Summary of Inhalation Carcinogenicity Study of 1,2-Dichloropropane in B6D2F1 Mice

March 2006

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 29, 2006.

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

Summary of Inhalation Carcinogenicity Study of 1,2-Dichloropropane in B6D2F1 Mice

Purpose, materials and methods

1,2-Dichloropropane (1,2DCP, CAS No. 78-87-5) is a colorless liquid with a boiling point of 96.4°C and a vapor pressure of 53.3 mm Hg at 25°C. It is poorly soluble in water and soluble in ethanol and diethyl ether.

The carcinogenicity and chronic toxicity of 1,2DCP were examined by inhalation exposure of groups of 50 B6D2F1/Crlj mice of both sexes to 1,2DCP vapor at a target concentration of 0 (clean air), 32, 80 or 200 ppm (v/v) for 6 hours/day, 5 days/week for 2 years (104 weeks). 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. 1,2DCP was analyzed for purity and stability by both infrared spectrometry and gas chromatography before and after its use. Stainless-steel inhalation exposure chambers (volume: 3700 L) were used throughout the 2-year exposure period. 1,2DCP vapor-air mixture was generated by bubbling clean air through the 1,2DCP liquid, and supplied to the inhalation exposure chambers. Clean air was bubbled through the liquid 1,2DCP. Air concentrations of 1,2DCP 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. Animals found dead, in a moribund state, or 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, the surviving animals were bled under ether anesthesia, after they were fasted overnight, at the terminal necropsy. Organs and tissues were removed, weighed and examined for macroscopic lesions at necropsy. The organs and tissues were fixed and embedded in paraffin. Tissue sections of 5 μm thick were prepared and stained with hematoxylin and eosin and examined for histopathology. Incidences of neoplastic lesions were statistically analyzed by Fisher's exact test. A positive trend of the dose-response relation for the neoplastic incidence was analyzed by Peto's test. Incidences of non-neoplastic lesions and urinalysis were analyzed by 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 study was conducted in accordance with the Organisation for Economic Co-operation and Development (OECD) Good Laboratory Practice and with reference to the OECD Guideline for Testing of Chemicals 451 "Carcinogenicity Studies".

Results

There was no significant difference in survival rate or body weights between any 1,2DCP-exposed group of either sex and the respective control.

The incidence of Harderian gland adenomas in males and the combined incidence of bronchiolor-alveolar adenomas and carcinomas in females were increased dose-dependently. The significantly increased incidences of Harderian gland tumor in the 200 ppm-exposed males and lung tumors in the 200 ppm-exposed females were noted. As non-neoplastic lesions, changes in the nasal cavity (atrophy in the olfactory epithelium, respiratory metaplasia in the olfactory epithelium and submucosal gland) and in the kidney (increased kidney weight, basophilic change in the proximal tubules and mineralization of cortex) were observed.

Conclusions

In mice, there was some evidence of carcinogenic activity of 1,2DCP in males, based on the increased incidence of Harderian gland adenomas, and there was some evidence of carcinogenic activity of 1,2DCP in females, based on the increased combined incidence of bronchiolar-alveolar adenomas and carcinomas.

TABLES

TABLE 1 CONCENTRATIONS OF 1,2-DICHLOROPROPANE IN THE INHALATION CHAMBER OF THE 2-YEAR INHALATION STUDY

TABLE 2 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

TABLE 3 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

TABLE 4 FOOD CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

TABLE 5 FOOD CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

TABLE 6 HEMATOLOGY OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

TABLE 7 HEMATOLOGY OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

TABLE 8 BIOCHEMISTRY OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

TABLE 9 BIOCHEMISTRY OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

TABLE 10 URINALYSIS OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

TABLE 11 ORGAN WEIGHTS OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

TABLES (CONTINUED)

TABLE 12 INCIDENCES OF SELECTED NEOPLASTIC LESIONS OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

TABLE 13 INCIDENCES OF SELECTED NEOPLASTIC LESIONS OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

TABLE 14 INCIDENCES OF SELECTED NON-NEOPLASTIC LESIONS OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

TABLE 15 INCIDENCES OF SELECTED NON-NEOPLASTIC LESIONS OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

TABLE 16 HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER : B6D2F1/Crlj MALE MICE

TABLE 17 HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER : B6D2F1/Crlj FEMALE MICE

TABLE 18 CAUSE OF DEATH OF MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

TABLE 1 CONCENTRATIONS OF 1,2-DICHLOROPROPANE IN THE INHALATION CHAMBER OF THE 2-YEAR INHALATION STUDY

Group Name	Concentration(ppm) Mean ± S.D.
Control	0.0 ± 0.0
32 ppm	32.1 ± 0.2
80 ppm	80.2 ± 0.4
200 ppm	200.5 ± 1.2

TABLE 2 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

Week on Study	Control		32 ppm			80 ppm			200 ppm		
	Av. Wt.	No. of Surviv. <50>	Av. Wt.	% of cont.	No. of Surviv. <50>	Av. Wt.	% of cont.	No. of Surviv. <50>	Av. Wt.	% of cont.	No. of Surviv. <50>
0	23.3 (50)	50 / 50	23.3 (50)	100	50 / 50	23.3 (50)	100	50 / 50	23.3 (50)	100	50 / 50
1	24.5 (50)	50 / 50	24.2 (50)	99	50 / 50	24.5 (50)	100	50 / 50	24.4 (50)	100	50 / 50
2	25.4 (50)	50 / 50	25.1 (50)	99	50 / 50	25.4 (50)	100	50 / 50	25.0 (50)	98	50 / 50
3	26.1 (50)	50 / 50	25.6 (50)	98	50 / 50	26.1 (50)	100	50 / 50	25.4 (50)	97	50 / 50
4	26.6 (50)	50 / 50	26.3 (50)	99	50 / 50	26.8 (50)	101	50 / 50	26.2 (50)	98	50 / 50
5	27.0 (50)	50 / 50	26.7 (50)	99	50 / 50	27.4 (50)	101	50 / 50	26.6 (50)	99	50 / 50
6	27.9 (50)	50 / 50	26.8 (50)	96	50 / 50	28.0 (50)	100	50 / 50	27.2 (50)	97	50 / 50
7	28.2 (50)	50 / 50	27.0 (50)	96	50 / 50	28.5 (50)	101	50 / 50	27.6 (50)	98	50 / 50
8	29.0 (50)	50 / 50	28.0 (50)	97	50 / 50	29.4 (50)	101	50 / 50	28.1 (50)	97	50 / 50
9	29.4 (50)	50 / 50	28.7 (50)	98	50 / 50	29.9 (50)	102	50 / 50	28.3 (50)	96	50 / 50
10	30.0 (50)	50 / 50	29.6 (50)	99	50 / 50	30.4 (50)	101	50 / 50	29.3 (50)	98	50 / 50
11	30.3 (50)	50 / 50	30.0 (50)	99	50 / 50	30.9 (50)	102	50 / 50	29.4 (50)	97	50 / 50
12	31.2 (50)	50 / 50	30.8 (50)	99	50 / 50	32.0 (50)	103	50 / 50	30.0 (50)	96	50 / 50
13	31.7 (50)	50 / 50	31.7 (50)	100	50 / 50	32.6 (50)	103	50 / 50	30.9 (50)	97	50 / 50
14	32.3 (50)	50 / 50	32.3 (50)	100	50 / 50	33.4 (50)	103	50 / 50	31.2 (50)	97	50 / 50
18	34.5 (50)	50 / 50	35.2 (50)	102	50 / 50	35.9 (50)	104	50 / 50	33.7 (50)	98	50 / 50
22	36.6 (50)	50 / 50	37.2 (50)	102	50 / 50	38.2 (50)	104	50 / 50	35.3 (50)	96	50 / 50
26	38.5 (50)	50 / 50	39.7 (50)	103	50 / 50	40.2 (50)	104	50 / 50	37.3 (50)	97	50 / 50
30	40.2 (50)	50 / 50	41.5 (50)	103	50 / 50	42.0 (50)	104	50 / 50	38.9 (50)	97	50 / 50
34	42.0 (50)	50 / 50	43.2 (50)	103	50 / 50	43.7 (49)	104	49 / 50	40.6 (50)	97	50 / 50
38	43.3 (50)	50 / 50	44.8 (50)	103	50 / 50	44.9 (49)	104	49 / 50	41.6 (50)	96	50 / 50
42	44.4 (50)	50 / 50	45.8 (50)	103	50 / 50	46.2 (49)	104	49 / 50	42.9 (50)	97	50 / 50
46	45.8 (49)	49 / 50	47.2 (49)	103	49 / 50	47.7 (49)	104	49 / 50	44.3 (50)	97	50 / 50
50	46.7 (49)	49 / 50	47.8 (48)	102	48 / 50	48.4 (49)	104	49 / 50	45.3 (50)	97	50 / 50
54	47.1 (48)	48 / 50	48.4 (48)	103	48 / 50	48.8 (49)	104	49 / 50	46.0 (50)	98	50 / 50
58	47.6 (48)	48 / 50	48.7 (48)	102	48 / 50	48.8 (48)	103	48 / 50	46.0 (50)	97	50 / 50
62	47.9 (48)	48 / 50	50.2 (47)	105	47 / 50	49.4 (48)	103	48 / 50	46.6 (50)	97	50 / 50
66	48.5 (48)	48 / 50	50.8 (47)	105	47 / 50	50.6 (47)	104	47 / 50	46.9 (50)	97	50 / 50
70	49.3 (47)	47 / 50	51.3 (47)	104	47 / 50	50.7 (47)	103	47 / 50	47.4 (50)	96	50 / 50
74	50.1 (46)	46 / 50	52.1 (45)	104	45 / 50	51.0 (46)	102	46 / 50	47.9 (50)	96	50 / 50
78	50.1 (46)	46 / 50	52.7 (44)	105	44 / 50	50.8 (46)	101	46 / 50	47.9 (50)	96	50 / 50
82	50.2 (44)	44 / 50	53.4 (43)	106	43 / 50	51.4 (45)	102	45 / 50	48.5 (47)	97	47 / 50
86	49.5 (43)	43 / 50	53.7 (43)	108	43 / 50	53.2 (41)	107	41 / 50	48.9 (47)	99	47 / 50
90	50.1 (40)	40 / 50	54.4 (39)	109	39 / 50	53.1 (41)	106	41 / 50	48.8 (47)	97	47 / 50
94	49.6 (40)	40 / 50	53.5 (37)	108	37 / 50	52.7 (39)	106	39 / 50	49.4 (45)	100	45 / 50
98	48.6 (35)	35 / 50	53.3 (35)	110	35 / 50	52.6 (35)	108	35 / 50	48.9 (45)	101	45 / 50
102	47.2 (34)	34 / 50	52.1 (33)	110	33 / 50	51.0 (34)	108	34 / 50	48.3 (41)	102	41 / 50
104	46.8 (32)	32 / 50	51.4 (33)	110	33 / 50	49.9 (33)	107	33 / 50	47.8 (41)	102	41 / 50

< > : No. of effective animals, ( ) : No. of measured animals, Av. Wt. : Averaged body weight (Unit : g).

TABLE 3 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

Week on Study	Control		32 ppm			80 ppm			200 ppm		
	Av. Wt.	No. of Surviv. <50>	Av. Wt.	% of cont.	No. of Surviv. <50>	Av. Wt.	% of cont.	No. of Surviv. <50>	Av. Wt.	% of cont.	No. of Surviv. <50>
0	19.2 (50)	50 / 50	19.2 (50)	100	50 / 50	19.2 (50)	100	50 / 50	19.2 (50)	100	50 / 50
1	19.6 (50)	50 / 50	19.6 (50)	100	50 / 50	19.5 (50)	99	50 / 50	19.9 (50)	102	50 / 50
2	20.5 (50)	50 / 50	20.4 (50)	100	50 / 50	20.4 (50)	100	50 / 50	20.7 (50)	101	50 / 50
3	20.6 (50)	50 / 50	21.1 (50)	102	50 / 50	21.0 (50)	102	50 / 50	21.3 (50)	103	50 / 50
4	21.7 (50)	50 / 50	21.6 (50)	100	50 / 50	21.6 (50)	100	50 / 50	21.9 (50)	101	50 / 50
5	21.8 (50)	50 / 50	22.0 (50)	101	50 / 50	22.1 (50)	101	50 / 50	22.6 (50)	104	50 / 50
6	22.7 (50)	50 / 50	22.6 (50)	100	50 / 50	22.8 (50)	100	50 / 50	23.1 (50)	102	50 / 50
7	23.1 (50)	50 / 50	22.9 (50)	99	50 / 50	23.2 (50)	100	50 / 50	23.5 (50)	102	50 / 50
8	23.4 (50)	50 / 50	23.4 (50)	100	50 / 50	23.6 (50)	101	50 / 50	24.0 (50)	103	50 / 50
9	23.8 (50)	50 / 50	24.0 (50)	101	50 / 50	23.7 (50)	100	50 / 50	24.0 (50)	101	50 / 50
10	24.3 (50)	50 / 50	24.3 (50)	100	50 / 50	24.0 (50)	99	50 / 50	24.3 (50)	100	50 / 50
11	24.3 (50)	50 / 50	24.3 (50)	100	50 / 50	24.6 (50)	101	50 / 50	24.5 (50)	101	50 / 50
12	24.8 (50)	50 / 50	24.8 (50)	100	50 / 50	25.0 (50)	101	50 / 50	24.9 (50)	100	50 / 50
13	25.0 (50)	50 / 50	25.1 (50)	100	50 / 50	25.1 (50)	100	50 / 50	25.3 (50)	101	50 / 50
14	25.2 (50)	50 / 50	25.2 (50)	100	50 / 50	25.1 (50)	100	50 / 50	25.3 (50)	100	50 / 50
18	26.3 (50)	50 / 50	26.2 (50)	100	50 / 50	26.7 (50)	102	50 / 50	26.5 (50)	101	50 / 50
22	27.0 (50)	50 / 50	26.9 (50)	100	50 / 50	27.4 (50)	101	50 / 50	27.1 (50)	100	50 / 50
26	28.0 (50)	50 / 50	28.0 (50)	100	50 / 50	28.1 (50)	100	50 / 50	27.7 (50)	99	50 / 50
30	28.5 (50)	50 / 50	28.4 (50)	100	50 / 50	29.0 (50)	102	50 / 50	28.6 (50)	100	50 / 50
34	29.4 (50)	50 / 50	29.3 (50)	100	50 / 50	29.7 (50)	101	50 / 50	29.2 (50)	99	50 / 50
38	30.2 (50)	50 / 50	30.0 (50)	99	50 / 50	30.4 (50)	101	50 / 50	29.3 (49)	97	49 / 50
42	30.6 (50)	50 / 50	30.6 (50)	100	50 / 50	30.8 (50)	101	50 / 50	29.6 (49)	97	49 / 50
46	31.2 (50)	50 / 50	31.3 (49)	100	49 / 50	32.1 (50)	103	50 / 50	30.3 (49)	97	49 / 50
50	31.4 (50)	50 / 50	31.1 (48)	99	48 / 50	32.6 (50)	104	50 / 50	30.3 (49)	96	49 / 50
54	32.1 (50)	50 / 50	31.6 (48)	98	48 / 50	32.9 (50)	102	50 / 50	30.8 (49)	96	49 / 50
58	32.0 (50)	50 / 50	32.1 (48)	100	48 / 50	33.0 (50)	103	50 / 50	30.6 (47)	96	47 / 50
62	32.0 (49)	49 / 50	31.8 (47)	99	47 / 50	33.7 (48)	105	48 / 50	31.3 (46)	98	46 / 50
66	32.6 (49)	49 / 50	32.9 (46)	101	46 / 50	34.6 (47)	106	47 / 50	31.7 (44)	97	44 / 50
70	32.5 (48)	48 / 50	32.9 (45)	101	45 / 50	34.8 (45)	107	45 / 50	31.8 (44)	98	44 / 50
74	33.0 (48)	48 / 50	33.7 (43)	102	43 / 50	35.0 (43)	106	43 / 50	32.3 (44)	98	44 / 50
78	32.9 (46)	46 / 50	33.3 (42)	101	42 / 50	35.0 (41)	106	41 / 50	32.5 (43)	99	43 / 50
82	33.9 (46)	46 / 50	34.2 (42)	101	42 / 50	35.8 (41)	106	41 / 50	32.9 (42)	97	42 / 50
86	34.1 (46)	46 / 50	34.4 (40)	101	40 / 50	36.2 (38)	106	38 / 50	33.2 (40)	97	40 / 50
90	33.6 (44)	44 / 50	34.4 (39)	102	39 / 50	35.9 (36)	107	36 / 50	33.7 (38)	100	38 / 50
94	34.4 (41)	41 / 50	34.2 (36)	99	36 / 50	36.2 (33)	105	33 / 50	33.5 (34)	97	34 / 50
98	33.9 (36)	36 / 50	35.5 (33)	105	33 / 50	36.6 (31)	108	31 / 50	33.2 (31)	98	31 / 50
102	34.1 (32)	32 / 50	34.7 (29)	102	29 / 50	35.9 (28)	105	28 / 50	33.3 (30)	98	30 / 50
104	33.3 (29)	29 / 50	34.5 (28)	104	28 / 50	35.4 (26)	106	26 / 50	33.5 (30)	101	30 / 50

< > : No. of effective animals, ( ) : No. of measured animals, Av. Wt. : Averaged body weight (Unit : g).

TABLE 4 FOOD CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

Week on Study	Control		32 ppm			80 ppm			200 ppm		
	Av. FC.	No. of Surviv. <50>	Av. FC.	% of cont.	No. of Surviv. <50>	Av. FC.	% of cont.	No. of Surviv. <50>	Av. FC.	% of cont.	No. of Surviv. <50>
1	3.9 (50)	50 / 50	3.8 (50)	97	50 / 50	3.9 (50)	100	50 / 50	3.7 (50)	95	50 / 50
2	3.9 (50)	50 / 50	3.9 (50)	100	50 / 50	3.9 (50)	100	50 / 50	3.8 (50)	97	50 / 50
3	3.9 (50)	50 / 50	3.8 (50)	97	50 / 50	3.9 (50)	100	50 / 50	3.8 (50)	97	50 / 50
4	4.0 (50)	50 / 50	3.9 (50)	98	50 / 50	4.0 (50)	100	50 / 50	4.0 (50)	100	50 / 50
5	4.0 (50)	50 / 50	4.0 (50)	100	50 / 50	4.1 (50)	103	50 / 50	4.1 (50)	103	50 / 50
6	4.3 (50)	50 / 50	4.1 (50)	95	50 / 50	4.2 (50)	98	50 / 50	4.3 (50)	100	50 / 50
7	4.1 (50)	50 / 50	4.2 (50)	102	50 / 50	4.2 (50)	102	50 / 50	4.3 (50)	105	50 / 50
8	4.2 (50)	50 / 50	4.3 (50)	102	50 / 50	4.2 (50)	100	50 / 50	4.3 (50)	102	50 / 50
9	4.2 (50)	50 / 50	4.3 (50)	102	50 / 50	4.3 (50)	102	50 / 50	4.3 (50)	102	50 / 50
10	4.3 (50)	50 / 50	4.5 (50)	105	50 / 50	4.3 (50)	100	50 / 50	4.5 (50)	105	50 / 50
11	4.4 (50)	50 / 50	4.4 (50)	100	50 / 50	4.4 (50)	100	50 / 50	4.3 (50)	98	50 / 50
12	4.4 (50)	50 / 50	4.5 (50)	102	50 / 50	4.4 (50)	100	50 / 50	4.4 (50)	100	50 / 50
13	4.5 (50)	50 / 50	4.5 (50)	100	50 / 50	4.4 (50)	98	50 / 50	4.5 (50)	100	50 / 50
14	4.5 (50)	50 / 50	4.4 (50)	98	50 / 50	4.4 (50)	98	50 / 50	4.5 (50)	100	50 / 50
18	4.6 (50)	50 / 50	4.6 (50)	100	50 / 50	4.5 (50)	98	50 / 50	4.6 (50)	100	50 / 50
22	4.5 (50)	50 / 50	4.5 (50)	100	50 / 50	4.5 (50)	100	50 / 50	4.5 (50)	100	50 / 50
26	4.6 (50)	50 / 50	4.7 (50)	102	50 / 50	4.6 (50)	100	50 / 50	4.7 (50)	102	50 / 50
30	4.6 (50)	50 / 50	4.7 (50)	102	50 / 50	4.6 (50)	100	50 / 50	4.6 (50)	100	50 / 50
34	4.7 (50)	50 / 50	4.7 (50)	100	50 / 50	4.7 (49)	100	49 / 50	4.7 (50)	100	50 / 50
38	4.8 (50)	50 / 50	4.8 (50)	100	50 / 50	4.9 (48)	102	49 / 50	4.7 (49)	98	50 / 50
42	4.9 (50)	50 / 50	4.9 (50)	100	50 / 50	4.9 (49)	100	49 / 50	4.9 (50)	100	50 / 50
46	4.9 (49)	49 / 50	4.9 (49)	100	49 / 50	4.9 (49)	100	49 / 50	4.9 (50)	100	50 / 50
50	5.1 (49)	49 / 50	5.1 (46)	100	48 / 50	5.0 (49)	98	49 / 50	5.0 (50)	98	50 / 50
54	4.9 (48)	48 / 50	4.9 (48)	100	48 / 50	4.9 (49)	100	49 / 50	4.9 (50)	100	50 / 50
58	4.8 (48)	48 / 50	4.8 (48)	100	48 / 50	4.8 (48)	100	48 / 50	4.8 (50)	100	50 / 50
62	5.1 (48)	48 / 50	5.2 (47)	102	47 / 50	5.2 (48)	102	48 / 50	5.1 (50)	100	50 / 50
66	5.1 (48)	48 / 50	5.2 (47)	102	47 / 50	5.1 (47)	100	47 / 50	5.0 (50)	98	50 / 50
70	5.2 (47)	47 / 50	5.1 (47)	98	47 / 50	5.0 (47)	96	47 / 50	5.1 (50)	98	50 / 50
74	5.2 (46)	46 / 50	5.3 (45)	102	45 / 50	5.1 (46)	98	46 / 50	5.1 (50)	98	50 / 50
78	5.1 (46)	46 / 50	5.3 (44)	104	44 / 50	5.1 (46)	100	46 / 50	5.0 (50)	98	50 / 50
82	5.1 (44)	44 / 50	5.4 (43)	106	43 / 50	5.3 (45)	104	45 / 50	5.2 (47)	102	47 / 50
86	5.2 (43)	43 / 50	5.4 (43)	104	43 / 50	5.4 (41)	104	41 / 50	5.3 (47)	102	47 / 50
90	5.2 (40)	40 / 50	5.3 (39)	102	39 / 50	5.4 (41)	104	41 / 50	5.2 (47)	100	47 / 50
94	5.1 (40)	40 / 50	5.1 (37)	100	37 / 50	5.2 (39)	102	39 / 50	5.1 (45)	100	45 / 50
98	5.0 (35)	35 / 50	5.4 (35)	108	35 / 50	5.1 (35)	102	35 / 50	5.2 (45)	104	45 / 50
102	5.0 (34)	34 / 50	5.3 (33)	106	33 / 50	5.1 (34)	102	34 / 50	5.2 (41)	104	41 / 50
104	5.1 (32)	32 / 50	5.2 (33)	102	33 / 50	4.9 (33)	96	33 / 50	5.1 (41)	100	41 / 50

< > : No. of effective animals, ( ) : No. of measured animals, Av. FC. : Averaged food consumption (Unit : g).

TABLE 5 FOOD CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

Week on Study	Control		32 ppm			80 ppm			200 ppm		
	Av. FC.	No. of Surviv. <50>	Av. FC.	% of cont.	No. of Surviv. <50>	Av. FC.	% of cont.	No. of Surviv. <50>	Av. FC.	% of cont.	No. of Surviv. <50>
1	3.3 (50)	50 / 50	3.3 (50)	100	50 / 50	3.1 (50)	94	50 / 50	3.0 (50)	91	50 / 50
2	3.3 (50)	50 / 50	3.4 (50)	103	50 / 50	3.4 (50)	103	50 / 50	3.4 (50)	103	50 / 50
3	3.4 (50)	50 / 50	3.5 (50)	103	50 / 50	3.5 (50)	103	50 / 50	3.5 (50)	103	50 / 50
4	3.6 (50)	50 / 50	3.7 (50)	103	50 / 50	3.7 (50)	103	50 / 50	3.7 (50)	103	50 / 50
5	3.7 (50)	50 / 50	3.8 (50)	103	50 / 50	3.8 (50)	103	50 / 50	3.9 (50)	105	50 / 50
6	4.0 (50)	50 / 50	4.0 (50)	100	50 / 50	4.1 (50)	103	50 / 50	4.1 (50)	103	50 / 50
7	4.1 (50)	50 / 50	4.1 (50)	100	50 / 50	4.1 (50)	100	50 / 50	4.2 (50)	102	50 / 50
8	4.0 (50)	50 / 50	4.1 (50)	103	50 / 50	4.1 (50)	103	50 / 50	4.2 (50)	105	50 / 50
9	4.1 (50)	50 / 50	4.2 (50)	102	50 / 50	4.2 (50)	102	50 / 50	4.2 (50)	102	50 / 50
10	4.2 (50)	50 / 50	4.2 (50)	100	50 / 50	4.3 (50)	102	50 / 50	4.3 (50)	102	50 / 50
11	4.2 (50)	50 / 50	4.2 (50)	100	50 / 50	4.3 (45)	102	50 / 50	4.2 (50)	100	50 / 50
12	4.2 (50)	50 / 50	4.2 (50)	100	50 / 50	4.2 (50)	100	50 / 50	4.2 (50)	100	50 / 50
13	4.2 (50)	50 / 50	4.2 (50)	100	50 / 50	4.3 (50)	102	50 / 50	4.5 (50)	107	50 / 50
14	4.2 (50)	50 / 50	4.1 (50)	98	50 / 50	4.2 (50)	100	50 / 50	4.4 (50)	105	50 / 50
18	4.3 (50)	50 / 50	4.2 (50)	98	50 / 50	4.3 (50)	100	50 / 50	4.4 (50)	102	50 / 50
22	4.2 (50)	50 / 50	4.1 (50)	98	50 / 50	4.2 (50)	100	50 / 50	4.2 (48)	100	50 / 50
26	4.4 (50)	50 / 50	4.3 (50)	98	50 / 50	4.3 (50)	98	50 / 50	4.4 (50)	100	50 / 50
30	4.5 (50)	50 / 50	4.3 (50)	96	50 / 50	4.4 (50)	98	50 / 50	4.4 (50)	98	50 / 50
34	4.5 (50)	50 / 50	4.4 (50)	98	50 / 50	4.4 (50)	98	50 / 50	4.5 (50)	100	50 / 50
38	4.6 (50)	50 / 50	4.4 (50)	96	50 / 50	4.5 (50)	98	50 / 50	4.4 (49)	96	49 / 50
42	4.6 (50)	50 / 50	4.5 (50)	98	50 / 50	4.5 (50)	98	50 / 50	4.5 (49)	98	49 / 50
46	4.6 (50)	50 / 50	4.6 (49)	100	49 / 50	4.6 (50)	100	50 / 50	4.6 (49)	100	49 / 50
50	4.7 (50)	50 / 50	4.7 (48)	100	48 / 50	4.7 (50)	100	50 / 50	4.6 (49)	98	49 / 50
54	4.6 (50)	50 / 50	4.5 (48)	98	48 / 50	4.5 (50)	98	50 / 50	4.4 (49)	96	49 / 50
58	4.4 (50)	50 / 50	4.4 (48)	100	48 / 50	4.4 (50)	100	50 / 50	4.3 (47)	98	47 / 50
62	4.6 (49)	49 / 50	4.4 (47)	96	47 / 50	4.7 (48)	102	48 / 50	4.6 (46)	100	46 / 50
66	4.7 (48)	49 / 50	4.6 (46)	98	46 / 50	4.5 (47)	96	47 / 50	4.5 (44)	96	44 / 50
70	4.5 (48)	48 / 50	4.5 (45)	100	45 / 50	4.6 (45)	102	45 / 50	4.6 (44)	102	44 / 50
74	4.6 (48)	48 / 50	4.5 (43)	98	43 / 50	4.6 (43)	100	43 / 50	4.5 (44)	98	44 / 50
78	4.5 (46)	46 / 50	4.4 (42)	98	42 / 50	4.7 (41)	104	41 / 50	4.6 (43)	102	43 / 50
82	4.7 (46)	46 / 50	4.7 (42)	100	42 / 50	4.7 (41)	100	41 / 50	4.7 (42)	100	42 / 50
86	4.8 (46)	46 / 50	4.7 (40)	98	40 / 50	5.0 (38)	104	38 / 50	4.7 (40)	98	40 / 50
90	4.6 (44)	44 / 50	4.6 (39)	100	39 / 50	4.9 (36)	107	36 / 50	4.9 (38)	107	38 / 50
94	4.8 (41)	41 / 50	4.5 (36)	94	36 / 50	4.8 (33)	100	33 / 50	4.7 (34)	98	34 / 50
98	4.7 (36)	36 / 50	4.7 (33)	100	33 / 50	4.8 (31)	102	31 / 50	4.7 (31)	100	31 / 50
102	4.9 (32)	32 / 50	4.8 (29)	98	29 / 50	4.9 (28)	100	28 / 50	4.8 (30)	98	30 / 50
104	4.7 (29)	29 / 50	4.7 (28)	100	28 / 50	4.7 (26)	100	26 / 50	4.6 (30)	98	30 / 50

< > : No. of effective animals, ( ) : No. of measured animals, Av. FC. : Averaged food consumption (Unit : g).

TABLE 6 HEMATOLOGY OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

Group Name	Control	32 ppm	80 ppm	200 ppm
No. of examined animals	32	33	32	40
MCHC (g/dL)	32.4 ± 1.5	32.3 ± 0.9	31.9 ± 1.3 *	31.9 ± 0.9 **

Mean ± S.D.
Significant difference: * : p≦0.05 ** : p≦0.01 Test of Dunnett

TABLE 7 HEMATOLOGY OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

Group Name	Control	32 ppm	80 ppm	200 ppm
No. of examined animals	29	26	25	28
MCV (fL)	44.3 ± 2.2	44.6 ± 1.7	45.2 ± 2.7	46.7 ± 4.9 **
MCHC (g/dL)	33.0 ± 0.9	33.0 ± 1.0	32.5 ± 1.1	32.0 ± 2.1 *

Mean ± S.D.
Significant difference: * : p≦0.05 ** : p≦0.01 Test of Dunnett

TABLE 8 BIOCHEMISTRY OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

Group Name	Control	32 ppm	80 ppm	200 ppm
No. of examined animals	32	33	32	40
UREA NITROGEN (mg/dL)	25.9 ± 12.0	22.3 ± 15.7 **	21.1 ± 5.5 **	21.3 ± 5.2 **
POTASSIUM (mEq/L)	4.2 ± 0.4	4.1 ± 0.3	4.4 ± 0.7 *	4.1 ± 0.3

Mean ± S.D.
Significant difference: * : p≦0.05 ** : p≦0.01 Test of Dunnett

TABLE 9 BIOCHEMISTRY OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

Group Name	Control	32 ppm	80 ppm	200 ppm
No. of examined animals	29	27	25	28
A/G RATIO	1.1 ± 0.1	1.3 ± 0.3	1.2 ± 0.3	1.4 ± 0.3 **

Mean ± S.D.
Significant difference: * : p≦0.05 ** : p≦0.01 Test of Dunnett

TABLE 10 URINALYSIS OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

Group Name		Control	32 ppm	80 ppm	200 ppm
No. of examined animals		32	33	33	41
	Grade				
Protein	−	0	0	0	0
	±	11	22	14	16
	+	18	8	16	23
	2+	2	3	3	2
	3+	1	0	0	0
	4+	0	0	0	0
	Chi square test		*		

Significant difference: * : p≦0.05 ** : p≦0.01

TABLE 11 ORGAN WEIGHTS OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

Group Name	Control	32 ppm		80 ppm		200 ppm	
No. of examined animals	32	33		33		41	
Body weight (g)	41.9 ± 7.5	46.8 ± 7.4		45.5 ± 8.0		44.0 ± 8.1	
Testes (g)	0.230 ± 0.027	0.230 ± 0.041		0.215 ± 0.038		0.224 ± 0.038	
Testes (%)	0.562 ± 0.101	0.496 ± 0.080	*	0.487 ± 0.127	*	0.519 ± 0.096	
Kidneys (g)	0.634 ± 0.048	0.705 ± 0.048	**	0.764 ± 0.212	**	0.989 ± 1.690	**
Kidneys (%)	1.551 ± 0.269	1.540 ± 0.251		1.732 ± 0.560		2.290 ± 3.833	*
Spleen (g)	0.192 ± 0.556	0.163 ± 0.350		0.117 ± 0.105		0.145 ± 0.107	*
Spleen (%)	0.496 ± 1.456	0.424 ± 1.085		0.276 ± 0.292		0.343 ± 0.262	
Brain (g)	0.453 ± 0.020	0.445 ± 0.017		0.451 ± 0.014		0.456 ± 0.013	
Brain (%)	1.115 ± 0.211	0.976 ± 0.169	*	1.028 ± 0.226		1.074 ± 0.206	

Mean ± S.D.
Significant difference: * : $p \leqq 0.05$ ** : $p \leqq 0.01$ Test of Dunnett

TABLE 12 INCIDENCES OF SELECTED NEOPLASTIC LESIONS OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

Group Name	Control	32 ppm	80 ppm	200 ppm	Peto	Cochran-
Number of examined animals	50	50	50	50	test	Armitage test
lung	<50>	<50>	<50>	<50>		
bronchiolar-alveolar adenoma	5 (10 %)	14 (28 %) *	9 (18 %)	12 (24 %)		
bronchiolar-alveolar carcinoma	4 (8 %)	6 (12 %)	6 (12 %)	8 (16 %)		
spleen	<50>	<50>	<50>	<50>		
hemangioma	0 (0 %)	1 (2 %)	0 (0 %)	1 (2 %)		
hemangiosarcoma	0 (0 %)	3 (6 %)	3 (6 %)	5 (10 %) *		
liver	<50>	<50>	<50>	<50>		
histiocytic sarcoma	1 (2 %)	4 (8 %)	7 (14 %) *	0 (0 %)		
Harderian gland	<50>	<50>	<49>	<50>		
adenoma	1 (2 %)	2 (4 %)	3 (6 %)	6 (12 %)	↑	↑

Significant difference : * : p≦0.05 ** : p≦0.01 Fisher's exact test for neoplastic lesion
↑(↓) : p≦0.05 ↑ ↑(↓ ↓) : p≦0.01 Peto or Cochran-Armitage test for neoplastic lesion
< > : Number of animals examined at the site

TABLE 13 INCIDENCES OF SELECTED NEOPLASTIC LESIONS OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

Group Name	Control	32 ppm	80 ppm	200 ppm	Peto	Cochran-
Number of examined animals	50	50	50	50	test	Armitage test
lung	<50>	<50>	<50>	<50>		
bronchiolar-alveolar adenoma	1 (2 %)	4 (8 %)	4 (8 %)	4 (8 %)		
bronchiolar-alveolar carcinoma	1 (2 %)	1 (2 %)	1 (2 %)	4 (8 %)	↑	

Significant difference : * : p≦0.05 ** : p≦0.01 Fisher's exact test for neoplastic lesion
↑(↓) : p≦0.05 ↑ ↑(↓ ↓) : p≦0.01 Peto or Cochran-Armitage test for neoplastic lesion
< > : Number of animals examined at the site

TABLE 14 INCIDENCES OF SELECTED NON-NEOPLASTIC LESIONS OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

Group Name	Control				32 ppm				80 ppm				200 ppm			
Number of examined animals	50				50				50				50			
Grade of non-neoplastic lesion	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
kidney	<50>				<50>				<50>				<50>			
basophilic change	8	2	1	0	30	0	0	0 **	26	2	0	0 **	22	9	2	0 **
mineralization:cortex	7	0	0	0	20	3	0	0 **	26	4	0	0 **	15	3	0	0 *
nasal cavity	<50>				<50>				<50>				<50>			
atrophy:olfactory epithelium	1	0	0	0	0	1	0	0	19	0	0	0 **	20	0	0	0 **
eosinophilic change:olfactory epithelium	7	0	0	0	21	0	0	0 **	9	0	0	0	14	1	0	0

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< > : Number of animals examined at the site
Significant difference : * : p ≦ 0.05 ** : p ≦ 0.01 Test of Chi Square

TABLE 15 INCIDENCES OF SELECTED NON-NEOPLASTIC LESIONS OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

Group Name	Control				32 ppm				80 ppm				200 ppm			
Number of examined animals	50				50				50				50			
Grade of non-neoplastic lesion	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
nasal cavity	<50>				<50>				<50>				<50>			
atrophy:olfactory epithelium	8	0	0	0	7	1	0	0	19	0	0	0 *	16	0	0	0
respiratory metaplasia:olfactory epithelium	32	0	0	0	14	0	0	0 **	34	0	0	0	43	1	0	0 *
eosinophilic change:olfactory epithelium	23	3	0	0	11	0	0	0 **	12	2	0	0 *	19	2	0	0
respiratory metaplasia:gland	16	0	0	0	11	0	0	0	13	0	0	0	40	3	0	0 **
eosinophilic change:respiratory epithelium	31	14	2	0	34	5	2	0	29	6	0	0 **	35	8	2	0
nasopharynx	<50>				<50>				<50>				<50>			
eosinophilic change	8	4	1	0	3	1	2	0	2	0	1	0 *	4	1	1	0
adrenal	<50>				<50>				<50>				<50>			
spindle-cell hyperplasia	2	22	26	0	5	25	20	0	4	29	16	0	7	32	10	0 **

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< > : Number of animals examined at the site
Significant difference : * : p ≦ 0.05 ** : p ≦ 0.01 Test of Chi Square

TABLE 16 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. (%)
Harderian gland	1695			
Adenoma		83	4.9	0 - 10
Lung	1695			
Bronchiolar-alveolar adenoma [1)]		136	8.3	2 - 18
Bronchiolar-alveolar carcinoma [2)]		185	10.7	0 - 24
1)+2)		319	18.8	2 - 30
Spleen	1695			
Hemangioma [3)]		41	2.4	0 - 10
Hemangiosarcoma [4)]		49	2.9	0 - 10
3)+4)		145	8.6	0 - 14

Thirty four 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

TABLE 17 HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER : B6D2F1/Crlj FEMALE MICE

Organs Tumors	No. of animals examined	No. of animals bearing tumor	Incidence (%)	Min. - Max. (%)
Lung	1697			
Bronchiolar-alveolar adenoma [1)]		64	3.6	0 - 14
Bronchiolar-alveolar carcinoma [2)]		50	2.9	0 - 8
1)+2)		114	6.7	0 - 14

Thirty four 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

TABLE 18 CAUSE OF DEATH OF MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

	Male				Female			
Group name	Control	32 ppm	80 ppm	200 ppm	Control	32 ppm	80 ppm	200 ppm
Number of dead or moribund animals	18	17	17	9	21	22	24	20
Integumentary system lesions	1	0	0	0	0	0	0	0
Urinary retention	2	1	0	0	0	0	0	0
Hydronephrosis	0	0	1	1	2	0	1	1
Cardiovascular lesions	0	0	0	0	0	1	0	1
Tumor death : leukemia	4	5	3	2	5	13	9	6
subcutis	1	0	1	0	0	0	0	0
nasal cavity	1	0	0	0	0	0	0	0
lung	0	0	1	0	0	0	0	1
spleen	0	1	0	1	0	0	0	0
stomach	0	1	0	0	0	0	0	0
liver	6	5	10	3	0	1	0	0
pituitary gland	1	0	0	0	2	0	1	1
mammary gland	0	0	0	1	0	0	2	0
peripheral nerve	0	2	0	0	0	0	0	0
epididymis	1	0	0	1	—	—	—	—
uterus	—	—	—	—	10	6	11	6
peritoneum	0	0	0	0	0	0	0	1
retroperitoneum	0	0	0	0	0	1	0	0
No microscopical confirmation	1	2	1	0	2	0	0	3

FIGURES

FIGURE 1 1,2-DICHLOROPROPANE VAPOR GENERATION SYSTEM AND INHALATION SYSTEM

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

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

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

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

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

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

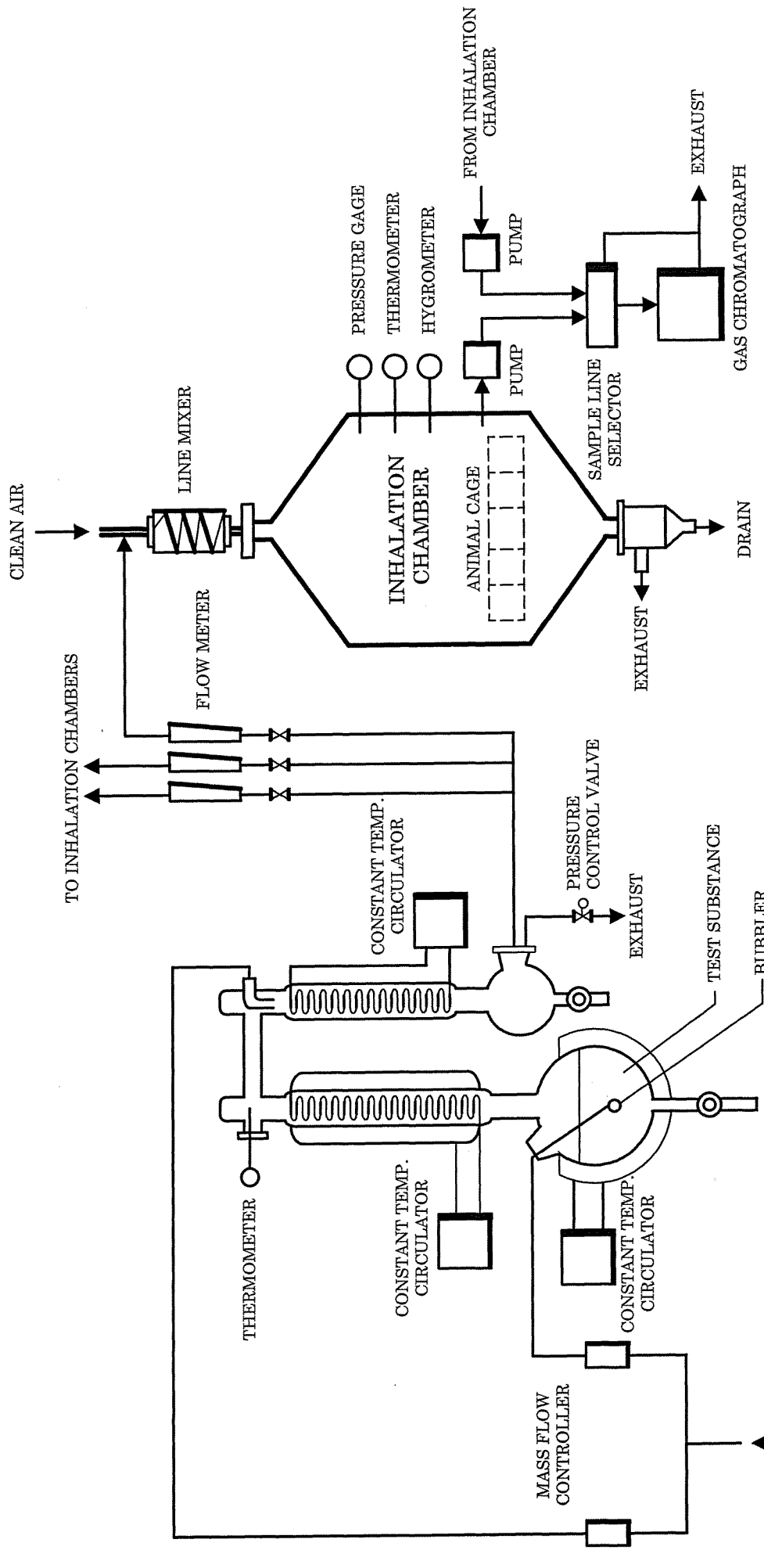


FIGURE 1 1,2-DICHLOROPROPANE VAPOR GENERATION SYSTEM AND INHALATION SYSTEM

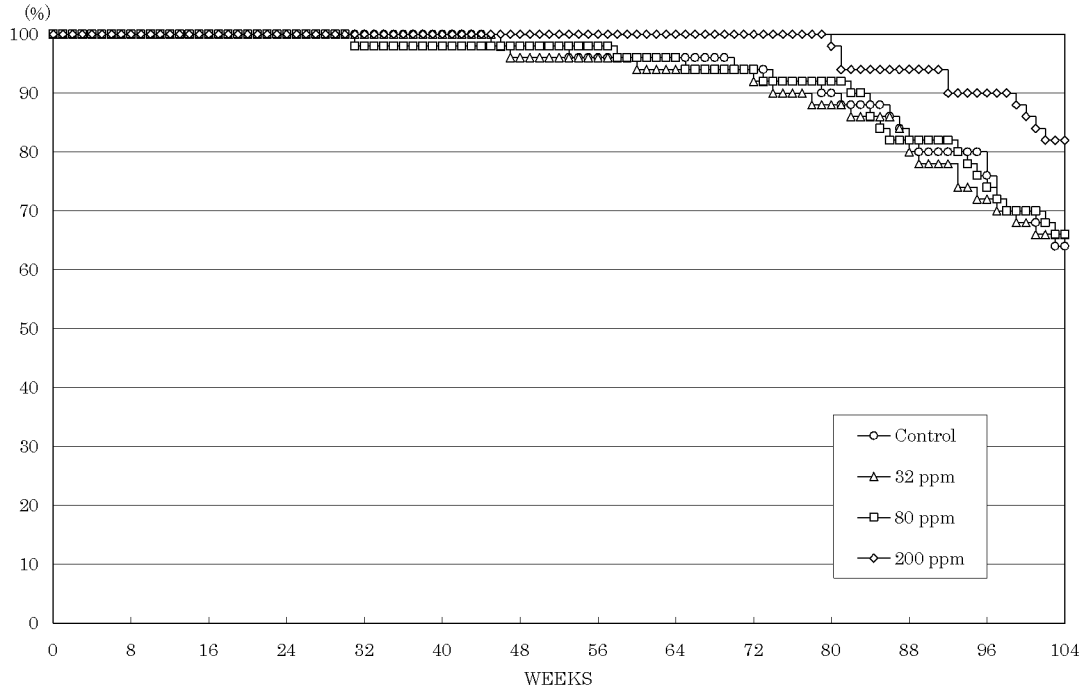


FIGURE 2 SURVIVAL ANIMAL RATE OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

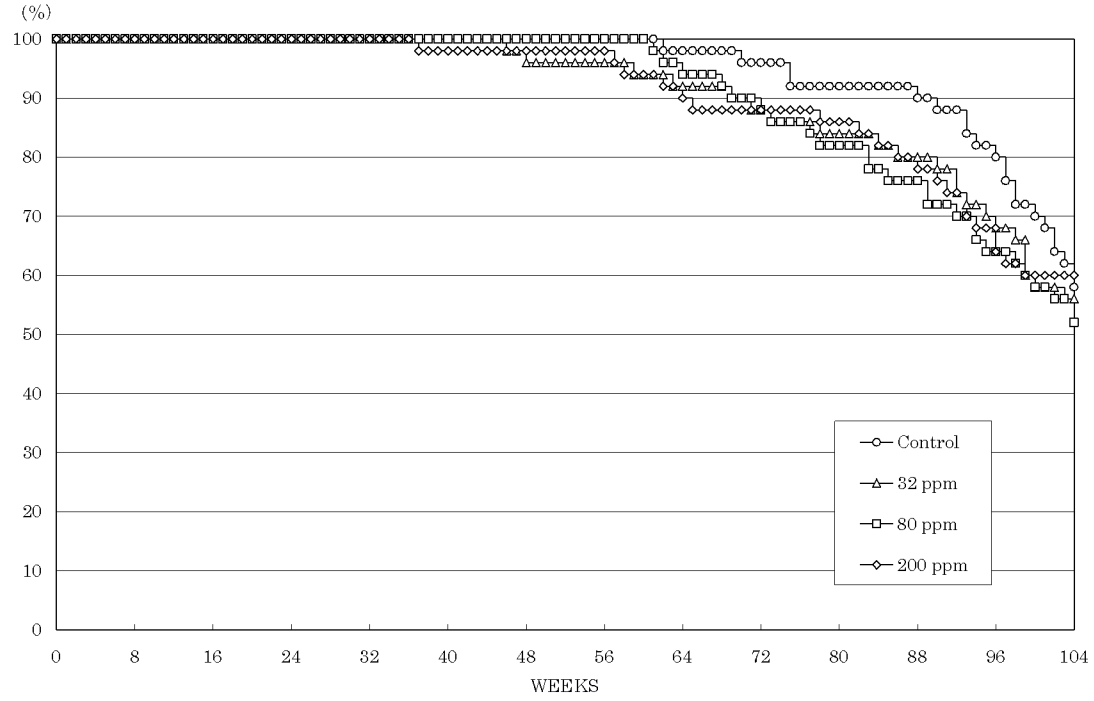


FIGURE 3 SURVIVAL ANIMAL RATE OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

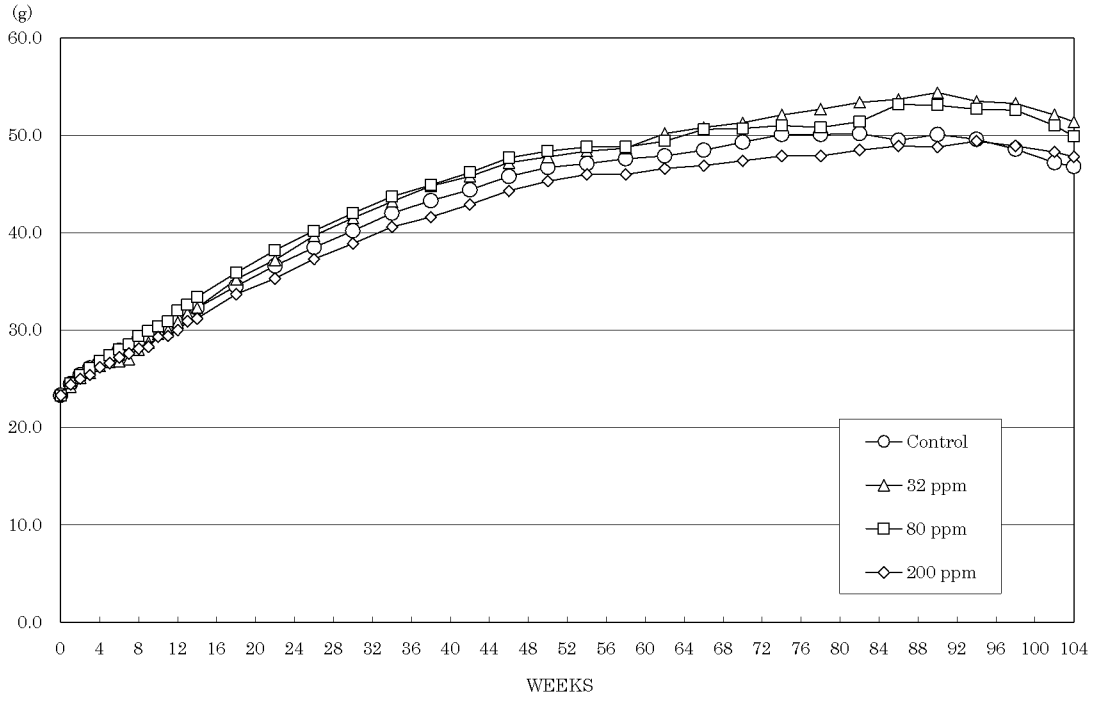


FIGURE 4 BODY WEIGHT CHANGES OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

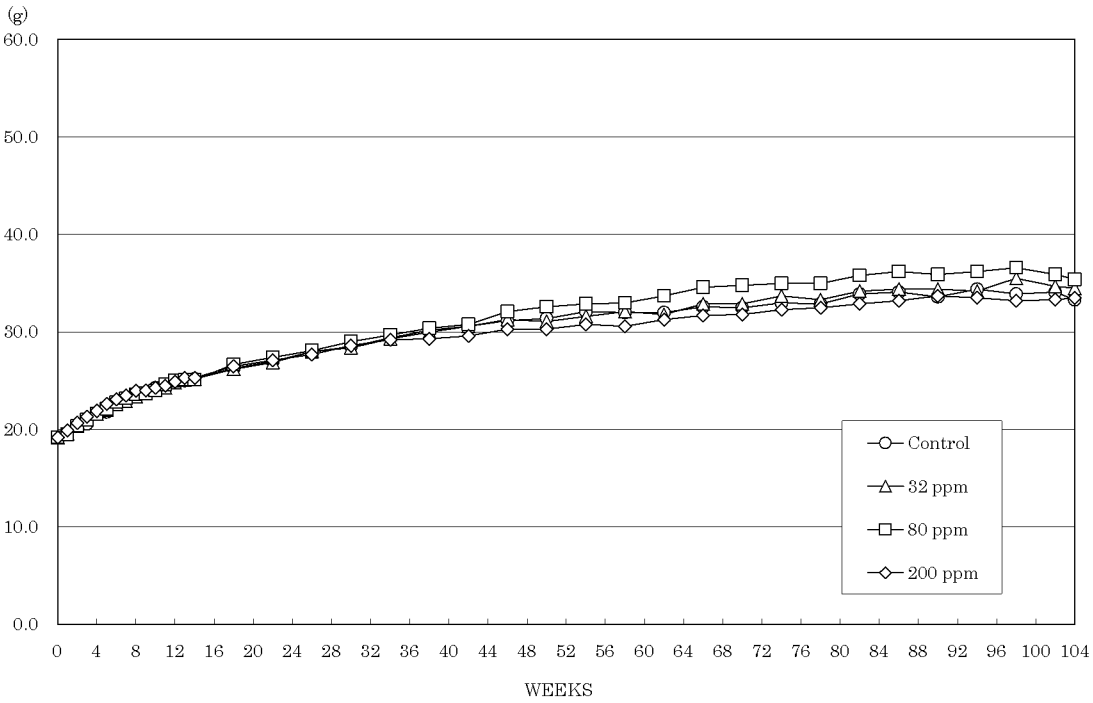


FIGURE 5 BODY WEIGHT CHANGES OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

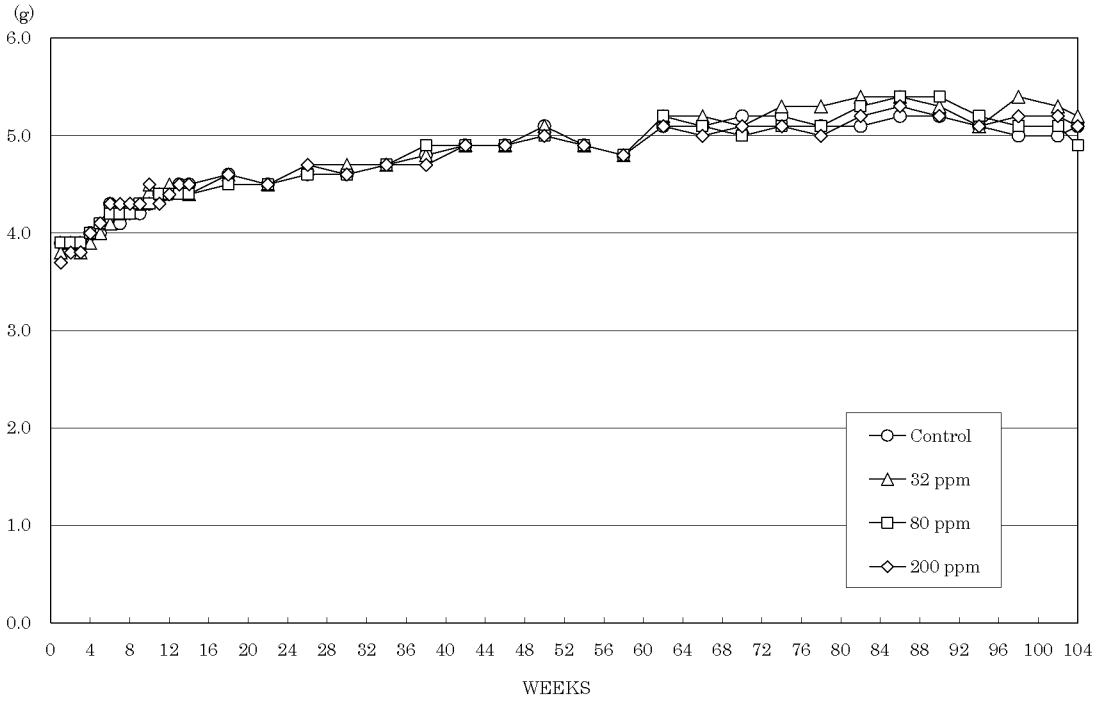


FIGURE 6 FOOD CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

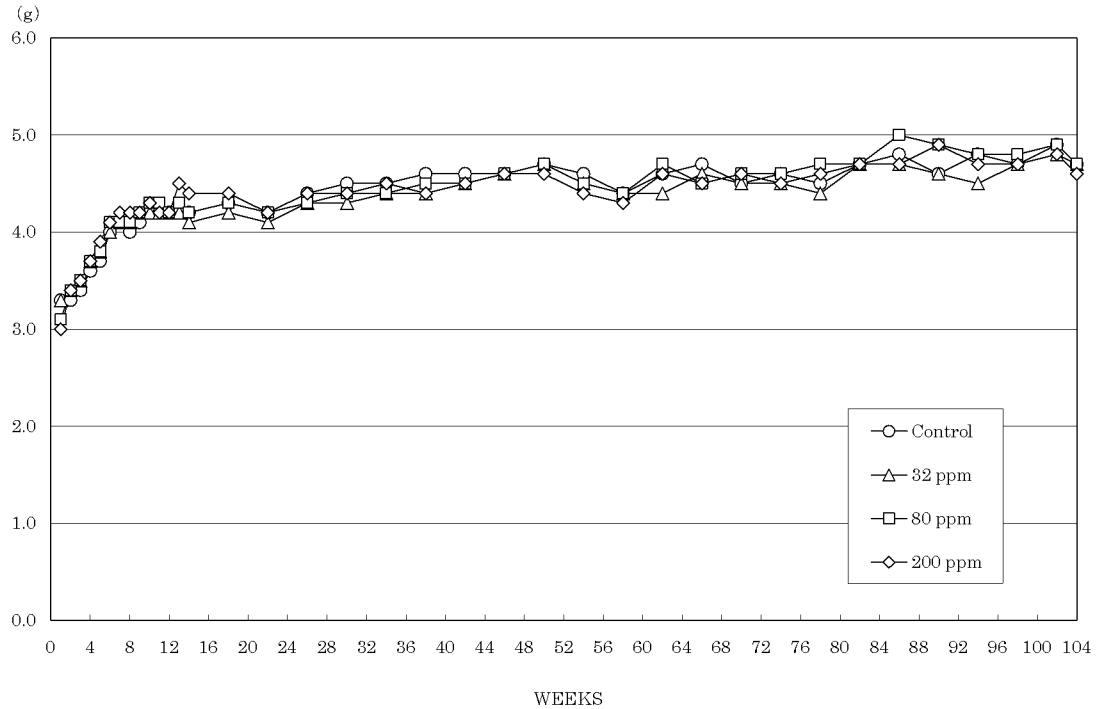
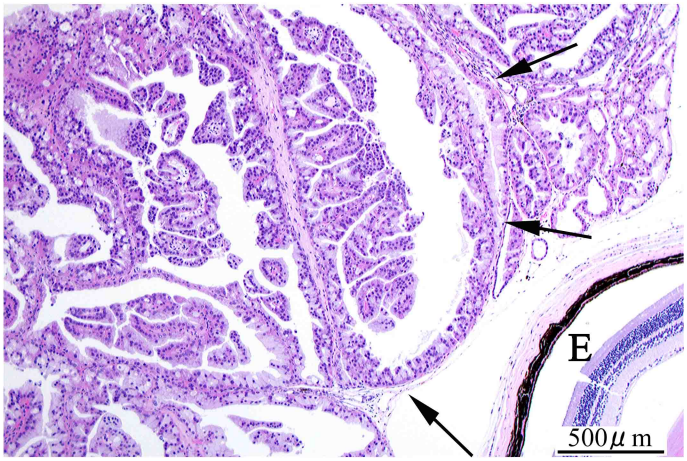
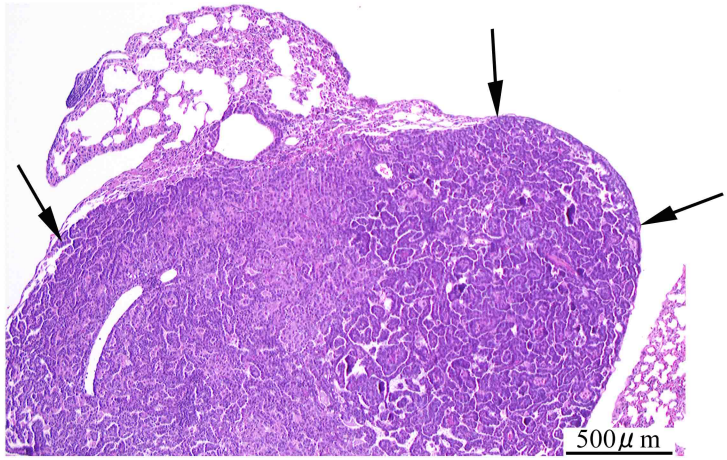


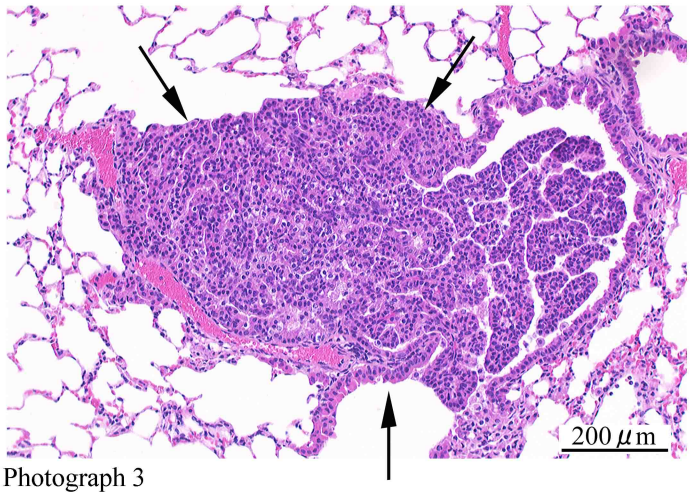
FIGURE 7 FOOD CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE



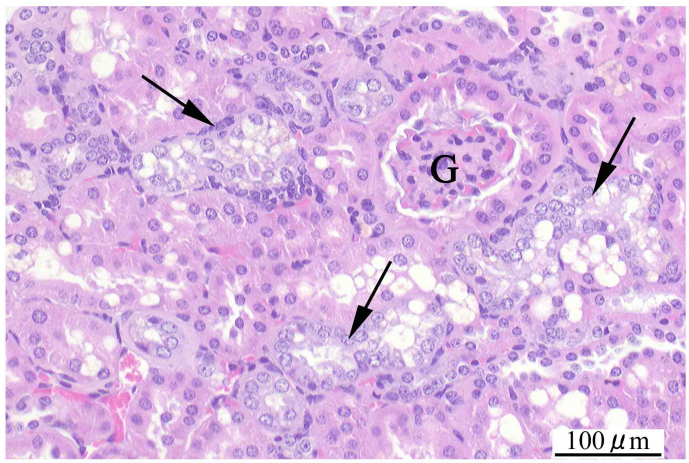
Photograph 1
Harderian gland: Adenoma (Arrows), Eye (E)
Mouse, Male, 200 ppm, Animal No. 0458-1310 (H&E)



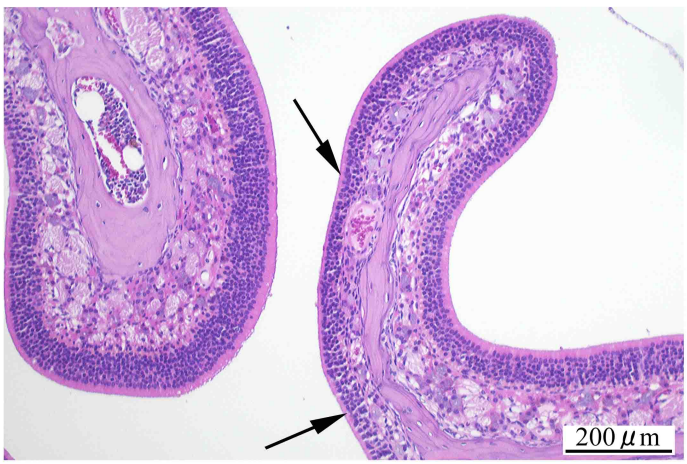
Photograph 2
Lung: Bronchiolar-alveolar carcinoma (Arrows)
Mouse, Female, 200 ppm, Animal No. 0458-2306 (H&E)



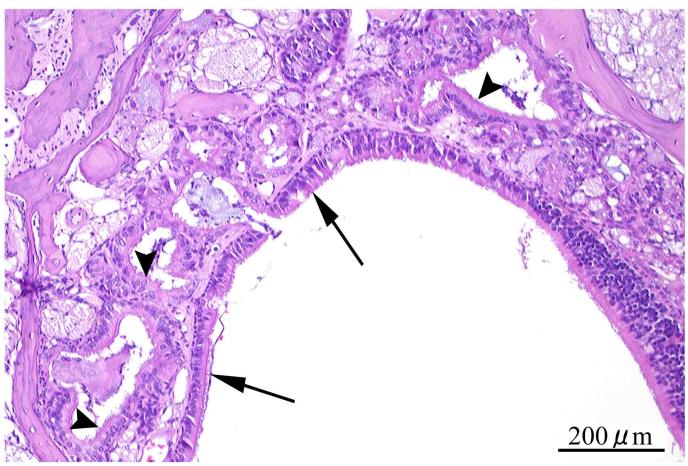
Photograph 3
Lung: Bronchiolar-alveolar adenoma (Arrows)
Mouse, Female, 200 ppm, Animal No. 0458-2301 (H&E)



Photograph 4
Kidney: Basophilic change (Arrows), Glomerulus(G)
Mouse, Male, 200 ppm, Animal No. 0458-1303 (H&E)



Photograph 5
Nasal cavity: Atrophy of olfactory epithelium (Arrows)
Mouse, Male, 200 ppm, Animal No. 0458-1338 (H&E)



Photograph 6
Nasal cavity: Respiratory metaplasia of olfactory epithelium (Arrows), Respiratory metaplasia of submucosal gland (Arrow heads)
Mouse, Female, 200 ppm, Animal No. 0458-2315 (H&E)