

メタリルクロライドのマウスを用いた
吸入によるがん原性試験報告書

試験番号：0270

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

2-year study

<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	
Crj:BDF ₁ mouse	
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	: 0, 50, 100, or 200 ppm
Female	: 0, 50, 100, or 200 ppm
<Duration of Dosing>	
6h/d, 5d/wk, for 104wk	
<Animal Maintenance>	
Feed	
CRF-1 (Oriental Yeast Co., Ltd.)	
Sterilized by γ -ray	
Available <i>ad libitum</i>	
Water	
Filtrated and sterilized by ultraviolet ray	
Automatic watering system in duration of quarantine	
Available <i>ad libitum</i>	
Animal per Cage	
Single (stainless steel wire)	
Animal Room Environment	
Barrier system	
Temperature	
Fluorescent light 12h/d	
Chamber Environment	: $23 \pm 3^{\circ}\text{C}$
Temperature	: $22 \pm 2^{\circ}\text{C}$
Humidity	: $55 \pm 15\%$
Air changes	: $12 \pm 1/\text{h}$
Pressure	: $0 \sim -15\text{mmAq}$
<Type and Frequency of Observation>	
Clinical sign	
Observed 1 per d	
Body weight	
Weighed 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 EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE 2-YEAR
(continued) INHALATION STUDY OF 2-METHALLYL CHLORIDE

2-year study

<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,
Glutamic oxaloacetic transaminase (GOT),
Glutamic pyruvic transaminase (GPT),
Lactate dehydrogenase (LDH),
Alkaline phosphatase (ALP),
Creatine phosphokinase (CPK),
Urea nitrogen,
Sodium, Potassium, Chloride,
Calcium, Inorganic phosphorus.

<Urinalysis>

pH, Protein, Glucose, Ketone body,
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, 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, 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 MICE IN THE 2-YEAR INHALATION STUDY OF 2-METHALLYL CHLORIDE

Week on Study	Control		50 ppm			100 ppm			200 ppm		
	Au.Wt.	No.of Surviv. <50>	Au.Wt.	% of cont. <50>	No.of Surviv.	Au.Wt.	% of cont. <50>	No.of Surviv.	Au.Wt.	% of cont. <50>	No.of Surviv.
0	22.2 (50)	50/50	22.2 (50)	100	50/50	22.2 (50)	100	50/50	22.2 (50)	100	50/50
1	22.5 (50)	50/50	22.2 (50)	99	50/50	22.5 (50)	100	50/50	22.2 (50)	99	50/50
1	23.8 (50)	50/50	23.6 (50)	99	50/50	23.9 (50)	100	50/50	22.6 (50)	95	50/50
2	25.0 (50)	50/50	24.6 (50)	98	50/50	24.8 (50)	99	50/50	23.9 (50)	96	50/50
3	25.8 (50)	50/50	25.1 (50)	97	50/50	25.7 (50)	100	50/50	25.0 (50)	97	50/50
4	26.5 (50)	50/50	26.0 (50)	98	50/50	26.4 (49)	100	49/50	25.7 (50)	97	50/50
5	27.1 (50)	50/50	26.6 (50)	98	50/50	27.0 (49)	100	49/50	26.7 (50)	99	50/50
6	27.8 (50)	50/50	27.4 (50)	99	50/50	27.4 (49)	99	49/50	26.8 (50)	96	50/50
7	28.4 (50)	50/50	27.9 (50)	98	50/50	28.0 (49)	99	49/50	27.2 (50)	96	50/50
8	29.1 (50)	50/50	28.5 (50)	98	50/50	28.6 (49)	98	49/50	27.8 (50)	96	50/50
9	29.7 (50)	50/50	29.1 (50)	98	50/50	29.0 (49)	98	49/50	28.4 (50)	96	50/50
10	30.4 (50)	50/50	29.8 (50)	98	50/50	29.5 (49)	97	49/50	28.8 (50)	95	50/50
11	31.0 (50)	50/50	30.3 (50)	98	50/50	29.9 (49)	96	49/50	28.7 (50)	93	50/50
12	31.5 (50)	50/50	30.5 (50)	97	50/50	30.4 (49)	97	49/50	29.1 (50)	92	50/50
13	32.2 (50)	50/50	31.1 (50)	97	50/50	31.2 (49)	97	49/50	29.5 (50)	92	50/50
14	32.7 (50)	50/50	31.6 (50)	97	50/50	31.6 (49)	97	49/50	30.2 (50)	92	50/50
18	34.2 (50)	50/50	33.2 (50)	97	50/50	33.0 (49)	96	49/50	31.3 (50)	92	50/50
22	35.8 (50)	50/50	34.9 (50)	97	50/50	34.4 (49)	96	49/50	32.8 (50)	92	50/50
26	37.6 (50)	50/50	36.6 (50)	97	50/50	36.2 (49)	96	49/50	33.9 (50)	90	50/50
30	39.5 (50)	50/50	37.9 (50)	96	50/50	37.7 (49)	95	49/50	35.9 (49)	91	49/50
34	41.3 (50)	50/50	39.5 (50)	96	50/50	38.9 (49)	94	49/50	37.3 (49)	90	49/50
38	41.7 (50)	50/50	40.0 (50)	96	50/50	39.1 (49)	94	49/50	37.3 (49)	89	49/50
42	43.4 (50)	50/50	41.3 (49)	95	49/50	39.7 (49)	91	49/50	37.9 (49)	87	49/50
46	44.7 (50)	50/50	42.5 (49)	95	49/50	40.9 (49)	91	49/50	38.8 (49)	87	49/50
50	46.0 (50)	50/50	43.8 (49)	95	49/50	41.6 (49)	90	49/50	39.5 (49)	86	49/50
54	47.0 (49)	49/50	44.6 (49)	95	49/50	42.0 (49)	89	49/50	39.9 (49)	85	49/50
58	48.2 (48)	48/50	45.8 (49)	95	49/50	42.7 (49)	89	49/50	40.1 (48)	83	48/50
62	48.6 (48)	48/50	46.0 (49)	95	49/50	42.7 (49)	88	49/50	40.1 (48)	83	48/50
66	48.8 (48)	48/50	46.0 (49)	94	49/50	42.6 (49)	87	49/50	39.9 (48)	82	48/50
70	48.5 (48)	48/50	45.3 (49)	93	49/50	42.1 (49)	87	49/50	39.1 (48)	81	48/50
74	49.3 (47)	47/50	45.2 (49)	92	49/50	41.3 (49)	84	49/50	38.7 (48)	78	48/50
78	49.1 (46)	46/50	45.3 (49)	92	49/50	41.7 (49)	85	49/50	38.9 (48)	79	48/50
82	49.4 (46)	46/50	46.2 (48)	94	48/50	42.1 (49)	85	49/50	39.1 (48)	79	48/50
86	49.4 (46)	46/50	47.0 (48)	95	48/50	42.6 (49)	86	49/50	40.0 (48)	81	48/50
90	49.6 (46)	46/50	46.8 (47)	94	47/50	43.3 (47)	87	47/50	40.6 (48)	82	48/50
94	50.2 (44)	44/50	46.6 (46)	93	46/50	43.2 (47)	86	47/50	40.1 (46)	80	46/50
98	49.8 (43)	43/50	46.7 (45)	94	45/50	42.6 (46)	86	45/50	40.5 (46)	81	46/50
102	49.5 (40)	40/50	46.8 (44)	95	44/50	42.7 (45)	86	45/50	40.6 (46)	82	46/50
104	49.2 (40)	40/50	46.8 (44)	95	44/50	43.0 (43)	87	43/50	40.4 (46)	82	46/50

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

Au.Wt.: g

TABLE 3 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 2-METHALLYL CHLORIDE

Week on Study	Control		50 ppm		No. of Surviv.	100 ppm		No. of Surviv.	200 ppm		No. of Surviv.
	Au. Wt.	No. of Surviv. <50>	Au. Wt.	% of cont. <48>		Au. Wt.	% of cont. <50>		Au. Wt.	% of cont. <49>	
0	18.6 (50)	50/50	18.6 (48)	100	50/50	18.6 (50)	100	50/50	18.6 (49)	100	50/50
1	18.3 (50)	50/50	18.2 (48)	99	50/50	18.3 (50)	100	50/50	18.2 (49)	99	50/50
1	19.4 (50)	50/50	19.4 (48)	100	50/50	19.4 (50)	100	50/50	19.2 (49)	99	50/50
2	20.6 (50)	50/50	20.3 (48)	99	49/49	20.4 (50)	99	50/50	19.7 (49)	96	50/50
3	21.1 (50)	50/50	20.9 (48)	99	49/49	20.9 (50)	99	50/50	20.5 (49)	97	50/50
4	22.1 (50)	50/50	21.8 (48)	99	49/49	21.7 (50)	98	50/50	21.3 (49)	96	50/50
5	22.4 (50)	50/50	22.1 (48)	99	49/49	22.0 (50)	98	50/50	22.1 (49)	99	50/50
6	23.2 (50)	50/50	22.7 (48)	98	49/49	22.5 (50)	97	50/50	22.2 (49)	96	50/50
7	23.5 (50)	50/50	23.1 (48)	98	49/49	22.9 (50)	97	50/50	22.4 (49)	95	50/50
8	23.9 (50)	50/50	23.3 (48)	97	49/49	23.4 (50)	98	50/50	22.8 (49)	95	50/50
9	24.0 (50)	50/50	23.3 (48)	97	49/49	23.2 (50)	97	50/50	23.1 (49)	96	50/50
10	24.0 (50)	50/50	23.6 (48)	98	49/49	23.4 (50)	98	50/50	23.1 (49)	96	50/50
11	24.3 (50)	50/50	23.9 (48)	98	49/49	23.8 (50)	98	50/50	23.4 (49)	96	50/50
12	24.8 (50)	50/50	24.3 (48)	98	49/49	24.2 (50)	98	50/50	23.4 (49)	94	50/50
13	24.8 (50)	50/50	24.5 (48)	99	49/49	24.0 (50)	97	50/50	23.7 (49)	96	50/50
14	25.1 (50)	50/50	24.7 (48)	98	49/49	24.0 (50)	96	50/50	23.8 (49)	95	50/50
18	26.4 (50)	50/50	25.1 (48)	95	49/49	24.8 (50)	94	50/50	24.4 (49)	92	50/50
22	26.8 (50)	50/50	25.5 (48)	95	49/49	25.3 (50)	94	50/50	24.5 (49)	91	50/50
26	27.5 (50)	50/50	25.7 (48)	93	49/49	25.4 (50)	92	50/50	24.8 (49)	90	50/50
30	28.0 (50)	50/50	26.3 (48)	94	49/49	25.6 (50)	91	50/50	24.7 (49)	88	50/50
34	29.0 (50)	50/50	27.0 (48)	93	49/49	25.7 (50)	89	50/50	25.1 (49)	87	50/50
38	29.3 (50)	50/50	26.8 (48)	91	49/49	26.1 (50)	89	50/50	25.2 (49)	86	50/50
42	30.3 (50)	50/50	27.5 (48)	91	49/49	26.6 (50)	88	50/50	25.3 (49)	83	50/50
46	31.0 (50)	50/50	28.0 (48)	90	49/49	26.5 (50)	85	50/50	25.7 (48)	83	49/50
50	31.3 (48)	48/50	28.4 (48)	91	49/49	26.9 (50)	86	50/50	26.0 (48)	83	49/50
54	31.7 (48)	48/50	28.8 (47)	91	48/49	27.2 (50)	86	50/50	26.1 (48)	82	49/50
58	32.2 (48)	48/50	29.6 (47)	92	48/49	27.2 (50)	84	50/50	26.3 (48)	82	49/50
62	32.4 (48)	48/50	29.8 (47)	92	48/49	27.8 (50)	86	50/50	26.5 (46)	82	47/50
66	32.0 (47)	47/50	29.5 (46)	92	47/49	27.9 (49)	87	49/50	26.5 (46)	83	47/50
70	32.0 (47)	47/50	29.6 (46)	93	47/49	28.2 (49)	88	49/50	26.8 (46)	84	46/49
74	32.3 (47)	47/50	30.3 (45)	94	46/49	28.0 (47)	87	47/50	26.5 (46)	82	46/49
78	32.1 (43)	43/50	30.3 (45)	94	45/48	28.3 (44)	88	44/50	27.1 (46)	84	46/49
82	32.2 (41)	41/50	31.0 (43)	96	43/48	28.4 (42)	88	42/50	27.3 (45)	85	45/49
86	32.9 (40)	40/50	31.1 (41)	95	41/48	28.9 (41)	88	41/50	27.9 (44)	85	44/49
90	33.0 (39)	39/50	32.2 (39)	98	39/48	29.0 (40)	88	40/50	28.1 (42)	85	42/49
94	32.6 (38)	38/50	32.4 (37)	99	37/48	28.9 (38)	89	38/50	28.1 (41)	86	41/49
98	33.0 (35)	35/50	32.6 (35)	99	35/48	29.6 (38)	90	38/50	27.8 (38)	84	38/49
102	33.6 (30)	30/50	32.9 (31)	98	31/48	30.9 (34)	92	34/50	28.6 (33)	85	33/49
104	34.2 (29)	29/50	32.6 (29)	95	29/48	30.6 (31)	89	31/50	28.8 (33)	84	33/49

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

Au. Wt.: g

TABLE 4 INCIDENCE OF EXTERNAL AND INTERNAL MASS IN CLINICAL OBSERVATION OF MALE MICE
IN THE 2-YEAR INHALATION STUDY OF 2-METHALLYL CHLORIDE

Time of mass occurrence (week)		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	1/50	2/49	3/48	4/46	4/44	5/50(2/10)
50ppm		0/50	0/50	0/50	0/49	0/49	0/49	0/49	1/46	1/50(1/ 6)
100ppm		0/50	0/49	0/49	0/49	1/49	2/49	5/49	7/47	7/50(2/ 7)
200ppm		0/50	0/50	0/49	0/49	0/49	0/48	0/48	3/47	3/50(0/ 4)
Internal mass										
Control		0/50	2/50	2/50	2/50	1/49	1/48	3/46	7/44	8/50(2/10)
50ppm		0/50	3/50	3/50	3/49	3/49	3/49	4/49	3/46	5/50(2/ 6)
100ppm		0/50	0/49	0/49	0/49	1/49	2/49	2/49	2/47	3/50(0/ 7)
200ppm		0/50	0/50	1/49	1/49	1/49	1/48	2/48	2/47	3/50(2/ 4)

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 MICE
IN THE 2-YEAR INHALATION STUDY OF 2-METHALLYL CHLORIDE

Time of mass occurrence (week)		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	2/48	2/47	1/42	3/39	6/50(4/21)
50ppm		0/48	0/48	0/48	0/48	0/47	1/46	2/45	4/37	5/48(2/19)
100ppm		0/50	0/50	0/50	0/50	0/50	0/49	0/43	3/39	3/50(2/19)
200ppm		0/49	0/49	0/49	0/49	0/48	1/46	2/46	4/42	5/49(3/16)
Internal mass										
Control		0/50	0/50	0/50	1/50	0/48	4/47	5/42	6/39	11/50(8/21)
50ppm		0/48	0/48	0/48	1/48	2/47	4/46	7/45	11/37	18/48(10/19)
100ppm		0/50	0/50	0/50	0/50	3/50	6/49	5/43	12/39	19/50(13/19)
200ppm		0/49	0/49	0/49	1/49	0/48	2/46	5/46	10/42	12/49(7/16)

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 MICE IN THE 2-YEAR INHALATION STUDY OF 2-METHALLYL CHLORIDE

Week on Study	Control			50 ppm			100 ppm			200 ppm		
	Au.FC.	No.of Surviv. <50>		Au.FC.	% of cont. <50>	No.of Surviv.	Au.FC.	% of cont. <50>	No.of Surviv.	Au.FC.	% of cont. <50>	No.of Surviv.
1	4.2 (50)	50/50		4.2 (50)	100	50/50	4.2 (50)	100	50/50	3.7 (50)	88	50/50
2	4.1 (50)	50/50		4.0 (50)	98	50/50	4.3 (50)	105	50/50	4.4 (50)	107	50/50
3	4.2 (50)	50/50		4.0 (50)	95	50/50	4.3 (50)	102	50/50	4.2 (50)	100	50/50
4	4.3 (50)	50/50		4.1 (50)	95	50/50	4.4 (49)	102	49/50	4.3 (50)	100	50/50
5	4.3 (50)	50/50		4.1 (50)	95	50/50	4.2 (49)	98	49/50	4.1 (50)	95	50/50
6	4.3 (50)	50/50		4.2 (50)	98	50/50	4.4 (49)	102	49/50	4.2 (50)	98	50/50
7	4.4 (50)	50/50		4.2 (50)	95	50/50	4.5 (49)	102	49/50	4.3 (50)	98	50/50
8	4.5 (50)	50/50		4.3 (50)	96	50/50	4.5 (49)	100	49/50	4.4 (50)	98	50/50
9	4.4 (50)	50/50		4.3 (50)	98	50/50	4.4 (49)	100	49/50	4.4 (50)	100	50/50
10	4.5 (50)	50/50		4.3 (50)	96	50/50	4.4 (49)	98	49/50	4.3 (50)	96	50/50
11	4.5 (50)	50/50		4.2 (50)	93	50/50	4.3 (49)	96	49/50	4.1 (50)	91	50/50
12	4.4 (50)	50/50		4.2 (50)	95	50/50	4.4 (49)	100	49/50	4.4 (50)	100	50/50
13	4.4 (50)	50/50		4.2 (50)	95	50/50	4.3 (49)	98	49/50	4.4 (50)	100	50/50
14	4.4 (50)	50/50		4.3 (50)	98	50/50	4.4 (49)	100	49/50	4.4 (50)	100	50/50
18	4.4 (50)	50/50		4.3 (50)	98	50/50	4.3 (49)	98	49/50	4.2 (50)	95	50/50
22	4.5 (50)	50/50		4.4 (50)	98	50/50	4.5 (49)	100	49/50	4.4 (50)	98	50/50
26	4.7 (50)	50/50		4.6 (50)	98	50/50	4.6 (49)	98	49/50	4.5 (50)	96	50/50
30	4.8 (50)	50/50		4.6 (50)	96	50/50	4.6 (49)	96	49/50	4.6 (49)	96	49/50
34	4.7 (50)	50/50		4.6 (50)	98	50/50	4.5 (49)	96	49/50	4.3 (49)	91	49/50
38	4.8 (50)	50/50		4.7 (50)	98	50/50	4.5 (49)	94	49/50	4.4 (49)	92	49/50
42	5.0 (50)	50/50		4.7 (49)	94	49/50	4.6 (49)	92	49/50	4.5 (49)	90	49/50
46	5.0 (50)	50/50		4.7 (49)	94	49/50	4.7 (49)	94	49/50	4.6 (49)	92	49/50
50	5.0 (50)	50/50		4.8 (49)	96	49/50	4.8 (48)	96	49/50	4.6 (49)	92	49/50
54	5.2 (49)	49/50		4.9 (49)	94	49/50	4.8 (49)	92	49/50	4.7 (49)	90	49/50
58	5.2 (48)	48/50		5.0 (49)	96	49/50	4.9 (49)	94	49/50	4.7 (48)	90	48/50
62	5.2 (48)	48/50		4.8 (49)	92	49/50	4.8 (49)	92	49/50	4.6 (47)	88	48/50
66	5.0 (48)	48/50		4.7 (49)	94	49/50	4.6 (49)	92	49/50	4.4 (48)	88	48/50
70	5.0 (48)	48/50		4.7 (49)	94	49/50	4.6 (49)	92	49/50	4.5 (48)	90	48/50
74	5.2 (47)	47/50		4.7 (49)	90	49/50	4.7 (49)	90	49/50	4.6 (48)	88	48/50
78	5.2 (46)	46/50		4.7 (49)	90	49/50	4.8 (49)	92	49/50	4.6 (48)	88	48/50
82	5.4 (46)	46/50		5.0 (48)	93	48/50	4.8 (49)	89	49/50	4.6 (48)	85	48/50
86	5.4 (46)	46/50		5.1 (48)	94	48/50	4.9 (49)	91	49/50	4.7 (48)	87	48/50
90	5.4 (46)	46/50		5.1 (47)	94	47/50	5.0 (47)	93	47/50	4.8 (48)	89	48/50
94	5.3 (44)	44/50		5.0 (46)	94	46/50	5.2 (47)	98	47/50	5.2 (46)	98	46/50
98	5.3 (43)	43/50		4.9 (45)	92	45/50	4.7 (46)	89	45/50	4.7 (46)	89	46/50
102	5.1 (40)	40/50		4.9 (44)	96	44/50	4.7 (45)	92	45/50	4.6 (46)	90	46/50
104	5.1 (40)	40/50		4.9 (44)	96	44/50	4.8 (43)	94	43/50	4.7 (46)	92	46/50

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

Au.FC.:g

TABLE 7 FOOD CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 2-METHALLYL CHLORIDE

Week on Study	Control			50 ppm			100 ppm			200 ppm		
	Au.FC.	No.of Surviv. <50>		Au.FC.	% of cont. <48>	No.of Surviv.	Au.FC.	% of cont. <50>	No.of Surviv.	Au.FC.	% of cont. <49>	No.of Surviv.
1	3.6 (50)	50/50		3.5 (48)	97	50/50	3.6 (50)	100	50/50	3.4 (49)	94	50/50
2	3.6 (50)	50/50		3.5 (48)	97	49/49	3.8 (50)	106	50/50	3.7 (49)	103	50/50
3	3.9 (50)	50/50		3.7 (48)	95	49/49	3.8 (50)	97	50/50	3.7 (49)	95	50/50
4	4.1 (50)	50/50		3.9 (48)	95	49/49	4.0 (50)	98	50/50	3.8 (49)	93	50/50
5	4.1 (50)	50/50		3.9 (48)	95	49/49	4.0 (50)	98	50/50	3.8 (49)	93	50/50
6	4.3 (50)	50/50		4.1 (48)	95	49/49	4.2 (50)	98	50/50	3.9 (49)	91	50/50
7	4.4 (50)	50/50		4.1 (48)	93	49/49	4.4 (50)	100	50/50	4.0 (49)	91	50/50
8	4.5 (50)	50/50		4.2 (48)	93	49/49	4.3 (50)	96	50/50	4.1 (49)	91	50/50
9	4.3 (50)	50/50		4.1 (48)	95	49/49	4.2 (50)	98	50/50	4.1 (49)	95	50/50
10	4.3 (50)	50/50		4.1 (48)	95	49/49	4.2 (50)	98	50/50	4.1 (49)	95	50/50
11	4.3 (50)	50/50		4.0 (48)	93	49/49	4.1 (50)	95	50/50	3.9 (49)	91	50/50
12	4.4 (50)	50/50		4.1 (48)	93	49/49	4.2 (50)	95	50/50	4.1 (49)	93	50/50
13	4.2 (50)	50/50		4.0 (48)	95	49/49	4.0 (50)	95	50/50	4.3 (49)	102	50/50
14	4.3 (50)	50/50		4.0 (48)	93	49/49	4.1 (50)	95	50/50	4.1 (49)	95	50/50
18	4.3 (50)	50/50		4.0 (48)	93	49/49	4.0 (50)	93	50/50	3.9 (49)	91	50/50
22	4.3 (50)	50/50		3.9 (48)	91	49/49	4.0 (50)	93	50/50	3.9 (49)	91	50/50
26	4.4 (50)	50/50		4.0 (48)	91	49/49	4.1 (50)	93	50/50	3.9 (49)	89	50/50
30	4.4 (50)	50/50		4.1 (48)	93	49/49	4.0 (50)	91	50/50	3.8 (49)	86	50/50
34	4.4 (50)	50/50		4.0 (48)	91	49/49	3.9 (50)	89	50/50	3.6 (49)	82	50/50
38	4.5 (50)	50/50		4.1 (48)	91	49/49	4.0 (50)	89	50/50	3.8 (49)	84	50/50
42	4.7 (50)	50/50		4.1 (48)	87	49/49	4.2 (50)	89	50/50	3.9 (49)	83	50/50
46	4.6 (50)	50/50		4.2 (48)	91	49/49	4.1 (50)	89	50/50	3.9 (48)	85	49/50
50	4.5 (49)	48/50		4.1 (48)	91	49/49	4.2 (50)	93	50/50	3.9 (48)	87	49/50
54	4.7 (48)	48/50		4.3 (47)	91	48/49	4.3 (50)	91	50/50	4.0 (48)	85	49/50
58	4.7 (48)	48/50		4.4 (47)	94	48/49	4.3 (50)	91	50/50	4.1 (48)	87	49/50
62	4.7 (48)	48/50		4.3 (47)	91	48/49	4.3 (50)	91	50/50	4.1 (46)	87	47/50
66	4.4 (47)	47/50		4.1 (46)	93	47/49	4.1 (49)	93	49/50	3.9 (46)	89	47/50
70	4.4 (47)	47/50		4.2 (46)	95	47/49	4.1 (49)	93	49/50	4.0 (46)	91	46/49
74	4.5 (47)	47/50		4.3 (45)	96	46/49	4.2 (47)	93	47/50	4.0 (46)	89	46/49
78	4.4 (43)	43/50		4.1 (45)	93	45/48	4.2 (44)	95	44/50	4.0 (46)	91	46/49
82	4.5 (41)	41/50		4.4 (43)	98	43/48	4.2 (42)	93	42/50	4.0 (45)	89	45/49
86	4.7 (40)	40/50		4.3 (41)	91	41/48	4.4 (41)	94	41/50	4.1 (44)	87	44/49
90	4.9 (39)	39/50		4.6 (39)	94	39/48	4.4 (40)	90	40/50	4.3 (42)	88	42/49
94	4.6 (38)	38/50		4.4 (37)	96	37/48	4.8 (38)	104	38/50	4.8 (41)	104	41/49
98	4.6 (35)	35/50		4.4 (35)	96	35/48	4.4 (38)	96	38/50	4.2 (38)	91	38/49
102	4.7 (30)	30/50		4.5 (31)	96	31/48	4.4 (34)	94	34/50	4.2 (33)	89	33/49
104	4.8 (29)	29/50		4.4 (29)	92	29/48	4.4 (31)	92	31/50	4.2 (33)	88	33/49

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

Au.FC.: g

TABLE 8 NEOPLASTIC LESIONS INCIDENCE AND STATISTICAL ANALYSIS OF MALE MICE
IN THE 2-YEAR INHALATION STUDY OF 2-METHALLYL CHLORIDE

Group Name	Control	50ppm	100ppm	200ppm
SITE : stomach				
TUMOR : squamous cell papilloma ^(f)				
Tumor rate				
Overall rates(a)	1/50(2.0)	0/49(0.0)	3/50(6.0)	4/50(8.0)
Adjusted rates(b)	2.50	0.0	6.98	8.70
Terminal rates(c)	1/40(2.5)	0/43(0.0)	3/43(7.0)	4/46(8.7)
Statistical analysis				
Peto test				
Standard method(d)	P=-----			
Prevalence method(d)	P=0.0392*			
Combined analysis (d)	P=-----			
Cochran-Armitage test(e)	P=0.0523			
Fisher Exact test(e)		P=0.4900	P=0.3235	P=0.1998
SITE : lymph node				
TUMOR : malignant lymphoma ^(g)				
Tumor rate				
Overall rates(a)	10/50(20.0)	8/50(16.0)	6/50(12.0)	1/50(2.0)
Adjusted rates(b)	20.00	13.64	6.98	0.00
Terminal rates(c)	8/40(20.0)	6/44(13.6)	3/43(7.0)	0/46(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P=0.6952			
Prevalence method(d)	P=0.9998			
Combined analysis (d)	P=0.9990			
Cochran-Armitage test(e)	P=0.0043**			
Fisher Exact test(e)		P=0.4300	P=0.2557	P=0.0088**
SITE : ALL SITE				
TUMOR : malignant lymphoma				
Tumor rate				
Overall rates(a)	14/50(28.0)	8/50(16.0)	6/50(12.0)	3/50(6.0)
Adjusted rates(b)	25.00	13.64	6.98	2.17
Terminal rates(c)	10/40(25.0)	6/44(13.6)	3/43(7.0)	1/46(2.2)
Statistical analysis				
Peto test				
Standard method(d)	P=0.7613			
Prevalence method(d)	P=0.9997			
Combined analysis (d)	P=0.9991			
Cochran-Armitage test(e)	P=0.0033**			
Fisher Exact test(e)		P=0.1781	P=0.0810	P=0.0114*

(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 method :Incidental tumor test

Combined analysis :Death analysis + Incidental tumor test

(e):The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.

(f):Historical incidence for 2-year studies: 0/847(0.0%); range 0% to 0%

(g):Historical incidence for 2-year studies: 82/847(9.7%);range 2% to 18%

?: The conditional probabilities of the largest and smallest possible outcomes 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 9 NEOPLASTIC LESIONS INCIDENCE AND STATISTICAL ANALYSIS OF FEMALE MICE
IN THE 2-YEAR INHALATION STUDY OF 2-METHALLYL CHLORIDE

Group Name	Control	50ppm	100ppm	200ppm
SITE : stomach				
TUMOR : squamous cell papilloma ^(f)				
Tumor rate				
Overall rates(a)	1/50(2.0)	0/48(0.0)	5/50(10.0)	4/49(8.2)
Adjusted rates(b)	3.45	0.00	12.90	9.30
Terminal rates(c)	1/29(3.4)	0/29(0.0)	4/31(12.9)	3/33(9.1)
Statistical analysis				
Peto test				
Standard method(d)	P=-----			
Prevalence method(d)	P=0.0437*			
Combined analysis (d)	P=-----			
Cochran-Armitage test(e)	P=0.0611			
Fisher Exact test(e)		P=0.4848	P=0.1210	P=0.1936
SITE : Harderian gland				
TUMOR : adenoma ^(g)				
Tumor rate				
Overall rates(a)	0/50(0.0)	4/48(8.3)	7/50(14.0)	8/49(16.3)
Adjusted rates(b)	0.0	13.79	17.07	23.53
Terminal rates(c)	0/29(0.0)	4/29(13.8)	5/31(16.1)	7/33(21.2)
Statistical analysis				
Peto test				
Standard method(d)	P=-----			
Prevalence method(d)	P=0.0056**			
Combined analysis (d)	P=-----			
Cochran-Armitage test(e)	P=0.0061**			
Fisher Exact test(e)		P=0.0637	P=0.0101*	P=0.0051**
SITE : pituitary gland				
TUMOR : adenoma ^(h)				
Tumor rate				
Overall rates(a)	11/49(22.4)	4/48(8.3)	4/50(8.0)	2/48(4.2)
Adjusted rates(b)	31.43	10.34	11.43	3.03
Terminal rates(c)	9/29(31.0)	3/29(10.3)	3/31(9.7)	1/33(3.0)
Statistical analysis				
Peto test				
Standard method(d)	P=0.2620			
Prevalence method(d)	P=0.9995			
Combined analysis (d)	P=0.9978			
Cochran-Armitage test(e)	P=0.0092**			
Fisher Exact test(e)		P=0.0838	P=0.0727	P=0.0187*

(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 method :Incidental tumor test

Combined analysis :Death analysis + Incidental tumor test

(e):The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.

(f):Historical incidence for 2-year studies: 1/849(0.1%); range 0% to 2%

(g):Historical incidence for 2-year studies: 29/849(3.4%);range 0% to 12%

(h):Historical incidence for 2-year studies: 124/849(14.6%); range 2% to 35%

?: The conditional probabilities 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 10 NUMBER OF MICE WITH SELECTED NON-NEOPLASTIC LESIONS IN THE 2-YEAR INHALATION STUDY OF 2-METHALLYL CHLORIDE

Group name	Male				Female			
	Control	50ppm	100ppm	200ppm	Control	50ppm	100ppm	200ppm
Nasal cavity exudate	<50>(40)	<50>(44)	<50>(43)	<50>(46)	<49>(29)	<48>(29)	<48>(30)	<49>(33)
	0 (0)	0 (0)	6 * (5)	23**(21)**	0 (0)	5 (3)	23**(15)**	43**(28)**
+	0 (0)	0 (0)	2 (2)	2 (2)	0 (0)	3 (2)	4 (1)	2 (2)
2+	0 (0)	0 (0)	4 (3)	21 (19)	0 (0)	2 (1)	19 (14)	41 (26)
3+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
4+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
eosinophilic change:respiratory ep.	7 (6)	31**(28)**	36**(33)**	47**(44)**	38 (27)	40 (29)*	40**(28)**	49**(33)**
+	5 (5)	28 (25)	31 (28)	21 (19)	26 (19)	18 (11)	11 (6)	14 (6)
2+	1 (1)	3 (3)	4 (4)	24 (23)	10 (6)	15 (13)	25 (19)	30 (23)
3+	1 (0)	0 (0)	1 (1)	2 (2)	2 (2)	7 (5)	4 (3)	4 (3)
4+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)
eosinophilic change:olfactory ep.	7 (6)	11 (11)	23**(21)**	33**(31)**	24 (20)	19 (16)	45**(30)**	41**(29)
+	5 (4)	8 (8)	20 (18)	29 (27)	22 (18)	18 (15)	41 (28)	38 (26)
2+	2 (2)	3 (3)	3 (3)	4 (4)	2 (2)	1 (1)	4 (2)	3 (3)
3+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
4+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
respiratory metaplasia:olfactory ep.	9 (8)	4 (4)	15 (13)	49**(46)**	2 (1)	5 (4)	15**(13)**	49**(33)**
+	9 (8)	4 (4)	15 (13)	4 (3)	2 (1)	5 (4)	15 (13)	2 (1)
2+	0 (0)	0 (0)	0 (0)	45 (43)	0 (0)	0 (0)	0 (0)	46 (31)
3+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)
4+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
respiratory metaplasia:gland	4 (3)	3 (3)	5 (4)	48**(45)**	4 (4)	9 (8)	6**(4)**	49**(33)**
+	4 (3)	3 (3)	5 (4)	1 (1)	4 (4)	8 (7)	6 (4)	5 (3)
2+	0 (0)	0 (0)	0 (0)	47 (44)	0 (0)	1 (1)	0 (0)	44 (30)
3+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
4+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade +:Slight 2+:Moderate 3+:Marked 4+:Severe

< >:Number of animals examined at the site

():Sacrificed animals

Significant difference

*:P≤0.05 **P≤0.01

Test of Chi square

TABLE 10 NUMBER OF MICE WITH SELECTED NON-NEOPLASTIC LESIONS IN THE 2-YEAR INHALATION STUDY
(continued) OF 2-METHALLYL CHLORIDE

Group name	Male				Female			
	Control	50ppm	100ppm	200ppm	Control	50ppm	100ppm	200ppm
Nasal cavity								
atrophy:olfactory ep.	<50>(40)	<50>(44)	<50>(43)	<50>(46)	<49>(29)	<48>(29)	<48>(30)	<49>(33)
	0 (0)	0 (0)	3 (2)	21**(19)**	0 (0)	2 (1)	9**(6)*	39**(25)**
+	0 (0)	0 (0)	3 (2)	13 (12)	0 (0)	1 (1)	7 (4)	10 (7)
2+	0 (0)	0 (0)	0 (0)	8 (7)	0 (0)	1 (0)	2 (2)	29 (18)
3+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
4+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Stomach								
hyperplasia:forestomach	<50>(40)	<49>(43)	<50>(46)	<50>(46)	<50>(29)	<48>(29)	<50>(31)	<49>(33)
	3 (3)	0 (0)	9 (8)	21**(20)**	0 (0)	1 (1)	4 (4)	19**(17)**
+	3 (3)	0 (0)	9 (8)	21 (20)	0 (0)	0 (0)	3 (3)	17 (16)
2+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)	1 (1)	2 (1)
3+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
4+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
hyperplasia:glandular stomach								
	40 (37)	36 (35)	40 (37)	34 (33)**	28 (20)	31 (24)	22 (18)	24 (21)
+	20 (19)	17 (16)	21 (19)	20 (19)	21 (14)	22 (16)	18 (14)	20 (18)
2+	20 (18)	19 (19)	19 (18)	14 (14)	7 (6)	9 (8)	4 (4)	4 (3)
3+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
4+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Brain								
mineralization	<50>(40)	<50>(44)	<50>(43)	<50>(46)	<50>(29)	<48>(29)	<50>(31)	<49>(33)
	19 (16)	24 (21)	31* (27)	21 (21)	24 (17)	22 (13)	6**(3)**	9**(8)
+	19 (16)	24 (21)	31 (27)	21 (21)	24 (17)	22 (13)	6 (3)	9 (8)
2+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
3+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
4+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Grade	+	Slight	2+:Moderate	3+:Marked	4+:Severe			
< >:Number of animals examined at the site								
():Sacrificed animals								
Significant difference								

*:P≤0.05 **:P≤0.01 Test of Chi square

TABLE 11

CAUSE OF DEATH OF MICE IN THE 2-YEAR INHALATION STUDY
OF 2-METHALLYL CHLORIDE

Group	Male				Female			
	Control	50ppm	100ppm	200ppm	Control	50ppm	100ppm	200ppm
Number of dead or moribund animals	10	6	7	4	21	19	19	16
No microscopical confirmation	1	1	0	1	1	0	0	1
Urinary retention	1	0	0	0	0	0	0	0
Hydronephrosis	0	0	1	0	0	0	1	0
Tumor death : leukemia	4	2	3	1	11	9	8	6
subcutis	1	0	0	0	0	0	0	1
lymph node	0	0	0	1	0	1	0	0
spleen	0	1	0	0	0	1	0	0
oral cavity	0	0	0	0	1	0	0	0
liver	2	2	3	1	2	0	3	0
pituitary	0	0	0	0	0	1	0	1
ovary	-	-	-	-	1	0	0	1
uterus	-	-	-	-	4	6	7	5
peripheral nerve	0	0	0	0	0	1	0	0
muscle	1	0	0	0	0	0	0	0
bone	0	0	0	0	1	0	0	1