Summary of Inhalation Carcinogenicity Study of 1,2-Dichloropropane in F344 Rats

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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.

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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 F344/DuCrlCrlj rats of both sexes to 1,2DCP vapor at a target concentration of 0 (clean air), 80, 200 or 500 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: 7600 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 between any 1,2DCP-exposed group of either sex and the respective control. Body weights of males were slightly decreased in a dose-dependent manner, and the terminal body weight of the 500 ppm-exposed males was decreased to 89% as compared with the male control. Body weights of the 200 ppm-exposed females were slightly decreased until the 22nd week, and those of the 500 ppm-exposed females were slightly decreased until the 22nd week and after the 78th week, and the terminal body weight was decreased to 92% as compared with the control.

The incidence of squamous cell papillomas in the nasal cavity was increased dose-dependently in both the 1,2DCP-exposed males and females. Adenomas and adenoacanthomas were also observed in the nasal cavity of 1,2DCP-exposed males. The increased incidences of the nasal tumors were noted in the males exposed to 200 ppm and above, and in the females exposed to 500 ppm. The 1,2DCP-induced nasal lesions in males and females were observed in the respiratory epithelium (inflammation, squamous cell metaplasia, squamous cell hyperplasia, transitional epithelial hyperplasia and goblet cell hyperplasia), in the olfactory epithelium (atrophy, respiratory metaplasia and sclerosis of lamina propria), in the submucosal gland (hyperplasia), and in the nasal turbinate (adhesion).

Conclusions

In rats, there was some evidence of carcinogenic activity of 1,2DCP in males and females, based on the increased incidences of nasal cavity tumors (squamous cell papillomas, adenomas and adenoacanthomas).

TABLES

TABLES (CONTINUED)

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
80 ppm	80.2 ± 0.5
200 ppm	200.5 ± 1.3
500 ppm	500.2 ± 2.4

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

Week on Study	Control		80 ppm			200 ppm			500 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	122 (50)	50 / 50	122 (50)	100	50 / 50	122 (50)	100	50 / 50	122 (50)	100	50 / 50
1	153 (50)	50 / 50	144 (50)	94	50 / 50	142 (50)	93	50 / 50	138 (50)	90	50 / 50
2	185 (50)	50 / 50	177 (50)	96	50 / 50	173 (50)	94	50 / 50	168 (50)	91	50 / 50
3	212 (50)	50 / 50	200 (50)	94	50 / 50	194 (50)	92	50 / 50	187 (50)	88	50 / 50
4	232 (50)	50 / 50	221 (50)	95	50 / 50	214 (50)	92	50 / 50	204 (50)	88	50 / 50
5	250 (50)	50 / 50	241 (50)	96	50 / 50	233 (50)	93	50 / 50	223 (50)	89	50 / 50
6	264 (50)	50 / 50	253 (50)	96	50 / 50	244 (50)	92	50 / 50	234 (50)	89	50 / 50
7	278 (50)	50 / 50	266 (50)	96	50 / 50	256 (50)	92	50 / 50	246 (50)	88	50 / 50
8	292 (50)	50 / 50	277 (50)	95	50 / 50	269 (50)	92	50 / 50	258 (50)	88	50 / 50
9	301 (50)	50 / 50	287 (50)	95	50 / 50	277 (50)	92	50 / 50	267 (50)	89	50 / 50
10	307 (50)	50 / 50	294 (50)	96	50 / 50	285 (50)	93	50 / 50	274 (50)	89	50 / 50
11	314 (50)	50 / 50	302 (50)	96	50 / 50	290 (50)	92	50 / 50	280 (50)	89	50 / 50
12	321 (50)	50 / 50	309 (50)	96	50 / 50	299 (50)	93	50 / 50	288 (50)	90	50 / 50
13	327 (50)	50 / 50	315 (50)	96	50 / 50	304 (50)	93	50 / 50	292 (50)	89	50 / 50
14	332 (50)	50 / 50	315 (50)	95	50 / 50	304 (50)	92	50 / 50	293 (50)	88	50 / 50
18	347 (50)	50 / 50	330 (50)	95	50 / 50	318 (50)	92	50 / 50	309 (50)	89	50 / 50
22	363 (50)	50 / 50	345 (50)	95	50 / 50	334 (50)	92	50 / 50	324 (50)	89	50 / 50
26	375 (50)	50 / 50	356 (50)	95	50 / 50	346 (50)	92	50 / 50	336 (50)	90	50 / 50
30	383 (50)	50 / 50	364 (50)	95	50 / 50	355 (50)	93	50 / 50	346 (50)	90	50 / 50
34	391 (50)	50 / 50	371 (50)	95	50 / 50	364 (50)	93	50 / 50	356 (49)	91	49 / 50
38	399 (50)	50 / 50	378 (50)	95	50 / 50	373 (50)	93	50 / 50	365 (49)	91	49 / 50
42	405 (50)	50 / 50	385 (49)	95	49 / 50	379 (50)	94	50 / 50	373 (49)	92	49 / 50
46	411 (50)	50 / 50	390 (49)	95	49 / 50	383 (50)	93	50 / 50	377 (49)	92	49 / 50
50	420 (50)	50 / 50	399 (49)	95	49 / 50	392 (50)	93	50 / 50	386 (49)	92	49 / 50
54	421 (50)	50 / 50	401 (49)	95	49 / 50	396 (50)	94	50 / 50	387 (49)	92	49 / 50
58	424 (50)	50 / 50	402 (49)	95	49 / 50	397 (50)	94	50 / 50	389 (48)	92	48 / 50
62	426 (50)	50 / 50	405 (49)	95	49 / 50	400 (50)	94	50 / 50	392 (48)	92	48 / 50
66	430 (49)	49 / 50	406 (49)	94	49 / 50	402 (50)	93	50 / 50	394 (47)	92	47 / 50
70	430 (49)	49 / 50	407 (48)	95	48 / 50	402 (50)	93	50 / 50	395 (47)	92	47 / 50
74	431 (49)	49 / 50	409 (47)	95	47 / 50	403 (50)	94	50 / 50	394 (46)	91	46 / 50
78	432 (48)	48 / 50	410 (47)	95	47 / 50	405 (50)	94	50 / 50	393 (44)	91	44 / 50
82	428 (47)	47 / 50	409 (45)	96	45 / 50	404 (50)	94	50 / 50	391 (43)	91	43 / 50
86	424 (47)	47 / 50	407 (43)	96	43 / 50	402 (49)	95	49 / 50	388 (43)	92	43 / 50
90	423 (46)	46 / 50	408 (42)	96	42 / 50	401 (49)	95	49 / 50	386 (41)	91	41 / 50
94	421 (45)	45 / 50	409 (42)	97	42 / 50	394 (48)	94	48 / 50	385 (41)	91	41 / 50
98	416 (45)	45 / 50	403 (41)	97	41 / 50	387 (46)	93	46 / 50	380 (39)	91	39 / 50
102	407 (42)	42 / 50	400 (40)	98	40 / 50	382 (43)	94	43 / 50	381 (37)	94	37 / 50
104	409 (40)	40 / 50	396 (39)	97	39 / 50	382 (41)	93	41 / 50	362 (36)	89	36 / 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 RATS IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

Week on Study	Control		80 ppm			200 ppm			500 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	96 (50)	50 / 50	96 (50)	100	50 / 50	96 (50)	100	50 / 50	96 (50)	100	50 / 50
1	111 (50)	50 / 50	106 (50)	95	50 / 50	105 (50)	95	50 / 50	103 (50)	93	50 / 50
2	124 (50)	50 / 50	119 (50)	96	50 / 50	118 (50)	95	50 / 50	117 (50)	94	50 / 50
3	134 (50)	50 / 50	129 (50)	96	50 / 50	127 (50)	95	50 / 50	124 (50)	93	50 / 50
4	142 (50)	50 / 50	136 (50)	96	50 / 50	135 (50)	95	50 / 50	133 (50)	94	50 / 50
5	150 (50)	50 / 50	145 (50)	97	50 / 50	144 (50)	96	50 / 50	141 (50)	94	50 / 50
6	155 (50)	50 / 50	151 (50)	97	50 / 50	148 (50)	95	50 / 50	146 (50)	94	50 / 50
7	160 (50)	50 / 50	156 (50)	98	50 / 50	152 (50)	95	50 / 50	151 (50)	94	50 / 50
8	165 (50)	50 / 50	160 (50)	97	50 / 50	157 (50)	95	50 / 50	156 (50)	95	50 / 50
9	170 (50)	50 / 50	164 (50)	96	50 / 50	160 (50)	94	50 / 50	160 (50)	94	50 / 50
10	173 (50)	50 / 50	167 (50)	97	50 / 50	165 (50)	95	50 / 50	164 (50)	95	50 / 50
11	176 (50)	50 / 50	172 (50)	98	50 / 50	167 (50)	95	50 / 50	166 (50)	94	50 / 50
12	179 (50)	50 / 50	174 (50)	97	50 / 50	171 (50)	96	50 / 50	170 (50)	95	50 / 50
13	182 (50)	50 / 50	177 (50)	97	50 / 50	171 (50)	94	50 / 50	170 (50)	93	50 / 50
14	183 (50)	50 / 50	176 (50)	96	50 / 50	171 (50)	93	50 / 50	169 (50)	92	50 / 50
18	189 (50)	50 / 50	182 (50)	96	50 / 50	179 (50)	95	50 / 50	177 (50)	94	50 / 50
22	196 (50)	50 / 50	188 (50)	96	50 / 50	187 (50)	95	50 / 50	186 (50)	95	50 / 50
26	201 (50)	50 / 50	194 (50)	97	50 / 50	194 (50)	97	50 / 50	194 (50)	97	50 / 50
30	205 (50)	50 / 50	200 (50)	98	50 / 50	199 (50)	97	50 / 50	200 (50)	98	50 / 50
34	208 (50)	50 / 50	202 (50)	97	50 / 50	203 (50)	98	50 / 50	204 (50)	98	50 / 50
38	212 (50)	50 / 50	207 (50)	98	50 / 50	210 (50)	99	50 / 50	208 (50)	98	50 / 50
42	214 (50)	50 / 50	210 (50)	98	50 / 50	212 (50)	99	50 / 50	212 (50)	99	50 / 50
46	220 (50)	50 / 50	216 (50)	98	50 / 50	217 (50)	99	50 / 50	217 (50)	99	50 / 50
50	225 (50)	50 / 50	219 (49)	97	49 / 50	225 (50)	100	50 / 50	224 (48)	100	48 / 50
54	227 (50)	50 / 50	221 (49)	97	49 / 50	226 (49)	100	49 / 50	226 (48)	100	48 / 50
58	229 (50)	50 / 50	224 (49)	98	49 / 50	227 (48)	99	48 / 50	228 (47)	100	47 / 50
62	234 (50)	50 / 50	228 (49)	97	49 / 50	232 (47)	99	47 / 50	232 (46)	99	46 / 50
66	237 (49)	49 / 50	232 (49)	98	49 / 50	236 (47)	100	47 / 50	236 (46)	100	46 / 50
70	243 (47)	47 / 50	237 (49)	98	49 / 50	240 (47)	99	47 / 50	238 (46)	98	46 / 50
74	247 (46)	46 / 50	240 (48)	97	48 / 50	247 (46)	100	46 / 50	240 (46)	97	46 / 50
78	255 (46)	46 / 50	244 (47)	96	47 / 50	250 (46)	98	46 / 50	241 (44)	95	44 / 50
82	257 (45)	45 / 50	248 (47)	96	47 / 50	253 (46)	98	46 / 50	240 (43)	93	43 / 50
86	258 (44)	44 / 50	249 (47)	97	47 / 50	258 (46)	100	46 / 50	241 (41)	93	41 / 50
90	262 (43)	43 / 50	252 (47)	96	47 / 50	260 (46)	99	46 / 50	243 (40)	93	40 / 50
94	262 (43)	43 / 50	255 (47)	97	47 / 50	262 (44)	100	44 / 50	246 (38)	94	38 / 50
98	268 (40)	40 / 50	253 (45)	94	45 / 50	264 (42)	99	42 / 50	243 (36)	91	36 / 50
102	267 (38)	38 / 50	254 (42)	95	42 / 50	264 (40)	99	40 / 50	245 (34)	92	34 / 50
104	267 (37)	37 / 50	252 (41)	94	41 / 50	266 (38)	100	38 / 50	246 (32)	92	32 / 50

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

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

Week on Study	Control		80 ppm			200 ppm			500 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	15.7 (50)	50 / 50	13.5 (50)	86	50 / 50	13.1 (50)	83	50 / 50	12.3 (50)	78	50 / 50
2	16.1 (50)	50 / 50	15.2 (50)	94	50 / 50	14.5 (50)	90	50 / 50	14.6 (50)	91	50 / 50
3	16.6 (50)	50 / 50	15.8 (50)	95	50 / 50	14.9 (50)	90	50 / 50	14.8 (50)	89	50 / 50
4	17.5 (50)	50 / 50	17.0 (50)	97	50 / 50	16.9 (50)	97	50 / 50	16.8 (50)	96	50 / 50
5	17.0 (50)	50 / 50	17.2 (50)	101	50 / 50	16.6 (50)	98	50 / 50	16.4 (50)	96	50 / 50
6	17.0 (50)	50 / 50	16.7 (50)	98	50 / 50	15.9 (50)	94	50 / 50	16.2 (50)	95	50 / 50
7	16.7 (50)	50 / 50	16.7 (50)	100	50 / 50	16.0 (50)	96	50 / 50	16.2 (50)	97	50 / 50
8	17.0 (50)	50 / 50	16.7 (50)	98	50 / 50	15.9 (50)	94	50 / 50	15.8 (50)	93	50 / 50
9	16.8 (50)	50 / 50	16.6 (50)	99	50 / 50	16.0 (50)	95	50 / 50	16.0 (50)	95	50 / 50
10	16.9 (50)	50 / 50	16.9 (50)	100	50 / 50	16.1 (50)	95	50 / 50	15.7 (50)	93	50 / 50
11	16.4 (50)	50 / 50	16.2 (50)	99	50 / 50	15.6 (50)	95	50 / 50	15.5 (50)	95	50 / 50
12	16.4 (50)	50 / 50	16.4 (50)	100	50 / 50	15.5 (50)	95	50 / 50	15.1 (50)	92	50 / 50
13	16.0 (50)	50 / 50	15.9 (50)	99	50 / 50	15.4 (50)	96	50 / 50	14.8 (50)	93	50 / 50
14	16.5 (50)	50 / 50	15.4 (50)	93	50 / 50	14.4 (50)	87	50 / 50	14.0 (50)	85	50 / 50
18	16.3 (50)	50 / 50	15.7 (50)	96	50 / 50	14.9 (50)	91	50 / 50	14.9 (50)	91	50 / 50
22	16.5 (50)	50 / 50	16.2 (50)	98	50 / 50	15.5 (50)	94	50 / 50	15.3 (50)	93	50 / 50
26	16.5 (50)	50 / 50	15.9 (50)	96	50 / 50	15.5 (50)	94	50 / 50	15.2 (50)	92	50 / 50
30	16.7 (50)	50 / 50	16.2 (50)	97	50 / 50	16.0 (50)	96	50 / 50	16.0 (50)	96	50 / 50
34	16.7 (50)	50 / 50	16.3 (50)	98	50 / 50	16.3 (50)	98	50 / 50	16.0 (49)	96	49 / 50
38	16.9 (50)	50 / 50	16.5 (50)	98	50 / 50	16.4 (50)	97	50 / 50	16.4 (49)	97	49 / 50
42	17.2 (50)	50 / 50	16.9 (49)	98	49 / 50	16.7 (50)	97	50 / 50	16.7 (49)	97	49 / 50
46	17.1 (50)	50 / 50	16.7 (49)	98	49 / 50	16.4 (50)	96	50 / 50	16.5 (49)	96	49 / 50
50	17.3 (50)	50 / 50	17.3 (49)	100	49 / 50	17.0 (50)	98	50 / 50	16.8 (49)	97	49 / 50
54	16.7 (50)	50 / 50	16.7 (49)	100	49 / 50	16.4 (50)	98	50 / 50	16.4 (49)	98	49 / 50
58	16.9 (50)	50 / 50	16.7 (49)	99	49 / 50	16.4 (50)	97	50 / 50	16.3 (48)	96	48 / 50
62	16.7 (50)	50 / 50	16.5 (49)	99	49 / 50	16.4 (50)	98	50 / 50	16.3 (48)	98	48 / 50
66	17.0 (49)	49 / 50	16.3 (49)	96	49 / 50	16.3 (50)	96	50 / 50	16.2 (47)	95	47 / 50
70	16.9 (49)	49 / 50	16.4 (48)	97	48 / 50	16.4 (50)	97	50 / 50	16.4 (47)	97	47 / 50
74	16.6 (49)	49 / 50	16.5 (47)	99	47 / 50	16.4 (50)	99	50 / 50	16.1 (46)	97	46 / 50
78	16.9 (48)	48 / 50	16.3 (47)	96	47 / 50	16.7 (50)	99	50 / 50	16.2 (44)	96	44 / 50
82	16.5 (47)	47 / 50	16.5 (45)	100	45 / 50	16.5 (50)	100	50 / 50	16.1 (43)	98	43 / 50
86	16.8 (47)	47 / 50	16.8 (43)	100	43 / 50	16.7 (49)	99	49 / 50	16.2 (43)	96	43 / 50
90	16.8 (46)	46 / 50	16.8 (42)	100	42 / 50	16.9 (49)	101	49 / 50	16.6 (41)	99	41 / 50
94	16.9 (45)	45 / 50	17.3 (42)	102	42 / 50	16.1 (48)	95	48 / 50	16.6 (41)	98	41 / 50
98	16.6 (45)	45 / 50	16.6 (41)	100	41 / 50	15.6 (46)	94	46 / 50	15.7 (39)	95	39 / 50
102	16.6 (42)	42 / 50	17.0 (40)	102	40 / 50	16.1 (43)	97	43 / 50	16.0 (36)	96	37 / 50
104	16.5 (40)	40 / 50	16.2 (39)	98	39 / 50	16.2 (41)	98	41 / 50	15.2 (36)	92	36 / 50

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

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

Week on Study	Control		80 ppm			200 ppm			500 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	11.8 (50)	50 / 50	10.6 (50)	90	50 / 50	9.9 (50)	84	50 / 50	9.4 (50)	80	50 / 50
2	10.9 (50)	50 / 50	10.5 (50)	96	50 / 50	10.8 (50)	99	50 / 50	11.1 (50)	102	50 / 50
3	11.1 (50)	50 / 50	11.1 (50)	100	50 / 50	10.4 (50)	94	50 / 50	10.5 (50)	95	50 / 50
4	11.4 (50)	50 / 50	11.3 (50)	99	50 / 50	11.5 (50)	101	50 / 50	11.7 (50)	103	50 / 50
5	11.2 (50)	50 / 50	11.8 (50)	105	50 / 50	11.1 (50)	99	50 / 50	11.4 (50)	102	50 / 50
6	11.0 (50)	50 / 50	11.2 (50)	102	50 / 50	11.0 (50)	100	50 / 50	11.3 (50)	103	50 / 50
7	10.7 (50)	50 / 50	11.3 (50)	106	50 / 50	10.5 (50)	98	50 / 50	10.9 (50)	102	50 / 50
8	10.7 (50)	50 / 50	10.6 (50)	99	50 / 50	10.8 (50)	101	50 / 50	11.2 (50)	105	50 / 50
9	11.1 (50)	50 / 50	11.1 (50)	100	50 / 50	10.4 (50)	94	50 / 50	10.9 (50)	98	50 / 50
10	11.0 (50)	50 / 50	11.1 (50)	101	50 / 50	10.9 (50)	99	50 / 50	11.3 (50)	103	50 / 50
11	11.0 (50)	50 / 50	10.9 (50)	99	50 / 50	10.2 (50)	93	50 / 50	10.6 (50)	96	50 / 50
12	10.6 (50)	50 / 50	10.9 (50)	103	50 / 50	10.6 (50)	100	50 / 50	10.8 (50)	102	50 / 50
13	10.9 (50)	50 / 50	11.0 (50)	101	50 / 50	10.0 (50)	92	50 / 50	10.3 (50)	94	50 / 50
14	10.7 (50)	50 / 50	10.5 (50)	98	50 / 50	9.9 (50)	93	50 / 50	9.9 (50)	93	50 / 50
18	10.6 (50)	50 / 50	10.5 (50)	99	50 / 50	10.7 (50)	101	50 / 50	10.8 (50)	102	50 / 50
22	10.5 (50)	50 / 50	10.7 (50)	102	50 / 50	11.2 (50)	107	50 / 50	11.2 (50)	107	50 / 50
26	10.9 (50)	50 / 50	10.8 (50)	99	50 / 50	10.9 (50)	100	50 / 50	11.2 (50)	103	50 / 50
30	11.2 (50)	50 / 50	11.3 (50)	101	50 / 50	11.5 (50)	103	50 / 50	11.8 (50)	105	50 / 50
34	10.5 (50)	50 / 50	10.7 (50)	102	50 / 50	11.3 (50)	108	50 / 50	11.6 (50)	110	50 / 50
38	11.2 (50)	50 / 50	11.2 (50)	100	50 / 50	11.9 (50)	106	50 / 50	11.8 (50)	105	50 / 50
42	11.1 (50)	50 / 50	11.6 (50)	105	50 / 50	11.9 (50)	107	50 / 50	12.0 (50)	108	50 / 50
46	11.4 (50)	50 / 50	11.6 (50)	102	50 / 50	12.0 (50)	105	50 / 50	12.1 (50)	106	50 / 50
50	11.4 (50)	50 / 50	11.2 (49)	98	49 / 50	12.3 (50)	108	50 / 50	12.4 (48)	109	48 / 50
54	10.8 (50)	50 / 50	11.2 (49)	104	49 / 50	11.4 (49)	106	49 / 50	11.9 (48)	110	48 / 50
58	11.1 (50)	50 / 50	11.5 (49)	104	49 / 50	11.5 (48)	104	48 / 50	11.7 (47)	105	47 / 50
62	11.3 (50)	50 / 50	11.5 (49)	102	49 / 50	12.0 (47)	106	47 / 50	12.1 (46)	107	46 / 50
66	11.3 (49)	49 / 50	11.3 (49)	100	49 / 50	11.8 (47)	104	47 / 50	12.1 (46)	107	46 / 50
70	11.7 (47)	47 / 50	11.8 (49)	101	49 / 50	12.0 (47)	103	47 / 50	12.0 (46)	103	46 / 50
74	11.7 (46)	46 / 50	11.8 (48)	101	48 / 50	12.4 (46)	106	46 / 50	11.7 (46)	100	46 / 50
78	12.0 (46)	46 / 50	12.1 (47)	101	47 / 50	12.3 (46)	103	46 / 50	12.1 (44)	101	44 / 50
82	11.8 (45)	45 / 50	11.9 (47)	101	47 / 50	12.2 (46)	103	46 / 50	11.8 (43)	100	43 / 50
86	12.5 (44)	44 / 50	12.4 (47)	99	47 / 50	12.8 (46)	102	46 / 50	12.3 (41)	98	41 / 50
90	12.5 (43)	43 / 50	12.3 (47)	98	47 / 50	12.6 (46)	101	46 / 50	12.4 (40)	99	40 / 50
94	12.4 (43)	43 / 50	12.7 (47)	102	47 / 50	12.7 (44)	102	44 / 50	12.6 (38)	102	38 / 50
98	12.7 (40)	40 / 50	11.9 (45)	94	45 / 50	12.3 (42)	97	42 / 50	11.8 (36)	93	36 / 50
102	12.9 (38)	38 / 50	12.6 (42)	98	42 / 50	12.4 (40)	96	40 / 50	12.5 (34)	97	34 / 50
104	12.7 (37)	37 / 50	11.9 (41)	94	41 / 50	12.4 (38)	98	38 / 50	12.6 (32)	99	32 / 50

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

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

Group Name	Control	80 ppm	200 ppm	500 ppm
No. of examined animals	40	39	41	36
WBC ($10^3/\mu$ L)	5.85 ± 1.47	11.11 ± 25.55	5.59 ± 1.40	5.04 ± 1.49 *

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

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

Group Name	Control	80 ppm	200 ppm	500 ppm
No. of examined animals	37	41	38	32
RED BLOOD CELL ($10^6/\mu$ L)	7.96 ± 1.13	7.90 ± 1.06	8.03 ± 0.52	7.67 ± 0.78 *
MCV (fL)	52.7 ± 4.8	52.7 ± 4.2	52.5 ± 1.6	54.1 ± 1.9 **
MCHC (g/dL)	35.6 ± 1.2	35.3 ± 1.7	35.5 ± 0.6	34.9 ± 1.2 **
Differential WBC (%)				
EOSINO	2 ± 1	2 ± 1	1 ± 1 *	1 ± 1 **

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

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

Group Name	Control	80 ppm	200 ppm	500 ppm	
No. of examined animals	40	39	41	36	
POTASSIUM (mEq/L)	3.5 ± 0.2	3.7 ± 0.3	3.6 ± 0.3	3.8 ± 0.4	**

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

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

Group Name	Control	80 ppm		200 ppm	500 ppm	
No. of examined animals	37	41		38	32	
G-GTP (IU/L)	3 ± 2	3 ± 2		3 ± 2	5 ± 4	**
UREA NITOROGEN (mg/dL)	17.3 ± 1.9	18.4 ± 2.3	*	17.5 ± 1.8	17.8 ± 2.8	

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

TABLE 10 ORGAN WEIGHTS OF MALE RATS IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

Group Name	Control	80 ppm		200 ppm		500 ppm	
No. of examined animals	40	39		41		36	
Body weight (g)	381 ± 28	372 ± 44		357 ± 31	**	339 ± 39	**
Testes (g)	3.193 ± 1.411	3.730 ± 1.553		3.589 ± 1.278		4.639 ± 1.865	**
Testes (%)	0.838 ± 0.365	0.999 ± 0.406		1.001 ± 0.341		1.358 ± 0.492	**
Heart (g)	1.229 ± 0.084	1.232 ± 0.089		1.211 ± 0.096		1.197 ± 0.102	
Heart (%)	0.324 ± 0.029	0.335 ± 0.037		0.341 ± 0.036		0.357 ± 0.049	**
Lungs (g)	1.438 ± 0.141	1.476 ± 0.225		1.379 ± 0.099		1.365 ± 0.085	*
Lungs (%)	0.379 ± 0.046	0.404 ± 0.094		0.388 ± 0.040		0.408 ± 0.054	**
Kidneys (g)	2.709 ± 0.171	2.753 ± 0.253		2.761 ± 0.310		2.706 ± 0.265	
Kidneys (%)	0.714 ± 0.069	0.746 ± 0.070	*	0.777 ± 0.099	**	0.808 ± 0.125	**
Spleen (g)	1.029 ± 0.506	1.625 ± 3.568		0.853 ± 0.219	*	0.835 ± 0.373	**
Spleen (%)	0.270 ± 0.136	0.476 ± 1.211		0.238 ± 0.055		0.248 ± 0.125	
Liver (g)	11.016 ± 1.269	11.094 ± 2.037		10.346 ± 1.156	*	10.105 ± 1.530	*
Liver (%)	2.896 ± 0.331	2.994 ± 0.532		2.903 ± 0.301		2.982 ± 0.291	
Brain (g)	2.041 ± 0.050	2.017 ± 0.050		2.000 ± 0.063	**	1.967 ± 0.041	**
Brain (%)	0.538 ± 0.040	0.549 ± 0.063		0.563 ± 0.046	*	0.589 ± 0.080	**

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

TABLE 11 ORGAN WEIGHTS OF FEMALE RATS IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

Group Name	Control	80 ppm		200 ppm		500 ppm	
No. of examined animals	37	41		38		32	
Body weight (g)	249 ± 35	234 ± 19		249 ± 21		230 ± 35	**
Adrenals (g)	0.107 ± 0.228	0.069 ± 0.006		0.077 ± 0.023		0.094 ± 0.115	
Adrenals (%)	0.043 ± 0.089	0.030 ± 0.003		0.031 ± 0.010		0.043 ± 0.058	**
Ovaries (g)	0.137 ± 0.064	0.320 ± 1.231		0.131 ± 0.028		0.181 ± 0.216	
Ovaries (%)	0.055 ± 0.024	0.150 ± 0.608		0.053 ± 0.012		0.083 ± 0.109	*
Heart (g)	0.884 ± 0.082	0.868 ± 0.073		0.885 ± 0.067		0.894 ± 0.085	
Heart (%)	0.359 ± 0.037	0.373 ± 0.043		0.357 ± 0.031		0.394 ± 0.043	**
Lungs (g)	1.041 ± 0.138	1.025 ± 0.143		1.025 ± 0.047		1.046 ± 0.107	
Lungs (%)	0.423 ± 0.065	0.441 ± 0.089		0.414 ± 0.039		0.463 ± 0.075	**
Kidneys (g)	1.789 ± 0.159	1.729 ± 0.100		1.767 ± 0.097		1.810 ± 0.159	
Kidneys (%)	0.729 ± 0.092	0.741 ± 0.061		0.714 ± 0.066		0.799 ± 0.107	**
Liver (g)	6.717 ± 1.111	6.412 ± 0.893		6.724 ± 0.603		6.764 ± 1.190	
Liver (%)	2.715 ± 0.401	2.743 ± 0.380		2.710 ± 0.249		2.958 ± 0.415	**
Brain (g)	1.855 ± 0.055	1.824 ± 0.042	*	1.828 ± 0.055	*	1.789 ± 0.046	**
Brain (%)	0.759 ± 0.099	0.783 ± 0.064		0.740 ± 0.076		0.793 ± 0.099	

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

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

Group Name	Control	80 ppm	200 ppm	500 ppm	Peto	Cochran-
Number of examined animals	50	50	50	50	test	Armitage test
subcutis	<50>	<50>	<50>	<50>		
fibroma	2 (4 %)	4 (8 %)	8 (16 %) *	6 (12 %)	↑	
fibrosarcoma	0 (0 %)	1 (2 %)	0 (0 %)	0 (0 %)		
nasal cavity	<50>	<50>	<50>	<50>		
squamous cell papilloma	0 (0 %)	0 (0 %)	2 (4 %)	14 (28 %) **	↑ ↑	↑ ↑
adenoma	0 (0 %)	0 (0 %)	1 (2 %)	1 (2 %)		
adenoacanthoma	0 (0 %)	0 (0 %)	0 (0 %)	1 (2 %)		
ethesioneuroepithelioma	0 (0 %)	2 (4 %)	1 (2 %)	0 (0 %)		
pancreas	<50>	<50>	<50>	<50>		
islet cell adenoma	6 (12 %)	2 (4 %)	0 (0 %) *	2 (4 %)		
thyroid	<50>	<50>	<50>	<50>		
follicular adenoma	1 (2 %)	0 (0 %)	0 (0 %)	3 (6 %)	↑	
follicular adenocarcinoma	0 (0 %)	0 (0 %)	1 (2 %)	1 (2 %)		

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 RATS IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

Group Name	Control	80 ppm	200 ppm	500 ppm	Peto	Cochran-
Number of examined animals	50	50	50	50	test	Armitage test
nasal cavity	<50>	<50>	<50>	<50>		
squamous cell papilloma	0 (0 %)	0 (0 %)	0 (0 %)	9 (18 %) **	↑ ↑	↑ ↑
spleen	<50>	<50>	<50>	<50>		
mononuclear cell leukemia	8 (16 %)	6 (12 %)	3 (6 %)	2 (4 %) *		↓
uterus	<50>	<50>	<50>	<50>		
endometrial stromal polyp	10 (20 %)	15 (30 %)	2 (4 %) *	3 (6 %) *		↓ ↓
mammary gland	<50>	<50>	<50>	<50>		
adenoma	0 (0 %)	2 (4 %)	0 (0 %)	4 (8 %)	↑	↑
fibroadenoma	2 (4 %)	4 (8 %)	3 (6 %)	5 (10 %)		

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 RATS IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

Group Name	Control				80 ppm				200 ppm				500 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>			
inflammation:respiratory epithelium	20	0	0	0	35	0	0	0 **	46	1	0	0 **	37	10	0	0 **
squamous cell metaplasia:respiratory epithelium	5	0	0	0	30	1	0	0 **	40	1	0	0 **	37	12	0	0 **
hyperplasia:transitional epithelium	0	0	0	0	27	4	0	0 **	36	3	0	0 **	20	17	11	0 **
goblet cell hyperplasia	0	0	0	0	15	0	0	0 **	39	2	0	0 **	37	7	1	0 **
squamous cell hyperplasia	0	0	0	0	2	0	0	0	6	0	0	0 *	23	4	0	0 **
atrophy:olfactory epithelium	0	0	0	0	41	7	0	0 **	4	46	0	0 **	0	49	0	0 **
respiratory metaplasia:olfactory epithelium	21	0	0	0	49	1	0	0 **	50	0	0	0 **	2	42	5	0 **
sclerosis:lamina propria	0	0	0	0	2	0	0	0	9	0	0	0 **	15	0	0	0 **
hyperplasia:gland	0	0	0	0	44	2	0	0 **	8	37	5	0 **	3	19	27	0 **
adhesion	0	0	0	0	0	0	0	0	2	0	0	0	5	0	0	0
eosinophilic change:olfactory epithelium	40	6	0	0	0	0	0	0 **	0	0	0	0 **	0	0	0	0 **
eosinophilic change:respiratory epithelium	36	0	0	0	0	0	0	0 **	1	0	0	0 **	1	0	0	0 **
liver	<50>				<50>				<50>				<50>			
bile duct hyperplasia	49	0	0	0	48	0	0	0	45	0	0	0	42	0	0	0 *

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

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

Group Name	Control				80 ppm					200 ppm					500 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>				
inflammation:respiratory epithelium	10	0	0	0	29	1	0	0	**	38	1	0	0	**	35	5	0	0	**
squamous cell metaplasia:respiratory epithelium	3	0	0	0	15	0	0	0	**	31	6	0	0	**	25	21	0	0	**
hyperplasia:transitional epithelium	2	0	0	0	17	3	1	0	**	35	4	0	0	**	31	10	7	0	**
goblet cell hyperplasia	0	0	0	0	0	0	0	0		15	0	0	0	**	41	0	0	0	**
squamous cell hyperplasia	0	0	0	0	0	0	0	0		3	0	0	0		15	5	0	0	**
atrophy:olfactory epithelium	0	0	0	0	50	0	0	0	**	3	47	0	0	**	2	48	0	0	**
respiratory metaplasia:olfactory epithelium	0	0	0	0	49	0	0	0	**	18	32	0	0	**	1	48	1	0	**
sclerosis:lamina propria	0	0	0	0	8	0	0	0	**	12	0	0	0	**	24	0	0	0	**
hyperplasia:gland	0	0	0	0	41	1	0	0	**	7	41	2	0	**	4	31	15	0	**
adhesion	0	0	0	0	0	0	0	0		3	0	0	0		1	0	0	0	
eosinophilic change:olfactory epithelium	7	42	0	0	1	0	0	0	**	1	0	0	0	**	0	0	0	0	**
eosinophilic change:respiratory epithelium	41	0	0	0	12	0	0	0	**	5	0	0	0	**	2	0	0	0	**
liver	<50>				<50>					<50>					<50>				
granulation	10	0	1	0	19	3	0	0	*	23	3	1	0	**	16	0	0	0	
pancreas	<50>				<50>					<50>					<50>				
atrophy	11	0	0	0	8	0	0	0		2	0	0	0	*	4	0	1	0	

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

TABLE 16 HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER : F344/DuCrlCrlj MALE RATS

Organs Tumors	No. of animals examined	No. of animals bearing tumor	Incidence (%)	Min. - Max. (%)
Nasal cavity	1949			
Adenoma		2	0.1	0 - 2
Adenoacanthoma		0	0.0	0 - 0
Squamous cell papilloma		0	0.0	0 - 0
Ethesioneuroepithelioma		0	0.0	0 - 0
Thyroid	1942			
Follicular adenoma 1)		16	0.8	0 - 4
Follicular adenocarcinoma 2)		34	1.8	0 - 8
1)+2)		50	2.6	0 - 8
Subcutis	1949			
Fibroma		151	7.7	2 - 20

Thirty nine carcinogenicity studies examined in Japan Bioassay Research Center were used.
Study No. : 0043, 0059, 0061, 0063, 0065, 0067, 0095, 0104, 0115, 0130, 0141, 0158, 0162, 0189, 0205, 0210, 0224, 0242, 0267, 0269, 0278, 0284, 0288, 0294, 0296, 0318, 0328, 0342, 0347, 0365, 0371, 0396, 0399, 0401, 0407, 0417, 0421, 0437, 0448

TABLE 17 HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER : F344/DuCrlCrlj FEMALE RATS

Organs Tumors	No. of animals examined	No. of animals bearing tumor	Incidence (%)	Min. - Max. (%)
Nasal cavity	1797			
Squamous cell papilloma		0	0.0	0 - 0
Mammary gland	1797			
Adenoma 1)		202	11.2	0 - 20
Fibroadenoma 2)		55	3.1	0 - 18
1)+2)		254	14.1	4 - 24

Thirty six carcinogenicity studies examined in Japan Bioassay Research Center were used.
Study No. : 0043, 0059, 0061, 0063, 0065, 0067, 0095, 0104, 0115, 0130, 0141, 0158, 0162, 0189, 0205, 0210, 0224, 0242, 0267, 0269, 0278, 0284, 0296, 0303, 0318, 0328, 0342, 0347, 0365, 0371, 0399, 0401, 0417, 0421, 0437, 0448

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

	Male				Female			
Group name	Control	80 ppm	200 ppm	500 ppm	Control	80 ppm	200 ppm	500 ppm
Number of dead or moribund animals	10	11	9	14	13	9	12	18
Urinary retention	1	2	0	0	0	0	0	0
Hepatic lesion	0	0	0	0	1	0	0	0
Renal lesion	0	0	0	0	0	0	0	2
Nasal lesion	0	0	0	2	0	0	0	0
Endcrine system lesion	0	0	0	0	1	1	0	1
Central nervous system lesion	0	0	0	0	0	0	0	1
Deglutition disorder	0	0	0	0	0	0	0	2
Arteritis	0	0	0	1	0	0	0	0
Tumor death : leukemia	5	0	4	4	5	3	3	1
skin / appendage	0	0	0	0	0	0	0	1
subcutis	0	1	2	2	0	0	0	1
bone marrow	0	0	0	1	0	0	0	0
liver	0	0	0	1	0	0	0	0
pituitary gland	2	0	2	0	3	3	4	3
thyroid	1	0	1	0	0	0	0	0
adrenal gland	0	1	0	0	0	0	0	0
ovary	—	—	—	—	1	0	0	0
uterus	—	—	—	—	0	0	2	1
brain	0	0	0	1	0	0	0	0
spinal cord	0	0	0	0	0	1	0	0
Zymbal gland	0	1	0	0	0	0	1	1
muscle	0	1	0	0	0	0	0	0
bone	0	1	0	0	0	0	1	0
peritoneum	0	1	0	0	0	0	0	0
retroperitoneum	1	1	0	0	0	0	0	0
No microscopical confirmation	0	2	0	2	2	1	1	4

FIGURES

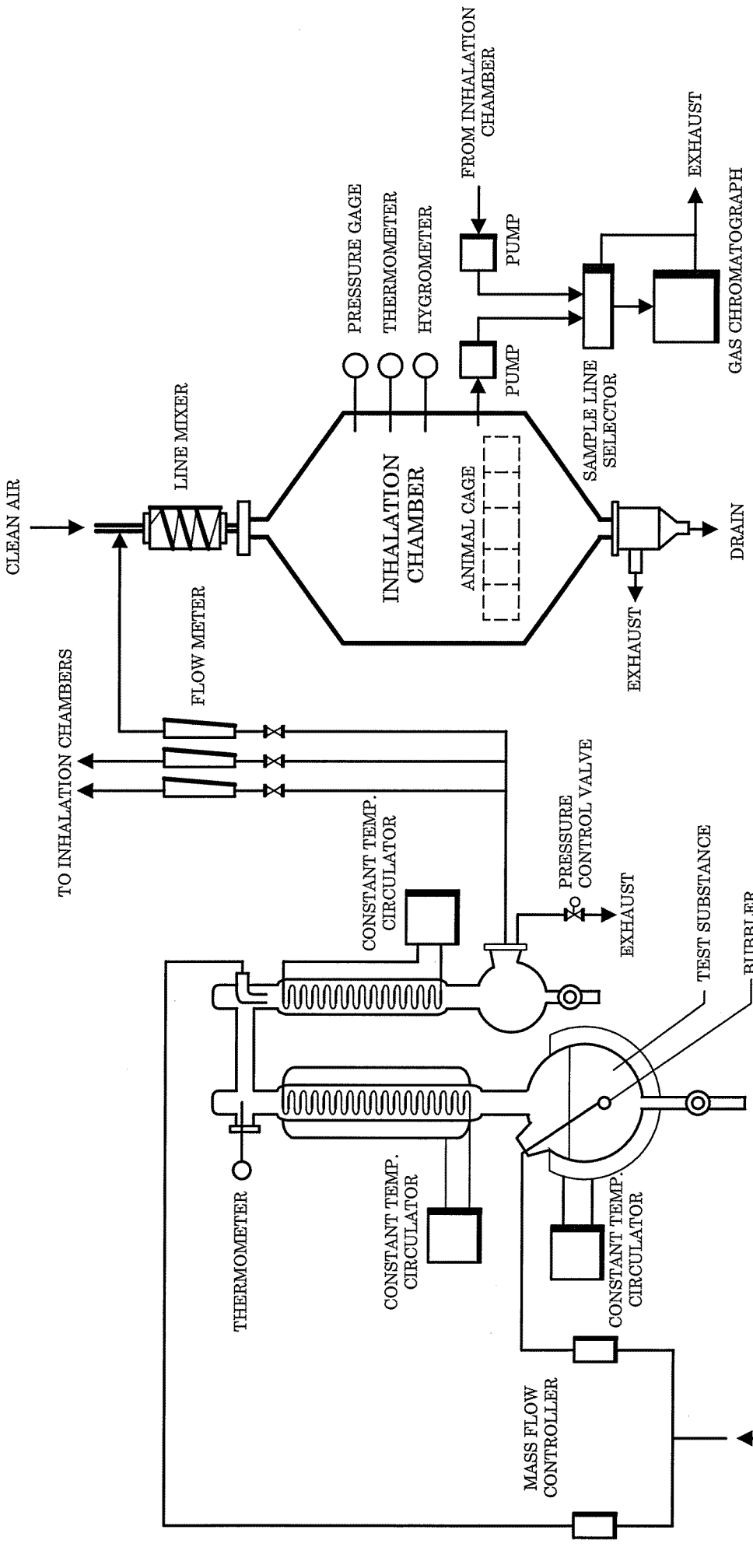


FIGURE 1 1,2-DICHLOROPROPANE VAPOR GENERATION SYSTEM AND INHALATION SYSTEM

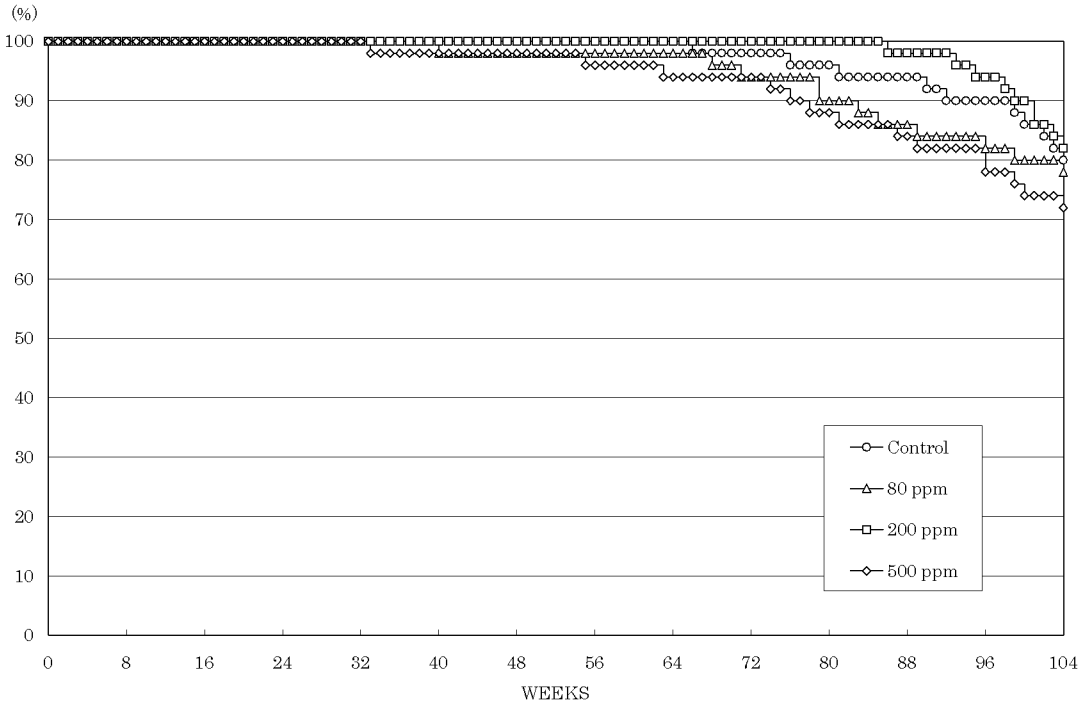


FIGURE 2 SURVIVAL ANIMAL RATE OF MALE RATS IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

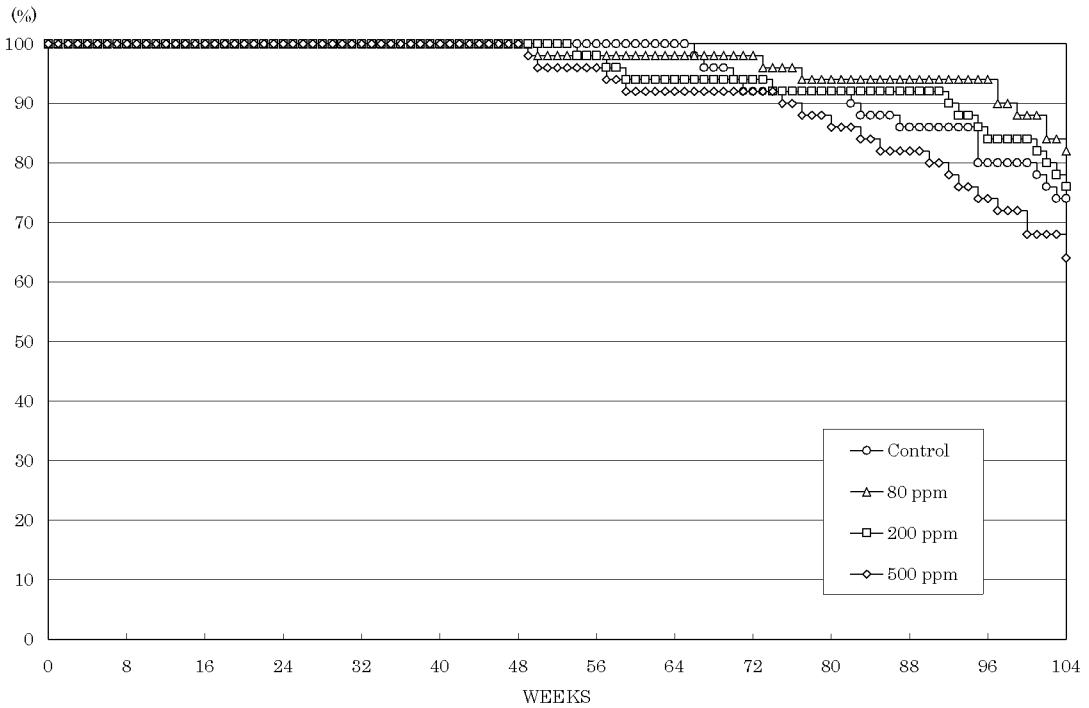


FIGURE 3 SURVIVAL ANIMAL RATE OF FEMALE RATS IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

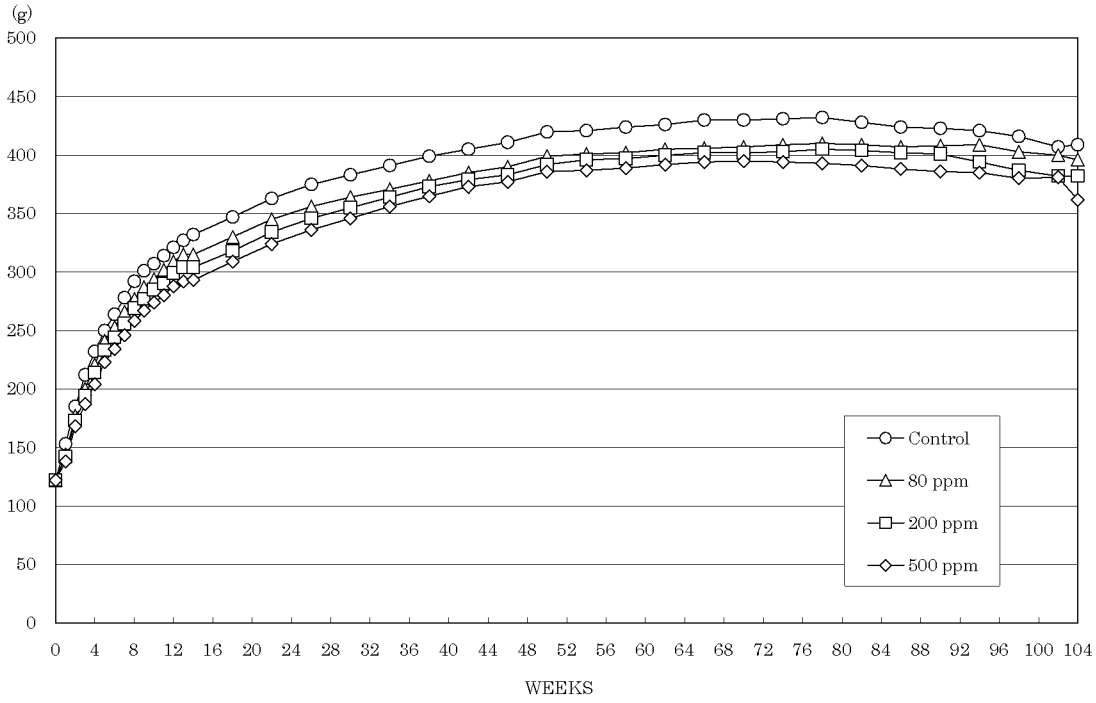


FIGURE 4 BODY WEIGHT CHANGES OF MALE RATS IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

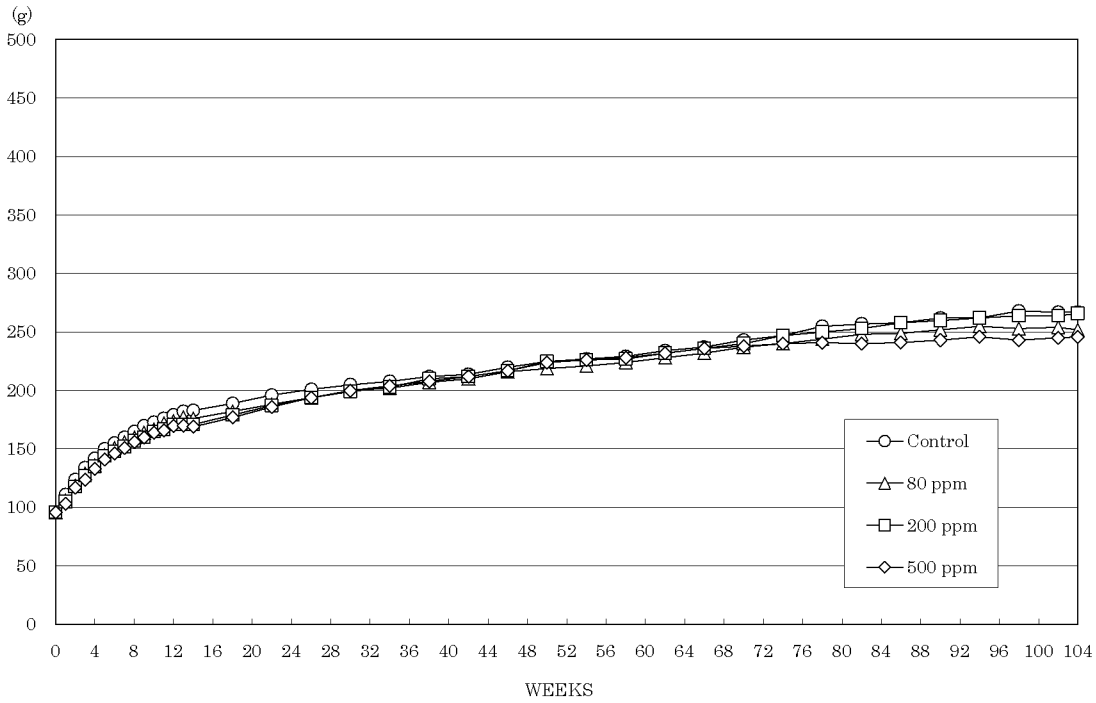


FIGURE 5 BODY WEIGHT CHANGES OF FEMALE RATS IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

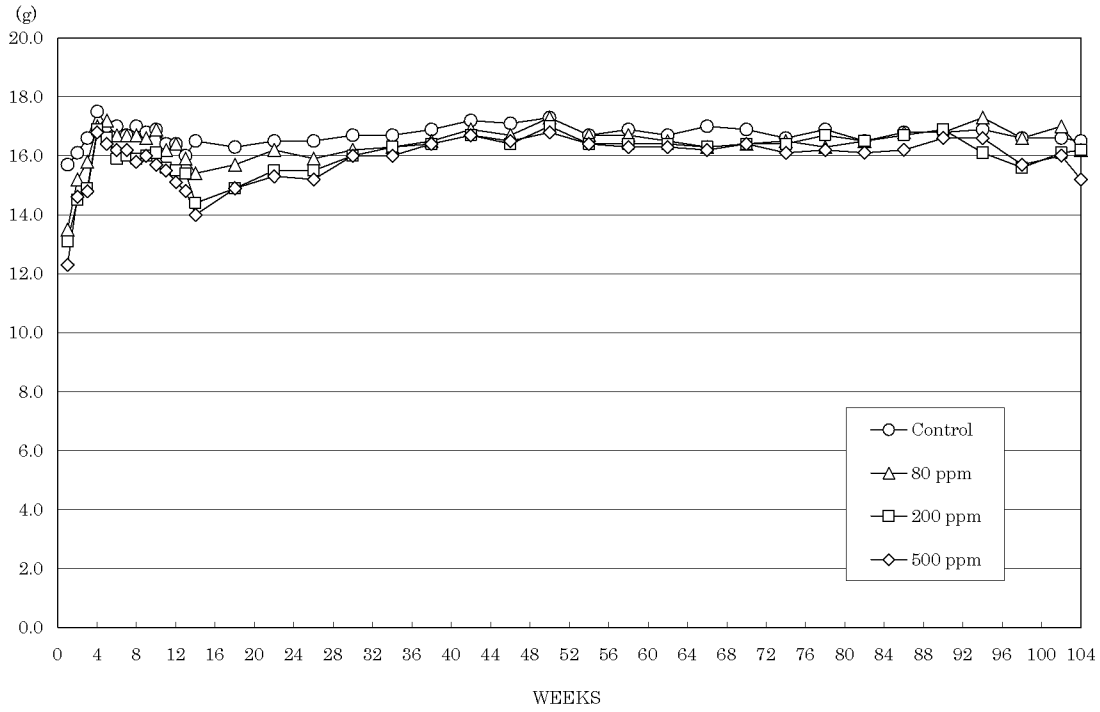


FIGURE 6 FOOD CONSUMPTION CHANGES OF MALE RATS IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

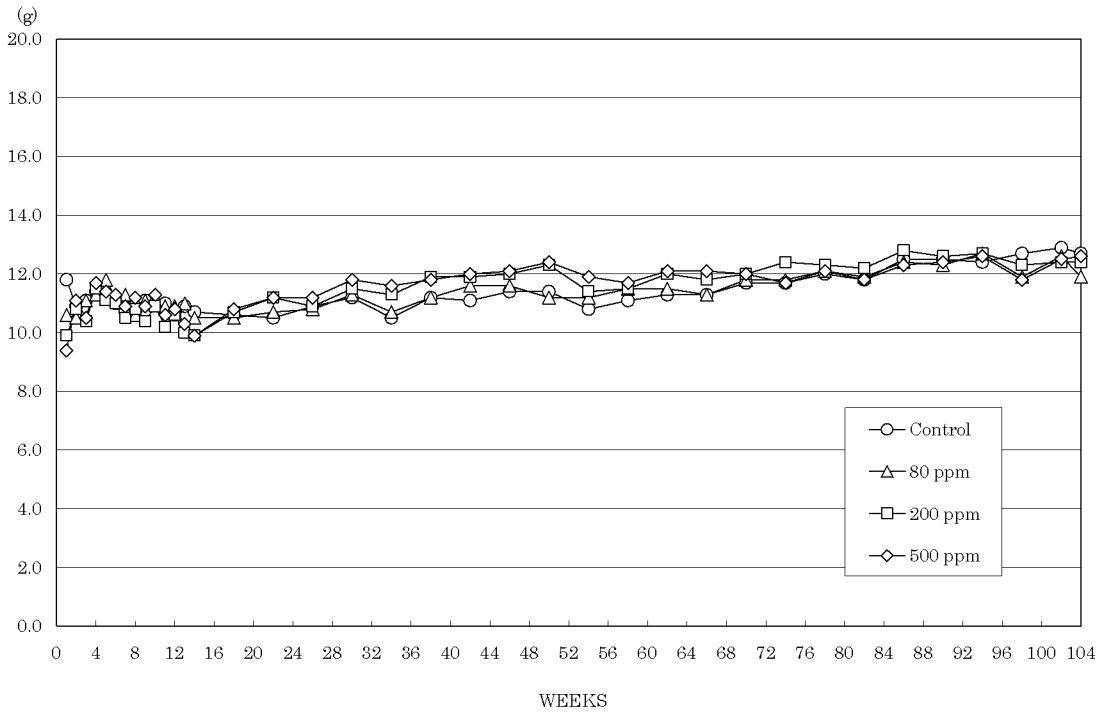
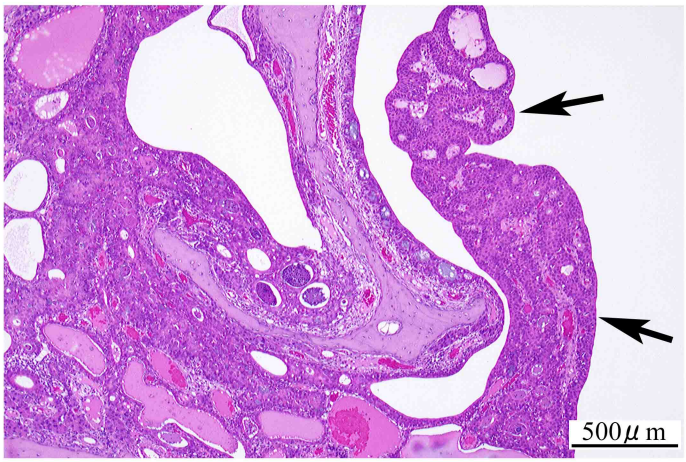
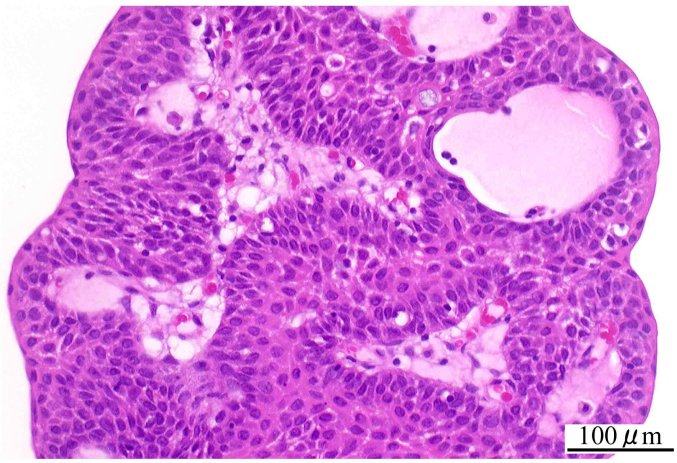


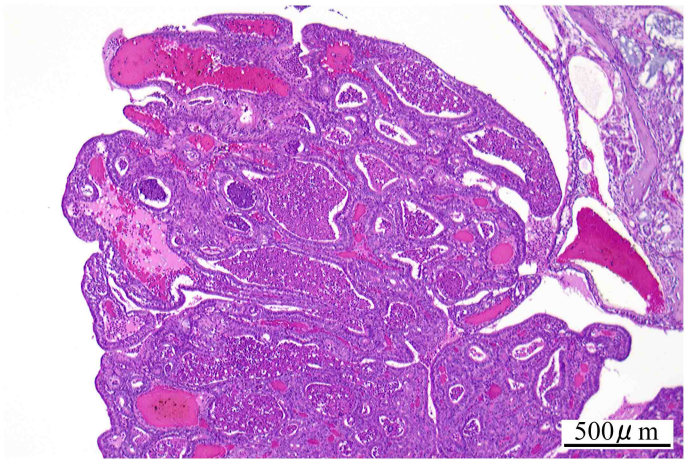
FIGURE 7 FOOD CONSUMPTION CHANGES OF FEMALE RATS IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE



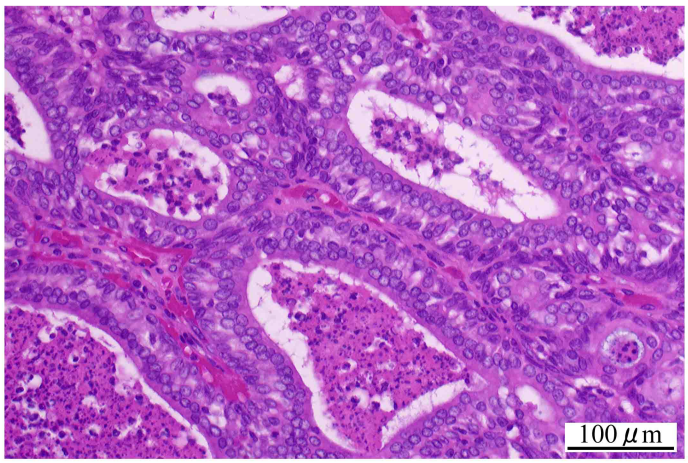
Photograph 1
Nasal cavity: Squamous cell papilloma (Arrows)
Rat, Female, 500 ppm, Animal No. 0457-2303 (H&E)



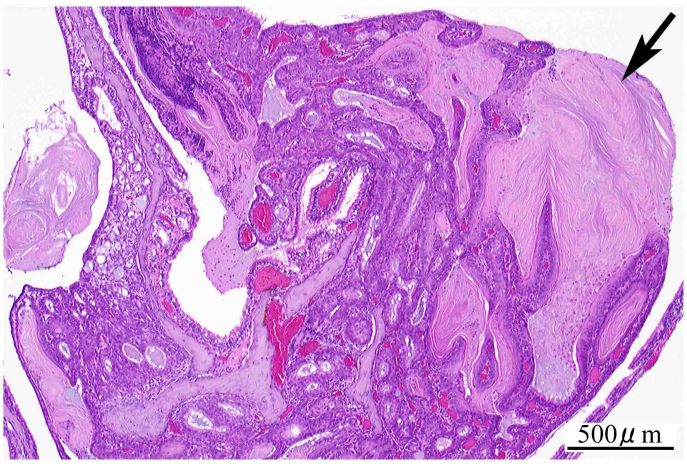
Photograph 2
Nasal cavity: Squamous cell papilloma
Higher magnification of photograph 1.
Rat, Female, 500 ppm, Animal No. 0457-2303 (H&E)



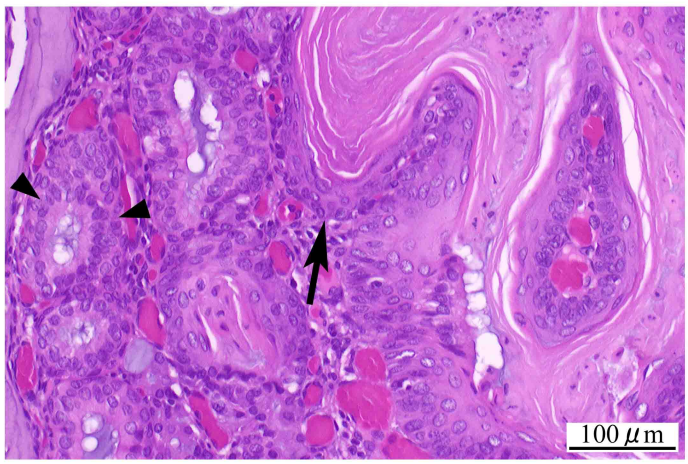
Photograph 3
Nasal cavity: Adenoma
Rat, Male, 200 ppm, Animal No. 0457-1210 (H&E)



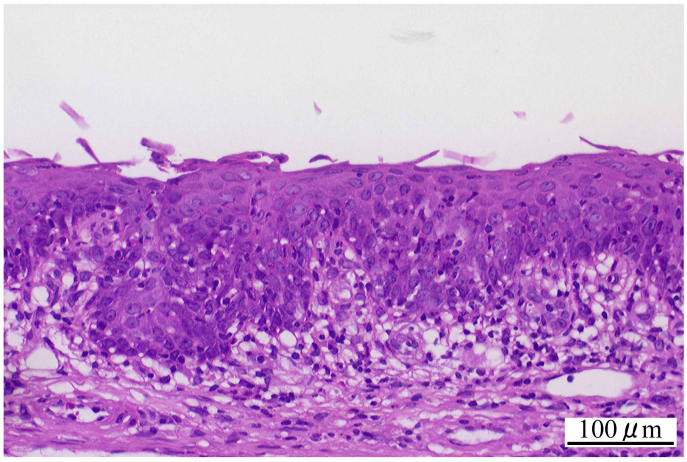
Photograph 4
Nasal cavity: Adenoma
Higher magnification of photograph 3.
Rat, Male, 200 ppm, Animal No. 0457-1210 (H&E)



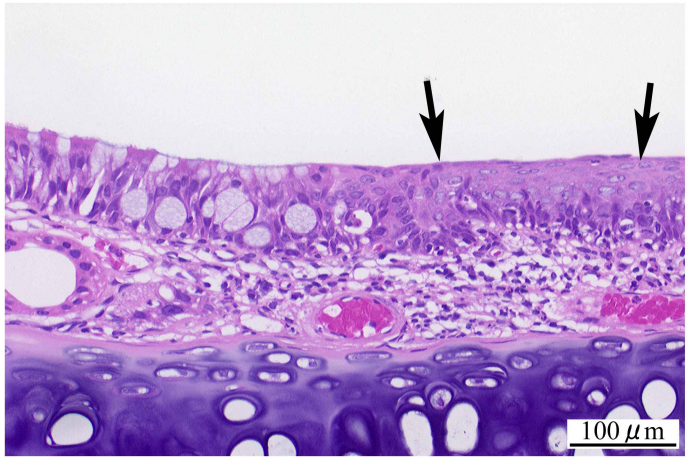
Photograph 5
Nasal cavity: Adenoacanthoma (Arrow)
Rat, Male, 500 ppm, Animal No. 0457-1302 (H&E)



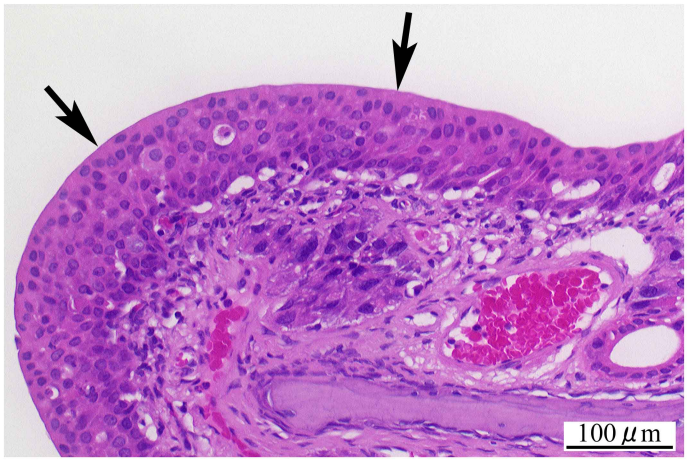
Photograph 6
Nasal cavity: Adenoacanthoma
Higher magnification of photograph 5.
Glandular structures (arrowheads) and keratinnizing squamous epithelium (arrow) are noted.
Rat, Male, 500 ppm, Animal No. 0457-1302 (H&E)



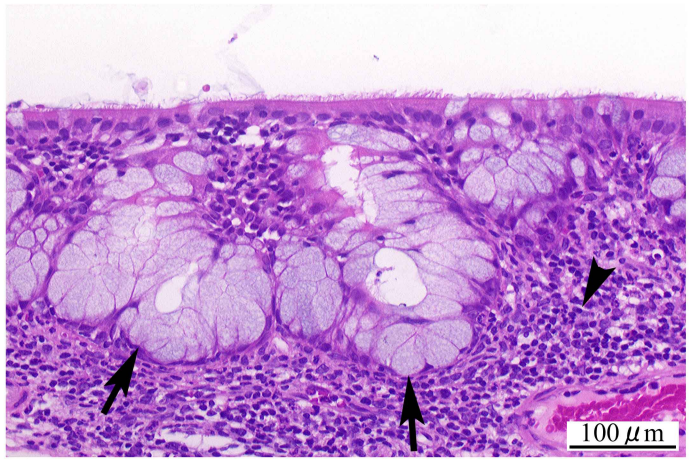
Photograph 7
Nasal cavity: Squamous cell hyperplasia
Rat, Male, 200 ppm, Animal No. 0457-1205 (H&E)



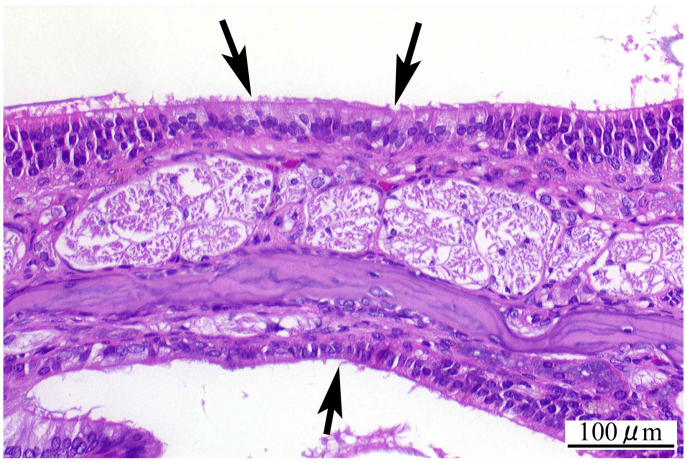
Photograph 8
Nasal cavity: Squamous metaplasia of respratory epithelium (Arrows)
Rat, Male, 200 ppm, Animal No. 0457-1202 (H&E)



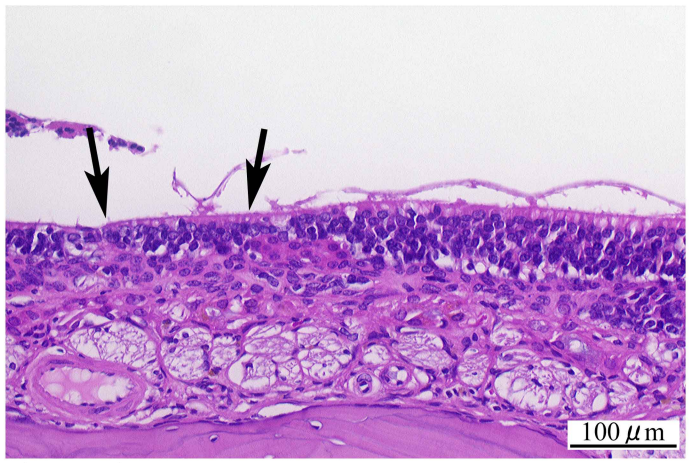
Photograph 9
Nasal cavity: Transitional cell hyperplasia (Arrows)
Rat, Male, 500 ppm, Animal No. 0457-1305 (H&E)



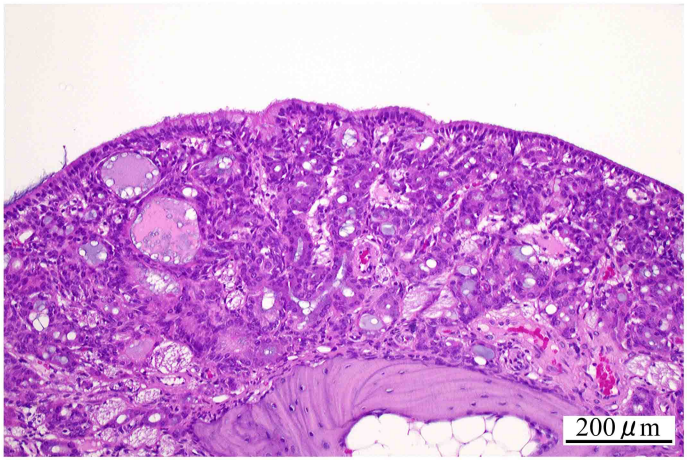
Photograph 10
Nasal cavity: Goblet cell hyperplasia (Arrows) and inflammation of respiratory epithelium (Arrowhead)
Rat, Male, 500 ppm, Animal No. 0457-1330 (H&E)



Photograph 11
Nasal cavity: Respiratory metaplasia of olfactory epithelium (Arrows)
Rat, Male, 80 ppm, Animal No. 0457-1128 (H&E)



Photograph 12
Nasal cavity: atrophy of olfactory epithelium (Arrows)
Rat, Female, 80 ppm, Animal No. 0457-2144 (H&E)



Photograph 13
Nasal cavity: Hyperplasia of submucosal gland
Rat, Male, 500 ppm, Animal No. 0457-1304 (H&E)