± 0.5	2.7± 0.3	1.1± 0.1	0.13± 0.03	145± 37	92± 40	37± 23

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

(HCL074)

BA1S 4

STUDY NO. : 0580
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	34	128± 39	179± 346	74± 160	711± 1367	224± 93	1± 1	126± 249
512 ppm	28	130± 32	115± 99	58± 70	437± 476	212± 63	1± 1	66± 50
1280 ppm	28	138± 51	84± 23	36± 15	353± 183	198± 78	1± 1	127± 252
3200 ppm	30	155± 39*	101± 72	41± 31	449± 409	181± 75	1± 1	85± 127

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

(HCL074)

STUDY NO. : 0580
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	34	20.7± 19.9	153± 1	4.3± 0.8	122± 2	9.0± 0.6	6.3± 2.0
512 ppm	28	15.8± 3.3	152± 2	4.0± 0.3	122± 2	8.9± 0.4	5.8± 0.8
1280 ppm	28	18.0± 10.4	152± 1	4.1± 0.4	122± 3	9.0± 0.4	6.1± 1.0
3200 ppm	30	20.8± 17.5	152± 2	4.2± 0.4	121± 2	9.3± 0.9	6.5± 1.3

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

(HCL074)

BA1S4

TABLE H 1

URINALYSIS: MALE

STUDY NO. : 0580
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	8	15	7	3	0	0		0	3	24	6	0	0		33	0	0	0	0	0		21	6	6	0	0	0		27	0	1	0	5	
512 ppm	35	0	4	17	11	3	0	0		0	4	24	7	0	0		35	0	0	0	0	0		21	9	5	0	0	0		31	0	1	0	3	
1280 ppm	36	0	8	11	8	8	0	1		0	6	21	7	2	0		36	0	0	0	0	0		17	10	9	0	0	0		34	0	0	0	2	
3200 ppm	36	0	3	15	11	5	2	0		0	12	18	6	0	0	*	36	0	0	0	0	0		21	9	6	0	0	0		31	0	0	0	5	

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

(HCL101)

BAIS 4

STUDY NO. : 0580
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	
512 ppm	35	35	0	0	0	0	
1280 ppm	36	36	0	0	0	0	
3200 ppm	36	36	0	0	0	0	

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

(HCL101)

TABLE H 2

URINALYSIS: FEMALE

STUDY NO. : 0580
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein —	±	+	2+	3+	4+	CHI	Glucose —	±	+	2+	3+	4+	CHI	Ketone body —	±	+	2+	3+	4+	CHI	Occult blood —	±	+	2+	3+	CHI
Control	34	0	4	10	5	7	6	2		0	3	15	14	2	0		34	0	0	0	0	0		2	25	6	1	0	0		28	1	0	0	5	
512 ppm	29	0	1	6	12	4	4	2		0	2	18	8	1	0		29	0	0	0	0	0		3	20	6	0	0	0		26	1	0	1	1	
1280 ppm	28	0	0	8	4	9	4	3		0	3	18	6	1	0		28	0	0	0	0	0		3	19	4	2	0	0		22	1	0	2	3	
3200 ppm	30	0	0	4	9	7	9	1		1	4	18	6	1	0		30	0	0	0	0	0		2	24	3	1	0	0		29	0	0	0	1	

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

(HCL101)

BAIS 4

STUDY NO. : 0580
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	34	34	0	0	0	0	
512 ppm	29	29	0	0	0	0	
1280 ppm	28	28	0	0	0	0	
3200 ppm	30	30	0	0	0	0	

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

(HCL101)

TABLE J 1

ORGAN WEIGHT, ABSOLUTE: MALE

STUDY NO. : 0580
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	33	45.5± 8.2	0.010± 0.001	0.222± 0.028	0.220± 0.025	0.207± 0.050	0.640± 0.167
512 ppm	34	49.8± 7.1	0.010± 0.001	0.222± 0.030	0.215± 0.020	0.213± 0.070	0.665± 0.373
1280 ppm	36	45.8± 8.8	0.010± 0.002	0.222± 0.029	0.219± 0.025	0.211± 0.059	0.724± 0.479
3200 ppm	35	48.5± 7.2	0.012± 0.012	0.225± 0.033	0.222± 0.021	0.242± 0.147	0.653± 0.137

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

(HCL040)

BAIS 4

STUDY NO. : 0580
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	33	0.126±	0.113	1.879±	0.576	0.449±	0.014
512 ppm	34	0.161±	0.325	1.857±	0.728	0.453±	0.019
1280 ppm	36	0.168±	0.194	1.799±	0.687	0.451±	0.017
3200 ppm	35	0.094±	0.054	1.782±	0.537	0.449±	0.019

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

TABLE J 2

ORGAN WEIGHT, ABSOLUTE: FEMALE

STUDY NO. : 0580
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	34	36.4± 6.3	0.014± 0.003	0.106± 0.211	0.170± 0.024	0.198± 0.042	0.558± 0.642
512 ppm	28	35.9± 5.4	0.013± 0.001	0.055± 0.157	0.176± 0.031	0.189± 0.054	0.432± 0.057
1280 ppm	28	37.4± 4.7	0.014± 0.002	0.057± 0.147	0.176± 0.025	0.181± 0.013	0.472± 0.225
3200 ppm	30	35.1± 6.8	0.014± 0.004	0.067± 0.210	0.167± 0.020	0.224± 0.204	0.471± 0.153

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

(HCL040)

BAIS 4

STUDY NO. : 0580
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	34	0.232±	0.307	1.404±	0.425	0.468±	0.019
512 ppm	28	0.167±	0.188	1.403±	0.262	0.467±	0.013
1280 ppm	28	0.138±	0.081	1.368±	0.235	0.467±	0.015
3200 ppm	30	0.178±	0.247	1.412±	0.291	0.468±	0.013

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

TABLE K 1

ORGAN WEIGHT, RELATIVE: MALE

STUDY NO. : 0580
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	33	45.5± 8.2	0.023± 0.006	0.507± 0.119	0.498± 0.097	0.473± 0.144	1.441± 0.385
512 ppm	34	49.8± 7.1	0.020± 0.004	0.454± 0.080	0.441± 0.074**	0.443± 0.203	1.330± 0.576*
1280 ppm	36	45.8± 8.8	0.024± 0.008	0.501± 0.115	0.498± 0.127	0.477± 0.151	1.660± 1.221
3200 ppm	35	48.5± 7.2	0.030± 0.050	0.476± 0.108	0.468± 0.088	0.554± 0.601	1.392± 0.450

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

(HCL042)

BAIS 4

STUDY NO. : 0580
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	33	0.299± 0.279	4.323± 1.775	1.024± 0.223
512 ppm	34	0.331± 0.688	3.883± 2.140	0.928± 0.140
1280 ppm	36	0.391± 0.437	4.149± 2.229	1.025± 0.216
3200 ppm	35	0.209± 0.147	3.878± 1.871	0.952± 0.182

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

TABLE K 2

ORGAN WEIGHT, RELATIVE: FEMALE

STUDY NO. : 0580
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	34	36.4± 6.3	0.039± 0.008	0.296± 0.607	0.477± 0.085	0.553± 0.101	1.505± 1.331
512 ppm	28	35.9± 5.4	0.037± 0.007	0.163± 0.476	0.499± 0.111	0.548± 0.248	1.228± 0.227
1280 ppm	28	37.4± 4.7	0.038± 0.007	0.151± 0.382	0.475± 0.075	0.491± 0.073	1.282± 0.669
3200 ppm	30	35.1± 6.8	0.041± 0.016	0.211± 0.696	0.490± 0.100	0.752± 1.176	1.400± 0.598

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

(HCL042)

STUDY NO. : 0580
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	34	0.625± 0.765	3.873± 0.929	1.325± 0.244
512 ppm	28	0.506± 0.655	4.005± 1.022	1.333± 0.214
1280 ppm	28	0.371± 0.214	3.665± 0.503	1.268± 0.182
3200 ppm	30	0.487± 0.546	4.094± 0.831	1.391± 0.324

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

(HCL042)

TABLE L 1

HISTOPATHOLOGICAL FINDINGS:

NON-NEOPLASTIC LESIONS:MALE: ALL ANIMALS

STUDY NO. : 0580
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				512 ppm				1280 ppm				3200 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	0	0	0	0	0	0	1	1	0	0	0	1	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(2)	(0)	(0)	(0)	(2)	(0)	(0)
	squamous cell hyperplasia		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)
	scab		0	1	0	0	0	1	0	0	0	2	0	0	0	0	0	0
			(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)
	epidermal 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)
	duct ectasia:sebaceous gland		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)
subcutis			<50>				<50>				<50>				<50>			
	thrombus		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)	(0)	(0)	(0)
{Respiratory system}																		
nasal cavit			<50>				<50>				<50>				<50>			
	mineralization		1	0	0	0	2	0	0	0	0	0	0	0	1	0	0	0
			(2)	(0)	(0)	(0)	(4)	(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				512 ppm				1280 ppm				3200 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		0	1	0	0	0	0	1	0	0	1	0	0	0	0	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)
	eosinophilic change:olfactory epithelium		30	2	1	0	27	7	0	0	27	10	0	0	26	2	0	0
			(60)	(4)	(2)	(0)	(54)	(14)	(0)	(0)	(54)	(20)	(0)	(0)	(52)	(4)	(0)	(0)
	eosinophilic change:respiratory epithelium		12	14	1	0	30	3	0	0 **	25	6	0	0 *	14	1	0	0 **
			(24)	(28)	(2)	(0)	(60)	(6)	(0)	(0)	(50)	(12)	(0)	(0)	(28)	(2)	(0)	(0)
	inflammation:respiratory epithelium		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)
	respiratory metaplasia:olfactory epithelium		23	3	0	0	27	3	0	0	17	4	0	0	18	1	0	0
			(46)	(6)	(0)	(0)	(54)	(6)	(0)	(0)	(34)	(8)	(0)	(0)	(36)	(2)	(0)	(0)
	respiratory metaplasia:gland		21	8	3	0	28	14	0	0 *	20	16	0	0	26	6	0	0
			(42)	(16)	(6)	(0)	(56)	(28)	(0)	(0)	(40)	(32)	(0)	(0)	(52)	(12)	(0)	(0)
	squamous cell metaplasia:respiratory epithelium		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)
	epithelial hyperplasia:transitional cell type		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)

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
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Organ	Findings	Group Name	Control				512 ppm				1280 ppm				3200 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>			
	necrosis:olfactory epithelium		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)
nasopharynx			<50>				<50>				<50>				<50>			
	eosinophilic change		1	0	1	0	1	0	0	0	3	0	0	0	0	0	0	0
			(2)	(0)	(2)	(0)	(2)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	inflammation		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)
lung			<50>				<50>				<50>				<50>			
	hemorrhage		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)
	edema		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)
	inflammatory infiltration		1	0	0	0	0	0	0	0	1	1	0	0	1	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(2)	(0)	(0)	(2)	(0)	(0)	(0)
	lymphocytic infiltration		2	0	0	0	2	0	0	0	2	0	0	0	0	0	0	0
			(4)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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Organ	Findings	Group Name	Control				512 ppm				1280 ppm				3200 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>			
	accumulation of foamy cells		5	0	0	0	2	0	0	0	5	0	0	0	7	0	0	0
			(10)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(14)	(0)	(0)	(0)
	bronchiolar-alveolar cell hyperplasia		0	1	0	0	0	0	0	0	0	1	0	0	1	0	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(2)	(0)	(0)	(0)
{Hematopoietic system}																		
bone marrow			<50>				<50>				<50>				<50>			
	mastcell 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)
	myelofibrosis		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)
	granulopoiesis:increased		2	0	0	0	0	1	0	0	0	3	0	0	0	0	0	0
			(4)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)
lymph node			<50>				<50>				<50>				<50>			
	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)

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Organ	Findings	Group Name	Control				512 ppm				1280 ppm				3200 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>			
	atrophy		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)
	congestion		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)
	angiectasis		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)
	deposit of hemosiderin		1	0	0	0	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)
	deposit of melanin		1	0	0	0	2	0	0	0	1	0	0	0	1	0	0	0
			(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	extramedullary hematopoiesis		10	13	6	0	19	9	2	0	12	9	6	0	16	11	5	0
			(20)	(26)	(12)	(0)	(38)	(18)	(4)	(0)	(24)	(18)	(12)	(0)	(32)	(22)	(10)	(0)
	follicular hyperplasia		1	1	1	0	3	0	0	0	2	0	0	0	2	1	0	0
			(2)	(2)	(2)	(0)	(6)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(2)	(0)	(0)
{Circulatory system}																		
heart			<50>				<50>				<50>				<50>			
	mineralization		0	0	0	0	2	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)

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Organ	Findings	Group Name	Control				512 ppm				1280 ppm				3200 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Circulatory system}																		
heart			<50>				<50>				<50>				<50>			
	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)
	scar		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)
	myocarditis		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)
	arteritis		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)
{Digestive system}																		
oral cavity			<50>				<50>				<50>				<50>			
	ulcer		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)	(0)	(0)
tooth			<50>				<50>				<50>				<50>			
	dysplasia		3	1	0	0	3	2	0	0	7	3	0	0	2	3	0	0
			(6)	(2)	(0)	(0)	(6)	(4)	(0)	(0)	(14)	(6)	(0)	(0)	(4)	(6)	(0)	(0)

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Organ	Findings	Group Name	Control				512 ppm				1280 ppm				3200 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}																		
tooth			<50>				<50>				<50>				<50>			
	odontogenic cyst		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)
tongue			<50>				<50>				<50>				<50>			
	arteritis		1	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
salivary gl			<50>				<50>				<50>				<50>			
	atrophy:focal		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		1	0	0	0	1	0	0	0	0	0	0	0	2	0	0	0
			(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	granulation		0	0	0	0	1	0	0	0	0	0	0	0	1	1	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(2)	(0)	(0)
	xanthogranuloma		0	0	0	0	0	1	1	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(2)	(2)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
stomach			<50>				<50>				<50>				<50>			
	ulcer:forestomach		1	0	0	0	0	0	0	0	1	0	1	0	3	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(2)	(0)	(6)	(0)	(0)	(0)

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Organ	Findings	Group Name	Control				512 ppm				1280 ppm				3200 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>			
	hyperplasia:forestomach		0	0	0	0	2	0	0	0	2	0	0	0	1	1	0	0
			(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(2)	(0)	(0)
	erosion:glandular stomach		5	0	0	0	4	1	0	0	4	1	0	0	3	0	0	0
			(10)	(0)	(0)	(0)	(8)	(2)	(0)	(0)	(8)	(2)	(0)	(0)	(6)	(0)	(0)	(0)
	ulcer:glandular stomach		1	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(2)	(0)	(0)	(0)	(0)	(0)	(0)
	hyperplasia:glandular stomach		15	0	0	0	13	0	0	0	10	0	0	0	7	0	0	0
			(30)	(0)	(0)	(0)	(26)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(14)	(0)	(0)	(0)
	degeneration:glandular stomach		2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
large intes			<50>				<50>				<50>				<50>			
	inflammation		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)	(0)	(0)
liver			<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)

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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				512 ppm				1280 ppm				3200 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>			
	necrosis:focal		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)	(0)	(0)	(0)
	fatty change:central		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)
	inflammatory infiltration		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)
	granulation		0	0	0	0	0	0	0	0	1	0	0	0	1	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(2)	(0)	(0)
	inflammatory cell nest		5	0	0	0	3	0	0	0	4	0	0	0	2	0	0	0
			(10)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	clear cell focus		1	0	0	0	1	0	3	0	0	1	0	0	2	1	0	0
			(2)	(0)	(0)	(0)	(2)	(0)	(6)	(0)	(0)	(2)	(0)	(0)	(4)	(2)	(0)	(0)
	acidophilic cell focus		2	2	1	0	1	3	0	0	2	1	1	0	4	0	1	0
			(4)	(4)	(2)	(0)	(2)	(6)	(0)	(0)	(4)	(2)	(2)	(0)	(8)	(0)	(2)	(0)
	basophilic cell focus		1	1	0	0	0	0	1	0	1	0	0	0	1	0	0	0
			(2)	(2)	(0)	(0)	(0)	(0)	(2)	(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				512 ppm				1280 ppm				3200 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>			
	biliary cyst		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)
pancreas			<50>				<50>				<50>				<50>			
	islet cell hyperplasia		4	0	0	0	1	0	0	0	7	0	0	0	3	0	0	0
			(8)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(14)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
{Urinary system}																		
kidney			<50>				<50>				<50>				<50>			
	atrophy		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)
	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)
	hyaline droplet		0	0	0	0	2	0	0	0	1	0	0	0	1	1	0	0
			(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(2)	(0)	(0)
	deposit of hemosiderin		1	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				512 ppm				1280 ppm				3200 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>			
	lymphocytic infiltration		1	0	0	0	3	0	0	0	1	0	0	0	1	0	0	0
			(2)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	scar		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)
	inflammatory polyp		0	1	0	0	0	1	1	0	0	1	1	0	0	0	0	0
			(0)	(2)	(0)	(0)	(0)	(2)	(2)	(0)	(0)	(2)	(2)	(0)	(0)	(0)	(0)	(0)
	ossification		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)
	hydronephrosis		2	0	3	0	1	0	2	0	1	1	2	0	0	1	2	0
			(4)	(0)	(6)	(0)	(2)	(0)	(4)	(0)	(2)	(2)	(4)	(0)	(0)	(2)	(4)	(0)
	papillary necrosis		0	0	0	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)
	mineralization:cortex		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)
	regeneration:proximal tubule		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 (%)	512 ppm 50 1 (%)	512 ppm 50 2 (%)	512 ppm 50 3 (%)	512 ppm 50 4 (%)	1280 ppm 50 1 (%)	1280 ppm 50 2 (%)	1280 ppm 50 3 (%)	1280 ppm 50 4 (%)	3200 ppm 50 1 (%)	3200 ppm 50 2 (%)	3200 ppm 50 3 (%)	3200 ppm 50 4 (%)
{Urinary system}																		
urin bladd		<50>					<50>				<50>				<50>			
	dilatation		0 (0)	1 (2)	3 (6)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	1 (2)	1 (2)	4 (8)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)
	inflammation		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)
urethra		<50>					<50>				<50>				<50>			
	inflammation		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)
{Endocrine system}																		
pituitary		<49>					<49>				<50>				<49>			
	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)	0 (0)	0 (0)	0 (0)
	inflammatory infiltration		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hyperplasia		3 (6)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)

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

Organ	Findings	Group Name	Control				512 ppm				1280 ppm				3200 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			<49>				<49>				<50>				<49>			
	Rathke pouch		2	0	0	0	2	0	0	0	4	0	0	0	1	0	0	0
			(4)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
thyroid			<50>				<50>				<50>				<50>			
	cyst		2	0	0	0	0	0	0	0	4	0	0	0	3	0	0	0
			(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
	focal follicular cell hyperplasia		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)
parathyroid			<50>				<50>				<50>				<50>			
	cyst		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)	(0)	(0)	(0)	(0)
adrenal			<50>				<50>				<49>				<50>			
	spindle-cell hyperplasia		28	4	0	0	21	2	0	0	21	1	0	0	16	4	0	0 *
			(56)	(8)	(0)	(0)	(42)	(4)	(0)	(0)	(43)	(2)	(0)	(0)	(32)	(8)	(0)	(0)
	hyperplasia:cortical cell		0	0	0	0	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)
	hyperplasia:medulla		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				512 ppm				1280 ppm				3200 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>			
	mineralization		11	0	0	0	13	1	0	0	11	0	0	0	13	0	0	0
			(22)	(0)	(0)	(0)	(26)	(2)	(0)	(0)	(22)	(0)	(0)	(0)	(26)	(0)	(0)	(0)
epididymis			<50>				<50>				<50>				<50>			
	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)
	granulation		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)
	spermatogenic granuloma		1	1	0	0	3	0	0	0	2	0	0	0	5	0	0	0
			(2)	(2)	(0)	(0)	(6)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	xanthogranuloma		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)
semin ves			<50>				<50>				<50>				<50>			
	hemorrhage		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)
	mineralization		2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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				512 ppm				1280 ppm				3200 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}																		
mammary gl			<50>				<50>				<50>				<50>			
	duct ectasia		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)
{Nervous system}																		
brain			<50>				<50>				<50>				<50>			
	mineralization		12	0	0	0	9	0	0	0	6	0	0	0	12	0	0	0
			(24)	(0)	(0)	(0)	(18)	(0)	(0)	(0)	(12)	(0)	(0)	(0)	(24)	(0)	(0)	(0)
{Special sense organs/appendage}																		
eye			<50>				<50>				<50>				<50>			
	keratitis		0	0	1	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
Harder gl			<50>				<50>				<50>				<50>			
	hyperplasia		1	0	0	0	1	0	0	0	1	0	0	0	0	1	0	0
			(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(2)	(0)	(0)
{Musculoskeletal system}																		
bone			<50>				<50>				<50>				<50>			
	osteosclerosis		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				512 ppm				1280 ppm				3200 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Body cavities}																		
pleura			<50>				<50>				<50>				<50>			
	inflammatory infiltration		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	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)
mesenterium			<50>				<50>				<50>				<50>			
	hemorrhage		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

TABLE L 4

HISTOPATHOLOGICAL FINDINGS: NON-NEOPLASTIC

LESIONS: FEMALE: ALL ANIMALS

Organ	Findings	Group Name	Control				512 ppm				1280 ppm				3200 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	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)
	inflammation		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		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)
	epidermal cyst		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 system}																		
nasal cavit			<50>				<50>				<50>				<50>			
	mineralization		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)
	inflammation		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)
	eosinophilic change:olfactory epithelium		23	5	0	0	18	1	0	0	23	2	0	0	16	0	0	0 *
			(46)	(10)	(0)	(0)	(36)	(2)	(0)	(0)	(46)	(4)	(0)	(0)	(32)	(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 (%)	512 ppm 50 1 (%)	512 ppm 50 2 (%)	512 ppm 50 3 (%)	512 ppm 50 4 (%)	1280 ppm 50 1 (%)	1280 ppm 50 2 (%)	1280 ppm 50 3 (%)	1280 ppm 50 4 (%)	3200 ppm 50 1 (%)	3200 ppm 50 2 (%)	3200 ppm 50 3 (%)	3200 ppm 50 4 (%)
{Respiratory system}																		
nasal cavit			<50>				<50>				<50>				<50>			
	eosinophilic change:respiratory epithelium		19 (38)	24 (48)	0 (0)	0 (0)	16 (32)	16 (32)	4 (8)	0 * (0)	19 (38)	17 (34)	3 (6)	0 (0)	18 (36)	13 (26)	1 (2)	0 * (0)
	respiratory metaplasia:olfactory epithelium		13 (26)	2 (4)	0 (0)	0 (0)	10 (20)	0 (0)	0 (0)	0 (0)	8 (16)	1 (2)	0 (0)	0 (0)	13 (26)	1 (2)	0 (0)	0 (0)
	respiratory metaplasia:gland		35 (70)	9 (18)	0 (0)	0 (0)	34 (68)	9 (18)	0 (0)	0 (0)	40 (80)	5 (10)	0 (0)	0 (0)	36 (72)	5 (10)	0 (0)	0 (0)
	squamous cell metaplasia:respiratory epithelium		2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	ulcer: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)	0 (0)	0 (0)	0 (0)	0 (0)
nasopharynx			<50>				<50>				<50>				<50>			
	eosinophilic change		3 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)
lung			<50>				<50>				<50>				<50>			
	lymphocytic infiltration		1 (2)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)

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

Organ	Findings	Group Name	Control				512 ppm				1280 ppm				3200 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>			
	accumulation of foamy cells		7	0	0	0	12	0	0	0	4	0	0	0	10	0	0	0
			(14)	(0)	(0)	(0)	(24)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	bronchiolar-alveolar cell hyperplasia		3	0	0	0	0	0	0	0	3	0	0	0	0	0	0	0
			(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}																		
bone marrow			<50>				<50>				<50>				<50>			
	angiectasis		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)
	granulation		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)
	increased hematopoiesis		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)
	myelofibrosis		1	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(2)	(2)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen			<50>				<50>				<50>				<50>			
	deposit of hemosiderin		5	0	0	0	2	0	0	0	4	0	0	0	11	0	0	0
			(10)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(22)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				512 ppm				1280 ppm				3200 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>			
	deposit of melanin		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)	(0)	(0)	(0)	(0)
	extramedullary hematopoiesis		7	5	2	0	11	2	0	0	14	3	6	0	13	6	3	0
			(14)	(10)	(4)	(0)	(22)	(4)	(0)	(0)	(28)	(6)	(12)	(0)	(26)	(12)	(6)	(0)
	follicular hyperplasia		0	1	0	0	0	3	0	0	1	1	1	0	0	0	1	0
			(0)	(2)	(0)	(0)	(0)	(6)	(0)	(0)	(2)	(2)	(2)	(0)	(0)	(0)	(2)	(0)
{Circulatory system}																		
heart			<50>				<50>				<50>				<50>			
	thrombus		0	1	0	0	1	0	0	0	1	0	0	0	0	1	0	0
			(0)	(2)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(2)	(0)	(0)
	mineralization		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	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)
	arteritis		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)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
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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				512 ppm				1280 ppm				3200 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
oral cavity			<50>				<50>				<50>				<50>			
	thrombus		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)
tooth			<50>				<50>				<50>				<50>			
	dysplasia		2	0	0	0	0	2	0	0	3	0	0	0	0	0	0	0
			(4)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
tongue			<50>				<50>				<50>				<50>			
	inflammation		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>			
	lymphocytic infiltration		4	0	0	0	3	0	0	0	4	0	0	0	4	0	0	0
			(8)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(8)	(0)	(0)	(0)
stomach			<50>				<50>				<50>				<50>			
	ulcer:forestomach		2	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
			(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	hyperplasia:forestomach		2	1	0	0	3	0	0	0	0	0	0	0	1	0	0	0
			(4)	(2)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	erosion:glandular stomach		3	1	0	0	8	0	0	0	1	0	0	0	3	0	0	0
			(6)	(2)	(0)	(0)	(16)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(6)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
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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				512 ppm				1280 ppm				3200 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>			
	ulcer:glandular stomach		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)
	hyperplasia:glandular stomach		13	0	0	0	6	0	0	0	4	0	0	0 *	6	0	0	0
			(26)	(0)	(0)	(0)	(12)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(12)	(0)	(0)	(0)
small intes			<50>				<50>				<50>				<50>			
	lymphocytic infiltration		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
liver			<50>				<50>				<50>				<50>			
	angiectasis		3	0	0	0	2	0	0	0	1	0	0	0	0	2	0	0
			(6)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(4)	(0)	(0)
	necrosis:central		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)
	necrosis:focal		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)	(0)	(0)
	inflammatory infiltration		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)

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				512 ppm				1280 ppm				3200 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>			
	lymphocytic infiltration		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)
	granulation		11	1	0	0	16	1	0	0	20	1	0	0	17	1	0	0
			(22)	(2)	(0)	(0)	(32)	(2)	(0)	(0)	(40)	(2)	(0)	(0)	(34)	(2)	(0)	(0)
	inflammatory cell nest		4	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	extramedullary hematopoiesis		1	0	0	0	0	0	0	0	3	0	0	0	1	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	clear cell focus		0	0	0	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)
	acidophilic cell focus		1	1	2	0	1	1	4	0	1	2	3	0	1	1	2	0
			(2)	(2)	(4)	(0)	(2)	(2)	(8)	(0)	(2)	(4)	(6)	(0)	(2)	(2)	(4)	(0)
	basophilic cell focus		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)
	biliary 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)

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				512 ppm				1280 ppm				3200 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>			
	mineralization:central		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:Ito-cell		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)
gall bladd			<50>				<50>				<50>				<50>			
	hyperplasia		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)
pancreas			<50>				<50>				<50>				<50>			
	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)
	islet cell hyperplasia		0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
{Urinary system}																		
kidney			<50>				<50>				<50>				<50>			
	cyst		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)

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				512 ppm				1280 ppm				3200 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		3	3	1	0	1	6	0	0	4	4	2	0	3	7	5	0
			(6)	(6)	(2)	(0)	(2)	(12)	(0)	(0)	(8)	(8)	(4)	(0)	(6)	(14)	(10)	(0)
	deposit of amyloid		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)	(0)	(0)
	inflammatory infiltration		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)
	lymphocytic infiltration		8	2	0	0	3	0	0	0	5	0	0	0	3	0	0	0
			(16)	(4)	(0)	(0)	(6)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
	scar		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)
	inflammatory polyp		1	2	0	0	2	1	0	0	1	0	1	0	0	2	0	0
			(2)	(4)	(0)	(0)	(4)	(2)	(0)	(0)	(2)	(0)	(2)	(0)	(0)	(4)	(0)	(0)
	ossification		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)
	hydronephrosis		0	2	2	0	1	0	0	0	0	0	2	0	0	1	5	0
			(0)	(4)	(4)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(2)	(10)	(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				512 ppm				1280 ppm				3200 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		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)
urin bladd			<50>				<50>				<50>				<50>			
	dilatation		1	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(2)	(2)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	inflammatory infiltration		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)
	lymphocytic infiltration		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)
{Endocrine system}																		
pituitary			<50>				<50>				<50>				<50>			
	angiectasis		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)
	cyst		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)	(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				512 ppm				1280 ppm				3200 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>			
	hyperplasia		9	5	3	0	11	5	1	0	8	4	4	0	7	6	4	0
			(18)	(10)	(6)	(0)	(22)	(10)	(2)	(0)	(16)	(8)	(8)	(0)	(14)	(12)	(8)	(0)
	Rathke pouch		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)
thyroid			<50>				<50>				<50>				<50>			
	cyst		2	0	0	0	0	0	0	0	2	0	0	0	3	0	0	0
			(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(6)	(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)
parathyroid			<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)
adrenal			<50>				<50>				<50>				<50>			
	fatty change		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)
	extramedullary hematopoiesis		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				512 ppm				1280 ppm				3200 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}																		
adrenal			<50>				<50>				<50>				<50>			
	spindle-cell hyperplasia		34	13	0	0	35	11	0	0	37	10	0	0	40	9	0	0
			(68)	(26)	(0)	(0)	(70)	(22)	(0)	(0)	(74)	(20)	(0)	(0)	(80)	(18)	(0)	(0)
	hyperplasia:cortical cell		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)
	focal fatty change:cortex		1	0	0	0	2	1	0	0	0	0	0	0	2	0	0	0
			(2)	(0)	(0)	(0)	(4)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
{Reproductive system}																		
ovary			<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)
	thrombus		0	0	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)
	cyst		3	1	0	0	0	0	1	0	3	0	2	0	0	0	1	0
			(6)	(2)	(0)	(0)	(0)	(0)	(2)	(0)	(6)	(0)	(4)	(0)	(0)	(0)	(2)	(0)
	lymphocytic infiltration		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)

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				512 ppm				1280 ppm				3200 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>			
	stromal hyperplasia		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)
	cystic endometrial hyperplasia		28	0	0	0	32	1	0	0	29	0	0	0	29	0	0	0
			(56)	(0)	(0)	(0)	(64)	(2)	(0)	(0)	(58)	(0)	(0)	(0)	(58)	(0)	(0)	(0)
{Nervous system}																		
brain			<50>				<50>				<50>				<50>			
	mineralization		5	0	0	0	10	0	0	0	3	0	0	0	4	0	0	0
			(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(8)	(0)	(0)	(0)
{Special sense organs/appendage}																		
eye			<50>				<50>				<50>				<50>			
	keratitis		2	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(4)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	degeneration:cornea		0	1	0	0	2	0	0	0	0	0	0	0	1	0	0	0
			(0)	(2)	(0)	(0)	(4)	(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				512 ppm				1280 ppm				3200 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}																		
eye			<50>				<50>				<50>				<50>			
	mineralization:cornea		0	0	0	0	0	0	0	0	2	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
Harder gl			<50>				<50>				<50>				<50>			
	hyperplasia		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)
{Musculoskeletal system}																		
muscle			<50>				<50>				<50>				<50>			
	mineralization		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)
bone			<50>				<50>				<50>				<50>			
	osteosclerosis		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

TABLE O 1

NEOPLASTIC LESIONS-INCIDENCE AND

STATISTICAL ANALYSIS: MALE

Group Name	Control	512 ppm	1280 ppm	3200 ppm
SITE : lung				
TUMOR : bronchiolar-alveolar adenoma				
Tumor rate				
Overall rates(a)	3/50(6.0)	6/50(12.0)	2/50(4.0)	2/50(4.0)
Adjusted rates(b)	9.09	13.04	5.56	5.00
Terminal rates(c)	3/33(9.1)	4/34(11.8)	2/36(5.6)	1/35(2.9)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P = 0.8596			
Combined analysis(d)	P = ----------			
Cochran-Armitage test(e)	P = 0.3226			
Fisher Exact test(e)		P = 0.2435	P = 0.5000	P = 0.5000
SITE : lung				
TUMOR : bronchiolar-alveolar carcinoma				
Tumor rate				
Overall rates(a)	6/50(12.0)	4/50(8.0)	8/50(16.0)	7/50(14.0)
Adjusted rates(b)	17.65	11.76	16.67	20.00
Terminal rates(c)	5/33(15.2)	4/34(11.8)	6/36(16.7)	7/35(20.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.4556			
Prevalence method(d)	P = 0.2959			
Combined analysis(d)	P = 0.3046			
Cochran-Armitage test(e)	P = 0.5395			
Fisher Exact test(e)		P = 0.3703	P = 0.3871	P = 0.5000
SITE : lung				
TUMOR : bronchiolar-alveolar adenoma,bronchiolar-alveolar carcinoma				
Tumor rate				
Overall rates(a)	9/50(18.0)	9/50(18.0)	10/50(20.0)	9/50(18.0)
Adjusted rates(b)	26.47	20.59	22.22	22.86
Terminal rates(c)	8/33(24.2)	7/34(20.6)	8/36(22.2)	8/35(22.9)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.4556			
Prevalence method(d)	P = 0.5620			
Combined analysis(d)	P = 0.5600			
Cochran-Armitage test(e)	P = 0.9962			
Fisher Exact test(e)		P = 0.6024	P = 0.5000	P = 0.6024

Group Name	Control	512 ppm	1280 ppm	3200 ppm
SITE : lung				
TUMOR : bronchiolar-alveolar adenoma, bronchiolar-alveolar carcinoma, squamous cell carcinoma				
Tumor rate				
Overall rates(a)	9/50(18.0)	9/50(18.0)	11/50(22.0)	9/50(18.0)
Adjusted rates(b)	26.47	20.59	25.00	22.86
Terminal rates(c)	8/33(24.2)	7/34(20.6)	9/36(25.0)	8/35(22.9)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.4556			
Prevalence method(d)	P = 0.5610			
Combined analysis(d)	P = 0.5591			
Cochran-Armitage test(e)	P = 0.9924			
Fisher Exact test(e)		P = 0.6024	P = 0.4016	P = 0.6024
SITE : lymph node				
TUMOR : malignant lymphoma				
Tumor rate				
Overall rates(a)	3/50(6.0)	6/50(12.0)	8/50(16.0)	2/50(4.0)
Adjusted rates(b)	9.09	5.88	22.22	2.86
Terminal rates(c)	3/33(9.1)	2/34(5.9)	8/36(22.2)	1/35(2.9)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.6351			
Prevalence method(d)	P = 0.7743			
Combined analysis(d)	P = 0.8057			
Cochran-Armitage test(e)	P = 0.4275			
Fisher Exact test(e)		P = 0.2435	P = 0.0999	P = 0.5000
SITE : spleen				
TUMOR : hemangiosarcoma				
Tumor rate				
Overall rates(a)	4/50(8.0)	2/50(4.0)	0/50(0.0)	1/50(2.0)
Adjusted rates(b)	8.89	0.0	0.0	0.0
Terminal rates(c)	1/33(3.0)	0/34(0.0)	0/36(0.0)	0/35(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.4010			
Prevalence method(d)	P = 0.9962			
Combined analysis(d)	P = 0.9335			
Cochran-Armitage test(e)	P = 0.1532			
Fisher Exact test(e)		P = 0.3389	P = 0.0587	P = 0.1811

Group Name	Control	512 ppm	1280 ppm	3200 ppm
	SITE : spleen			
	TUMOR : hemangioma, hemangiosarcoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	3/50(6.0)	2/50(4.0)	1/50(2.0)
Adjusted rates(b)	8.89	2.86	4.26	0.0
Terminal rates(c)	1/33(3.0)	0/34(0.0)	1/36(2.8)	0/35(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.4010			
Prevalence method(d)	P = 0.9755			
Combined analysis(d)	P = 0.9246			
Cochran-Armitage test(e)	P = 0.1665			
Fisher Exact test(e)		P = 0.5000	P = 0.3389	P = 0.1811
	SITE : stomach			
	TUMOR : squamous cell papilloma			
Tumor rate				
Overall rates(a)	0/50(0.0)	4/50(8.0)	3/50(6.0)	6/50(12.0)
Adjusted rates(b)	0.0	8.51	8.33	13.95
Terminal rates(c)	0/33(0.0)	2/34(5.9)	3/36(8.3)	3/35(8.6)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P = 0.0273*			
Combined analysis(d)	P = ----------			
Cochran-Armitage test(e)	P = 0.0365*			
Fisher Exact test(e)		P = 0.0587	P = 0.1212	P = 0.0133*
	SITE : liver			
	TUMOR : hepatocellular adenoma			
Tumor rate				
Overall rates(a)	14/50(28.0)	13/50(26.0)	13/50(26.0)	19/50(38.0)
Adjusted rates(b)	33.33	31.43	33.33	42.86
Terminal rates(c)	11/33(33.3)	10/34(29.4)	12/36(33.3)	15/35(42.9)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.2429			
Prevalence method(d)	P = 0.1761			
Combined analysis(d)	P = 0.1335			
Cochran-Armitage test(e)	P = 0.1820			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.1976

Group Name	Control	512 ppm	1280 ppm	3200 ppm
	SITE : liver			
	TUMOR : histiocytic sarcoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	3/50(6.0)	0/50(0.0)	2/50(4.0)
Adjusted rates(b)	0.0	0.0	0.0	0.0
Terminal rates(c)	0/33(0.0)	0/34(0.0)	0/36(0.0)	0/35(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.2791			
Prevalence method(d)	P = -------			
Combined analysis(d)	P = 0.2791			
Cochran-Armitage test(e)	P = 0.5274			
Fisher Exact test(e)		P = 0.1212	P = N.C.	P = 0.2475
	SITE : liver			
	TUMOR : hemangiosarcoma			
Tumor rate				
Overall rates(a)	5/50(10.0)	3/50(6.0)	0/50(0.0)	1/50(2.0)
Adjusted rates(b)	15.15	4.35	0.0	2.86
Terminal rates(c)	5/33(15.2)	1/34(2.9)	0/36(0.0)	1/35(2.9)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5616			
Prevalence method(d)	P = 0.9708			
Combined analysis(d)	P = 0.9781			
Cochran-Armitage test(e)	P = 0.0683			
Fisher Exact test(e)		P = 0.3575	P = 0.0281*	P = 0.1022
	SITE : liver			
	TUMOR : hepatocellular carcinoma			
Tumor rate				
Overall rates(a)	20/50(40.0)	7/50(14.0)	7/50(14.0)	8/50(16.0)
Adjusted rates(b)	42.42	18.92	11.11	15.38
Terminal rates(c)	14/33(42.4)	6/34(17.6)	4/36(11.1)	5/35(14.3)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8323			
Prevalence method(d)	P = 0.9744			
Combined analysis(d)	P = 0.9859			
Cochran-Armitage test(e)	P = 0.0415*			
Fisher Exact test(e)		P = 0.0031**	P = 0.0031**	P = 0.0067**

Group Name	Control	512 ppm	1280 ppm	3200 ppm
	SITE : liver			
	TUMOR : hemangioma, hemangiosarcoma			
Tumor rate				
Overall rates(a)	6/50(12.0)	4/50(8.0)	1/50(2.0)	1/50(2.0)
Adjusted rates(b)	16.67	6.52	2.70	2.86
Terminal rates(c)	5/33(15.2)	2/34(5.9)	0/36(0.0)	1/35(2.9)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5616			
Prevalence method(d)	P = 0.9855			
Combined analysis(d)	P = 0.9890			
Cochran-Armitage test(e)	P = 0.0385*			
Fisher Exact test(e)		P = 0.3703	P = 0.0559	P = 0.0559
	SITE : liver			
	TUMOR : hepatocellular adenoma, hepatocellular carcinoma			
Tumor rate				
Overall rates(a)	28/50(56.0)	17/50(34.0)	18/50(36.0)	23/50(46.0)
Adjusted rates(b)	58.82	41.67	38.89	48.57
Terminal rates(c)	19/33(57.6)	13/34(38.2)	14/36(38.9)	17/35(48.6)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.6439			
Prevalence method(d)	P = 0.6382			
Combined analysis(d)	P = 0.6942			
Cochran-Armitage test(e)	P = 0.8157			
Fisher Exact test(e)		P = 0.0219*	P = 0.0352*	P = 0.2119

Group Name	Control	512 ppm	1280 ppm	3200 ppm
SITE : liver				
TUMOR : hepatocellular adenoma, hepatocellular carcinoma, hepatoblastoma				
Tumor rate				
Overall rates(a)	29/50(58.0)	18/50(36.0)	18/50(36.0)	24/50(48.0)
Adjusted rates(b)	58.82	44.44	38.89	48.57
Terminal rates(c)	19/33(57.6)	14/34(41.2)	14/36(38.9)	17/35(48.6)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5872			
Prevalence method(d)	P = 0.6446			
Combined analysis(d)	P = 0.6717			
Cochran-Armitage test(e)	P = 0.8135			
Fisher Exact test(e)		P = 0.0223*	P = 0.0223*	P = 0.2115

(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	512 ppm	1280 ppm	3200 ppm
	SITE : ALL SITE			
	TUMOR : histiocytic sarcoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	5/50(10.0)	3/50(6.0)	6/50(12.0)
Adjusted rates(b)	0.0	2.94	5.56	8.57
Terminal rates(c)	0/33(0.0)	1/34(2.9)	2/36(5.6)	3/35(8.6)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3363			
Prevalence method(d)	P = 0.0504			
Combined analysis(d)	P = 0.0873			
Cochran-Armitage test(e)	P = 0.1286			
Fisher Exact test(e)		P = 0.1022	P = 0.3087	P = 0.0559
	SITE : ALL SITE			
	TUMOR : malignant lymphoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	6/50(12.0)	8/50(16.0)	2/50(4.0)
Adjusted rates(b)	9.09	5.88	22.22	2.86
Terminal rates(c)	3/33(9.1)	2/34(5.9)	8/36(22.2)	1/35(2.9)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.6351			
Prevalence method(d)	P = 0.7743			
Combined analysis(d)	P = 0.8057			
Cochran-Armitage test(e)	P = 0.4275			
Fisher Exact test(e)		P = 0.2435	P = 0.0999	P = 0.5000

Group Name	Control	512 ppm	1280 ppm	3200 ppm
	SITE : ALL SITE			
	TUMOR : hemangiosarcoma			
Tumor rate				
Overall rates(a)	9/50(18.0)	4/50(8.0)	0/50(0.0)	2/50(4.0)
Adjusted rates(b)	20.00	2.94	0.0	2.86
Terminal rates(c)	6/33(18.2)	1/34(2.9)	0/36(0.0)	1/35(2.9)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5266			
Prevalence method(d)	P = 0.9984			
Combined analysis(d)	P = 0.9930			
Cochran-Armitage test(e)	P = 0.0233*			
Fisher Exact test(e)		P = 0.1168	P = 0.0013**	P = 0.0256*

(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 O 2

NEOPLASTIC LESIONS-INCIDENCE AND

STATISTICAL ANALYSIS: FEMALE

Group Name	Control	512 ppm	1280 ppm	3200 ppm
	SITE : lung			
	TUMOR : bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	1/50(2.0)	2/50(4.0)	4/50(8.0)
Adjusted rates(b)	2.94	3.57	6.25	13.33
Terminal rates(c)	1/34(2.9)	1/28(3.6)	1/28(3.6)	4/30(13.3)
Statistical analysis				
Peto test				
Standard method(d)	P = 1.0000 ?			
Prevalence method(d)	P = 0.0359*			
Combined analysis(d)	P = 0.0842			
Cochran-Armitage test(e)	P = 0.1929			
Fisher Exact test(e)		P = 0.5000	P = 0.6913	P = 0.3389
	SITE : lung			
	TUMOR : bronchiolar-alveolar adenoma, bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	2/50(4.0)	2/50(4.0)	5/50(10.0)
Adjusted rates(b)	8.82	4.00	6.25	16.67
Terminal rates(c)	3/34(8.8)	1/28(3.6)	1/28(3.6)	5/30(16.7)
Statistical analysis				
Peto test				
Standard method(d)	P = 1.0000 ?			
Prevalence method(d)	P = 0.1080			
Combined analysis(d)	P = 0.1809			
Cochran-Armitage test(e)	P = 0.4279			
Fisher Exact test(e)		P = 0.3389	P = 0.3389	P = 0.5000
	SITE : lymph node			
	TUMOR : malignant lymphoma			
Tumor rate				
Overall rates(a)	12/50(24.0)	16/50(32.0)	7/50(14.0)	7/50(14.0)
Adjusted rates(b)	14.71	14.29	0.0	13.33
Terminal rates(c)	5/34(14.7)	4/28(14.3)	0/28(0.0)	4/30(13.3)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.9462			
Prevalence method(d)	P = 0.5803			
Combined analysis(d)	P = 0.9286			
Cochran-Armitage test(e)	P = 0.0662			
Fisher Exact test(e)		P = 0.2522	P = 0.1540	P = 0.1540

Group Name	Control	512 ppm	1280 ppm	3200 ppm
	SITE : spleen			
	TUMOR : hemangioma, hemangiosarcoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	1/50(2.0)	3/50(6.0)	0/50(0.0)
Adjusted rates(b)	2.94	3.23	7.32	0.0
Terminal rates(c)	1/34(2.9)	0/28(0.0)	2/28(7.1)	0/30(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P = 0.6950			
Combined analysis(d)	P = --------			
Cochran-Armitage test(e)	P = 0.4818			
Fisher Exact test(e)		P = 0.7525	P = 0.3087	P = 0.5000
	SITE : stomach			
	TUMOR : squamous cell papilloma			
Tumor rate				
Overall rates(a)	0/50(0.0)	1/50(2.0)	1/50(2.0)	3/50(6.0)
Adjusted rates(b)	0.0	2.70	2.63	9.09
Terminal rates(c)	0/34(0.0)	0/28(0.0)	0/28(0.0)	2/30(6.7)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P = 0.0279*			
Combined analysis(d)	P = --------			
Cochran-Armitage test(e)	P = 0.0549			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.1212
	SITE : liver			
	TUMOR : hemangioma			
Tumor rate				
Overall rates(a)	2/50(4.0)	1/50(2.0)	2/50(4.0)	4/50(8.0)
Adjusted rates(b)	5.88	3.57	5.13	13.33
Terminal rates(c)	2/34(5.9)	1/28(3.6)	1/28(3.6)	4/30(13.3)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P = 0.0872			
Combined analysis(d)	P = --------			
Cochran-Armitage test(e)	P = 0.1929			
Fisher Exact test(e)		P = 0.5000	P = 0.6913	P = 0.3389

Group Name	Control	512 ppm	1280 ppm	3200 ppm
	SITE : liver			
	TUMOR : hepatocellular adenoma			
Tumor rate				
Overall rates(a)	5/50(10.0)	6/50(12.0)	4/50(8.0)	3/50(6.0)
Adjusted rates(b)	14.71	21.43	11.11	10.00
Terminal rates(c)	5/34(14.7)	6/28(21.4)	3/28(10.7)	3/30(10.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P = 0.7948			
Combined analysis(d)	P = -------			
Cochran-Armitage test(e)	P = 0.3423			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.3575
	SITE : liver			
	TUMOR : hemangiosarcoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	3/50(6.0)	0/50(0.0)	0/50(0.0)
Adjusted rates(b)	11.76	6.45	0.0	0.0
Terminal rates(c)	4/34(11.8)	1/28(3.6)	0/28(0.0)	0/30(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5483			
Prevalence method(d)	P = 0.9945			
Combined analysis(d)	P = 0.9950			
Cochran-Armitage test(e)	P = 0.0227*			
Fisher Exact test(e)		P = 0.5000	P = 0.0587	P = 0.0587
	SITE : liver			
	TUMOR : hepatocellular carcinoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	3/50(6.0)	1/50(2.0)	1/50(2.0)
Adjusted rates(b)	0.0	9.68	3.13	2.94
Terminal rates(c)	0/34(0.0)	2/28(7.1)	0/28(0.0)	0/30(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P = 0.4950			
Combined analysis(d)	P = -------			
Cochran-Armitage test(e)	P = 0.9335			
Fisher Exact test(e)		P = 0.1212	P = 0.5000	P = 0.5000

Group Name	Control	512 ppm	1280 ppm	3200 ppm
	SITE : liver			
	TUMOR : hemangioma, hemangiosarcoma			
Tumor rate				
Overall rates(a)	6/50(12.0)	4/50(8.0)	2/50(4.0)	4/50(8.0)
Adjusted rates(b)	17.65	9.68	5.13	13.33
Terminal rates(c)	6/34(17.6)	2/28(7.1)	1/28(3.6)	4/30(13.3)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5483			
Prevalence method(d)	P = 0.5917			
Combined analysis(d)	P = 0.6467			
Cochran-Armitage test(e)	P = 0.5831			
Fisher Exact test(e)		P = 0.3703	P = 0.1343	P = 0.3703
	SITE : liver			
	TUMOR : hepatocellular adenoma, hepatocellular carcinoma			
Tumor rate				
Overall rates(a)	5/50(10.0)	8/50(16.0)	5/50(10.0)	4/50(8.0)
Adjusted rates(b)	14.71	25.81	13.89	11.76
Terminal rates(c)	5/34(14.7)	7/28(25.0)	3/28(10.7)	3/30(10.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P = 0.7368			
Combined analysis(d)	P = ----------			
Cochran-Armitage test(e)	P = 0.4393			
Fisher Exact test(e)		P = 0.2768	P = 0.6297	P = 0.5000
	SITE : pituitary gland			
	TUMOR : adenoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	7/50(14.0)	5/50(10.0)	6/50(12.0)
Adjusted rates(b)	0.0	17.86	12.50	20.00
Terminal rates(c)	0/34(0.0)	5/28(17.9)	3/28(10.7)	6/30(20.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.9012			
Prevalence method(d)	P = 0.0427*			
Combined analysis(d)	P = 0.1642			
Cochran-Armitage test(e)	P = 0.4128			
Fisher Exact test(e)		P = 0.0798	P = 0.2180	P = 0.1343

Group Name	Control	512 ppm	1280 ppm	3200 ppm
	SITE : uterus			
	TUMOR : histiocytic sarcoma			
Tumor rate				
Overall rates(a)	12/50(24.0)	7/50(14.0)	12/50(24.0)	13/50(26.0)
Adjusted rates(b)	17.65	7.14	7.14	10.00
Terminal rates(c)	6/34(17.6)	2/28(7.1)	2/28(7.1)	3/30(10.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.0484*			
Prevalence method(d)	P = 0.7898			
Combined analysis(d)	P = 0.1667			
Cochran-Armitage test(e)	P = 0.4290			
Fisher Exact test(e)		P = 0.1540	P = 0.5924	P = 0.5000
	SITE : Harderian gland			
	TUMOR : adenoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	1/50(2.0)	4/50(8.0)	2/50(4.0)
Adjusted rates(b)	0.0	3.57	9.30	5.71
Terminal rates(c)	0/34(0.0)	1/28(3.6)	2/28(7.1)	1/30(3.3)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.1228			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.2968			
Fisher Exact test(e)		P = 0.5000	P = 0.0587	P = 0.2475

(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	512 ppm	1280 ppm	3200 ppm
	SITE : ALL SITE			
	TUMOR : histiocytic sarcoma			
Tumor rate				
Overall rates(a)	14/50(28.0)	9/50(18.0)	12/50(24.0)	17/50(34.0)
Adjusted rates(b)	20.59	14.29	7.14	10.00
Terminal rates(c)	7/34(20.6)	4/28(14.3)	2/28(7.1)	3/30(10.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.0076**			
Prevalence method(d)	P = 0.9033			
Combined analysis(d)	P = 0.0837			
Cochran-Armitage test(e)	P = 0.2091			
Fisher Exact test(e)		P = 0.1710	P = 0.4100	P = 0.3329
	SITE : ALL SITE			
	TUMOR : malignant lymphoma			
Tumor rate				
Overall rates(a)	12/50(24.0)	16/50(32.0)	7/50(14.0)	7/50(14.0)
Adjusted rates(b)	14.71	14.29	0.0	13.33
Terminal rates(c)	5/34(14.7)	4/28(14.3)	0/28(0.0)	4/30(13.3)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.9462			
Prevalence method(d)	P = 0.5803			
Combined analysis(d)	P = 0.9286			
Cochran-Armitage test(e)	P = 0.0662			
Fisher Exact test(e)		P = 0.2522	P = 0.1540	P = 0.1540

Group Name	Control	512 ppm	1280 ppm	3200 ppm
	SITE : ALL SITE			
	TUMOR : hemangiosarcoma			
Tumor rate				
Overall rates(a)	5/50(10.0)	3/50(6.0)	1/50(2.0)	0/50(0.0)
Adjusted rates(b)	14.71	6.45	2.44	0.0
Terminal rates(c)	5/34(14.7)	1/28(3.6)	0/28(0.0)	0/30(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5483			
Prevalence method(d)	P = 0.9934			
Combined analysis(d)	P = 0.9945			
Cochran-Armitage test(e)	P = 0.0182*			
Fisher Exact test(e)		P = 0.3575	P = 0.1022	P = 0.0281*

(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 Q 1

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

TABLE Q1 HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER : B6D2F1/Crlj MALE MICE

Organs Tumors	No. of animals examined	No. of animals bearing tumor	Incidence (%)	Min. - Max. (%)
Stomach	1946			
Squamous cell papilloma		5	0.3	0 - 2

39 carcinogenicity studies examined in Japan Bioassay Research Center were used.
Study No. : 0044, 0060, 0062, 0064, 0066, 0068, 0096, 0105, 0116, 0140, 0159, 0163, 0190, 0206, 0211, 0225, 0243, 0268, 0270, 0279, 0285, 0297, 0319, 0329, 0343, 0348, 0366, 0372, 0402, 0406, 0418, 0422, 0438, 0449, 0458, 0462, 0498, 0515, 0561

TABLE Q 2

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

TABLE Q2 HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER : B6D2F1/Crlj FEMALE MICE

Organs Tumors	No. of animals examined	No. of animals bearing tumor	Incidence (%)	Min. - Max. (%)
Stomach	1947			
Squamous cell papilloma		8	0.4	0 - 6
Lung	1947			
Bronchiolar-alveolar carcinoma		55	2.8	0 - 8
Pituitary gland	1938			
Adenoma		277	14.3	2 - 34
Uterus	1947			
Histiocytic sarcoma		401	20.6	10 - 32
All organ	1947			
Histiocytic sarcoma		456	23.4	12 - 36

39 carcinogenicity studies examined in Japan Bioassay Research Center were used.
Study No. : 0044, 0060, 0062, 0064, 0066, 0068, 0096, 0105, 0116, 0140, 0159, 0163, 0190, 0206, 0211, 0225, 0243, 0268, 0270, 0279, 0285, 0297, 0319, 0329, 0343, 0348, 0366, 0372, 0402, 0406, 0418, 0422, 0438, 0449, 0458, 0462, 0498, 0515, 0561

TABLE R

CAUSE OF DEATH OF MICE IN THE 2-YEAR FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

STUDY NO. : 0580
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
SEX : MALE

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

Group Name	Control	512 ppm	1280 ppm	3200 ppm
Number of Dead and Moribund Animal	17	16	14	15
no microscop confirm	0	0	1	2
digestive sy les	0	1	0	0
urinary retention	4	1	4	2
arteritis	1	0	0	0
tooth lesion	0	0	1	0
hydronephrosis	2	0	0	1
peritonitis	0	0	1	0
tumor d:leukemia	0	4	0	1
tumor d:subcutis	1	1	1	0
tumor d:lung	0	0	2	0
tumor d:lymph node	1	0	0	0
tumor d:spleen	0	2	0	1
tumor d:liver	8	5	3	7
tumor d:epididymis	0	0	1	0
tumor d:periph nerv	0	1	0	1
tumor d:Harder gl	0	1	0	0

STUDY NO. : 0580
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
SEX : FEMALE

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

Group Name	Control	512 ppm	1280 ppm	3200 ppm
Number of Dead and Moribund Animal	16	22	22	20
no microscop confirm	0	0	1	0
cardiovascular les	0	0	0	1
renal lesion	0	0	1	0
thrombosis	0	0	0	1
tooth lesion	0	1	0	0
hydronephrosis	0	0	1	0
tumor d:leukemia	7	12	7	3
tumor d:lung	1	0	0	0
tumor d:spleen	1	0	0	2
tumor d:liver	0	1	0	2
tumor d:pituitary	2	1	1	0
tumor d:ovary	0	1	0	1
tumor d:uterus	5	5	11	10
tumor d:bone	0	1	0	0

FIGURES

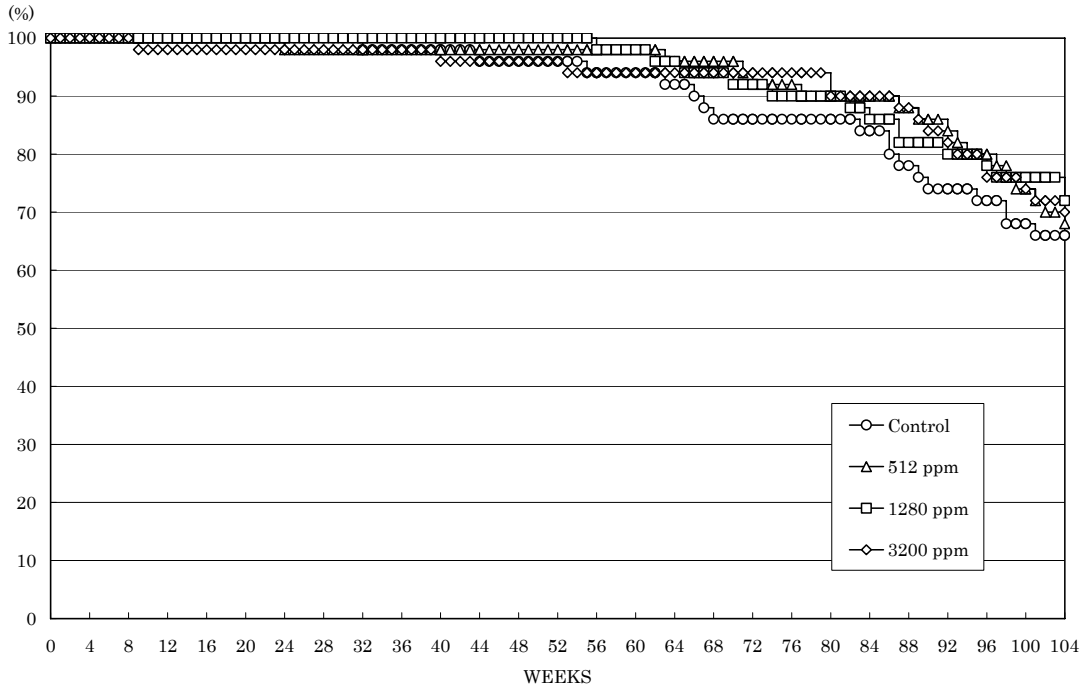

FIGURE 1 SURVIVAL ANIMAL RATE OF MALE MICE IN THE 2-YEAR FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

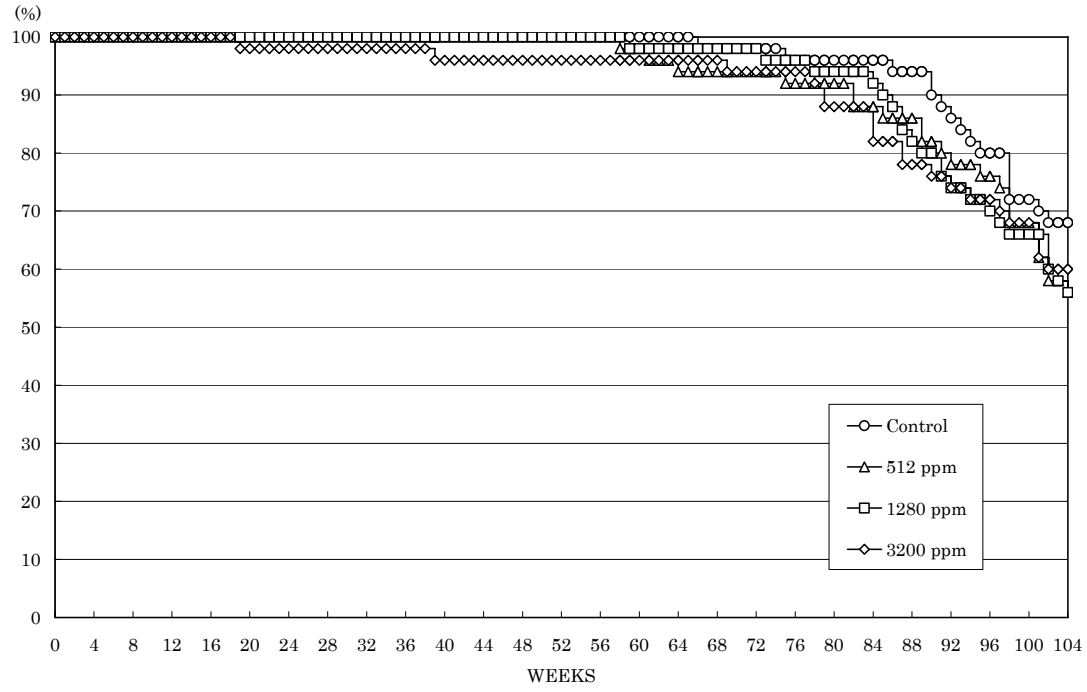

FIGURE 2 SURVIVAL ANIMAL RATE OF FEMALE MICE IN THE 2-YEAR FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

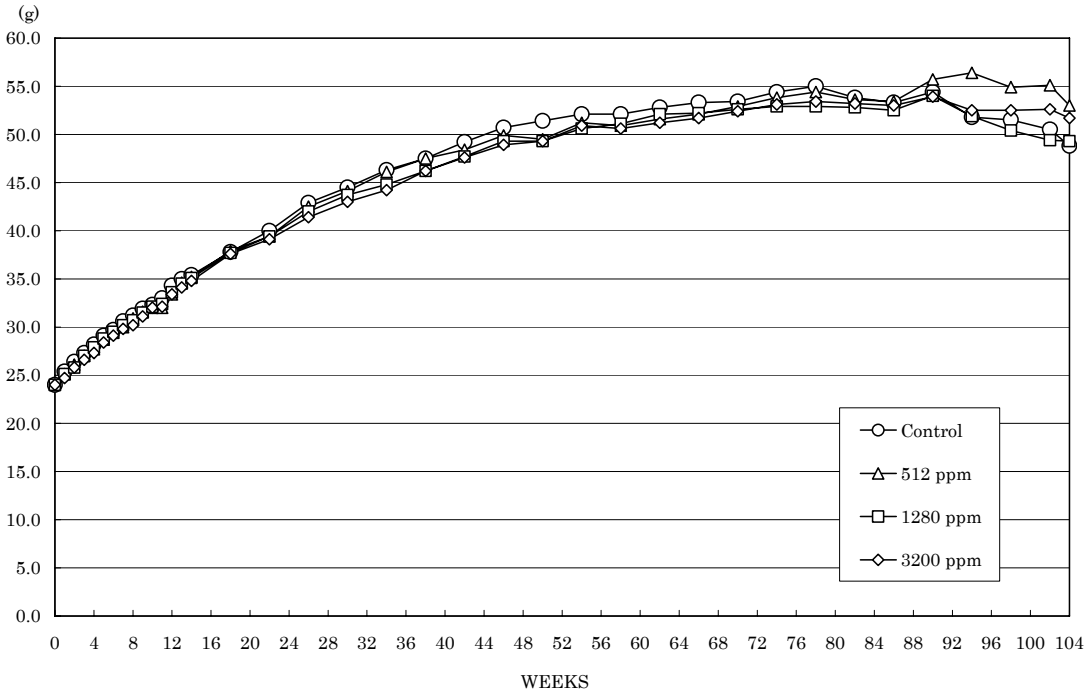

FIGURE 3 BODY WEIGHT CHANGES OF MALE MICE IN THE 2-YEAR FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

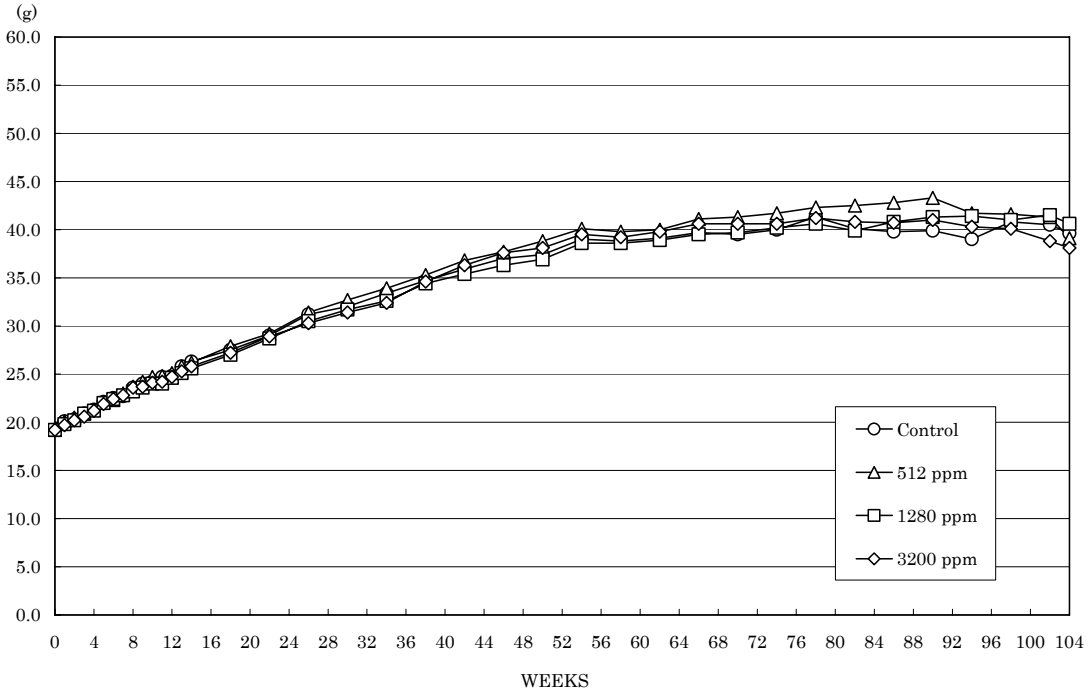

FIGURE 4 BODY WEIGHT CHANGES OF FEMALE MICE IN THE 2-YEAR FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

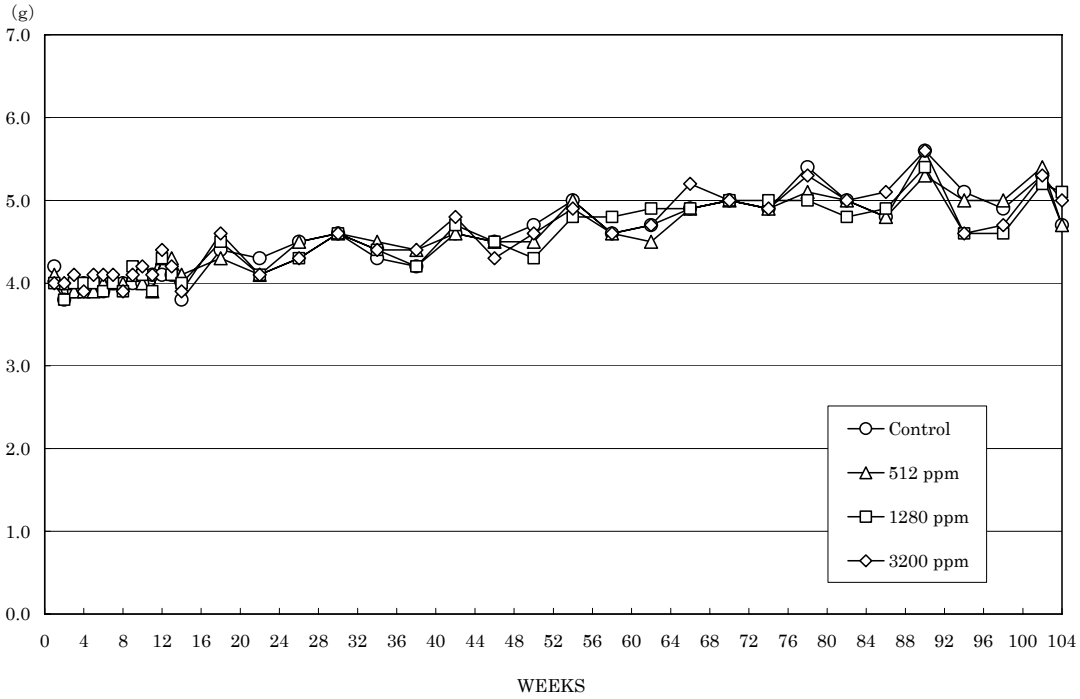

FIGURE 5 FOOD CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

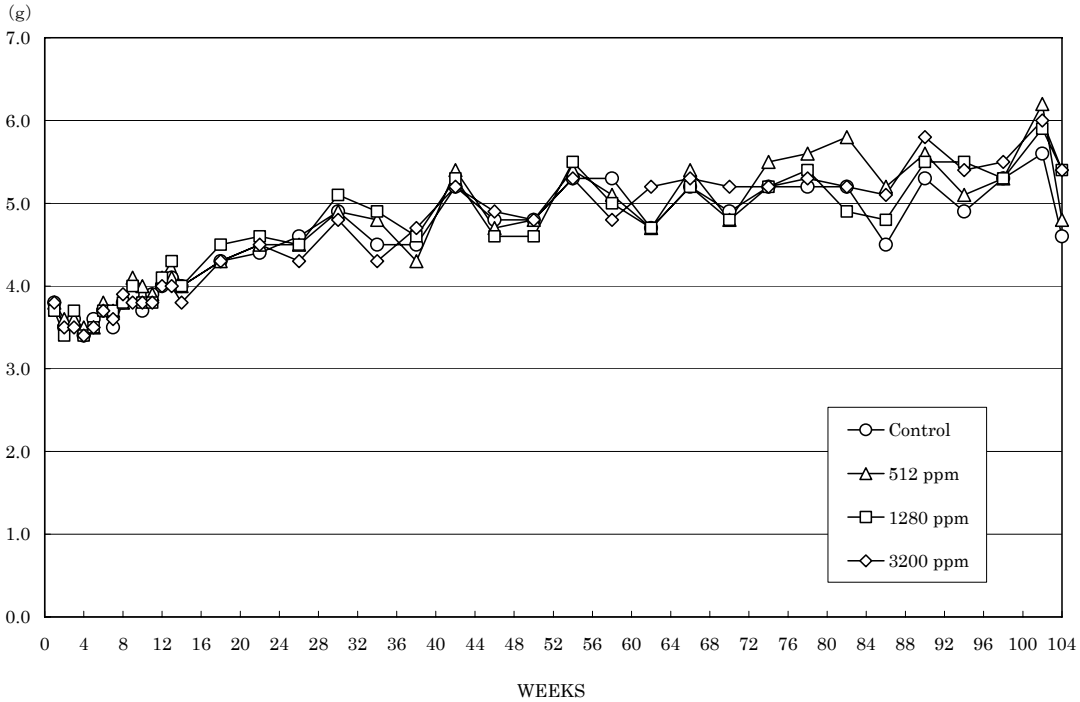

FIGURE 6 FOOD CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-YEAR FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

Photograph 1
Forestomach: Squamous cell papilloma
Mouse, Male, 1280 ppm, Animal No. 0580-1236 (H&E)