ジクロロメタンのラットを用いた
吸入によるがん原性試験報告書

試験番号：0278

TABLES

TABLES

TABLES (CONTINUED)

TABLE 1 EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE 2-YEAR INHALATION STUDY OF DICHLOROMETHANE

<Method of Administration>
Inhalation
<Number of Groups>
Male 4, Female 4
<Size of Groups>
50 males and 50 females of each group
<Animals>
Strain and Species
F344/DuCrj (Fischer) rat
Animal Source
Charles River Japan, Inc.
Duration Held Before Study
2 wk
Age When Placed on Study
6 wk
Age When Killed
110～111 wk
<Doses>
Male and Female
0, 1000, 2000, or 4000ppm
<Duration of Dosing>
6h/d, 5d/wk, for 104wk
<Animal Maintenance>
Feed
CRF-1 (Oriental Yeast Co., Ltd.)
Sterilized by γ-ray
Available *ad libitum*
Water
Filtrated and sterilized by ultraviolet ray
Automatic watering system in duration of quarantine
Available *ad libitum*
Animal per Cage
Single (stainless steel wire)
Animal Room Environment
Barrier system
Temperatu: : 23±3℃
Fluorescent light 12h/d
Chamber Environment
Temperatu: : 22±2℃
Humidity : 55±15%
Pressure : 0～-15mmAq
12±1 chamber air changes/h
(6±1 chamber air changes/h during exposure)
<Type and Frequency of Observation>
Clinical Sign
Observed 1 per d
Body Weight
Weighed first exposure and 1 per wk for 14wk
Weighed 1 per 4wks thereafter
Food Consumption
Weighed 1 per wk for 14wk
Weighed 1 per 4wks thereafter

TABLE 1 (continued) EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE 2-YEAR INHALATION STUDY OF DICHLOROMETHANE

<Hematology>
Red blood cell (RBC), Hemoglobin, Hematocrit,
Mean Corpuscular Volume (MCV),
Mean Corpuscular hemoglobin (MCH),
Mean Corpuscular hemoglobin concentrate (MCHC),
Platelet, White blood cell (WBC),
Differential WBC.

<Biochemistry>
Total protein, Albumin, A/G ratio,
Total bilirubin, Glucose, Total cholesterol
Triglyceride, Phospholipid ,
Glutamic oxaloacetic transaminase (GOT),
Glutamic pyruvic transaminase (GPT),
Lactate dehydrogenase (LDH),
Alkaline phosphatase (ALP),
γ-Glutamyl transpeptidase (γ-GTP) ,
Creatine phosphokinase (CPK),
Urea nitrogen, Creatinine ,
Sodium, Potassium, Chloride,
Calcium, Inorganic phosphorus.

<Urinalysis>
pH, Protein, Glucose, Ketone body,
Bilirubin, Occult blood, Urobilinogen.

<Necropsy>
Necropsy performed on all animals.

<Organ Weight>
Organ weight measurement performed on scheduled sacrificed animals.
The following organs were weighed;
brain, lung, liver, spleen, heart, kidney, adrenal, testis, ovary.

<Histopathologic Examination>
Histopathologic examination performed on all animals.
The following organs were examined;
skin, nasal cavity, nasopharynx, larynx, trachea, lung, bone marrow, lymph node, thymus, spleen, heart, tongue, salivary gland, esophagus, stomach, small intestine, large intestine, liver, pancreas, kidney, urinary bladder, pituitary, thyroid, parathyroid, adrenal, testis, epididymis, seminal vesicle, prostate, ovary, uterus, vagina, mammary gland, brain, spinal cord, peripheral nerve, eye, Harderian gland, muscle, bone, other organs/tissues with gross lesions.

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

Weeks on Study	Control		1000ppm			2000ppm			4000ppm		
	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	117 (50)	50/50	117 (50)	100	50/50	117 (50)	100	50/50	117 (50)	100	50/50
1	120 (50)	50/50	120 (50)	100	50/50	120 (50)	100	50/50	120 (50)	100	50/50
1	145 (50)	50/50	144 (50)	99	50/50	146 (50)	101	50/50	142 (50)	98	50/50
2	175 (50)	50/50	173 (50)	99	50/50	175 (50)	100	50/50	168 (50)	96	50/50
3	202 (50)	50/50	201 (50)	100	50/50	200 (50)	99	50/50	192 (50)	95	50/50
4	226 (50)	50/50	224 (50)	99	50/50	222 (50)	98	50/50	214 (50)	95	50/50
5	246 (50)	50/50	244 (50)	99	50/50	241 (50)	98	50/50	232 (50)	94	50/50
6	263 (50)	50/50	260 (50)	99	50/50	257 (50)	98	50/50	248 (50)	94	50/50
7	279 (50)	50/50	276 (50)	99	50/50	272 (50)	97	50/50	262 (50)	94	50/50
8	293 (50)	50/50	290 (50)	99	50/50	286 (50)	98	50/50	275 (50)	94	50/50
9	306 (50)	50/50	303 (50)	99	50/50	298 (50)	97	50/50	287 (50)	94	50/50
10	316 (50)	50/50	312 (50)	99	50/50	308 (50)	97	50/50	297 (50)	94	50/50
11	326 (50)	50/50	321 (50)	98	50/50	317 (50)	97	50/50	306 (50)	94	50/50
12	334 (50)	50/50	328 (50)	98	50/50	324 (50)	97	50/50	312 (50)	93	50/50
13	343 (50)	50/50	337 (50)	98	50/50	332 (50)	97	50/50	322 (50)	94	50/50
14	350 (50)	50/50	344 (50)	98	50/50	340 (50)	97	50/50	328 (50)	94	50/50
18	373 (50)	50/50	367 (50)	98	50/50	362 (50)	97	50/50	351 (50)	94	50/50
22	389 (50)	50/50	386 (50)	99	50/50	381 (50)	98	50/50	369 (50)	95	50/50
26	402 (50)	50/50	398 (50)	99	50/50	394 (50)	98	50/50	381 (50)	95	50/50
30	417 (50)	50/50	412 (50)	99	50/50	410 (50)	98	50/50	397 (50)	95	50/50
34	429 (50)	50/50	426 (50)	99	50/50	423 (50)	99	50/50	408 (50)	95	50/50
38	438 (50)	50/50	434 (50)	99	50/50	431 (50)	98	50/50	417 (50)	95	50/50
42	446 (50)	50/50	443 (50)	99	50/50	441 (50)	99	50/50	424 (50)	95	50/50
46	452 (50)	50/50	448 (50)	99	50/50	447 (50)	99	50/50	431 (50)	95	50/50
50	459 (50)	50/50	455 (50)	99	50/50	455 (50)	99	50/50	436 (50)	95	50/50
54	461 (50)	50/50	460 (50)	100	50/50	452 (50)	98	50/50	440 (50)	95	50/50
58	465 (50)	50/50	463 (50)	100	50/50	456 (50)	98	50/50	440 (50)	95	50/50
62	467 (50)	50/50	467 (50)	100	50/50	461 (50)	99	50/50	442 (50)	95	50/50
66	471 (50)	50/50	471 (50)	100	50/50	462 (50)	98	50/50	444 (50)	94	50/50
70	467 (50)	50/50	470 (50)	101	50/50	461 (50)	99	50/50	440 (49)	94	49/50
74	466 (48)	48/50	472 (49)	101	49/50	459 (50)	98	50/50	440 (48)	94	48/50
78	463 (48)	48/50	466 (49)	101	49/50	464 (49)	100	49/50	444 (46)	96	46/50
82	463 (46)	46/50	473 (48)	102	48/50	460 (49)	99	48/50	448 (45)	97	45/50
86	448 (46)	46/50	475 (48)	106	48/50	462 (48)	103	48/50	445 (43)	99	43/50
90	455 (42)	42/50	468 (48)	103	48/50	462 (47)	102	47/50	443 (43)	97	43/50
94	446 (39)	39/50	463 (48)	104	48/50	454 (47)	102	47/50	438 (41)	98	41/50
98	436 (37)	37/50	459 (44)	105	44/50	437 (44)	100	44/50	430 (37)	99	36/50
102	419 (36)	36/50	448 (43)	107	43/50	423 (42)	101	41/50	424 (30)	101	30/50
104	412 (32)	32/50	437 (43)	106	43/50	416 (39)	101	38/50	417 (29)	101	28/50

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

TABLE 3 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF FEMALE RATS IN THE 2-YEAR INHALATION STUDY OF DICHLOROMETHANE

Weeks on Study	Control		1000ppm			2000ppm			4000ppm		
	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	97 (50)	50/50	97 (50)	100	50/50	97 (50)	100	50/50	97 (50)	100	50/50
1	110 (50)	50/50	109 (50)	99	50/50	110 (50)	100	50/50	107 (50)	97	50/50
2	124 (50)	50/50	122 (50)	98	50/50	123 (50)	99	50/50	118 (50)	95	50/50
3	135 (50)	50/50	133 (50)	99	50/50	134 (50)	99	50/50	128 (50)	95	50/50
4	144 (50)	50/50	142 (50)	99	50/50	143 (50)	99	50/50	135 (50)	94	50/50
5	154 (50)	50/50	152 (50)	99	50/50	151 (50)	98	50/50	144 (50)	94	50/50
6	161 (50)	50/50	160 (50)	99	50/50	158 (50)	98	50/50	150 (50)	93	50/50
7	168 (50)	50/50	166 (50)	99	50/50	164 (50)	98	50/50	155 (50)	92	50/50
8	174 (50)	50/50	171 (50)	98	50/50	168 (50)	97	50/50	160 (50)	92	50/50
9	179 (50)	50/50	177 (50)	99	50/50	174 (50)	97	50/50	166 (50)	93	50/50
10	184 (50)	50/50	181 (50)	98	50/50	178 (50)	97	50/50	170 (50)	92	50/50
11	189 (50)	50/50	187 (50)	99	50/50	185 (50)	98	50/50	177 (50)	94	50/50
12	193 (50)	50/50	189 (50)	98	50/50	187 (50)	97	50/50	179 (50)	93	50/50
13	197 (50)	50/50	194 (50)	98	50/50	191 (50)	97	50/50	184 (50)	93	50/50
14	199 (50)	50/50	196 (50)	98	50/50	194 (50)	97	50/50	186 (50)	93	50/50
18	209 (50)	50/50	206 (50)	99	50/50	204 (50)	98	50/50	196 (50)	94	50/50
22	215 (50)	50/50	214 (50)	100	50/50	210 (50)	98	50/50	205 (50)	95	50/50
26	222 (50)	50/50	219 (50)	99	50/50	217 (50)	98	50/50	210 (50)	95	50/50
30	233 (50)	50/50	231 (50)	99	50/50	228 (50)	98	50/50	222 (50)	95	50/50
34	240 (50)	50/50	237 (50)	99	50/50	234 (50)	98	50/50	227 (50)	95	50/50
38	242 (50)	50/50	241 (50)	100	50/50	236 (50)	98	50/50	230 (50)	95	50/50
42	248 (50)	50/50	248 (50)	100	50/50	243 (50)	98	50/50	239 (50)	96	50/50
46	253 (50)	50/50	251 (50)	99	50/50	248 (50)	98	50/50	244 (50)	96	50/50
50	263 (50)	50/50	261 (50)	99	50/50	259 (50)	98	50/50	251 (50)	95	50/50
54	268 (50)	50/50	266 (50)	99	50/50	260 (50)	97	50/50	257 (50)	96	50/50
58	271 (50)	50/50	273 (50)	101	50/50	264 (50)	97	50/50	259 (50)	96	50/50
62	274 (50)	50/50	276 (50)	101	50/50	269 (50)	98	50/50	264 (49)	96	49/50
66	282 (50)	50/50	284 (50)	101	50/50	277 (50)	98	50/50	270 (47)	96	47/50
70	288 (50)	50/50	291 (50)	101	50/50	284 (50)	99	50/50	278 (47)	97	47/50
74	295 (49)	49/50	300 (49)	102	49/50	291 (50)	99	50/50	281 (47)	95	47/50
78	301 (49)	49/50	305 (49)	101	49/50	298 (50)	99	50/50	286 (44)	95	44/50
82	308 (48)	48/50	312 (49)	101	49/50	303 (50)	98	50/50	293 (44)	95	44/50
86	314 (48)	48/50	321 (48)	102	48/50	316 (48)	101	48/50	298 (42)	95	42/50
90	323 (46)	46/50	320 (48)	99	48/50	322 (48)	100	48/50	306 (39)	95	39/50
94	326 (46)	46/50	323 (45)	99	45/50	329 (47)	101	47/50	307 (39)	94	39/50
98	324 (46)	46/50	319 (43)	98	42/50	324 (45)	100	45/50	309 (36)	95	36/50
102	324 (45)	45/50	320 (41)	99	41/50	322 (43)	99	43/50	301 (32)	93	31/50
104	315 (45)	45/50	312 (40)	99	40/50	315 (43)	100	43/50	293 (31)	93	30/50

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

TABLE 4 INCIDENCE OF EXTERNAL AND INTERNAL MASS IN CLINICAL OBSERVATION OF MALE RATS IN THE 2-YEAR INHALATION STUDY OF DICHLOROMETHANE

Time of mass occurrence (weeks)		0～13	14～26	27～39	40～52	53～65	66～78	79～91	92～104	0～104
External mass										
	Control	0/50	0/50	1/50	2/50	2/50	4/50	6/47	7/40	10/50(5/18)
	1000ppm	0/50	0/50	0/50	1/50	1/50	2/50	6/49	16/48	18/50(2/ 7)
	2000ppm	0/50	0/50	0/50	5/50	4/50	6/50	10/49	14/47	18/50(6/12)
	4000ppm	0/50	0/50	0/50	1/50	2/50	4/50	17/46	22/42	24/50(8/22)
Internal mass										
	Control	0/50	0/50	0/50	0/50	0/50	0/50	1/47	1/40	2/50(2/18)
	1000ppm	0/50	0/50	0/50	0/50	0/50	0/50	0/49	1/48	1/50(1/ 7)
	2000ppm	0/50	0/50	0/50	0/50	0/50	0/50	0/49	3/47	3/50(2/12)
	4000ppm	0/50	0/50	0/50	0/50	0/50	2/50	1/46	2/42	5/50(5/22)

No. of animals with mass / No. of survival animals at first week on each period.
(No. of dead and moribund animals with mass / No. of dead and moribund animals)

TABLE 5 INCIDENCE OF EXTERNAL AND INTERNAL MASS IN CLINICAL OBSERVATION OF FEMALE RATS IN THE 2-YEAR INHALATION STUDY OF DICHLOROMETHANE

Time of mass occurrence (weeks)		0～13	14～26	27～39	40～52	53～65	66～78	79～91	92～104	0～104
External mass										
	Control	0/50	0/50	0/50	0/50	0/50	1/50	5/49	10/46	11/50(1/ 5)
	1000ppm	0/50	0/50	0/50	1/50	1/50	1/50	3/49	6/46	7/50(1/10)
	2000ppm	0/50	0/50	0/50	0/50	0/50	0/50	1/50	9/47	9/50(1/ 7)
	4000ppm	0/50	0/50	0/50	0/50	2/50	2/47	2/44	12/39	12/50(2/20)
Internal mass										
	Control	0/50	0/50	0/50	0/50	0/50	0/50	0/49	0/46	0/50(0/ 5)
	1000ppm	0/50	0/50	0/50	0/50	0/50	0/50	0/49	2/46	2/50(2/10)
	2000ppm	0/50	0/50	0/50	0/50	0/50	0/50	2/50	0/47	2/50(1/ 7)
	4000ppm	0/50	0/50	0/50	1/50	1/50	0/47	5/44	3/39	9/50(9/20)

No. of animals with mass / No. of survival animals at first week on each period.
(No. of dead and moribund animals with mass / No. of dead and moribund animals)

TABLE 6 FOOD CONSUMPTION CHANGES OF MALE RATS
IN THE 2-YEAR INHALATION STUDY OF DICHLOROMETHANE

Weeks on Study	Control Av.FC.	Control No.of Surviv. <50>	1000ppm Av.FC.	1000ppm % of cont.	1000ppm No.of Surviv. <50>	2000ppm Av.FC.	2000ppm % of cont.	2000ppm No.of Surviv. <50>	4000ppm Av.FC.	4000ppm % of cont.	4000ppm No.of Surviv. <50>
1	15.0 (50)	50/50	15.0 (50)	100	50/50	15.0 (50)	100	50/50	14.3 (50)	95	50/50
2	16.5 (50)	50/50	16.3 (50)	99	50/50	16.2 (50)	98	50/50	15.0 (50)	91	50/50
3	17.8 (50)	50/50	17.5 (50)	98	50/50	17.0 (50)	96	50/50	16.1 (50)	90	50/50
4	18.7 (50)	50/50	18.3 (50)	98	50/50	17.8 (50)	95	50/50	17.0 (50)	91	50/50
5	19.0 (50)	50/50	18.9 (50)	99	50/50	18.1 (50)	95	50/50	17.6 (50)	93	50/50
6	18.9 (50)	50/50	18.6 (50)	98	50/50	18.3 (50)	97	50/50	17.5 (50)	93	50/50
7	18.5 (50)	50/50	18.2 (50)	98	50/50	17.8 (50)	96	50/50	17.2 (50)	93	50/50
8	18.7 (50)	50/50	18.5 (50)	99	50/50	18.0 (50)	96	50/50	17.4 (50)	93	50/50
9	19.2 (50)	50/50	19.0 (50)	99	50/50	18.4 (50)	96	50/50	17.8 (50)	93	50/50
10	19.0 (50)	50/50	18.8 (50)	99	50/50	18.3 (50)	96	50/50	17.9 (50)	94	50/50
11	19.1 (50)	50/50	18.6 (50)	97	50/50	18.2 (50)	95	50/50	18.2 (50)	95	50/50
12	18.8 (50)	50/50	18.2 (50)	97	50/50	17.6 (50)	94	50/50	17.4 (50)	93	50/50
13	18.9 (50)	50/50	18.2 (50)	96	50/50	18.0 (50)	95	50/50	17.9 (50)	95	50/50
14	18.6 (50)	50/50	18.1 (50)	97	50/50	17.8 (50)	96	50/50	17.5 (50)	94	50/50
18	18.6 (50)	50/50	18.2 (50)	98	50/50	17.8 (50)	96	50/50	17.6 (50)	95	50/50
22	18.7 (50)	50/50	18.4 (50)	98	50/50	18.4 (50)	98	50/50	17.9 (50)	96	50/50
26	18.7 (50)	50/50	18.3 (50)	98	50/50	18.3 (50)	98	50/50	18.1 (50)	97	50/50
30	18.8 (50)	50/50	18.3 (50)	97	50/50	18.2 (50)	97	50/50	18.4 (50)	98	50/50
34	18.7 (50)	50/50	18.5 (50)	99	50/50	18.4 (50)	98	50/50	18.5 (50)	99	50/50
38	18.9 (50)	50/50	18.3 (50)	97	50/50	18.2 (50)	96	50/50	18.3 (50)	97	50/50
42	18.8 (50)	50/50	18.4 (50)	98	50/50	18.4 (50)	98	50/50	18.0 (50)	96	50/50
46	18.5 (50)	50/50	18.1 (50)	98	50/50	18.3 (50)	99	50/50	18.2 (50)	98	50/50
50	18.6 (50)	50/50	18.1 (50)	97	50/50	18.5 (50)	99	50/50	18.1 (50)	97	50/50
54	18.1 (50)	50/50	18.5 (50)	102	50/50	17.3 (50)	96	50/50	18.2 (50)	101	50/50
58	18.9 (50)	50/50	19.0 (50)	101	50/50	18.6 (50)	98	50/50	18.4 (50)	97	50/50
62	18.6 (50)	50/50	18.8 (50)	101	50/50	18.5 (50)	99	50/50	18.7 (50)	101	50/50
66	18.7 (50)	50/50	18.8 (50)	101	50/50	18.5 (50)	99	50/50	18.1 (50)	97	50/50
70	18.5 (50)	50/50	18.5 (50)	100	50/50	18.2 (50)	98	50/50	18.1 (49)	98	49/50
74	19.0 (48)	48/50	18.9 (49)	99	49/50	18.6 (50)	98	50/50	19.0 (48)	100	48/50
78	19.0 (48)	48/50	18.4 (49)	97	49/50	19.0 (49)	100	49/50	18.9 (46)	99	46/50
82	19.3 (46)	46/50	18.7 (48)	97	48/50	18.2 (49)	94	48/50	18.8 (45)	97	45/50
86	17.8 (44)	46/50	19.5 (47)	110	48/50	18.6 (48)	104	48/50	20.1 (43)	113	43/50
90	18.5 (42)	42/50	18.8 (48)	102	48/50	19.4 (47)	105	47/50	20.0 (43)	108	43/50
94	18.3 (39)	39/50	18.3 (48)	100	48/50	18.0 (47)	98	47/50	18.6 (41)	102	41/50
98	17.9 (37)	37/50	18.0 (43)	101	44/50	17.9 (44)	100	44/50	19.5 (37)	109	36/50
102	17.2 (34)	36/50	18.3 (43)	106	43/50	17.5 (42)	102	41/50	19.0 (27)	110	30/50
104	17.3 (32)	32/50	17.4 (43)	101	43/50	16.6 (39)	96	38/10	18.6 (28)	108	28/50

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

TABLE 7 FOOD CONSUMPTION CHANGES OF FEMALE RATS
IN THE 2-YEAR INHALATION STUDY OF DICHLOROMETHANE

Weeks on Study	Control Av.FC.	Control No.of Surviv. <50>	1000ppm Av.FC.	1000ppm % of cont.	1000ppm No.of Surviv. <50>	2000ppm Av.FC.	2000ppm % of cont.	2000ppm No.of Surviv. <50>	4000ppm Av.FC.	4000ppm % of cont.	4000ppm No.of Surviv. <50>
1	12.0 (50)	50/50	12.0 (50)	100	50/50	12.0 (50)	100	50/50	11.2 (50)	93	50/50
2	12.2 (50)	50/50	12.1 (50)	99	50/50	11.9 (50)	98	50/50	11.0 (50)	90	50/50
3	12.0 (50)	50/50	12.1 (50)	101	50/50	12.0 (50)	100	50/50	11.4 (50)	95	50/50
4	12.4 (50)	50/50	12.5 (50)	101	50/50	12.3 (50)	99	50/50	11.4 (50)	92	50/50
5	13.1 (50)	50/50	13.0 (50)	99	50/50	12.6 (50)	96	50/50	12.1 (50)	92	50/50
6	12.9 (50)	50/50	12.6 (50)	98	50/50	12.4 (50)	96	50/50	11.8 (50)	91	50/50
7	12.6 (50)	50/50	12.5 (50)	99	50/50	11.8 (50)	94	50/50	11.3 (50)	90	50/50
8	12.6 (50)	50/50	12.4 (50)	98	50/50	11.8 (50)	94	50/50	11.4 (50)	90	50/50
9	13.1 (50)	50/50	12.7 (50)	97	50/50	12.3 (50)	94	50/50	11.9 (50)	91	50/50
10	12.9 (50)	50/50	12.8 (50)	99	50/50	12.5 (50)	97	50/50	11.9 (50)	92	50/50
11	12.8 (50)	50/50	13.0 (49)	102	50/50	12.8 (50)	100	50/50	12.3 (50)	96	50/50
12	13.2 (50)	50/50	12.7 (50)	96	50/50	12.3 (50)	93	50/50	11.9 (50)	90	50/50
13	13.2 (50)	50/50	12.8 (50)	97	50/50	12.5 (50)	95	50/50	12.5 (50)	95	50/50
14	12.8 (50)	50/50	12.9 (50)	101	50/50	12.3 (50)	96	50/50	12.1 (50)	95	50/50
18	12.4 (50)	50/50	12.7 (50)	102	50/50	12.3 (50)	99	50/50	12.1 (50)	98	50/50
22	12.9 (50)	50/50	12.8 (50)	99	50/50	12.3 (50)	95	50/50	12.7 (50)	98	50/50
26	12.5 (50)	50/50	12.9 (50)	103	50/50	12.4 (50)	99	50/50	12.6 (50)	101	50/50
30	13.5 (50)	50/50	13.7 (50)	101	50/50	13.2 (50)	98	50/50	13.3 (50)	99	50/50
34	12.9 (50)	50/50	13.3 (50)	103	50/50	12.7 (50)	98	50/50	13.1 (50)	102	50/50
38	12.6 (50)	50/50	12.8 (50)	102	50/50	12.2 (50)	97	50/50	13.0 (50)	103	50/50
42	13.3 (50)	50/50	13.2 (50)	99	50/50	12.8 (50)	96	50/50	13.2 (50)	99	50/50
46	13.2 (50)	50/50	13.0 (50)	98	50/50	12.8 (50)	97	50/50	13.1 (50)	99	50/50
50	13.7 (50)	50/50	13.5 (45)	99	50/50	13.3 (50)	97	50/50	13.5 (50)	99	50/50
54	12.9 (50)	50/50	13.1 (50)	102	50/50	12.2 (50)	95	50/50	13.3 (50)	103	50/50
58	13.2 (50)	50/50	13.9 (50)	105	50/50	12.7 (50)	96	50/50	12.9 (50)	98	50/50
62	13.2 (50)	50/50	13.1 (50)	99	50/50	13.0 (50)	98	50/50	13.6 (49)	103	49/50
66	13.7 (50)	50/50	13.9 (50)	101	50/50	13.6 (50)	99	50/50	14.0 (47)	102	47/50
70	13.7 (50)	50/50	14.0 (50)	102	50/50	13.7 (50)	100	50/50	14.3 (47)	104	47/50
74	14.2 (49)	49/50	14.9 (49)	105	49/50	14.3 (50)	101	50/50	14.4 (47)	101	47/50
78	14.3 (49)	49/50	14.7 (49)	103	49/50	14.8 (50)	103	50/50	14.8 (44)	103	44/50
82	14.3 (48)	48/50	14.6 (49)	102	49/50	13.8 (50)	97	50/50	14.7 (44)	103	44/50
86	14.8 (47)	48/50	15.1 (48)	102	48/50	15.1 (48)	102	48/50	15.6 (42)	105	42/50
90	15.1 (46)	46/50	14.3 (48)	95	48/50	15.4 (48)	102	48/50	15.6 (39)	103	39/50
94	14.5 (46)	46/50	14.6 (45)	101	45/50	15.0 (47)	103	47/50	14.6 (39)	101	39/50
98	14.4 (46)	46/50	13.6 (43)	94	42/50	13.7 (45)	95	45/50	15.2 (36)	106	36/50
102	15.2 (45)	45/50	14.0 (41)	92	41/50	14.5 (42)	95	43/50	14.5 (32)	95	31/50
104	13.6 (45)	45/50	13.3 (40)	98	40/50	13.7 (43)	101	43/50	13.9 (31)	102	30/50

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

TABLE 8 SELECTED NON NEOPLASTIC LESIONS OF MALE RATS IN THE 2-YEAR INHALATION STUDY OF DICHLOROMETHANE

	Group Name	Control				1000 ppm				2000 ppm				4000 ppm			
	No. of Animals	50				50				50				50			
Organ	Findings Grade a)	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
spleen		<50> b)				<50>				<50>				<50>			
	fibrosis	1	0	0	0	1	1	0	0	3	2	0	0	6	5	0	0 **
eye		<50>				<50>				<50>				<50>			
	mineralization:cornea	33	0	0	0	25	0	0	0	26	0	0	0	17	0	0	0 **
liver		<50>				<50>				<50>				<50>			
	acidophilic cell focus	2	1	0	0	8	0	0	0	9	5	0	0 *	13	10	0	0 **
	basophilic cell focus	18	0	0	0	28	8	1	0 **	15	25	0	0 **	11	23	2	0 **
	vacuolated cell focus	2	0	0	0	7	0	0	0	12	1	0	0 **	8	3	0	0 *

a) 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

b) : Number of animals examined at the site

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

TABLE 9 SELECTED NON NEOPLASTIC LESIONS OF FEMALE RATS IN THE 2-YEAR INHALATION STUDY OF DICHLOROMETHANE

	Group Name	Control				1000 ppm				2000 ppm				4000 ppm			
	No. of Animals	50				50				50				50			
Organ	Findings Grade a)	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
kidney		<50> b)				<50>				<50>				<50>			
	chronic nephropathy	8	23	14	3	22	21	2	0 **	19	17	5	0 **	27	6	5	0 **

a) 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

b) : Number of animals examined at the site

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

TABLE 10 NEOPLASTIC LESIONS INCIDENCE AND STATISTICAL ANALYSIS IN MALE RATS IN THE 2-YEAR INHALATION STUDY OF DICHLOROMETHANE

Group Name	Control	1000ppm	2000ppm	4000ppm
SITE : subcutis				
TUMOR : fibroma				
Tumor rate				
Overall rates(a)	1/50(2.0)	4/50(8.0)	7/50(14.0)	12/50(24.0)
Adjusted rates(b)	3.13	9.30	15.56	36.67
Terminal rates(c)	1/32(3.1)	4/43(9.3)	5/38(13.2)	10/28(35.7)
Statistical analysis				
Peto test				
Standard method(d)	P=0.0799 ?			
Prevalence method(d)	P=0.0001**			
Combined analysis (d)	P<0.0001**			
Cochran-Armitage test(e)	P=0.0004**			
Fisher Exact test(e)		P=0.1811	P=0.0297*	P=0.0009**
SITE : subcutis				
TUMOR : fibroma, fibrosarcoma				
Tumor rate				
Overall rates(a)	1/50(2.0)	4/50(8.0)	8/50(16.0)	12/50(24.0)
Adjusted rates(b)	3.13	9.30	17.78	36.67
Terminal rates(c)	1/32(3.1)	4/43(9.3)	6/38(15.8)	10/28(35.7)
Statistical analysis				
Peto test				
Standard method(d)	P=0.0799 ?			
Prevalence method(d)	P=0.0001**			
Combined analysis (d)	P<0.0001**			
Cochran-Armitage test(e)	P=0.0005**			
Fisher Exact test(e)		P=0.1811	P=0.0154*	P=0.0009**
SITE : mammary gland				
TUMOR : fibroadenoma				
Tumor rate				
Overall rates(a)	1/50(2.0)	2/50(4.0)	3/50(6.0)	8/50(16.0)
Adjusted rates(b)	3.13	4.65	6.12	25.00
Terminal rates(c)	1/32(3.1)	2/43(4.7)	2/38(5.3)	7/28(25.0)
Statistical analysis				
Peto test				
Standard method(d)	P=0.0923			
Prevalence method(d)	P=0.0020**			
Combined analysis (d)	P=0.0007**			
Cochran-Armitage test(e)	P=0.0037**			
Fisher Exact test(e)		P=0.5000	P=0.3086	P=0.0154*
SITE : mammary gland				
TUMOR : adenoma, fibroadenoma				
Tumor rate				
Overall rates(a)	2/50(4.0)	2/50(4.0)	3/50(6.0)	8/50(16.0)
Adjusted rates(b)	6.25	4.65	6.12	25.00
Terminal rates(c)	2/32(6.3)	2/43(4.7)	2/38(5.3)	7/28(25.0)
Statistical analysis				
Peto test				
Standard method(d)	P=0.0923			
Prevalence method(d)	P=0.0068**			
Combined analysis (d)	P=0.0026**			
Cochran-Armitage test(e)	P=0.0126*			
Fisher Exact test(e)		P=0.3088	P=0.4999	P=0.0458*

TABLE 10 NEOPLASTIC LESIONS INCIDENCE AND STATISTICAL ANALYSIS IN MALE RATS IN THE 2-YEAR INHALATION STUDY OF DICHLOROMETHANE(continued)

Group Name	Control	1000ppm	2000ppm	4000ppm
SITE : mammary gland				
TUMOR : adenoma, fibroadenoma, adenocarcinoma				
Tumor rate				
Overall rates(a)	3/50(6.0)	2/50(4.0)	3/50(6.0)	8/50(16.0)
Adjusted rates(b)	6.25	4.65	6.12	25.00
Terminal rates(c)	2/32(6.3)	2/43(4.7)	2/38(5.3)	7/28(25.0)
Statistical analysis				
Peto test				
Standard method(d)	P=0.3854			
Prevalence method(d)	P=0.0068**			
Combined analysis (d)	P=0.0086**			
Cochran-Armitage test(e)	P=0.0345*			
Fisher Exact test(e)		P=0.4999	P=0.3388	P=0.0999
SITE : peritoneum				
TUMOR : mesothelioma				
Tumor rate				
Overall rates(a)	3/50(6.0)	1/50(2.0)	0/50(0.0)	7/50(14.0)
Adjusted rates(b)	5.13	0.0	0.0	14.29
Terminal rates(c)	1/32(3.1)	0/43(0.0)	0/38(0.0)	4/28(14.3)
Statistical analysis				
Peto test				
Standard method(d)	P=0.0960			
Prevalence method(d)	P=0.0568			
Combined analysis (d)	P=0.0198*			
Cochran-Armitage test(e)	P=0.0409*			
Fisher Exact test(e)		P=0.3086	P=0.1212	P=0.1590
SITE : liver				
TUMOR : hepatocellular adenoma, hepatocellular carcinoma				
Tumor rate				
Overall rates(a)	1/50(2.0)	0/50(0.0)	2/50(4.0)	3/50(6.0)
Adjusted rates(b)	3.13	0.0	5.26	10.71
Terminal rates(c)	1/32(3.1)	0/43(0.0)	2/38(5.3)	3/28(10.7)
Statistical analysis				
Peto test				
Standard method(d)	P=---------			
Prevalence method(d)	P=0.0371*			
Combined analysis (d)	P=---------			
Cochran-Armitage test(e)	P=0.1232			
Fisher Exact test(e)		P=0.4999	P=0.5000	P=0.3086

(a):Number of tumor-bearing animals/number of animals examined at the site.
(b):Kaplan-Meire 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 metho :Incidental tumor test
Combined analysi :Death analysis + Incidental tumor test
(e):The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.
? :The conditional probabities of the largest and smallest possible out comes can not be 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

TABLE 11 NEOPLASTIC LESIONS INCIDENCE AND STATISTICAL ANALYSIS IN FEMALE RATS IN THE 2-YEAR INHALATION STUDY OF DICHLOROMETHANE

Group Name	Control	1000ppm	2000ppm	4000ppm
SITE : mammary gland				
TUMOR : fibroadenoma				
Tumor rate				
Overall rates(a)	7/50(14.0)	7/50(14.0)	9/50(18.0)	14/50(28.0)
Adjusted rates(b)	15.56	15.00	20.93	43.33
Terminal rates(c)	7/45(15.6)	6/40(4.7)	9/43(20.9)	13/30(43.3)
Statistical analysis				
Peto test				
Standard method(d)	P=---------			
Prevalence method(d)	P=0.0029**			
Combined analysis (d)	P=---------			
Cochran-Armitage test(e)	P=0.0454**			
Fisher Exact test(e)		P=0.3866	P=0.3932	P=0.0699
SITE : mammary gland				
TUMOR : adenoma, fibroadenoma				
Tumor rate				
Overall rates(a)	7/50(14.0)	8/50(16.0)	10/50(20.0)	14/50(28.0)
Adjusted rates(b)	15.56	17.50	23.26	43.33
Terminal rates(c)	7/45(15.6)	7/40(17.5)	10/43(23.3)	13/30(43.3)
Statistical analysis				
Peto test				
Standard method(d)	P=---------			
Prevalence method(d)	P=0.0035**			
Combined analysis (d)	P=---------			
Cochran-Armitage test(e)	P=0.0574			
Fisher Exact test(e)		P=0.4996	P=0.2980	P=0.0699
SITE : mammary gland				
TUMOR : adenoma, fibroadenoma, adenocarcinoma				
Tumor rate				
Overall rates(a)	7/50(14.0)	9/50(18.0)	10/50(20.0)	14/50(28.0)
Adjusted rates(b)	15.56	18.18	23.26	43.33
Terminal rates(c)	7/45(15.6)	7/40(17.5)	10/43(23.3)	13/30(43.3)
Statistical analysis				
Peto test				
Standard method(d)	P=0.5814			
Prevalence method(d)	P=0.0038**			
Combined analysis (d)	P=0.0056**			
Cochran-Armitage test(e)	P=0.0730			
Fisher Exact test(e)		P=0.3932	P=0.2980	P=0.0699
SITE : uterus				
TUMOR : endometrial stromal polyp				
Tumor rate				
Overall rates(a)	8/50(16.0)	11/50(22.0)	6/50(12.0)	9/50(18.0)
Adjusted rates(b)	17.39	21.28	13.95	20.00
Terminal rates(c)	7/45(15.6)	8/40(20.0)	6/43(14.0)	6/30(20.0)
Statistical analysis				
Peto test				
Standard method(d)	P=0.0152*			
Prevalence method(d)	P=0.6589			
Combined analysis (d)	P=0.3162			
Cochran-Armitage test(e)	P=0.9493			
Fisher Exact test(e)		P=0.3059	P=0.3875	P=0.4995

TABLE 11 NEOPLASTIC LESIONS INCIDENCE AND STATISTICAL ANALYSIS IN FEMALE RATS IN THE 2-YEAR INHALATION STUDY OF DICHLOROMETHANE(continued)

Group Name	Control	1000ppm	2000ppm	4000ppm
SITE : uterus				
TUMOR : endometrial stromal sarcoma, leiomyosarcoma				
Tumor rate				
Overall rates(a)	0/50(0.0)	0/50(0.0)	0/50(0.0)	3/50(6.0)
Adjusted rates(b)	0.0	0.0	0.0	0.0
Terminal rates(c)	0/50(0.0)	0/40(0.0)	0/43(0.0)	0/30(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P=0.0034**?			
Prevalence method(d)	P=---------			
Combined analysis (d)	P=0.0034**?			
Cochran-Armitage test(e)	P=0.0079**			
Fisher Exact test(e)		P=0.5000	P=0.5000	P=0.1212
SITE : spleen				
TUMOR : mononclear cell lukemia				
Tumor rate				
Overall rates(a)	2/50(4.0)	4/50(8.0)	8/50(16.0)	7/50(14.0)
Adjusted rates(b)	2.22	7.50	9.30	10.00
Terminal rates(c)	1/45(2.2)	3/40(7.5)	4/43(9.3)	3/30(10.0)
Statistical analysis				
Peto test				
Standard method(d)	P=0.0375*			
Prevalence method(d)	P=0.1001			
Combined analysis (d)	P=0.0151*			
Cochran-Armitage test(e)	P=0.0793			
Fisher Exact test(e)		P=0.3389	P=0.0458*	P=0.0798
SITE : pituitary gland				
TUMOR : adenoma				
Tumor rate				
Overall rates(a)	18/50(36.0)	28/50(56.0)	24/50(48.0)	19/50(38.0)
Adjusted rates(b)	37.78	53.19	51.16	42.42
Terminal rates(c)	17/45(37.8)	19/40(47.5)	22/43(51.2)	12/30(40.0)
Statistical analysis				
Peto test				
Standard method(d)	P=0.1991			
Prevalence method(d)	P=0.5048			
Combined analysis (d)	P=0.3817			
Cochran-Armitage test(e)	P=0.7183			
Fisher Exact test(e)		P=0.0353*	P=0.1558	P=0.4991

TABLE 11 NEOPLASTIC LESIONS INCIDENCE AND STATISTICAL ANALYSIS IN FEMALE RATS IN THE 2-YEAR INHALATION STUDY OF DICHLOROMETHANE(continued)

Group Name	Control	1000ppm	2000ppm	4000ppm
SITE : pituitary gland				
TUMOR : adenoma, adenocarcinoma				
Tumor rate				
Overall rates(a)	19/50(38.0)	29/50(58.0)	24/50(48.0)	19/50(38.0)
Adjusted rates(b)	37.78	55.32	51.16	42.42
Terminal rates(c)	17/45(37.8)	20/40(50.0)	22/43(51.2)	12/30(40.0)
Statistical analysis				
Peto test				
Standard method(d)	P=0.3387			
Prevalence method(d)	P=0.5659			
Combined analysis (d)	P=0.4988			
Cochran-Armitage test(e)	P=0.5485			
Fisher Exact test(e)		P=0.0356*	P=0.2101	P=0.4173

(a):Number of tumor-bearing animals/number of animals examined at the si
(b):Kaplan-Meire 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 metho :Incidental tumor test
Combined analysi :Death analysis + Incidental tumor test
(e):The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.
? :The conditional probabities of the largest and smallest possible out comes can not be 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

TABLE 12 CAUSE OF DEATH OF RATS IN THE 2-YEAR INHALATION STUDY OF DICHLOROMETHANE

	Male				Female			
Group	Control	1000ppm	2000ppm	4000ppm	Control	1000ppm	2000ppm	4000ppm
Number of dead or moribund animals	18	7	12	22	5	10	7	20
No microscopical confirmation	0	0	0	1	0	0	0	0
Cardiovascular lesion	0	1	0	0	0	0	0	1
Digestive system lesion	2	0	1	0	0	0	0	1
Renal lesion	0	0	0	2	0	0	1	2
Thrombosis	0	0	0	0	0	1	0	0
Hemorrhage	0	0	0	0	0	1	0	0
Urinary retention	0	0	1	0	0	0	0	0
Chronic nephropathy	2	0	2	3	0	0	0	0
Tumor death : leukemia	3	1	5	4	2	3	5	4
subcutis	1	0	1	3	0	0	0	0
lung	1	0	0	0	0	0	0	0
oral cavity	0	0	0	0	1	0	0	0
stomach	1	0	0	0	0	0	0	0
liver	1	0	0	0	0	0	0	0
pancreas	0	1	0	0	0	0	0	0
kidney	0	1	0	1	0	0	0	0
urinary bladder	0	0	0	2	0	0	0	0
pituitary	3	0	1	1	2	3	0	4
thyroid	0	1	0	0	0	0	0	1
ovary	-	-	-	-	0	0	0	1
uterus	-	-	-	-	0	1	0	6
brain	2	0	0	2	0	0	0	0
mamary gland	0	0	0	1	0	1	0	0
brain	1	0	1	0	0	0	0	0
Zymbal gland	1	1	0	0	0	0	0	0
bone	0	0	0	0	0	0	1	0
peritoneum	2	1	0	3	0	0	0	0
retroperit	0	0	0	1	0	0	0	0