Summary of Inhalation Carcinogenicity Study of 1-Bromobutane in B6D2F1 Mice

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Japan Bioassay Research Center

Japan Industrial Safety and Health Association

PREFACE

The tests were contracted and supported by the Ministry of Health, Labour and Welfare of Japan. The tests were conducted by Japan Bioassay Research Center (JBRC) and the report was prepared by JBRC and peer reviewed by outside expert pathologist. Complete report was submitted to Ministry of Health, Labour and Welfare of Japan on March 31, 2008.

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

Summary of Inhalation Carcinogenicity Study of 1-Bromobutane in B6D2F1 Mice

Purpose, materials and methods

1-Bromobutane (CAS No. 109-65-9) is a colorless liquid with a boiling point of 101.3°C. It is soluble in alcohol and ether and insoluble in water.

The carcinogenicity and chronic toxicity of 1-bromobutane (greater than 99.7% pure) were examined by inhalation exposure using groups of B6D2F1/Crlj mice. Each group of test animals consisted of either 50 male or 50 female mice. Test animals were exposed to 1-bromobutane vapor at a target concentration of 0 (clean air), 20, 50 or 125 ppm (v/v) for 6 hours/day, 5 days/week for 2 years (104 weeks). Both sexes were exposed to each concentration of 1-bromobutane vapor. The highest dose level was chosen so as not to exceed the maximum tolerated dose (MTD), based on both growth rate and toxicity in the previous 13-week toxicity study. The identity of the 1-Bromobutane 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. Stainless-steel inhalation exposure chambers (volume: 3900 L) were used throughout the 2-year exposure period. 1-Bromobutane vapor-air mixtures were generated by bubbling clean air through 1-bromobutane liquid and the mixtures supplied to the inhalation exposure chambers. Air concentrations of 1-bromobutane vapor in the inhalation exposure chambers were monitored at 15 min intervals by gas chromatography. The animals were observed daily for clinical signs and mortality. Body weight and food consumption were measured once a week for the first 14 weeks and every 4 weeks thereafter. All animals, including those found dead or in a moribund state as well as those surviving to the end of the 2-year exposure period, underwent complete necropsy. Urinalysis was performed near the end of the exposure period. 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 1-Bromobutane induction of neoplastic lesions were analyzed by Peto's test. Incidences of non-neoplastic lesions and urinalysis were analyzed by the Chi-square test. Changes in body weight, food consumption, hematological and blood biochemical parameters, and organ weights were analyzed by Dunnett's test. The present studies were conducted in accordance with the Organisation for Economic Co-operation and Development (OECD) Good

Laboratory Practice and with reference to the OECD Guideline for Testing of Chemicals 451 “Carcinogenicity Studies”.

Results

No significant difference in survival rate, clinical symptoms, body weight or food consumption was found between any 1-bromobutane-exposed group of either sex and their respective controls.

The incidence of bronchiolar-alveolar carcinomas in the lung was increased in males exposed to 50 ppm and 125 ppm 1-bromobutane. No significant increases in the incidence of neoplastic lesions was found in any of the 1-bromobutane-exposed female groups. There was, however, an increase in the incidence of eosinophilic change in the olfactory epithelium of females exposed to 125 ppm 1-bromobutane.

Conclusions

There was clear evidence of carcinogenic activity of 1-bromobutane in male mice. There was no evidence of carcinogenic activity of 1-bromobutane in females.

SELECTED TABLES

TABLE A

CONCENTRATIONS OF 1 - BROMOBUTANE IN THE INHALATION CHAMBER OF THE 2-YEAR INHALATION STUDY

CONCENTRATIONS OF 1-BROMOBUTANE IN THE INHALATION CHAMBER OF THE 2-YEAR INHALATION STUDY

Group Name	Concentration(ppm) Mean ± S.D.
Control	0.0 ± 0.0
20 ppm	20.1 ± 0.2
50 ppm	50.1 ± 0.4
125 ppm	125.2 ± 0.7

TABLE D1

BODY WEIGHT CHANGES AND SURVIVAL ANIMAL NUMBERS : MALE

STUDY NO. : 0561
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>	20 ppm Av. Wt.	20 ppm % of cont. <50>	20 ppm No. of Surviv.	50 ppm Av. Wt.	50 ppm % of cont. <50>	50 ppm No. of Surviv.	125 ppm Av. Wt.	125 ppm % of cont. <50>	125 ppm No. of Surviv.
0-0	23.6 (50)	50/50	23.6 (50)	100	50/50	23.6 (50)	100	50/50	23.6 (50)	100	50/50
1-7	25.0 (50)	50/50	25.2 (50)	101	50/50	25.1 (50)	100	50/50	25.0 (50)	100	50/50
2-7	26.0 (50)	50/50	25.9 (50)	100	50/50	25.9 (50)	100	50/50	25.7 (50)	99	50/50
3-7	26.8 (50)	50/50	26.7 (50)	100	50/50	26.7 (50)	100	50/50	26.1 (50)	97	50/50
4-7	27.4 (50)	50/50	27.1 (50)	99	50/50	27.4 (50)	100	50/50	26.5 (50)	97	50/50
5-7	27.9 (50)	50/50	27.6 (50)	99	50/50	28.0 (50)	100	50/50	26.9 (50)	96	50/50
6-7	28.6 (50)	50/50	28.0 (50)	98	50/50	28.6 (50)	100	50/50	27.5 (50)	96	50/50
7-7	29.1 (50)	50/50	28.5 (50)	98	50/50	29.0 (50)	100	50/50	27.9 (50)	96	50/50
8-7	29.8 (50)	50/50	29.0 (50)	97	50/50	29.6 (50)	99	50/50	28.5 (50)	96	50/50
9-7	30.5 (50)	50/50	29.6 (50)	97	50/50	30.2 (50)	99	50/50	29.2 (50)	96	50/50
10-7	31.2 (50)	50/50	30.5 (50)	98	50/50	31.0 (50)	99	50/50	29.7 (50)	95	50/50
11-7	31.7 (50)	50/50	30.7 (50)	97	50/50	31.4 (50)	99	50/50	29.8 (50)	94	50/50
12-7	32.8 (50)	50/50	31.9 (50)	97	50/50	32.2 (50)	98	50/50	31.0 (50)	95	50/50
13-7	33.5 (50)	50/50	32.5 (50)	97	50/50	33.1 (50)	99	50/50	31.9 (50)	95	50/50
14-7	34.2 (50)	50/50	33.1 (50)	97	50/50	33.8 (50)	99	50/50	32.7 (50)	96	50/50
18-7	36.0 (50)	50/50	35.5 (50)	99	50/50	35.9 (50)	100	50/50	35.4 (50)	98	50/50
22-7	38.3 (50)	50/50	37.6 (50)	98	50/50	37.7 (50)	98	50/50	37.2 (50)	97	50/50
26-7	40.5 (50)	50/50	39.9 (50)	99	50/50	40.0 (50)	99	50/50	39.6 (50)	98	50/50
30-7	42.1 (50)	50/50	41.6 (50)	99	50/50	41.4 (50)	98	50/50	40.8 (50)	97	50/50
34-7	43.8 (50)	50/50	42.8 (50)	98	50/50	42.7 (50)	97	50/50	42.2 (50)	96	50/50
38-7	45.5 (50)	50/50	44.7 (50)	98	50/50	43.7 (50)	96	50/50	43.5 (50)	96	50/50
42-7	46.7 (50)	50/50	45.7 (50)	98	50/50	44.9 (50)	96	50/50	44.5 (50)	95	50/50
46-7	47.6 (50)	50/50	47.0 (50)	99	50/50	46.2 (50)	97	50/50	45.8 (50)	96	50/50
50-7	48.2 (50)	50/50	47.8 (50)	99	50/50	47.1 (50)	98	50/50	46.5 (50)	96	50/50
54-7	49.1 (50)	50/50	48.2 (50)	98	50/50	47.7 (50)	97	50/50	47.0 (50)	96	50/50
58-7	49.7 (50)	50/50	48.2 (50)	97	50/50	48.4 (50)	97	50/50	47.4 (50)	95	50/50
62-7	50.1 (49)	49/50	48.9 (50)	98	50/50	48.8 (50)	97	50/50	48.2 (49)	96	49/50
66-7	51.0 (49)	49/50	49.4 (50)	97	50/50	49.5 (50)	97	50/50	48.6 (47)	95	47/50
70-7	51.5 (49)	49/50	49.2 (50)	96	50/50	49.8 (50)	97	50/50	48.9 (47)	95	47/50
74-7	52.2 (49)	49/50	50.2 (48)	96	48/50	50.2 (50)	96	50/50	49.5 (47)	95	47/50
78-7	53.2 (49)	49/50	51.0 (48)	96	48/50	50.9 (50)	96	50/50	50.6 (47)	95	47/50
82-7	52.9 (48)	48/50	50.9 (46)	96	46/50	51.0 (47)	96	47/50	50.8 (46)	96	46/50
86-7	52.6 (48)	48/50	50.2 (46)	95	46/50	50.6 (45)	96	45/50	50.7 (45)	96	45/50
90-7	52.9 (48)	48/50	50.6 (43)	96	43/50	51.4 (43)	97	43/50	51.8 (44)	98	44/50
94-7	52.3 (45)	45/50	52.1 (37)	100	37/50	51.6 (39)	99	39/50	51.1 (43)	98	43/50
98-7	51.4 (42)	42/50	52.3 (34)	102	34/50	50.9 (37)	99	37/50	50.3 (40)	98	40/50
102-7	50.0 (40)	40/50	51.6 (33)	103	33/50	49.9 (35)	100	35/50	48.6 (39)	97	39/50
104-7	49.8 (39)	39/50	51.9 (32)	104	32/50	49.7 (32)	100	32/50	48.5 (39)	97	39/50

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

TABLE D2

BODY WEIGHT CHANGES AND SURVIVAL ANIMAL NUMBERS : FEMALE

STUDY NO. : 0561
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>	20 ppm Av. Wt.	20 ppm % of cont. <50>	20 ppm No. of Surviv.	50 ppm Av. Wt.	50 ppm % of cont. <50>	50 ppm No. of Surviv.	125 ppm Av. Wt.	125 ppm % of cont. <50>	125 ppm No. of Surviv.
0-0	19.3 (50)	50/50	19.3 (50)	100	50/50	19.3 (50)	100	50/50	19.3 (50)	100	50/50
1-7	20.0 (50)	50/50	20.1 (50)	101	50/50	20.1 (50)	101	50/50	19.8 (50)	99	50/50
2-7	20.8 (50)	50/50	20.8 (50)	100	50/50	20.8 (50)	100	50/50	20.7 (50)	100	50/50
3-7	21.6 (50)	50/50	21.3 (50)	99	50/50	21.5 (50)	100	50/50	21.1 (50)	98	50/50
4-7	21.9 (50)	50/50	21.9 (50)	100	50/50	21.8 (50)	100	50/50	21.5 (50)	98	50/50
5-7	22.5 (50)	50/50	22.2 (50)	99	50/50	22.2 (50)	99	50/50	22.0 (50)	98	50/50
6-7	23.0 (50)	50/50	22.5 (50)	98	50/50	22.6 (50)	98	50/50	22.3 (50)	97	50/50
7-7	23.5 (50)	50/50	23.0 (50)	98	50/50	23.1 (50)	98	50/50	22.7 (50)	97	50/50
8-7	23.7 (50)	50/50	23.6 (50)	100	50/50	23.4 (50)	99	50/50	23.1 (50)	97	50/50
9-7	24.1 (50)	50/50	24.1 (50)	100	50/50	23.7 (50)	98	50/50	23.3 (50)	97	50/50
10-7	24.5 (50)	50/50	24.4 (50)	100	50/50	24.0 (50)	98	50/50	23.6 (50)	96	50/50
11-7	24.4 (50)	50/50	24.3 (50)	100	50/50	24.3 (50)	100	50/50	23.7 (50)	97	50/50
12-7	24.7 (50)	50/50	24.7 (50)	100	50/50	24.2 (50)	98	50/50	24.0 (50)	97	50/50
13-7	24.9 (50)	50/50	24.9 (50)	100	50/50	24.7 (50)	99	50/50	24.4 (50)	98	50/50
14-7	25.4 (50)	50/50	25.3 (50)	100	50/50	25.3 (50)	100	50/50	24.8 (50)	98	50/50
18-7	26.1 (50)	50/50	26.5 (50)	102	50/50	25.8 (50)	99	50/50	25.8 (50)	99	50/50
22-7	27.2 (50)	50/50	27.5 (50)	101	50/50	26.8 (50)	99	50/50	26.0 (50)	96	50/50
26-7	28.3 (50)	50/50	28.2 (50)	100	50/50	28.4 (50)	100	50/50	27.5 (50)	97	50/50
30-7	29.2 (50)	50/50	29.4 (50)	101	50/50	28.8 (50)	99	50/50	28.3 (49)	97	49/50
34-7	30.3 (50)	50/50	30.4 (50)	100	50/50	29.7 (50)	98	50/50	29.0 (49)	96	49/50
38-7	31.3 (50)	50/50	31.4 (50)	100	50/50	30.5 (50)	97	50/50	29.9 (49)	96	49/50
42-7	31.7 (50)	50/50	31.9 (50)	101	50/50	31.2 (50)	98	50/50	30.4 (49)	96	49/50
46-7	32.6 (50)	50/50	32.4 (50)	99	50/50	31.6 (50)	97	50/50	31.1 (49)	95	49/50
50-7	32.7 (50)	50/50	32.5 (50)	99	50/50	32.7 (50)	100	50/50	31.6 (49)	97	49/50
54-7	33.5 (50)	50/50	32.9 (50)	98	50/50	32.6 (50)	97	50/50	32.3 (49)	96	49/50
58-7	33.7 (50)	50/50	33.4 (50)	99	50/50	33.7 (49)	100	49/50	32.6 (48)	97	48/50
62-7	33.6 (50)	50/50	34.1 (50)	101	50/50	33.7 (48)	100	48/50	32.5 (44)	97	44/50
66-7	34.2 (49)	49/50	34.3 (50)	100	50/50	34.3 (48)	100	48/50	32.8 (44)	96	44/50
70-7	34.7 (49)	49/50	35.0 (47)	101	47/50	34.4 (47)	99	47/50	33.5 (44)	97	44/50
74-7	35.0 (48)	48/50	35.0 (46)	100	46/50	34.6 (44)	99	44/50	33.9 (44)	97	44/50
78-7	35.8 (45)	45/50	36.2 (46)	101	46/50	35.3 (43)	99	43/50	34.7 (43)	97	43/50
82-7	35.8 (43)	43/50	36.1 (46)	101	46/50	35.3 (40)	99	40/50	34.8 (41)	97	41/50
86-7	36.2 (38)	38/50	36.6 (44)	101	44/50	35.6 (38)	98	38/50	34.7 (41)	96	41/50
90-7	36.4 (36)	36/50	37.4 (41)	103	41/50	36.4 (35)	100	35/50	36.1 (37)	99	37/50
94-7	35.1 (29)	29/50	37.2 (37)	106	37/50	36.6 (30)	104	30/50	35.1 (34)	100	34/50
98-7	35.2 (26)	26/50	36.6 (34)	104	34/50	36.4 (28)	103	28/50	35.6 (31)	101	31/50
102-7	34.4 (20)	20/50	36.5 (32)	106	32/50	36.7 (25)	107	25/50	34.5 (26)	100	26/50
104-7	34.2 (18)	18/50	37.6 (31)	110	31/50	36.6 (24)	107	24/50	35.6 (26)	104	26/50

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

TABLE D3

BODY WEIGHT CHANGES : MALE

STUDY NO. : 0561
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7
Control	23.6± 0.9	25.0± 1.0	26.0± 1.2	26.8± 1.3	27.4± 1.4	27.9± 1.5	28.6± 1.6
20 ppm	23.6± 0.9	25.2± 1.1	25.9± 1.2	26.7± 1.4	27.1± 1.3	27.6± 1.5	28.0± 1.5
50 ppm	23.6± 0.9	25.1± 1.0	25.9± 1.1	26.7± 1.3	27.4± 1.4	28.0± 1.5	28.6± 1.6
125 ppm	23.6± 0.9	25.0± 1.0	25.7± 1.2	26.1± 1.4*	26.5± 1.6**	26.9± 1.7**	27.5± 1.9**

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

(HAN260)

BAIS 4

STUDY NO. : 0561
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	29.1± 1.7	29.8± 2.0	30.5± 2.2	31.2± 2.3	31.7± 2.5	32.8± 2.6	33.5± 2.6
20 ppm	28.5± 1.5	29.0± 1.7	29.6± 1.9	30.5± 1.9	30.7± 2.2	31.9± 2.4	32.5± 2.4
50 ppm	29.0± 1.9	29.6± 2.0	30.2± 2.0	31.0± 2.1	31.4± 2.3	32.2± 2.4	33.1± 2.5
125 ppm	27.9± 2.1**	28.5± 2.2**	29.2± 2.3**	29.7± 2.5**	29.8± 2.5**	31.0± 2.6**	31.9± 2.6**

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

STUDY NO. : 0561
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	34.2± 2.8	36.0± 3.1	38.3± 3.4	40.5± 3.9	42.1± 4.3	43.8± 4.4	45.5± 4.6
20 ppm	33.1± 2.4	35.5± 2.7	37.6± 2.9	39.9± 3.3	41.6± 3.5	42.8± 4.1	44.7± 4.1
50 ppm	33.8± 2.5	35.9± 2.8	37.7± 3.3	40.0± 3.9	41.4± 4.2	42.7± 4.2	43.7± 4.6
125 ppm	32.7± 2.7**	35.4± 3.0	37.2± 3.5	39.6± 3.8	40.8± 4.2	42.2± 4.2	43.5± 4.5

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

(HAN260)

BAIS 4

STUDY NO. : 0561
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 42-7	46-7	50-7	54-7	58-7	62-7	66-7
Control	46.7± 4.7	47.6± 4.6	48.2± 5.2	49.1± 5.3	49.7± 5.2	50.1± 5.1	51.0± 5.6
20 ppm	45.7± 4.0	47.0± 3.8	47.8± 3.9	48.2± 4.1	48.2± 4.2	48.9± 4.0	49.4± 4.4
50 ppm	44.9± 4.4	46.2± 4.5	47.1± 4.5	47.7± 4.6	48.4± 4.8	48.8± 5.1	49.5± 5.3
125 ppm	44.5± 4.7	45.8± 4.8	46.5± 4.8	47.0± 5.0	47.4± 5.2	48.2± 5.4	48.6± 5.5

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

(HAN260)

STUDY NO. : 0561
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	51.5± 6.1	52.2± 6.5	53.2± 6.9	52.9± 6.3	52.6± 6.8	52.9± 7.5	52.3± 8.2
20 ppm	49.2± 5.5	50.2± 5.9	51.0± 6.7	50.9± 6.8	50.2± 7.6	50.6± 8.9	52.1± 8.1
50 ppm	49.8± 5.8	50.2± 6.2	50.9± 7.7	51.0± 7.0	50.6± 6.9	51.4± 7.4	51.6± 7.2
125 ppm	48.9± 6.2	49.5± 6.5	50.6± 7.3	50.8± 6.2	50.7± 7.0	51.8± 6.6	51.1± 7.3

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

(HAN260)

BAIS 4

STUDY NO. : 0561
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	51.4± 8.3	50.0± 8.5	49.8± 8.6
20 ppm	52.3± 7.4	51.6± 7.8	51.9± 7.6
50 ppm	50.9± 7.6	49.9± 7.3	49.7± 7.4
125 ppm	50.3± 7.4	48.6± 8.5	48.5± 8.5

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

TABLE D4

BODY WEIGHT CHANGES : FEMALE

STUDY NO. : 0561
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	19.3± 0.8	20.0± 0.8	20.8± 0.7	21.6± 0.8	21.9± 0.7	22.5± 0.8	23.0± 0.8
20 ppm	19.3± 0.8	20.1± 0.8	20.8± 0.9	21.3± 0.8	21.9± 0.8	22.2± 1.0	22.5± 1.0*
50 ppm	19.3± 0.8	20.1± 1.0	20.8± 1.0	21.5± 1.1	21.8± 1.0	22.2± 1.0	22.6± 1.1
125 ppm	19.3± 0.8	19.8± 0.9	20.7± 0.9	21.1± 0.9**	21.5± 0.9	22.0± 0.9	22.3± 1.0**

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

(HAN260)

STUDY NO. : 0561
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 7-7	8-7	9-7	10-7	11-7	12-7	13-7
Control	23.5± 0.9	23.7± 0.8	24.1± 0.9	24.5± 1.0	24.4± 0.9	24.7± 1.2	24.9± 1.2
20 ppm	23.0± 1.1	23.6± 1.1	24.1± 1.4	24.4± 1.4	24.3± 1.3	24.7± 1.5	24.9± 1.7
50 ppm	23.1± 1.2	23.4± 1.2	23.7± 1.3	24.0± 1.3	24.3± 1.3	24.2± 1.8	24.7± 1.5
125 ppm	22.7± 1.2**	23.1± 1.2**	23.3± 1.3**	23.6± 1.5**	23.7± 1.5**	24.0± 1.4**	24.4± 1.5

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

(HAN260)

BAIS 4

STUDY NO. : 0561
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 14-7	18-7	22-7	26-7	30-7	34-7	38-7
Control	25.4± 1.3	26.1± 1.6	27.2± 1.8	28.3± 2.1	29.2± 2.2	30.3± 2.6	31.3± 3.0
20 ppm	25.3± 1.8	26.5± 2.0	27.5± 2.5	28.2± 3.0	29.4± 3.3	30.4± 3.8	31.4± 3.8
50 ppm	25.3± 1.4	25.8± 1.5	26.8± 1.6	28.4± 2.6	28.8± 2.7	29.7± 2.8	30.5± 3.3
125 ppm	24.8± 1.7	25.8± 1.8	26.0± 2.1**	27.5± 2.6	28.3± 2.3	29.0± 3.0	29.9± 3.3

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

(HAN260)

BAIS 4

STUDY NO. : 0561
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 42-7	46-7	50-7	54-7	58-7	62-7	66-7
Control	31.7± 3.0	32.6± 3.7	32.7± 3.4	33.5± 3.6	33.7± 3.3	33.6± 3.6	34.2± 3.5
20 ppm	31.9± 4.2	32.4± 4.5	32.5± 4.9	32.9± 4.3	33.4± 4.6	34.1± 5.0	34.3± 5.5
50 ppm	31.2± 3.3	31.6± 3.4	32.7± 3.5	32.6± 3.5	33.7± 3.7	33.7± 4.2	34.3± 3.8
125 ppm	30.4± 3.4	31.1± 4.1	31.6± 3.8	32.3± 4.1	32.6± 3.7	32.5± 3.5	32.8± 3.3

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

(HAN260)

BAIS 4

STUDY NO. : 0561
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	34.7± 4.0	35.0± 3.4	35.8± 3.8	35.8± 3.7	36.2± 3.6	36.4± 4.3	35.1± 5.9
20 ppm	35.0± 4.6	35.0± 4.8	36.2± 4.9	36.1± 4.9	36.6± 4.5	37.4± 4.8	37.2± 4.4
50 ppm	34.4± 3.5	34.6± 3.6	35.3± 3.9	35.3± 4.1	35.6± 3.3	36.4± 3.2	36.6± 3.7
125 ppm	33.5± 3.4	33.9± 3.8	34.7± 4.0	34.8± 3.9	34.7± 4.0	36.1± 6.9	35.1± 3.8

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

(HAN260)

BAIS 4

STUDY NO. : 0561
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	35.2± 5.0	34.4± 5.0	34.2± 5.5
20 ppm	36.6± 5.2	36.5± 5.2	37.6± 4.4
50 ppm	36.4± 3.9	36.7± 3.9	36.6± 3.6
125 ppm	35.6± 4.1	34.5± 4.2	35.6± 5.3

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

(HAN260)

BAIS 4

TABLE E1

FOOD CONSUMPTION CHANGES AND SURVIVAL ANIMAL NUMBERS : MALE

STUDY NO. : 0561
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

MEAN FOOD CONSUMPTION(FC) AND SURVIVAL

Week-Day on Study	Control Av. FC.	Control No. of Surviv. <50>	20 ppm Av. FC.	20 ppm % of cont. <50>	20 ppm No. of Surviv.	50 ppm Av. FC.	50 ppm % of cont. <50>	50 ppm No. of Surviv.	125 ppm Av. FC.	125 ppm % of cont. <50>	125 ppm No. of Surviv.
1-7	3.9 (50)	50/50	4.0 (50)	103	50/50	3.9 (50)	100	50/50	3.8 (50)	97	50/50
2-7	3.9 (50)	50/50	3.8 (50)	97	50/50	3.8 (50)	97	50/50	3.9 (50)	100	50/50
3-7	4.1 (50)	50/50	4.1 (50)	100	50/50	4.0 (50)	98	50/50	4.0 (50)	98	50/50
4-7	4.1 (50)	50/50	4.0 (50)	98	50/50	4.0 (50)	98	50/50	4.0 (50)	98	50/50
5-7	4.1 (50)	50/50	4.1 (50)	100	50/50	4.0 (50)	98	50/50	4.0 (50)	98	50/50
6-7	4.2 (50)	50/50	4.1 (50)	98	50/50	4.0 (50)	95	50/50	4.1 (50)	98	50/50
7-7	4.1 (50)	50/50	4.1 (50)	100	50/50	4.0 (50)	98	50/50	4.1 (50)	100	50/50
8-7	4.2 (50)	50/50	4.1 (50)	98	50/50	4.1 (50)	98	50/50	4.1 (50)	98	50/50
9-7	4.3 (50)	50/50	4.2 (50)	98	50/50	4.1 (50)	95	50/50	4.2 (50)	98	50/50
10-7	4.3 (50)	50/50	4.3 (50)	100	50/50	4.1 (50)	95	50/50	4.2 (50)	98	50/50
11-7	4.2 (50)	50/50	4.2 (50)	100	50/50	4.1 (50)	98	50/50	4.0 (50)	95	50/50
12-7	4.4 (50)	50/50	4.4 (50)	100	50/50	4.2 (50)	95	50/50	4.3 (50)	98	50/50
13-7	4.3 (50)	50/50	4.2 (50)	98	50/50	4.1 (50)	95	50/50	4.2 (50)	98	50/50
14-7	4.3 (50)	50/50	4.3 (50)	100	50/50	4.3 (50)	100	50/50	4.3 (50)	100	50/50
18-7	4.6 (50)	50/50	4.6 (50)	100	50/50	4.5 (50)	98	50/50	4.6 (50)	100	50/50
22-7	4.8 (50)	50/50	4.7 (50)	98	50/50	4.7 (50)	98	50/50	4.6 (50)	96	50/50
26-7	4.6 (50)	50/50	4.6 (50)	100	50/50	4.6 (50)	100	50/50	4.5 (50)	98	50/50
30-7	4.7 (50)	50/50	4.6 (50)	98	50/50	4.6 (50)	98	50/50	4.6 (50)	98	50/50
34-7	4.9 (50)	50/50	4.9 (50)	100	50/50	4.8 (50)	98	50/50	4.7 (50)	96	50/50
38-7	5.0 (50)	50/50	5.0 (50)	100	50/50	4.8 (50)	96	50/50	4.8 (50)	96	50/50
42-7	5.0 (50)	50/50	5.0 (50)	100	50/50	5.0 (50)	100	50/50	4.8 (50)	96	50/50
46-7	5.0 (50)	50/50	5.0 (50)	100	50/50	4.9 (50)	98	50/50	4.8 (50)	96	50/50
50-7	5.0 (50)	50/50	5.0 (50)	100	50/50	4.9 (50)	98	50/50	4.9 (50)	98	50/50
54-7	5.0 (50)	50/50	5.0 (50)	100	50/50	4.9 (50)	98	50/50	4.7 (50)	94	50/50
58-7	5.0 (50)	50/50	4.9 (50)	98	50/50	4.9 (50)	98	50/50	4.7 (50)	94	50/50
62-7	5.2 (49)	49/50	5.1 (50)	98	50/50	4.9 (50)	94	50/50	4.9 (49)	94	49/50
66-7	5.1 (49)	49/50	5.0 (50)	98	50/50	5.1 (50)	100	50/50	4.9 (47)	96	47/50
70-7	5.1 (49)	49/50	5.0 (50)	98	50/50	5.0 (50)	98	50/50	4.8 (47)	94	47/50
74-7	5.2 (49)	49/50	5.2 (48)	100	48/50	5.0 (50)	96	50/50	4.9 (47)	94	47/50
78-7	5.2 (49)	49/50	5.1 (48)	98	48/50	5.0 (50)	96	50/50	4.9 (47)	94	47/50
82-7	5.2 (48)	48/50	5.2 (46)	100	46/50	5.0 (47)	96	47/50	4.9 (46)	94	46/50
86-7	5.2 (48)	48/50	5.0 (46)	96	46/50	4.8 (45)	92	45/50	4.9 (45)	94	45/50
90-7	5.5 (48)	48/50	5.3 (43)	96	43/50	5.2 (43)	95	43/50	5.1 (44)	93	44/50
94-7	5.4 (45)	45/50	5.2 (37)	96	37/50	5.2 (39)	96	39/50	5.0 (43)	93	43/50
98-7	5.3 (42)	42/50	5.3 (32)	100	34/50	4.9 (37)	92	37/50	4.9 (40)	92	40/50
102-7	4.8 (40)	40/50	5.2 (33)	108	33/50	4.7 (35)	98	35/50	4.8 (39)	100	39/50
104-7	4.8 (39)	39/50	5.2 (32)	108	32/50	4.9 (32)	102	32/50	4.8 (39)	100	39/50

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

TABLE E2

FOOD CONSUMPTION CHANGES AND SURVIVAL ANIMAL NUMBERS : FEMALE

STUDY NO. : 0561
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>	20 ppm Av. FC.	20 ppm % of cont. <50>	20 ppm No. of Surviv.	50 ppm Av. FC.	50 ppm % of cont. <50>	50 ppm No. of Surviv.	125 ppm Av. FC.	125 ppm % of cont. <50>	125 ppm No. of Surviv.
1-7	3.3 (50)	50/50	3.3 (50)	100	50/50	3.2 (50)	97	50/50	3.2 (50)	97	50/50
2-7	3.4 (50)	50/50	3.3 (50)	97	50/50	3.3 (50)	97	50/50	3.3 (50)	97	50/50
3-7	3.7 (50)	50/50	3.6 (50)	97	50/50	3.5 (50)	95	50/50	3.5 (50)	95	50/50
4-7	3.7 (50)	50/50	3.6 (50)	97	50/50	3.5 (50)	95	50/50	3.6 (50)	97	50/50
5-7	3.8 (50)	50/50	3.7 (50)	97	50/50	3.6 (50)	95	50/50	3.7 (50)	97	50/50
6-7	3.9 (50)	50/50	3.7 (50)	95	50/50	3.7 (50)	95	50/50	3.7 (50)	95	50/50
7-7	4.0 (50)	50/50	3.9 (50)	98	50/50	3.8 (50)	95	50/50	3.8 (50)	95	50/50
8-7	3.9 (50)	50/50	3.9 (50)	100	50/50	3.9 (50)	100	50/50	3.8 (50)	97	50/50
9-7	4.1 (50)	50/50	4.0 (50)	98	50/50	3.9 (50)	95	50/50	3.9 (50)	95	50/50
10-7	4.0 (50)	50/50	4.0 (50)	100	50/50	3.9 (50)	98	50/50	3.9 (50)	98	50/50
11-7	3.8 (50)	50/50	3.8 (50)	100	50/50	3.9 (50)	103	50/50	3.9 (50)	103	50/50
12-7	4.0 (50)	50/50	4.0 (50)	100	50/50	3.9 (50)	98	50/50	3.9 (50)	98	50/50
13-7	3.9 (50)	50/50	3.8 (50)	97	50/50	3.9 (50)	100	50/50	3.9 (50)	100	50/50
14-7	4.0 (50)	50/50	4.0 (50)	100	50/50	4.1 (50)	103	50/50	4.0 (50)	100	50/50
18-7	4.3 (50)	50/50	4.4 (50)	102	50/50	4.3 (50)	100	50/50	4.3 (50)	100	50/50
22-7	4.4 (50)	50/50	4.4 (50)	100	50/50	4.4 (50)	100	50/50	4.3 (50)	98	50/50
26-7	4.4 (50)	50/50	4.3 (50)	98	50/50	4.4 (50)	100	50/50	4.3 (50)	98	50/50
30-7	4.4 (50)	50/50	4.4 (50)	100	50/50	4.4 (50)	100	50/50	4.4 (49)	100	49/50
34-7	4.6 (50)	50/50	4.6 (50)	100	50/50	4.5 (50)	98	50/50	4.4 (49)	96	49/50
38-7	4.8 (50)	50/50	4.6 (50)	96	50/50	4.5 (50)	94	50/50	4.6 (49)	96	49/50
42-7	4.7 (50)	50/50	4.6 (50)	98	50/50	4.6 (50)	98	50/50	4.6 (49)	98	49/50
46-7	4.8 (50)	50/50	4.7 (50)	98	50/50	4.6 (50)	96	50/50	4.5 (49)	94	49/50
50-7	4.6 (50)	50/50	4.6 (50)	100	50/50	4.5 (50)	98	50/50	4.5 (49)	98	49/50
54-7	4.7 (50)	50/50	4.5 (50)	96	50/50	4.5 (50)	96	50/50	4.5 (49)	96	49/50
58-7	4.6 (50)	50/50	4.6 (50)	100	50/50	4.7 (49)	102	49/50	4.6 (48)	100	48/50
62-7	4.7 (50)	50/50	4.8 (50)	102	50/50	4.7 (48)	100	48/50	4.6 (44)	98	44/50
66-7	4.6 (49)	49/50	4.5 (50)	98	50/50	4.6 (48)	100	48/50	4.5 (44)	98	44/50
70-7	4.7 (49)	49/50	4.8 (47)	102	47/50	4.6 (47)	98	47/50	4.7 (44)	100	44/50
74-7	4.7 (48)	48/50	4.7 (46)	100	46/50	4.6 (44)	98	44/50	4.7 (44)	100	44/50
78-7	4.7 (45)	45/50	4.7 (46)	100	46/50	4.7 (43)	100	43/50	4.7 (43)	100	43/50
82-7	4.7 (43)	43/50	4.9 (46)	104	46/50	4.7 (40)	100	40/50	4.6 (41)	98	41/50
86-7	4.7 (38)	38/50	4.6 (44)	98	44/50	4.5 (38)	96	38/50	4.4 (41)	94	41/50
90-7	4.9 (36)	36/50	5.0 (41)	102	41/50	4.9 (35)	100	35/50	4.8 (37)	98	37/50
94-7	4.9 (29)	29/50	5.1 (37)	104	37/50	5.0 (30)	102	30/50	4.8 (34)	98	34/50
98-7	5.0 (26)	26/50	4.9 (34)	98	34/50	4.9 (28)	98	28/50	4.7 (31)	94	31/50
102-7	4.7 (20)	20/50	4.8 (32)	102	32/50	4.8 (25)	102	25/50	4.5 (26)	96	26/50
104-7	4.6 (18)	18/50	4.9 (31)	107	31/50	4.8 (24)	104	24/50	4.5 (26)	98	26/50

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

TABLE E3

FOOD CONSUMPTION CHANGES : MALE

STUDY NO. : 0561
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(6)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	3.9± 0.3	3.9± 0.3	4.1± 0.3	4.1± 0.3	4.1± 0.3	4.2± 0.3	4.1± 0.3
20 ppm	4.0± 0.3	3.8± 0.3	4.1± 0.3	4.0± 0.3	4.1± 0.3	4.1± 0.3	4.1± 0.3
50 ppm	3.9± 0.3	3.8± 0.3	4.0± 0.3*	4.0± 0.3	4.0± 0.3	4.0± 0.3**	4.0± 0.3
125 ppm	3.8± 0.2	3.9± 0.3	4.0± 0.3	4.0± 0.2	4.0± 0.3	4.1± 0.3	4.1± 0.3

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

(HAN260)

BAIS 4

STUDY NO. : 0561
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)	14-7(7)
Control	4.2± 0.3	4.3± 0.3	4.3± 0.3	4.2± 0.3	4.4± 0.3	4.3± 0.2	4.3± 0.3
20 ppm	4.1± 0.3	4.2± 0.3	4.3± 0.3	4.2± 0.4	4.4± 0.3	4.2± 0.3	4.3± 0.3
50 ppm	4.1± 0.4	4.1± 0.3*	4.1± 0.3	4.1± 0.3*	4.2± 0.3*	4.1± 0.3*	4.3± 0.2
125 ppm	4.1± 0.3	4.2± 0.3	4.2± 0.4	4.0± 0.3*	4.3± 0.3	4.2± 0.3	4.3± 0.3

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

(HAN260)

BAIS 4

STUDY NO. : 0561
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 18-7(7)	22-7(7)	26-7(7)	30-7(7)	34-7(7)	38-7(7)	42-7(7)
Control	4.6± 0.3	4.8± 0.3	4.6± 0.3	4.7± 0.3	4.9± 0.2	5.0± 0.3	5.0± 0.3
20 ppm	4.6± 0.3	4.7± 0.3	4.6± 0.3	4.6± 0.3	4.9± 0.4	5.0± 0.3	5.0± 0.3
50 ppm	4.5± 0.2	4.7± 0.3	4.6± 0.3	4.6± 0.3	4.8± 0.3	4.8± 0.3	5.0± 0.3
125 ppm	4.6± 0.3	4.6± 0.3*	4.5± 0.2	4.6± 0.3	4.7± 0.3*	4.8± 0.4	4.8± 0.3*

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

(HAN260)

STUDY NO. : 0561
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 46-7(7)	50-7(7)	54-7(7)	58-7(7)	62-7(7)	66-7(7)	70-7(7)
Control	5.0± 0.3	5.0± 0.4	5.0± 0.3	5.0± 0.3	5.2± 0.3	5.1± 0.3	5.1± 0.3
20 ppm	5.0± 0.3	5.0± 0.3	5.0± 0.4	4.9± 0.3*	5.1± 0.3	5.0± 0.4	5.0± 0.5
50 ppm	4.9± 0.3	4.9± 0.3	4.9± 0.3	4.9± 0.3*	4.9± 0.4**	5.1± 0.3	5.0± 0.4
125 ppm	4.8± 0.3**	4.9± 0.3	4.7± 0.4**	4.7± 0.4**	4.9± 0.4**	4.9± 0.4**	4.8± 0.8**

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

(HAN260)

STUDY NO. : 0561
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 74-7(7)	78-7(7)	82-7(7)	86-7(7)	90-7(7)	94-7(7)	98-7(7)
Control	5.2± 0.3	5.2± 0.7	5.2± 0.4	5.2± 0.4	5.5± 0.5	5.4± 0.8	5.3± 0.7
20 ppm	5.2± 0.4	5.1± 0.4	5.2± 0.4	5.0± 0.6	5.3± 0.9	5.2± 0.8	5.3± 0.5
50 ppm	5.0± 0.4	5.0± 0.6	5.0± 0.6*	4.8± 0.6**	5.2± 0.7	5.2± 0.6	4.9± 0.7*
125 ppm	4.9± 0.4**	4.9± 0.6*	4.9± 0.6**	4.9± 0.6*	5.1± 0.5**	5.0± 0.7	4.9± 0.5*

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

(HAN260)

BAIS 4

STUDY NO. : 0561
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 102-7(7)	104-7(7)
Control	4.8± 0.6	4.8± 0.6
20 ppm	5.2± 0.7	5.2± 0.5*
50 ppm	4.7± 0.7	4.9± 0.5
125 ppm	4.8± 0.7	4.8± 0.7

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

(HAN260)

BAIS 4

TABLE E4

FOOD CONSUMPTION CHANGES : FEMALE

STUDY NO. : 0561
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(6)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	3.3± 0.2	3.4± 0.2	3.7± 0.2	3.7± 0.2	3.8± 0.2	3.9± 0.2	4.0± 0.3
20 ppm	3.3± 0.2	3.3± 0.2	3.6± 0.2*	3.6± 0.2	3.7± 0.2**	3.7± 0.2**	3.9± 0.3
50 ppm	3.2± 0.2	3.3± 0.2	3.5± 0.2**	3.5± 0.2**	3.6± 0.2**	3.7± 0.2**	3.8± 0.3**
125 ppm	3.2± 0.3**	3.3± 0.2	3.5± 0.2**	3.6± 0.2*	3.7± 0.2**	3.7± 0.2**	3.8± 0.3

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

(HAN260)

BAIS 4

STUDY NO. : 0561
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)	14-7(7)
Control	3.9± 0.2	4.1± 0.3	4.0± 0.2	3.8± 0.2	4.0± 0.2	3.9± 0.3	4.0± 0.3
20 ppm	3.9± 0.3	4.0± 0.3	4.0± 0.3	3.8± 0.3	4.0± 0.3	3.8± 0.3	4.0± 0.3
50 ppm	3.9± 0.3	3.9± 0.2*	3.9± 0.3	3.9± 0.3	3.9± 0.4	3.9± 0.3	4.1± 0.3
125 ppm	3.8± 0.2	3.9± 0.2	3.9± 0.3	3.9± 0.3	3.9± 0.2	3.9± 0.3	4.0± 0.3

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

(HAN260)

BAIS 4

STUDY NO. : 0561
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 18-7(7)	22-7(7)	26-7(7)	30-7(7)	34-7(7)	38-7(7)	42-7(7)
Control	4.3± 0.3	4.4± 0.4	4.4± 0.4	4.4± 0.4	4.6± 0.4	4.8± 0.5	4.7± 0.3
20 ppm	4.4± 0.3	4.4± 0.4	4.3± 0.5	4.4± 0.5	4.6± 0.5	4.6± 0.4	4.6± 0.5
50 ppm	4.3± 0.3	4.4± 0.3	4.4± 0.4	4.4± 0.5	4.5± 0.4	4.5± 0.5	4.6± 0.5
125 ppm	4.3± 0.3	4.3± 0.4	4.3± 0.4	4.4± 0.3	4.4± 0.4*	4.6± 0.5	4.6± 0.5

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

(HAN260)

BAIS 4

STUDY NO. : 0561
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 46-7(7)	50-7(7)	54-7(7)	58-7(7)	62-7(7)	66-7(7)	70-7(7)
Control	4.8± 0.5	4.6± 0.4	4.7± 0.5	4.6± 0.5	4.7± 0.4	4.6± 0.4	4.7± 0.6
20 ppm	4.7± 0.4	4.6± 0.6	4.5± 0.5	4.6± 0.5	4.8± 0.5	4.5± 0.8	4.8± 0.5
50 ppm	4.6± 0.4	4.5± 0.5	4.5± 0.5	4.7± 0.5	4.7± 0.5	4.6± 0.5	4.6± 0.6
125 ppm	4.5± 0.6*	4.5± 0.5	4.5± 0.6	4.6± 0.4	4.6± 0.5	4.5± 0.6	4.7± 0.9

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

STUDY NO. : 0561
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 74-7(7)	78-7(7)	82-7(7)	86-7(7)	90-7(7)	94-7(7)	98-7(7)
Control	4.7± 0.5	4.7± 0.7	4.7± 0.6	4.7± 0.7	4.9± 0.7	4.9± 1.2	5.0± 1.0
20 ppm	4.7± 0.5	4.7± 0.5	4.9± 0.6	4.6± 0.6	5.0± 0.9	5.1± 0.7	4.9± 0.7
50 ppm	4.6± 0.6	4.7± 0.5	4.7± 0.5	4.5± 0.6	4.9± 0.6	5.0± 0.8	4.9± 0.9
125 ppm	4.7± 0.5	4.7± 0.7	4.6± 0.5	4.4± 0.6	4.8± 0.7	4.8± 0.6	4.7± 0.6

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

STUDY NO. : 0561
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 102-7(7)	104-7(7)
Control	4.7± 0.7	4.6± 0.8
20 ppm	4.8± 0.6	4.9± 0.7
50 ppm	4.8± 0.7	4.8± 1.1
125 ppm	4.5± 0.5	4.5± 0.6

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

(HAN260)

TABLE F1

HEMATOLOGY : MALE

STUDY NO. : 0561
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	39	9.25± 1.94	13.4± 2.6	40.3± 7.4	43.7± 2.0	14.5± 0.8	33.2± 1.4	1538± 431
20 ppm	32	9.41± 1.16	13.5± 1.7	40.9± 4.5	43.7± 2.2	14.4± 0.6	33.0± 1.1	1649± 333
50 ppm	31	9.49± 0.65	13.6± 0.9	41.0± 2.4	43.2± 1.7	14.3± 0.5	33.1± 0.9	1646± 295
125 ppm	38	9.82± 1.28	14.0± 1.8	42.4± 5.3	43.2± 2.7	14.2± 1.0	32.9± 1.0	1545± 511

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

(HCL070)

BAIS 4

STUDY NO. : 0561
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	39	3.5± 4.1
20 ppm	32	2.9± 1.8
50 ppm	31	2.7± 1.2
125 ppm	38	2.8± 1.4

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

(HCL070)

BAIS 4

STUDY NO. : 0561
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	39	4.83±	3.47	2±	1	29±	13	2±	1	0±	0	5±	2	62±	13	2±	7
20 ppm	32	4.70±	2.72	2±	1	27±	12	2±	1	0±	0	5±	2	64±	12	1±	3
50 ppm	31	4.17±	2.02	1±	1	26±	11	2±	1	0±	0	5±	2	65±	12	1±	3
125 ppm	38	4.99±	2.38	2±	2	28±	12	2±	2	0±	0	4±	2	62±	13	1±	2

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

(HCL070)

TABLE F2

HEMATOLOGY : FEMALE

STUDY NO. : 0561
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 f ℓ	MCH p g	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	18	9.62± 0.80	14.1± 0.9	42.3± 2.4	44.0± 1.8	14.7± 0.5	33.5± 0.8	1002± 234
20 ppm	25	9.11± 1.66	13.5± 1.9	40.8± 4.4	45.9± 7.6	15.1± 1.5	33.0± 1.6	1010± 323
50 ppm	22	9.49± 1.86	13.8± 2.5	41.9± 6.6	45.1± 6.1	14.7± 0.9	32.8± 2.4	1025± 305
125 ppm	26	8.92± 2.08	13.2± 3.0	40.0± 8.1	46.0± 5.5	14.9± 0.6	32.7± 2.3	848± 332

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

(HCL070)

BAIS 4

STUDY NO. : 0561
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	18	2.6± 1.1
20 ppm	25	4.6± 6.8
50 ppm	22	3.6± 6.0
125 ppm	26	5.3± 8.2

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

(HCL070)

BAIS 4

STUDY NO. : 0561
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	18	3.15± 2.01	2± 2	25± 18	2± 1	0± 0	4± 2	66± 20	1± 2
20 ppm	25	3.70± 1.87	2± 2	27± 11	2± 2	0± 0	4± 2	63± 15	2± 4
50 ppm	22	6.19± 12.35	2± 2	24± 13	2± 1	0± 0	4± 2	62± 19	6± 17
125 ppm	26	10.67± 17.82	2± 3	26± 18	1± 2	0± 0	4± 3	55± 21	11± 20**

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

(HCL070)

BA1S 4

TABLE G1

BIOCHEMISTRY : MALE

STUDY NO. : 0561
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	39	5.1± 0.7	2.5± 0.4	1.0± 0.2	0.13± 0.03	161± 52	126± 111	46± 28
20 ppm	32	5.3± 0.6	2.7± 0.4	1.1± 0.1	0.13± 0.02	181± 32	120± 46	49± 25
50 ppm	32	5.3± 0.6	2.7± 0.4	1.0± 0.2	0.14± 0.03	182± 32	119± 38	50± 23
125 ppm	38	5.7± 0.9**	2.9± 0.4**	1.0± 0.2	0.14± 0.05	174± 32	131± 59	47± 32

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

(HCL074)

BAIS 4

STUDY NO. : 0561
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	39	206± 137	142± 205	80± 139	662± 1548	908± 4820	1± 1	248± 1065
20 ppm	32	215± 75	94± 79	55± 65	373± 270	139± 69	1± 1	56± 36
50 ppm	32	209± 55	213± 729	103± 322	549± 1368	121± 31	1± 1	50± 24
125 ppm	38	234± 88**	175± 276	114± 144	505± 488	159± 97	1± 1	121± 327

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

(HCL074)

BAIS 4

STUDY NO. : 0561
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	39	28.1± 15.3	155± 3	4.3± 0.5	122± 3	8.8± 0.5	6.5± 1.0
20 ppm	32	24.6± 11.5	154± 2	4.4± 0.5	122± 3	9.1± 1.0	6.3± 1.0
50 ppm	32	22.9± 4.9	154± 2	4.3± 0.5	123± 3	8.8± 0.4	6.2± 0.9
125 ppm	38	23.2± 7.0	153± 2	4.4± 0.4	121± 3	9.2± 0.6*	6.3± 0.9

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

(HCL074)

BAIS 4

TABLE G2

BIOCHEMISTRY : FEMALE

STUDY NO. : 0561
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	18	5.0± 0.4	2.5± 0.2	1.1± 0.2	0.17± 0.08	113± 49	84± 31	34± 17
20 ppm	26	5.0± 0.8	2.5± 0.4	1.0± 0.3	0.14± 0.07	129± 35	80± 18	45± 48
50 ppm	22	5.1± 0.5	2.7± 0.2*	1.1± 0.2	0.15± 0.05	133± 23	80± 40	42± 21
125 ppm	26	4.9± 0.9	2.6± 0.3	1.2± 0.3	0.16± 0.08	122± 35	70± 22	41± 23

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

(HCL074)

BAIS 4

STUDY NO. : 0561
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	18	137± 33	133± 90	61± 61	390± 415	179± 54	1± 3	128± 131
20 ppm	26	144± 39	135± 112	48± 35	1146± 3031	143± 55	1± 1	104± 116
50 ppm	22	150± 72	166± 177	82± 110	788± 1280	185± 92	1± 2	81± 56
125 ppm	26	131± 39	174± 161	64± 58	1962± 5395	188± 121	1± 0	265± 634

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

(HCL074)

BAIS 4

STUDY NO. : 0561
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	18	21.8±	15.3	152±	3	4.0±	0.5	121±	3	8.9±	0.2	6.7±	2.0
20 ppm	26	17.6±	7.8	153±	2	4.1±	0.6	123±	3	9.0±	0.5	6.4±	0.9
50 ppm	22	15.6±	3.2	152±	2	4.0±	0.7	122±	3	9.0±	0.6	6.5±	1.4
125 ppm	26	20.8±	14.6	153±	4	4.2±	0.7	124±	5*	8.9±	0.4	6.6±	1.2

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

(HCL074)

BAIS4

TABLE H1

URINALYSIS : MALE

STUDY NO. : 0561
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	40	0	5	10	6	17	2	0		0	1	14	23	1	1		40	0	0	0	0	0		8	32	0	0	0	0		37	0	1	0	2	
20 ppm	32	0	2	4	11	12	3	0		0	0	13	19	0	0		32	0	0	0	0	0		8	24	0	0	0	0		30	0	0	0	2	
50 ppm	33	0	4	9	4	8	8	0		0	0	13	19	1	0		33	0	0	0	0	0		6	26	1	0	0	0		31	0	0	0	2	
125 ppm	39	0	2	2	11	12	12	0	**	0	1	10	25	3	0		39	0	0	0	0	0		6	31	2	0	0	0		35	0	2	0	2	

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01

Test of CHI SQUARE

(HCL101)

STUDY NO. : 0561
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	40	40	0	0	0	0	
20 ppm	32	32	0	0	0	0	
50 ppm	33	33	0	0	0	0	
125 ppm	39	39	0	0	0	0	

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

(HCL101)

TABLE H2

URINALYSIS : FEMALE

STUDY NO. : 0561
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	18	0	0	1	3	4	9	1		0	2	9	6	1	0		18	0	0	0	0	0		10	7	0	1	0	0		13	0	0	0	5	
20 ppm	31	0	0	4	5	4	18	0		0	3	20	8	0	0		31	0	0	0	0	0		10	19	2	0	0	0		29	1	0	1	0	*
50 ppm	24	0	1	1	3	7	12	0		0	3	9	11	1	0		24	0	0	0	0	0		6	14	4	0	0	0		22	0	0	0	2	
125 ppm	26	0	0	4	4	5	13	0		0	1	11	11	3	0		26	0	0	0	0	0		1	18	5	2	0	0	**	19	1	2	2	2	

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01

Test of CHI SQUARE

(HCL101)

STUDY NO. : 0561
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	18	18	0	0	0	0	
20 ppm	31	31	0	0	0	0	
50 ppm	24	24	0	0	0	0	
125 ppm	26	26	0	0	0	0	

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

(HCL101)

TABLE J1

ORGAN WEIGHT, ABSOLUTE : MALE

STUDY NO. : 0561
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	39	45.6± 8.8	0.011± 0.002	0.228± 0.032	0.228± 0.028	0.228± 0.119	1.178± 3.250
20 ppm	32	47.9± 7.9	0.011± 0.002	0.223± 0.033	0.228± 0.022	0.220± 0.099	0.650± 0.052
50 ppm	32	45.7± 7.4	0.011± 0.002	0.225± 0.031	0.228± 0.020	0.229± 0.092	0.661± 0.061
125 ppm	39	44.3± 8.5	0.011± 0.002	0.219± 0.030	0.226± 0.022	0.254± 0.125	0.711± 0.446

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

STUDY NO. : 0561
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	39	0.187±	0.345	1.809±	0.606	0.450±	0.013
20 ppm	32	0.178±	0.427	1.898±	0.581	0.447±	0.011
50 ppm	32	0.115±	0.108	1.684±	0.327	0.451±	0.011
125 ppm	39	0.111±	0.104	2.161±	1.067	0.449±	0.012

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

(HCL040)

TABLE J2

ORGAN WEIGHT, ABSOLUTE : FEMALE

STUDY NO. : 0561
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	18	30.3± 5.3	0.014± 0.002	0.041± 0.030	0.179± 0.021	0.191± 0.014	0.445± 0.044
20 ppm	31	33.5± 4.5	0.014± 0.002	0.091± 0.184	0.179± 0.026	0.195± 0.020	0.474± 0.088
50 ppm	24	32.3± 4.2	0.016± 0.004	0.122± 0.306	0.188± 0.025	0.202± 0.031	0.472± 0.062
125 ppm	26	31.6± 5.4	0.014± 0.002	0.042± 0.023	0.181± 0.023	0.225± 0.112	0.464± 0.050

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

STUDY NO. : 0561
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	18	0.150±	0.174	1.396±	0.284	0.493±	0.067
20 ppm	31	0.232±	0.235	1.790±	1.218	0.473±	0.016
50 ppm	24	0.250±	0.376	1.676±	0.500	0.478±	0.018
125 ppm	26	0.311±	0.339	1.933±	1.340	0.474±	0.020

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

TABLE K1

ORGAN WEIGHT, RELATIVE : MALE

STUDY NO. : 0561
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	39	45.6± 8.8	0.026± 0.007	0.519± 0.128	0.517± 0.124	0.545± 0.453	2.480± 6.170
20 ppm	32	47.9± 7.9	0.023± 0.006	0.478± 0.099	0.487± 0.074	0.476± 0.268	1.388± 0.222
50 ppm	32	45.7± 7.4	0.025± 0.005	0.501± 0.085	0.511± 0.077	0.520± 0.250	1.476± 0.212
125 ppm	39	44.3± 8.5	0.026± 0.007	0.512± 0.115	0.528± 0.110	0.620± 0.437	1.718± 1.525

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

(HCL042)

BAIS 4

STUDY NO. : 0561
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	39	0.414± 0.719	4.149± 1.958	1.030± 0.234
20 ppm	32	0.424± 1.170	4.065± 1.545	0.960± 0.169
50 ppm	32	0.264± 0.254	3.770± 0.992	1.015± 0.178
125 ppm	39	0.266± 0.280	5.057± 2.630	1.056± 0.233

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

(HCL042)

BAIS 4

TABLE K2

ORGAN WEIGHT, RELATIVE : FEMALE

STUDY NO. : 0561
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	18	30.3± 5.3	0.049± 0.012	0.137± 0.096	0.610± 0.136	0.649± 0.127	1.505± 0.281
20 ppm	31	33.5± 4.5	0.043± 0.007	0.273± 0.530	0.540± 0.090	0.589± 0.074	1.425± 0.245
50 ppm	24	32.3± 4.2	0.049± 0.013	0.365± 0.918	0.585± 0.074	0.633± 0.115	1.469± 0.157
125 ppm	26	31.6± 5.4	0.045± 0.010	0.136± 0.084	0.588± 0.112	0.743± 0.493	1.500± 0.238

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

(HCL042)

BAIS 4

STUDY NO. : 0561
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	18	0.479± 0.508	4.627± 0.660	1.692± 0.484
20 ppm	31	0.702± 0.732	5.269± 2.975	1.435± 0.176
50 ppm	24	0.800± 1.300	5.179± 1.379	1.500± 0.189
125 ppm	26	0.959± 1.004	5.942± 3.042	1.542± 0.285

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

(HCL042)

BAIS 4

TABLE L1

HISTOPATHOLOGICAL FINDINGS :

NON-NEOPLASTIC LESIONS : MALE

ALL ANIMALS

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50				20 ppm 50				50 ppm 50				125 ppm 50			
			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 (0)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)
	erosion		2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	squamous cell hyperplasia		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)
	scab		2 (4)	1 (2)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	epidermal cyst		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
subcutis			<50>				<50>				<50>				<50>			
	cyst		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)
	inflammation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	xanthogranuloma		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1 (%)	Control 50 2 (%)	Control 50 3 (%)	Control 50 4 (%)	20 ppm 50 1 (%)	20 ppm 50 2 (%)	20 ppm 50 3 (%)	20 ppm 50 4 (%)	50 ppm 50 1 (%)	50 ppm 50 2 (%)	50 ppm 50 3 (%)	50 ppm 50 4 (%)	125 ppm 50 1 (%)	125 ppm 50 2 (%)	125 ppm 50 3 (%)	125 ppm 50 4 (%)
{Respiratory system}																		
nasal cavit			<50>				<50>				<50>				<50>			
	eosinophilic change:olfactory epithelium		24 (48)	0 (0)	0 (0)	0 (0)	32 (64)	0 (0)	0 (0)	0 (0)	24 (48)	2 (4)	0 (0)	0 (0)	19 (38)	2 (4)	0 (0)	0 (0)
	eosinophilic change:respiratory epithelium		18 (36)	0 (0)	0 (0)	0 (0)	15 (30)	0 (0)	0 (0)	0 (0)	17 (34)	0 (0)	0 (0)	0 (0)	20 (40)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:olfactory epithelium		12 (24)	0 (0)	0 (0)	0 (0)	13 (26)	0 (0)	0 (0)	0 (0)	9 (18)	0 (0)	0 (0)	0 (0)	10 (20)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:gland		21 (42)	1 (2)	0 (0)	0 (0)	23 (46)	2 (4)	0 (0)	0 (0)	25 (50)	2 (4)	0 (0)	0 (0)	22 (44)	0 (0)	0 (0)	0 (0)
	atrophy:olfactory epithelium		2 (4)	0 (0)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)
lung			<50>				<50>				<50>				<50>			
	hemorrhage		0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)
	edema		3 (6)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	2 (4)	1 (2)	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)	1 (2)	0 (0)	0 (0)	0 (0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1 (%)	Control 50 2 (%)	Control 50 3 (%)	Control 50 4 (%)	20 ppm 50 1 (%)	20 ppm 50 2 (%)	20 ppm 50 3 (%)	20 ppm 50 4 (%)	50 ppm 50 1 (%)	50 ppm 50 2 (%)	50 ppm 50 3 (%)	50 ppm 50 4 (%)	125 ppm 50 1 (%)	125 ppm 50 2 (%)	125 ppm 50 3 (%)	125 ppm 50 4 (%)
{Respiratory system}																		
lung			<50>				<50>				<50>				<50>			
	lymphocytic infiltration		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)
	bronchiolar-alveolar cell hyperplasia		1	0	0	0	3	1	0	0	0	2	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(6)	(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)
	uremic pneumonitis		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)
{Hematopoietic system}																		
bone marrow			<50>				<50>				<50>				<50>			
	thrombus		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)
	atrophy:focal		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)
	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)
	granulopoiesis:increased		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)

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				20 ppm				50 ppm				125 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}																		
lymph node			<50>				<50>				<50>				<50>			
	lymphadenitis		0	0	0	0	0	2	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen			<50>				<50>				<50>				<50>			
	angiectasis		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)
	increased extramedullary hematopoiesis		4	7	1	0	7	8	1	0	6	6	0	0	6	8	1	0
			(8)	(14)	(2)	(0)	(14)	(16)	(2)	(0)	(12)	(12)	(0)	(0)	(12)	(16)	(2)	(0)
	follicular hyperplasia		0	1	0	0	3	0	1	0	2	1	1	0	2	1	0	0
			(0)	(2)	(0)	(0)	(6)	(0)	(2)	(0)	(4)	(2)	(2)	(0)	(4)	(2)	(0)	(0)
{Circulatory system}																		
heart			<50>				<50>				<50>				<50>			
	mineralization		0	0	0	0	0	0	0	0	3	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	myocardial fibrosis		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)

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				20 ppm				50 ppm				125 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>			
	arteritis		1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}																		
tongue			<50>				<50>				<50>				<50>			
	arteritis		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
stomach			<50>				<50>				<50>				<50>			
	hyperplasia:forestomach		1	1	0	0	1	0	0	0	0	0	0	0	2	0	0	0
			(2)	(2)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	erosion:glandular stomach		4	0	0	0	4	0	0	0	0	0	0	0	1	0	0	0
			(8)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	hyperplasia:glandular stomach		11	15	0	0	16	10	0	0	17	9	0	0	15	11	0	0
			(22)	(30)	(0)	(0)	(32)	(20)	(0)	(0)	(34)	(18)	(0)	(0)	(30)	(22)	(0)	(0)
small intes			<50>				<50>				<50>				<50>			
	inflammation		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)

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				20 ppm				50 ppm				125 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>			
	angiectasis		1	0	1	0	0	0	0	0	3	1	0	0	1	1	0	0
			(2)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(6)	(2)	(0)	(0)	(2)	(2)	(0)	(0)
	hemorrhage		0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	necrosis:central		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)	(0)
	necrosis:focal		2	0	2	0	1	0	2	0	0	0	0	0	1	0	0	0
			(4)	(0)	(4)	(0)	(2)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	collapse		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)
	degeneration: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)
	granulation		11	0	0	0	13	0	0	0	15	0	0	0	15	1	0	0
			(22)	(0)	(0)	(0)	(26)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(30)	(2)	(0)	(0)
	scar		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				20 ppm				50 ppm				125 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
liver			<50>				<50>				<50>				<50>			
	clear cell focus		2	1	1	0	2	1	1	0	1	0	0	0	3	3	1	0
			(4)	(2)	(2)	(0)	(4)	(2)	(2)	(0)	(2)	(0)	(0)	(0)	(6)	(6)	(2)	(0)
	acidophilic cell focus		0	2	1	0	1	0	1	0	0	2	0	0	2	1	1	0
			(0)	(4)	(2)	(0)	(2)	(0)	(2)	(0)	(0)	(4)	(0)	(0)	(4)	(2)	(2)	(0)
	basophilic cell focus		2	1	0	0	1	1	0	0	0	2	0	0	1	2	0	0
			(4)	(2)	(0)	(0)	(2)	(2)	(0)	(0)	(0)	(4)	(0)	(0)	(2)	(4)	(0)	(0)
	bile duct 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)
	biliary cyst		0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
gall bladd			<50>				<50>				<50>				<50>			
	hyperplasia:epithelium		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)
{Urinary system}																		
kidney			<50>				<50>				<50>				<50>			
	cyst		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)

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 (%)	20 ppm 50 1 (%)	20 ppm 50 2 (%)	20 ppm 50 3 (%)	20 ppm 50 4 (%)	50 ppm 50 1 (%)	50 ppm 50 2 (%)	50 ppm 50 3 (%)	50 ppm 50 4 (%)	125 ppm 50 1 (%)	125 ppm 50 2 (%)	125 ppm 50 3 (%)	125 ppm 50 4 (%)
{Urinary system}																		
kidney			<50>				<50>				<50>				<50>			
	hyaline droplet		3	0	0	0	0	0	0	0	1	1	0	0	2	0	0	0
			(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(2)	(0)	(0)	(4)	(0)	(0)	(0)
	deposit of amyloid		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)
	inflammatory infiltration		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)
	lymphocytic infiltration		1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	scar		1	0	0	0	2	0	0	0	2	0	0	0	3	0	0	0
			(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
	inflammatory polyp		0	0	2	0	0	1	0	0	0	0	0	0	0	1	1	0
			(0)	(0)	(4)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(2)	(0)
	hydronephrosis		0	1	1	0	0	0	2	0	2	0	1	0	0	0	3	1
			(0)	(2)	(2)	(0)	(0)	(0)	(4)	(0)	(4)	(0)	(2)	(0)	(0)	(0)	(6)	(2)
	mineralization:cortex		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)

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				20 ppm				50 ppm				125 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		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)
	hemorrhage:papilla		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)
urin bladd			<50>				<50>				<50>				<50>			
	dilatation		0	0	3	0	0	0	3	0	2	0	4	0	0	0	5	0
			(0)	(0)	(6)	(0)	(0)	(0)	(6)	(0)	(4)	(0)	(8)	(0)	(0)	(0)	(10)	(0)
	ulcer		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)
	simple hyperplasia:transitional 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)
	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)
{Endocrine system}																		
pituitary			<50>				<50>				<50>				<50>			
	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)

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				20 ppm				50 ppm				125 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>			
	Rathke pouch		2	0	0	0	5	0	0	0	3	0	0	0	7	0	0	0
			(4)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(14)	(0)	(0)	(0)
thyroid			<50>				<50>				<50>				<50>			
	cyst		4	0	0	0	3	1	0	0	4	0	0	0	4	0	0	0
			(8)	(0)	(0)	(0)	(6)	(2)	(0)	(0)	(8)	(0)	(0)	(0)	(8)	(0)	(0)	(0)
	C-cell hyperplasia		21	0	0	0	22	0	0	0	23	0	0	0	22	0	0	0
			(42)	(0)	(0)	(0)	(44)	(0)	(0)	(0)	(46)	(0)	(0)	(0)	(44)	(0)	(0)	(0)
parathyroid			<50>				<50>				<50>				<50>			
	cyst		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
adrenal			<50>				<50>				<50>				<50>			
	deposit of amyloid		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)
	spindle-cell hyperplasia		24	0	0	0	29	0	0	0	28	1	0	0	27	0	0	0
			(48)	(0)	(0)	(0)	(58)	(0)	(0)	(0)	(56)	(2)	(0)	(0)	(54)	(0)	(0)	(0)
	hyperplasia:cortical cell		8	3	0	0	2	0	0	0 *	1	0	0	0 **	4	0	0	0
			(16)	(6)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(8)	(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				20 ppm				50 ppm				125 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>			
	atrophy		6	5	0	0	5	2	0	0	5	2	0	0	5	3	0	0
			(12)	(10)	(0)	(0)	(10)	(4)	(0)	(0)	(10)	(4)	(0)	(0)	(10)	(6)	(0)	(0)
	mineralization		23	0	0	0	18	0	0	0	29	0	0	0	25	0	0	0
			(46)	(0)	(0)	(0)	(36)	(0)	(0)	(0)	(58)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
epididymis			<50>				<50>				<50>				<50>			
	spermatogenic granuloma		3	0	0	0	3	3	0	0	1	0	0	0	1	1	0	0
			(6)	(0)	(0)	(0)	(6)	(6)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(2)	(0)	(0)
prostate			<50>				<50>				<50>				<50>			
	inflammation		0	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)
prep/cli gl			<50>				<50>				<50>				<50>			
	duct ectasia		0	1	0	0	1	1	0	0	0	2	0	0	0	0	0	0
			(0)	(2)	(0)	(0)	(2)	(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)
	inflammation		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)
{Nervous system}																		
brain			<50>				<50>				<50>				<50>			
	mineralization		22	0	0	0	21	0	0	0	29	0	0	0	20	0	0	0
			(44)	(0)	(0)	(0)	(42)	(0)	(0)	(0)	(58)	(0)	(0)	(0)	(40)	(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 (%)	20 ppm 50 1 (%)	20 ppm 50 2 (%)	20 ppm 50 3 (%)	20 ppm 50 4 (%)	50 ppm 50 1 (%)	50 ppm 50 2 (%)	50 ppm 50 3 (%)	50 ppm 50 4 (%)	125 ppm 50 1 (%)	125 ppm 50 2 (%)	125 ppm 50 3 (%)	125 ppm 50 4 (%)
{Special sense organs/appendage}																		
eye		<50>																
	keratitis		0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	mineralization:cornea		0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
Harder gl		<50>																
	lymphocytic infiltration		0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hyperplasia		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
{Musculoskeletal system}																		
muscle		<50>																
	mineralization		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)
{Body cavities}																		
adipose		<50>																
	granulation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

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

TABLE L4

HISTOPATHOLOGICAL FINDINGS :

NON-NEOPLASTIC LESIONS : FEMALE

ALL ANIMALS

Organ	Findings	Group Name	Control				20 ppm				50 ppm				125 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>			
	squamous cell hyperplasia		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)
	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)
{Respiratory system}																		
nasal cavit			<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)
	eosinophilic change:olfactory epithelium		22	1	0	0	26	0	0	0	27	2	0	0	34	1	0	0 *
			(44)	(2)	(0)	(0)	(52)	(0)	(0)	(0)	(54)	(4)	(0)	(0)	(68)	(2)	(0)	(0)
	eosinophilic change:respiratory epithelium		36	6	0	0	35	4	1	0	39	8	0	0	34	12	0	0
			(72)	(12)	(0)	(0)	(70)	(8)	(2)	(0)	(78)	(16)	(0)	(0)	(68)	(24)	(0)	(0)
	inflammation:foreign body		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)
	respiratory metaplasia:olfactory epithelium		9	0	0	0	7	0	0	0	1	0	0	0 *	6	0	0	0
			(18)	(0)	(0)	(0)	(14)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(12)	(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				20 ppm				50 ppm				125 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>			
	respiratory metaplasia:gland		28	0	0	0	39	1	0	0 *	41	0	0	0 **	33	0	0	0
			(56)	(0)	(0)	(0)	(78)	(2)	(0)	(0)	(82)	(0)	(0)	(0)	(66)	(0)	(0)	(0)
	hyperplasia:transitional epithelium		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)
	atrophy:olfactory epithelium		4	0	0	0	1	0	0	0	2	0	0	0	2	0	0	0
			(8)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
trachea			<50>				<50>				<50>				<50>			
	eosinophilic change		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		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)
	lymphocytic infiltration		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)	(0)
	bronchiolar-alveolar cell hyperplasia		2	0	0	0	1	2	0	0	0	3	0	0	2	1	0	0
			(4)	(0)	(0)	(0)	(2)	(4)	(0)	(0)	(0)	(6)	(0)	(0)	(4)	(2)	(0)	(0)

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

Organ	Findings	Group Name	Control				20 ppm				50 ppm				125 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>			
	uremic pneumonitis		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)
{Hematopoietic system}																		
bone marrow			<50>				<50>				<50>				<50>			
	granulation		1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lymph node			<50>				<50>				<50>				<50>			
	lymphadenitis		0	1	0	0	2	0	0	0	0	1	0	0	0	0	0	0
			(0)	(2)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)
spleen			<50>				<50>				<50>				<50>			
	increased extramedullary hematopoiesis		3	10	1	0	5	11	0	0	6	10	0	0	1	12	0	0
			(6)	(20)	(2)	(0)	(10)	(22)	(0)	(0)	(12)	(20)	(0)	(0)	(2)	(24)	(0)	(0)
	follicular hyperplasia		3	0	0	0	0	2	0	0	0	2	0	0	4	2	0	0
			(6)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(0)	(0)	(8)	(4)	(0)	(0)
{Circulatory system}																		
heart			<50>				<50>				<50>				<50>			
	dilatation		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)

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				20 ppm				50 ppm				125 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>			
	thrombus		1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	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)
	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)
	arteritis		0	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)
{Digestive system}																		
tongue			<50>				<50>				<50>				<50>			
	arteritis		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)
stomach			<50>				<50>				<50>				<50>			
	hyperplasia:forestomach		0	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)

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				20 ppm				50 ppm				125 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
stomach			<50>				<50>				<50>				<50>			
	erosion:glandular stomach		2	0	0	0	1	0	0	0	1	0	0	0	1	0	0	0
			(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	hyperplasia:glandular stomach		4	1	0	0	8	1	0	0	6	1	0	0	3	2	0	0
			(8)	(2)	(0)	(0)	(16)	(2)	(0)	(0)	(12)	(2)	(0)	(0)	(6)	(4)	(0)	(0)
liver			<50>				<50>				<50>				<50>			
	angiectasis		0	2	0	0	4	0	0	0 *	4	0	0	0 *	2	0	0	0
			(0)	(4)	(0)	(0)	(8)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	necrosis:central		0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:focal		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)
	degeneration:central		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		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		14	0	0	0	20	1	0	0	17	0	0	0	18	0	0	0
			(28)	(0)	(0)	(0)	(40)	(2)	(0)	(0)	(34)	(0)	(0)	(0)	(36)	(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 / No. of Animals on Study / Grade	Control 50 1 (%)	Control 50 2 (%)	Control 50 3 (%)	Control 50 4 (%)	20 ppm 50 1 (%)	20 ppm 50 2 (%)	20 ppm 50 3 (%)	20 ppm 50 4 (%)	50 ppm 50 1 (%)	50 ppm 50 2 (%)	50 ppm 50 3 (%)	50 ppm 50 4 (%)	125 ppm 50 1 (%)	125 ppm 50 2 (%)	125 ppm 50 3 (%)	125 ppm 50 4 (%)
{Digestive system}																		
liver			<50>				<50>				<50>				<50>			
	inflammatory cell nest		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)
	scar		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	extramedullary hematopoiesis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)
	clear cell focus		1 (2)	1 (2)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)	2 (4)	4 (8)	0 (0)	0 (0)	1 (2)	1 (2)	1 (2)	0 (0)
	acidophilic cell focus		3 (6)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 * (0)	1 (2)	2 (4)	1 (2)	0 (0)
	bile duct hyperplasia		2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	biliary cyst		1 (2)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	xanthogranuloma		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

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				20 ppm				50 ppm				125 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}																		
kidney			<50>				<50>				<50>				<50>			
	cyst		0	0	0	0	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)
	hyaline droplet		14	0	0	0	11	0	0	0	12	0	0	0	11	0	0	0
			(28)	(0)	(0)	(0)	(22)	(0)	(0)	(0)	(24)	(0)	(0)	(0)	(22)	(0)	(0)	(0)
	deposit of amyloid		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)
	hyaline cast		3	1	0	0	4	0	0	0	2	0	0	0	3	0	0	0
			(6)	(2)	(0)	(0)	(8)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
	lymphocytic infiltration		5	0	0	0	8	3	0	0	2	0	0	0	7	1	0	0
			(10)	(0)	(0)	(0)	(16)	(6)	(0)	(0)	(4)	(0)	(0)	(0)	(14)	(2)	(0)	(0)
	scar		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)	(0)	(0)	(0)	(0)
	inflammatory polyp		0	1	0	0	0	0	0	0	1	0	0	0	1	1	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(2)	(0)	(0)
	hydronephrosis		0	0	3	0	0	0	0	0	0	0	1	0	0	1	1	0
			(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(2)	(2)	(0)

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

Organ	Findings	Group Name	Control				20 ppm				50 ppm				125 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>			
	papillary necrosis		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)
urin bladd			<50>				<50>				<50>				<50>			
	dilatation		0	0	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)
{Endocrine system}																		
pituitary			<50>				<49>				<50>				<50>			
	angiectasis		6	0	0	0	1	1	0	0	1	0	0	0	1	0	0	0
			(12)	(0)	(0)	(0)	(2)	(2)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	hyperplasia		9	3	2	0	7	2	1	0	4	2	1	0	8	4	0	0
			(18)	(6)	(4)	(0)	(14)	(4)	(2)	(0)	(8)	(4)	(2)	(0)	(16)	(8)	(0)	(0)
	Rathke pouch		1	0	0	0	1	0	0	0	1	0	0	0	3	0	0	0
			(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
thyroid			<50>				<50>				<50>				<50>			
	cyst		3	0	0	0	1	0	0	0	2	0	0	0	4	2	0	0
			(6)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(8)	(4)	(0)	(0)

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

Organ	Findings	Group Name	Control				20 ppm				50 ppm				125 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Endocrine system}																		
thyroid			<50>				<50>				<50>				<50>			
	C-cell hyperplasia		23	0	0	0	30	0	0	0	26	0	0	0	26	0	0	0
			(46)	(0)	(0)	(0)	(60)	(0)	(0)	(0)	(52)	(0)	(0)	(0)	(52)	(0)	(0)	(0)
adrenal			<50>				<50>				<50>				<50>			
	thrombus		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	extramedullary 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)
	spindle-cell hyperplasia		17	25	0	0	22	26	0	0	19	26	1	0	24	19	0	0
			(34)	(50)	(0)	(0)	(44)	(52)	(0)	(0)	(38)	(52)	(2)	(0)	(48)	(38)	(0)	(0)
	focal fatty change:cortex		1	0	0	0	0	0	0	0	1	0	0	0	5	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	focal 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)
{Reproductive system}																		
ovary			<50>				<50>				<50>				<50>			
	thrombus		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)

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				20 ppm				50 ppm				125 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}																		
ovary			<50>				<50>				<50>				<50>			
	cyst		6	0	0	0	7	0	0	0	4	1	0	0	7	0	0	0
			(12)	(0)	(0)	(0)	(14)	(0)	(0)	(0)	(8)	(2)	(0)	(0)	(14)	(0)	(0)	(0)
uterus			<50>				<50>				<50>				<50>			
	cystic endometrial hyperplasia		16	5	0	0	16	5	0	0	14	9	0	0	14	6	0	0
			(32)	(10)	(0)	(0)	(32)	(10)	(0)	(0)	(28)	(18)	(0)	(0)	(28)	(12)	(0)	(0)
{Nervous system}																		
brain			<50>				<50>				<50>				<50>			
	hemorrhage		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)
	vacuolic change		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)
	mineralization		12	0	0	0	13	0	0	0	14	0	0	0	9	0	0	0
			(24)	(0)	(0)	(0)	(26)	(0)	(0)	(0)	(28)	(0)	(0)	(0)	(18)	(0)	(0)	(0)
{Special sense organs/appendage}																		
eye			<50>				<50>				<50>				<50>			
	keratitis		1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				20 ppm				50 ppm				125 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>			
	phthisis bulbi		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:cornea		8	0	0	0	2	0	0	0	1	0	0	0 *	3	0	0	0
			(16)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
Harder gl			<50>				<50>				<50>				<50>			
	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)
	lymphocytic infiltration		0	0	0	0	1	0	0	0	0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	hyperplasia		1	0	0	0	2	0	0	0	0	1	0	0	2	0	0	0
			(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(4)	(0)	(0)	(0)
{Musculoskeletal system}																		
muscle			<50>				<50>				<50>				<50>			
	mineralization		1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

TABLE O1

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS : MALE

STUDY No. : 0561
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

Group Name	Control	20 ppm	50 ppm	125 ppm
	SITE : lung			
	TUMOR : bronchiolar-alveolar adenoma			
Tumor rate				
Overall rates(a)	6/50(12.0)	4/50(8.0)	6/50(12.0)	8/50(16.0)
Adjusted rates(b)	15.38	10.53	17.14	18.18
Terminal rates(c)	6/39(15.4)	1/32(3.1)	5/32(15.6)	7/39(17.9)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.1641			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.3359			
Fisher Exact test(e)		P = 0.3703	P = 0.6202	P = 0.3871
	SITE : lung			
	TUMOR : bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	7/50(14.0)	13/50(26.0)	16/50(32.0)
Adjusted rates(b)	5.13	12.50	28.13	38.46
Terminal rates(c)	2/39(5.1)	4/32(12.5)	9/32(28.1)	15/39(38.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5009			
Prevalence method(d)	P = 0.0001**			
Combined analysis(d)	P = 0.0005**			
Cochran-Armitage test(e)	P = 0.0004**			
Fisher Exact test(e)		P = 0.0798	P = 0.0019**	P = 0.0002**
	SITE : lung			
	TUMOR : bronchiolar-alveolar adenoma,bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	7/50(14.0)	10/50(20.0)	18/50(36.0)	23/50(46.0)
Adjusted rates(b)	17.95	18.92	41.67	53.85
Terminal rates(c)	7/39(17.9)	4/32(12.5)	13/32(40.6)	21/39(53.8)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5009			
Prevalence method(d)	P = 0.0001**			
Combined analysis(d)	P = 0.0002**			
Cochran-Armitage test(e)	P = 0.0002**			
Fisher Exact test(e)		P = 0.2977	P = 0.0099**	P = 0.0004**

Group Name	Control	20 ppm	50 ppm	125 ppm
	SITE : lymph node			
	TUMOR : malignant lymphoma			
Tumor rate				
Overall rates(a)	14/50(28.0)	5/50(10.0)	4/50(8.0)	7/50(14.0)
Adjusted rates(b)	17.95	12.50	6.25	12.82
Terminal rates(c)	7/39(17.9)	4/32(12.5)	2/32(6.3)	5/39(12.8)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.9044			
Prevalence method(d)	P = 0.6819			
Combined analysis(d)	P = 0.8883			
Cochran-Armitage test(e)	P = 0.2305			
Fisher Exact test(e)		P = 0.0198*	P = 0.0087**	P = 0.0698
	SITE : spleen			
	TUMOR : hemangioma			
Tumor rate				
Overall rates(a)	1/50(2.0)	2/50(4.0)	4/50(8.0)	0/50(0.0)
Adjusted rates(b)	2.56	5.41	11.76	0.0
Terminal rates(c)	1/39(2.6)	1/32(3.1)	3/32(9.4)	0/39(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = -------			
Prevalence method(d)	P = 0.7910			
Combined analysis(d)	P = -------			
Cochran-Armitage test(e)	P = 0.4120			
Fisher Exact test(e)		P = 0.5000	P = 0.1811	P = 0.5000
	SITE : spleen			
	TUMOR : hemangioma, hemangiosarcoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	2/50(4.0)	4/50(8.0)	0/50(0.0)
Adjusted rates(b)	5.13	5.41	11.76	0.0
Terminal rates(c)	2/39(5.1)	1/32(3.1)	3/32(9.4)	0/39(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = -------			
Prevalence method(d)	P = 0.8767			
Combined analysis(d)	P = -------			
Cochran-Armitage test(e)	P = 0.2543			
Fisher Exact test(e)		P = 0.6913	P = 0.3389	P = 0.2475

Group Name	Control	20 ppm	50 ppm	125 ppm
	SITE : liver			
	TUMOR : hepatocellular adenoma			
Tumor rate				
Overall rates(a)	12/50(24.0)	13/50(26.0)	11/50(22.0)	20/50(40.0)
Adjusted rates(b)	28.21	34.29	27.78	51.28
Terminal rates(c)	11/39(28.2)	10/32(31.3)	8/32(25.0)	20/39(51.3)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.0308*			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.0544			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.0664
	SITE : liver			
	TUMOR : hemangiosarcoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	5/50(10.0)	5/50(10.0)	1/50(2.0)
Adjusted rates(b)	5.13	7.14	6.25	2.56
Terminal rates(c)	2/39(5.1)	1/32(3.1)	2/32(6.3)	1/39(2.6)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.6694			
Prevalence method(d)	P = 0.7593			
Combined analysis(d)	P = 0.8095			
Cochran-Armitage test(e)	P = 0.3376			
Fisher Exact test(e)		P = 0.2180	P = 0.2180	P = 0.5000
	SITE : liver			
	TUMOR : hepatocellular carcinoma			
Tumor rate				
Overall rates(a)	7/50(14.0)	10/50(20.0)	3/50(6.0)	9/50(18.0)
Adjusted rates(b)	16.67	21.88	6.25	21.43
Terminal rates(c)	5/39(12.8)	7/32(21.9)	2/32(6.3)	8/39(20.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.7106			
Prevalence method(d)	P = 0.3286			
Combined analysis(d)	P = 0.4204			
Cochran-Armitage test(e)	P = 0.7956			
Fisher Exact test(e)		P = 0.2977	P = 0.1589	P = 0.3929

Group Name	Control	20 ppm	50 ppm	125 ppm
	SITE : liver			
	TUMOR : hemangioma, hemangiosarcoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	7/50(14.0)	6/50(12.0)	3/50(6.0)
Adjusted rates(b)	7.14	11.90	9.38	7.69
Terminal rates(c)	2/39(5.1)	2/32(6.3)	3/32(9.4)	3/39(7.7)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.6694			
Prevalence method(d)	P = 0.5924			
Combined analysis(d)	P = 0.6800			
Cochran-Armitage test(e)	P = 0.5721			
Fisher Exact test(e)		P = 0.1589	P = 0.2435	P = 0.6611
	SITE : liver			
	TUMOR : hepatocellular adenoma, hepatocellular carcinoma			
Tumor rate				
Overall rates(a)	17/50(34.0)	19/50(38.0)	14/50(28.0)	25/50(50.0)
Adjusted rates(b)	38.10	42.86	33.33	61.54
Terminal rates(c)	14/39(35.9)	13/32(40.6)	10/32(31.3)	24/39(61.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.7106			
Prevalence method(d)	P = 0.0342*			
Combined analysis(d)	P = 0.0552			
Cochran-Armitage test(e)	P = 0.0914			
Fisher Exact test(e)		P = 0.4176	P = 0.3329	P = 0.0779
	SITE : liver			
	TUMOR : hepatocellular adenoma, hepatocellular carcinoma, hepatoblastoma			
Tumor rate				
Overall rates(a)	17/50(34.0)	19/50(38.0)	14/50(28.0)	25/50(50.0)
Adjusted rates(b)	38.10	42.86	33.33	61.54
Terminal rates(c)	14/39(35.9)	13/32(40.6)	10/32(31.3)	24/39(61.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.7906			
Prevalence method(d)	P = 0.0286*			
Combined analysis(d)	P = 0.0587			
Cochran-Armitage test(e)	P = 0.0914			
Fisher Exact test(e)		P = 0.4176	P = 0.3329	P = 0.0779

Group Name	Control	20 ppm	50 ppm	125 ppm
	SITE : gall bladder TUMOR : papillary adenoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	1/50(2.0)	0/50(0.0)	1/50(2.0)
Adjusted rates(b)	7.69	3.13	0.0	2.56
Terminal rates(c)	3/39(7.7)	1/32(3.1)	0/32(0.0)	1/39(2.6)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.8259			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.3462			
Fisher Exact test(e)		P = 0.3087	P = 0.1212	P = 0.3087
	SITE : Harderian gland TUMOR : adenoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	1/50(2.0)	4/50(8.0)	0/50(0.0)
Adjusted rates(b)	10.26	3.13	9.52	0.0
Terminal rates(c)	4/39(10.3)	1/32(3.1)	2/32(6.3)	0/39(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.9446			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.1161			
Fisher Exact test(e)		P = 0.1811	P = 0.6425	P = 0.0587

(HPT360A)

BAIS4

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

STUDY No. : 0561
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

Group Name	Control	20 ppm	50 ppm	125 ppm
	SITE : ALL SITE TUMOR : hemangioma			
Tumor rate				
Overall rates(a)	3/50(6.0)	5/50(10.0)	7/50(14.0)	3/50(6.0)
Adjusted rates(b)	4.76	12.50	16.67	7.14
Terminal rates(c)	1/39(2.6)	3/32(9.4)	4/32(12.5)	2/39(5.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 1.0000 ?			
Prevalence method(d)	P = 0.4691			
Combined analysis(d)	P = 0.5681			
Cochran-Armitage test(e)	P = 0.7847			
Fisher Exact test(e)		P = 0.3575	P = 0.1589	P = 0.6611
	SITE : ALL SITE TUMOR : histiocytic sarcoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	2/50(4.0)	5/50(10.0)	5/50(10.0)
Adjusted rates(b)	0.0	0.0	3.13	7.69
Terminal rates(c)	0/39(0.0)	0/32(0.0)	1/32(3.1)	3/39(7.7)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3425			
Prevalence method(d)	P = 0.0146*			
Combined analysis(d)	P = 0.0597			
Cochran-Armitage test(e)	P = 0.0893			
Fisher Exact test(e)		P = 0.5000	P = 0.1022	P = 0.1022
	SITE : ALL SITE TUMOR : malignant lymphoma			
Tumor rate				
Overall rates(a)	15/50(30.0)	7/50(14.0)	4/50(8.0)	7/50(14.0)
Adjusted rates(b)	20.51	18.18	6.25	12.82
Terminal rates(c)	8/39(20.5)	5/32(15.6)	2/32(6.3)	5/39(12.8)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.9044			
Prevalence method(d)	P = 0.8344			
Combined analysis(d)	P = 0.9449			
Cochran-Armitage test(e)	P = 0.1142			
Fisher Exact test(e)		P = 0.0448*	P = 0.0047**	P = 0.0448*

STUDY No. : 0561
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

Group Name	Control	20 ppm	50 ppm	125 ppm
	SITE : ALL SITE			
	TUMOR : hemangiosarcoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	6/50(12.0)	5/50(10.0)	2/50(4.0)
Adjusted rates(b)	5.13	7.14	6.25	5.13
Terminal rates(c)	2/39(5.1)	1/32(3.1)	2/32(6.3)	2/39(5.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.7419			
Prevalence method(d)	P = 0.5484			
Combined analysis(d)	P = 0.7074			
Cochran-Armitage test(e)	P = 0.5294			
Fisher Exact test(e)		P = 0.1343	P = 0.2180	P = 0.6913

(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 ; * : $P \leqq 0.05$ ** : $P \leqq 0.01$
N.C. :Statistical value cannot be calculated and was not significant.

TABLE O2

NEOPLASTIC LESIONS-INCIDENCE

AND STATISTICAL ANALYSIS : FEMALE

Group Name	Control	20 ppm	50 ppm	125 ppm
	SITE : lung			
	TUMOR : bronchiolar-alveolar adenoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	5/50(10.0)	6/50(12.0)	3/50(6.0)
Adjusted rates(b)	11.54	16.13	17.14	9.09
Terminal rates(c)	2/18(11.1)	5/31(16.1)	2/24(8.3)	2/26(7.7)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.7112			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.5938			
Fisher Exact test(e)		P = 0.5000	P = 0.3703	P = 0.5000
	SITE : lung			
	TUMOR : bronchiolar-alveolar adenoma, bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	5/50(10.0)	5/50(10.0)	6/50(12.0)	5/50(10.0)
Adjusted rates(b)	11.54	16.13	17.14	15.38
Terminal rates(c)	2/18(11.1)	5/31(16.1)	2/24(8.3)	4/26(15.4)
Statistical analysis				
Peto test				
Standard method(d)	P = 1.0000 ?			
Prevalence method(d)	P = 0.4259			
Combined analysis(d)	P = 0.5233			
Cochran-Armitage test(e)	P = 0.9952			
Fisher Exact test(e)		P = 0.6297	P = 0.5000	P = 0.6297
	SITE : lymph node			
	TUMOR : malignant lymphoma			
Tumor rate				
Overall rates(a)	15/50(30.0)	11/50(22.0)	12/50(24.0)	15/50(30.0)
Adjusted rates(b)	19.05	16.13	20.83	19.23
Terminal rates(c)	3/18(16.7)	5/31(16.1)	5/24(20.8)	5/26(19.2)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.4074			
Prevalence method(d)	P = 0.4160			
Combined analysis(d)	P = 0.3819			
Cochran-Armitage test(e)	P = 0.7074			
Fisher Exact test(e)		P = 0.2472	P = 0.3264	P = 0.5862

Group Name	Control	20 ppm	50 ppm	125 ppm
	SITE : spleen			
	TUMOR : malignant lymphoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	3/50(6.0)	3/50(6.0)	4/50(8.0)
Adjusted rates(b)	0.0	9.68	4.17	11.54
Terminal rates(c)	0/18(0.0)	3/31(9.7)	1/24(4.2)	3/26(11.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.6945			
Prevalence method(d)	P = 0.1525			
Combined analysis(d)	P = 0.3493			
Cochran-Armitage test(e)	P = 0.6451			
Fisher Exact test(e)		P = 0.6611	P = 0.6611	P = 0.5000
	SITE : liver			
	TUMOR : hemangioma			
Tumor rate				
Overall rates(a)	3/50(6.0)	4/50(8.0)	2/50(4.0)	6/50(12.0)
Adjusted rates(b)	11.11	9.68	5.71	12.20
Terminal rates(c)	2/18(11.1)	3/31(9.7)	1/24(4.2)	2/26(7.7)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.4719			
Prevalence method(d)	P = 0.1039			
Combined analysis(d)	P = 0.1319			
Cochran-Armitage test(e)	P = 0.2611			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.2435
	SITE : liver			
	TUMOR : hepatocellular adenoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	3/50(6.0)	1/50(2.0)	2/50(4.0)
Adjusted rates(b)	16.67	8.33	4.17	7.69
Terminal rates(c)	3/18(16.7)	2/31(6.5)	1/24(4.2)	2/26(7.7)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.8209			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.3837			
Fisher Exact test(e)		P = 0.5000	P = 0.1811	P = 0.3389

Group Name	Control	20 ppm	50 ppm	125 ppm
	SITE : liver			
	TUMOR : hemangioma, hemangiosarcoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	4/50(8.0)	2/50(4.0)	7/50(14.0)
Adjusted rates(b)	11.11	9.68	5.71	12.50
Terminal rates(c)	2/18(11.1)	3/31(9.7)	1/24(4.2)	2/26(7.7)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.2185			
Prevalence method(d)	P = 0.0967			
Combined analysis(d)	P = 0.0660			
Cochran-Armitage test(e)	P = 0.1312			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.1589
	SITE : liver			
	TUMOR : hepatocellular adenoma, hepatocellular carcinoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	4/50(8.0)	2/50(4.0)	3/50(6.0)
Adjusted rates(b)	16.67	11.11	8.33	10.34
Terminal rates(c)	3/18(16.7)	3/31(9.7)	2/24(8.3)	2/26(7.7)
Statistical analysis				
Peto test				
Standard method(d)	P = -------			
Prevalence method(d)	P = 0.6845			
Combined analysis(d)	P = -------			
Cochran-Armitage test(e)	P = 0.6343			
Fisher Exact test(e)		P = 0.6425	P = 0.3389	P = 0.5000
	SITE : pituitary gland			
	TUMOR : adenoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	6/49(12.2)	7/50(14.0)	3/50(6.0)
Adjusted rates(b)	10.53	19.35	25.00	11.54
Terminal rates(c)	1/18(5.6)	6/31(19.4)	6/24(25.0)	3/26(11.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 1.0000 ?			
Prevalence method(d)	P = 0.7083			
Combined analysis(d)	P = 0.7866			
Cochran-Armitage test(e)	P = 0.5100			
Fisher Exact test(e)		P = 0.3574	P = 0.2623	P = 0.5000

Group Name	Control	20 ppm	50 ppm	125 ppm
	SITE : pituitary gland			
	TUMOR : adenoma, adenocarcinoma			
Tumor rate				
Overall rates(a)	5/50(10.0)	6/49(12.2)	7/50(14.0)	3/50(6.0)
Adjusted rates(b)	15.79	19.35	25.00	11.54
Terminal rates(c)	2/18(11.1)	6/31(19.4)	6/24(25.0)	3/26(11.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 1.0000 ?			
Prevalence method(d)	P = 0.7901			
Combined analysis(d)	P = 0.8518			
Cochran-Armitage test(e)	P = 0.3778			
Fisher Exact test(e)		P = 0.4856	P = 0.3798	P = 0.3575
	SITE : uterus			
	TUMOR : histiocytic sarcoma			
Tumor rate				
Overall rates(a)	10/50(20.0)	14/50(28.0)	8/50(16.0)	15/50(30.0)
Adjusted rates(b)	5.56	22.58	4.17	24.14
Terminal rates(c)	1/18(5.6)	7/31(22.6)	1/24(4.2)	6/26(23.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.4312			
Prevalence method(d)	P = 0.1139			
Combined analysis(d)	P = 0.2036			
Cochran-Armitage test(e)	P = 0.3543			
Fisher Exact test(e)		P = 0.2415	P = 0.3976	P = 0.1779

(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	20 ppm	50 ppm	125 ppm
	SITE : ALL SITE TUMOR : hemangioma			
Tumor rate				
Overall rates(a)	3/50(6.0)	8/50(16.0)	4/50(8.0)	9/50(18.0)
Adjusted rates(b)	11.11	16.13	12.50	21.21
Terminal rates(c)	2/18(11.1)	5/31(16.1)	3/24(12.5)	4/26(15.4)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.6883			
Prevalence method(d)	P = 0.0348*			
Combined analysis(d)	P = 0.0888			
Cochran-Armitage test(e)	P = 0.1489			
Fisher Exact test(e)		P = 0.0999	P = 0.5000	P = 0.0606
	SITE : ALL SITE TUMOR : histiocytic sarcoma			
Tumor rate				
Overall rates(a)	12/50(24.0)	15/50(30.0)	9/50(18.0)	15/50(30.0)
Adjusted rates(b)	5.56	22.58	4.17	24.14
Terminal rates(c)	1/18(5.6)	7/31(22.6)	1/24(4.2)	6/26(23.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.6166			
Prevalence method(d)	P = 0.1183			
Combined analysis(d)	P = 0.3421			
Cochran-Armitage test(e)	P = 0.6355			
Fisher Exact test(e)		P = 0.3264	P = 0.3121	P = 0.3264

Group Name	Control	20 ppm	50 ppm	125 ppm
	SITE : ALL SITE			
	TUMOR : malignant lymphoma			
Tumor rate				
Overall rates(a)	18/50(36.0)	14/50(28.0)	15/50(30.0)	19/50(38.0)
Adjusted rates(b)	19.05	25.81	25.00	30.77
Terminal rates(c)	3/18(16.7)	8/31(25.8)	6/24(25.0)	8/26(30.8)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5007			
Prevalence method(d)	P = 0.2098			
Combined analysis(d)	P = 0.3265			
Cochran-Armitage test(e)	P = 0.5526			
Fisher Exact test(e)		P = 0.2603	P = 0.3355	P = 0.5000

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

TABLE Q

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

TABLE Q 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. (%)
Lung	1895			
Bronchiolar-alveolar adenoma 1)		165	8.7	2 - 18
Bronchiolar-alveolar carcinoma 2)		196	10.3	0 - 24
1) + 2)		361	19.1	2 - 34
Liver	1896			
Hepatocellular adenoma 1)		376	19.8	4 - 38
Hepatocellular carcinoma 2)		352	18.6	2 - 42
1) + 2)		657	34.7	8 - 68
All organ histiocytic sarcoma	1896	178	9.4	0 - 22

Thirty eight 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

TABLE R

CAUSE OF DEATH OF MICE IN THE 2-YEAR INHALATION STUDY OF 1 - BROMOBUTANE

TABLE R CAUSE OF DEATH OF MICE IN THE 2-YEAR INHALATION STUDY OF 1-BROMOBUTANE

	Male				Female			
Group name	Control	20 ppm	50 ppm	125 ppm	Control	20 ppm	50 ppm	125 ppm
Number of dead or moribund animals	11	18	18	11	32	19	26	24
Hepatic lesions	0	1	1	0	0	0	0	0
Urinary syatem lesions	0	1	0	0	0	0	0	0
Renal lesions	0	0	1	0	0	0	0	0
Urinary retention	1	1	3	2	0	1	0	0
Cardiovascular lesions	0	0	0	0	0	0	1	0
Arteritis	0	0	0	0	0	0	0	1
Hydronephrosis	0	2	1	3	1	0	1	1
Tumor death : leukemia	7	1	2	2	14	6	9	11
subcutis	1	1	0	1	2	1	1	0
lung	0	3	2	1	1	0	0	0
heart	0	0	0	0	0	0	1	0
bone marrow	0	1	0	0	0	0	0	0
liver	1	6	6	0	2	2	1	2
urinary bladder	0	0	0	0	0	1	0	0
pituitary gland	0	0	0	1	1	0	0	0
testis	1	0	0	0	-	-	-	-
epididymis	0	0	0	1	-	-	-	-
ovary	-	-	-	-	0	1	1	0
uterus	-	-	-	-	8	7	9	8
mammary gland	0	0	0	0	1	0	1	0
peripheral nerve	0	0	1	0	0	0	0	0
muscle	0	1	0	0	0	0	0	0
mediastinum	0	0	1	0	0	0	0	0
peritoneum	0	0	0	0	0	0	0	1
retroperitoneum	0	0	0	0	1	0	0	0
No microscopical confirmation	0	0	0	0	1	0	1	0

FIGURES

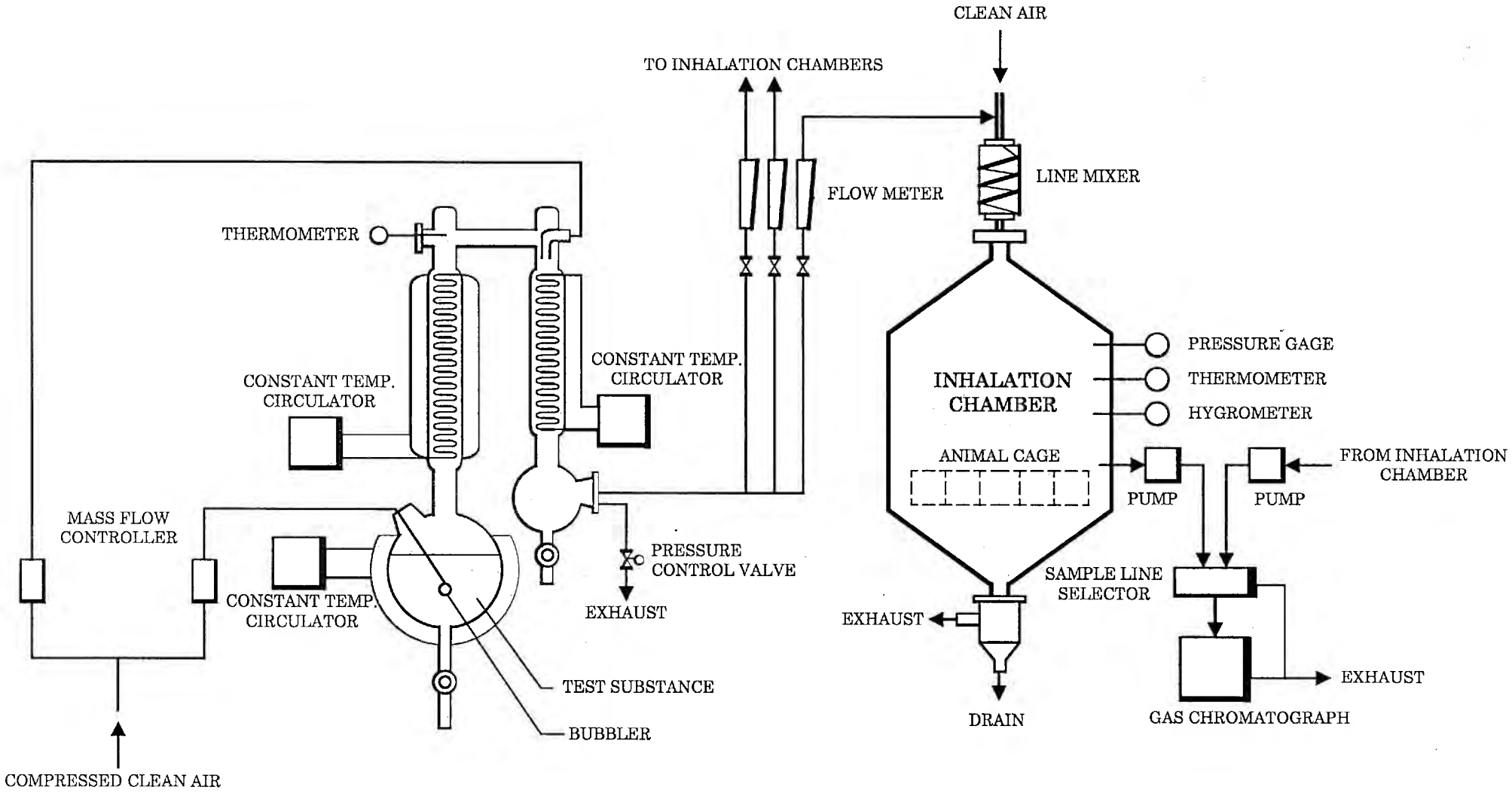


FIGURE 1 1-BROMOBUTANE VAPOR GENERATION SYSTEM AND INHALATION SYSTEM

(Study No. 0561)

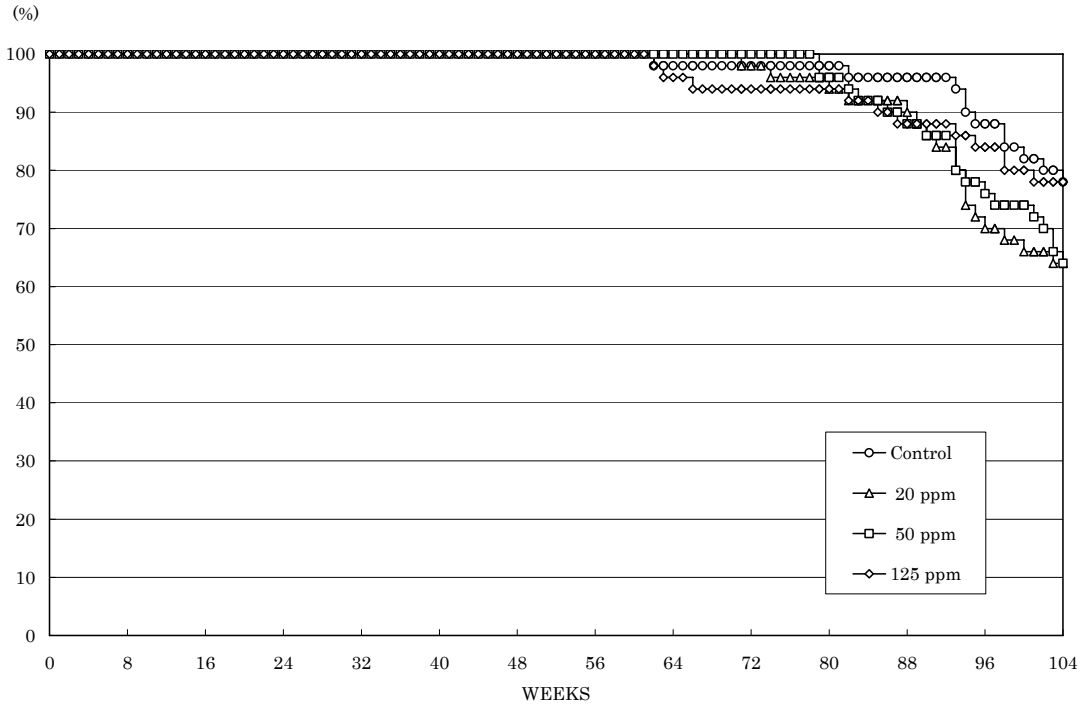


FIGURE 2 SURVIVAL ANIMAL RATE OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1-BROMOBUTANE

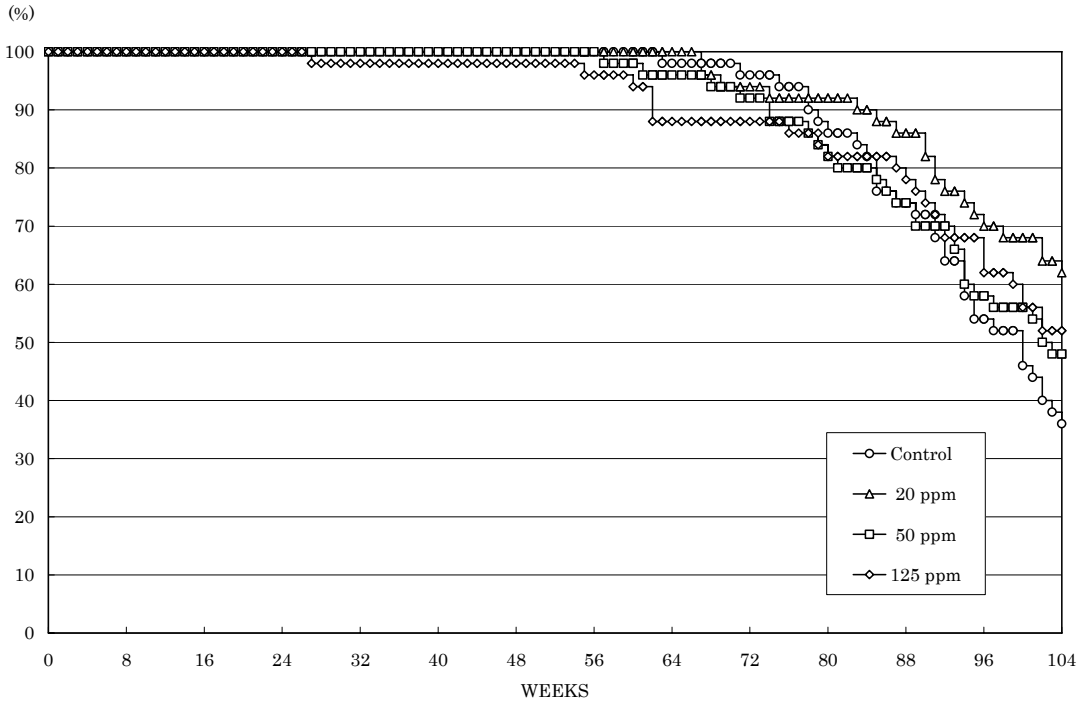


FIGURE 3 SURVIVAL ANIMAL RATE OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 1-BROMOBUTANE

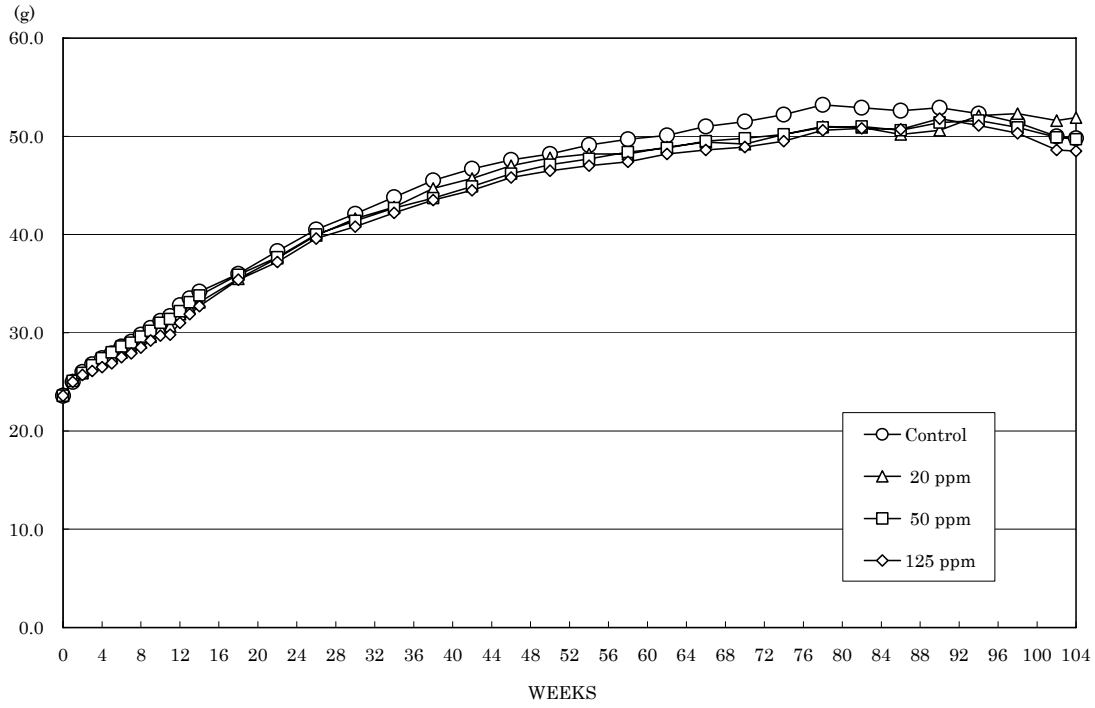


FIGURE 4　BODY WEIGHT CHANGES OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1-BROMOBUTANE

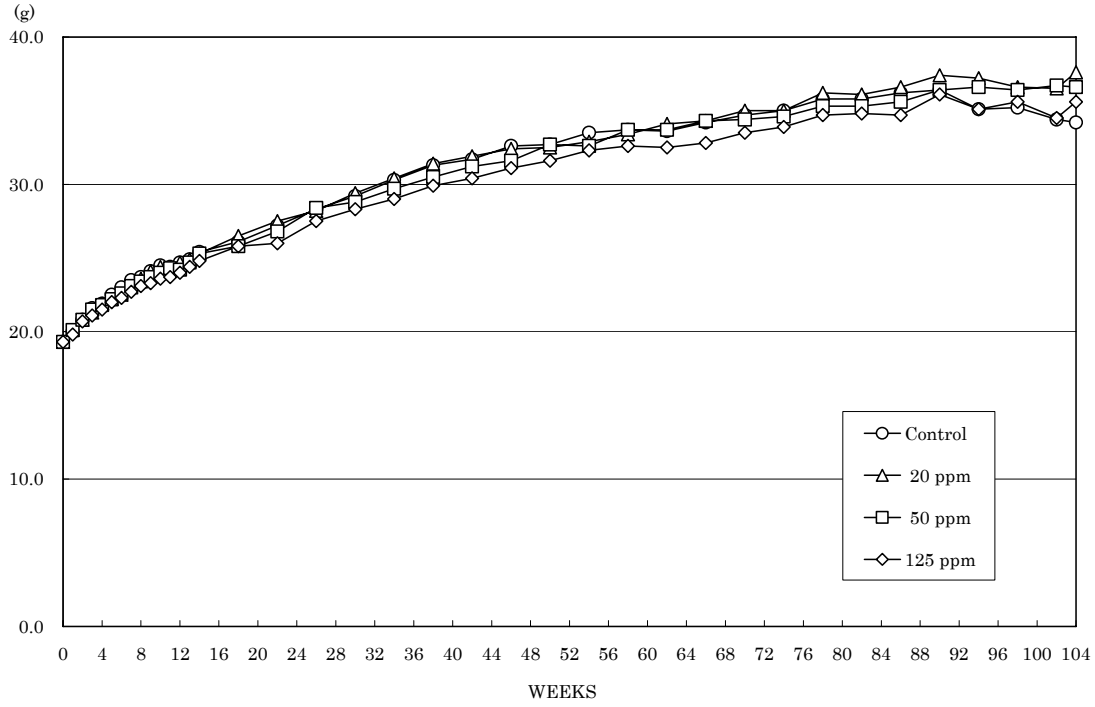


FIGURE 5　BODY WEIGHT CHANGES OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 1-BROMOBUTANE

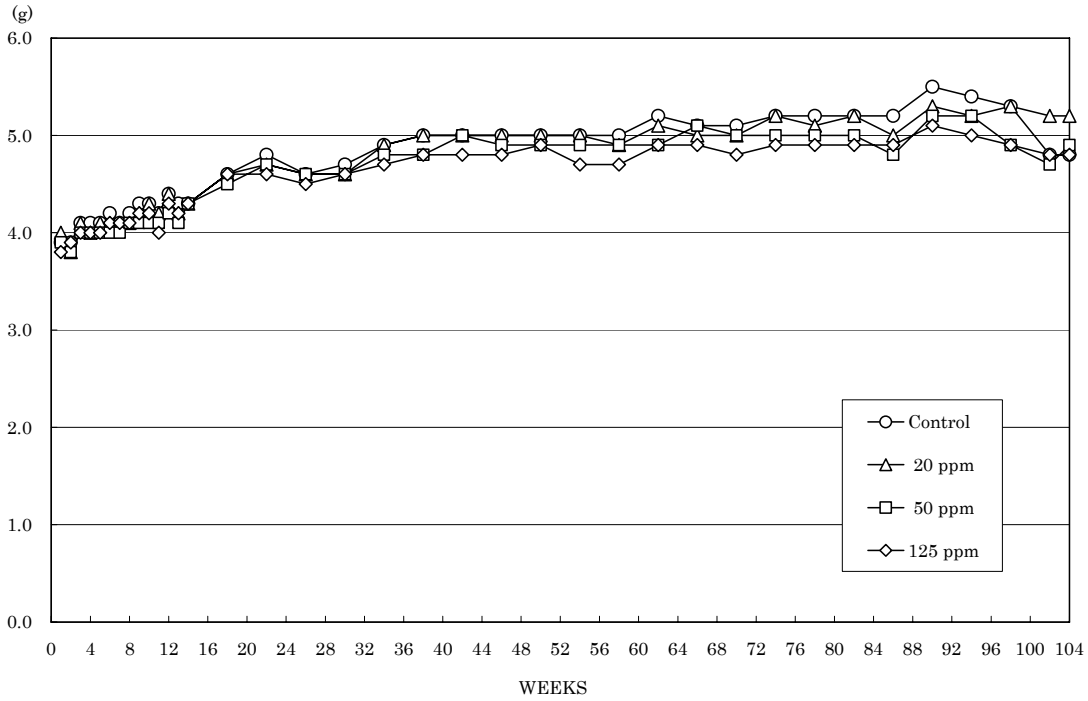


FIGURE 6 FOOD CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1-BROMOBUTANE

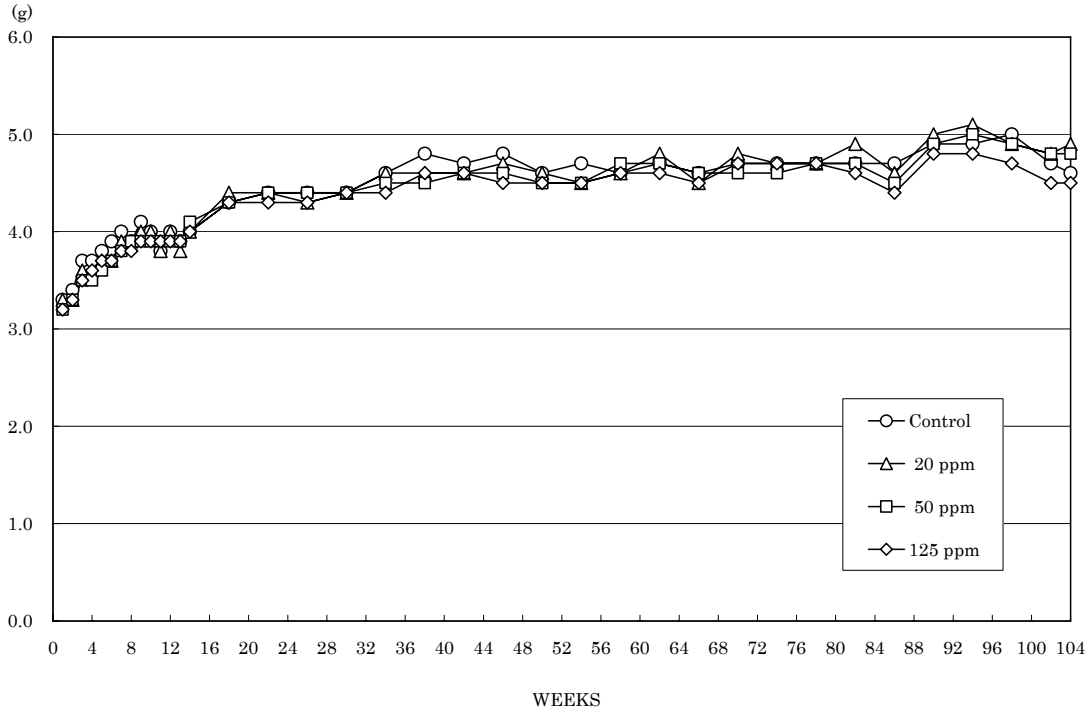
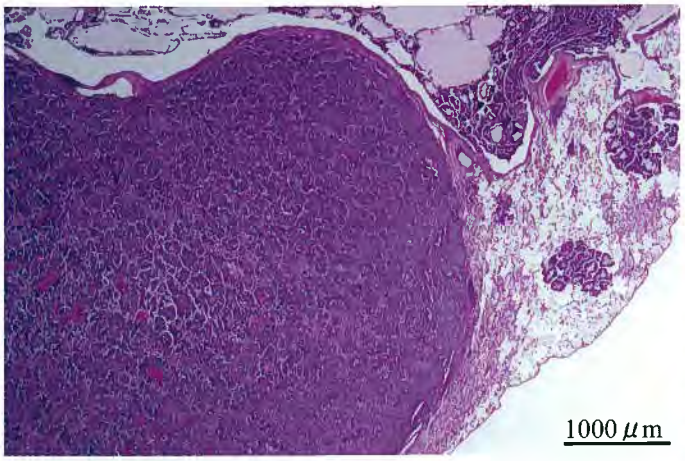
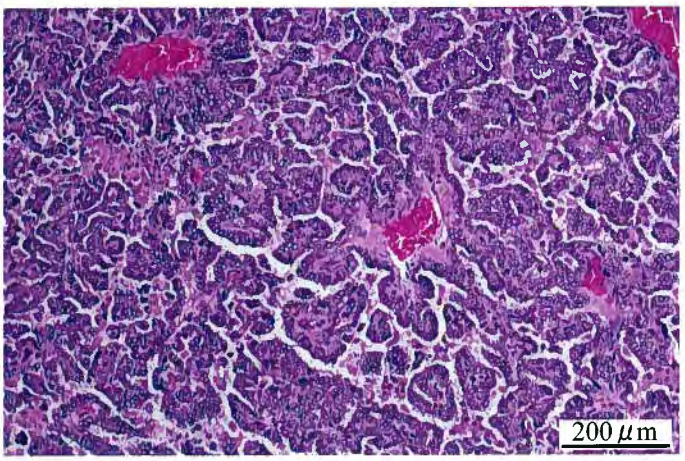


FIGURE 7 FOOD CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 1-BROMOBUTANE



Photograph 1
Lung: Bronchiolar-alveolar carcinoma
Mouse, Male, 125 ppm, Animal No. 0561-1347 (H&E)



Photograph 2
Lung: Bronchiolar-alveolar carcinoma
Higher magnification of photograph 1