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

TABLES

TABLES

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 *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
Temperature
Fluorescent light 12h/d
Chamber Environment : 23±3℃
Temperature : 22±2℃
Humidity : 55±15%
Air changes :12±1/h
Pressure :0～-15mmAq
<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 (continued) EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE 2-YEAR 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 Av.Wt.	Control No.of Surviv. <50>	50 ppm Av.Wt.	50 ppm % of cont. <50>	50 ppm No.of Surviv.	100 ppm Av.Wt.	100 ppm % of cont. <50>	100 ppm No.of Surviv.	200 ppm Av.Wt.	200 ppm % of cont. <50>	200 ppm 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 Av.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 Av.Wt.	Control No.of Surviv. <50>	50 ppm Av.Wt.	50 ppm % of cont. <48>	50 ppm No.of Surviv.	100 ppm Av.Wt.	100 ppm % of cont. <50>	100 ppm No.of Surviv.	200 ppm Av.Wt.	200 ppm % of cont. <49>	200 ppm No.of Surviv.
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 Av.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 Av.FC.	Control No.of Surviv. <50>	50 ppm Av.FC.	50 ppm % of cont. <50>	50 ppm No.of Surviv.	100 ppm Av.FC.	100 ppm % of cont. <50>	100 ppm No.of Surviv.	200 ppm Av.FC.	200 ppm % of cont. <50>	200 ppm 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 Av.FC.: g

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

Week on Study	Control Av.FC.	Control No.of Surviv. <50>	50 ppm Av.FC.	50 ppm % of cont. <48>	50 ppm No.of Surviv.	100 ppm Av.FC.	100 ppm % of cont. <50>	100 ppm No.of Surviv.	200 ppm Av.FC.	200 ppm % of cont. <49>	200 ppm 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 Av.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 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 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 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 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	<50>(40)	<50>(44)	<50>(43)	<50>(46)	<49>(29)	<48>(29)	<48>(30)	<49>(33)
exudate	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 (continued) 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		<50>(40)	<50>(44)	<50>(43)	<50>(46)	<49>(29)	<48>(29)	<48>(30)	<49>(33)
atrophy:olfactory ep.		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		<50>(40)	<49>(43)	<50>(46)	<50>(46)	<50>(29)	<48>(29)	<50>(31)	<49>(33)
hyperplasia:forestomach		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		<50>(40)	<50>(44)	<50>(43)	<50>(46)	<50>(29)	<48>(29)	<50>(31)	<49>(33)
mineralization		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

		Male				Female			
Group		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