N,N-ジメチルホルムアミ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：0297

TABLES

TABLES

TABLES (CONTINUED)

TABLE 1 EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE 2-YEAR INHALATION STUDY OF *N*,*N*-DIMETHYLFORMAMIDE

<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:BDF1 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 and Female
0, 200, 400, 800ppm
<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 : 22±2℃
Fluorescent light : 12 h/d
Air changes : 15～17 time/h
Chamber Environment
Temperature : 22±2℃
Humidity : 55±15%
Air changes : 12±1 time/h (6±0.5 time/h) ( ):during exposure
Pressure : 0～-15mmAq
<Type and Frequency of Observation>
Clinical Sign
Observed 1 per day for mortality, Detailed clinical observation performed on once weekly before exposure.
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 *N*,*N*-DIMETHYLFORMAMIDE

<Hematology>
Hematological examination performed on scheduled sacrificed animals.
The following measurement parameters were examined;
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>
Biochemistrical examination performed on scheduled sacrificed animals.
The following measurement parameters were examined;
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>
Urinalysis performed on all animals that survived to end of dosing period using fresh urine collection.
The following measurement parameters were examined;
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, nasopharynx, larynx, trachea, lung, bone marrow,
lymph node, thymus, spleen, heart, tongue, salivary gland, esophagus,
stomach, small intestine, large intestine, liver,gall bladder, 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 MICE IN THE 2-YEAR INHALATION STUDY OF *N*,*N*-DIMETHYLFORMAMIDE

Week on Study	Control		200ppm			400ppm			800ppm		
	Av.Wt.	No.of Surviv. <50>	Av.Wt.	% of cont. <50>	No.of Surviv.	Av.Wt.	% of cont. <49>	No.of Surviv.	Av.Wt.	% of cont. <50>	No.of Surviv.
0	22.6 (50)	50/50	22.6 (50)	100	50/50	22.6 (49)	100	50/50	22.6 (50)	100	50/50
1	24.0 (50)	50/50	23.6 (50)	98	50/50	24.1 (49)	100	50/50	23.3 (50)	97	50/50
2	24.9 (50)	50/50	24.6 (50)	99	50/50	25.1 (49)	101	50/50	23.9 (50)	96	50/50
3	25.5 (50)	50/50	25.1 (50)	98	50/50	25.9 (49)	102	50/50	24.2 (50)	95	50/50
4	26.1 (50)	50/50	25.8 (50)	99	50/50	26.4 (49)	101	50/50	24.5 (50)	94	50/50
5	26.7 (50)	50/50	26.3 (50)	99	50/50	26.8 (49)	100	50/50	24.7 (50)	93	50/50
6	27.4 (50)	50/50	26.9 (50)	98	50/50	27.1 (49)	99	50/50	25.1 (50)	92	50/50
7	27.6 (50)	50/50	27.1 (50)	98	50/50	27.3 (49)	99	49/49	24.2 (50)	88	50/50
8	28.6 (50)	50/50	28.0 (50)	98	50/50	28.2 (49)	99	49/49	25.9 (49)	91	49/50
9	29.4 (50)	50/50	28.6 (50)	97	50/50	28.5 (49)	97	49/49	25.7 (49)	87	49/50
10	29.9 (50)	50/50	29.2 (50)	98	50/50	29.0 (49)	97	49/49	26.5 (49)	89	49/50
11	30.4 (50)	50/50	29.6 (50)	97	50/50	29.1 (49)	96	49/49	26.6 (49)	88	49/50
12	31.1 (50)	50/50	30.1 (50)	97	50/50	29.1 (49)	94	49/49	26.5 (49)	85	49/50
13	31.4 (50)	50/50	30.7 (50)	98	50/50	29.9 (49)	95	49/49	27.7 (49)	88	49/50
14	32.0 (50)	50/50	31.2 (50)	98	50/50	30.2 (49)	94	49/49	27.9 (49)	87	49/50
18	34.8 (50)	50/50	34.1 (50)	98	50/50	31.8 (49)	91	49/49	29.1 (49)	84	49/50
22	36.7 (50)	50/50	36.2 (50)	99	50/50	33.5 (49)	91	49/49	30.3 (49)	83	49/50
26	38.4 (50)	50/50	37.9 (50)	99	50/50	34.2 (49)	89	49/49	30.8 (49)	80	49/50
30	40.0 (50)	50/50	39.5 (50)	99	50/50	35.5 (49)	89	49/49	32.2 (49)	81	49/50
34	42.3 (50)	50/50	41.4 (50)	98	50/50	36.9 (49)	87	49/49	32.9 (49)	78	49/50
38	43.4 (50)	50/50	42.5 (50)	98	50/50	37.8 (49)	87	49/49	33.7 (49)	78	49/50
42	45.1 (50)	50/50	42.9 (50)	95	50/50	38.6 (49)	86	49/49	34.1 (49)	76	49/50
46	45.9 (50)	50/50	43.8 (50)	95	50/50	39.0 (49)	85	49/49	34.5 (49)	75	49/50
50	46.2 (50)	50/50	44.3 (50)	96	50/50	39.2 (49)	85	49/49	35.0 (49)	76	49/50
54	46.6 (50)	50/50	44.5 (50)	95	50/50	39.2 (49)	84	49/49	35.1 (49)	75	49/50
58	47.6 (50)	50/50	45.2 (50)	95	50/50	39.8 (49)	84	49/49	35.9 (49)	75	49/50
62	48.2 (49)	49/50	45.2 (50)	94	50/50	39.6 (49)	82	49/49	36.0 (49)	75	49/50
66	49.0 (49)	49/50	45.8 (50)	93	50/50	40.6 (49)	83	49/49	36.5 (48)	74	48/50
70	50.0 (48)	48/50	46.9 (49)	94	49/50	41.1 (48)	82	48/49	36.6 (47)	73	47/50
74	50.2 (46)	46/50	47.9 (48)	95	48/50	41.0 (48)	82	48/49	36.2 (47)	72	47/50
78	50.9 (46)	46/50	48.6 (47)	95	47/50	41.4 (48)	81	48/49	36.0 (46)	71	46/50
82	51.6 (44)	44/50	48.2 (47)	93	47/50	40.6 (46)	79	46/49	35.2 (46)	68	46/50
86	51.9 (43)	43/50	48.0 (46)	92	46/50	40.5 (45)	78	45/49	34.6 (45)	67	45/50
90	52.1 (42)	42/50	47.9 (44)	92	44/50	40.4 (45)	78	45/49	34.7 (45)	67	45/50
94	52.4 (42)	42/50	46.6 (43)	89	43/50	39.9 (45)	76	45/49	34.2 (44)	65	44/50
98	51.7 (40)	40/50	45.2 (39)	87	39/50	39.4 (44)	76	44/49	34.6 (44)	67	44/50
102	50.4 (37)	37/50	43.5 (33)	86	33/50	38.5 (38)	76	38/49	34.2 (41)	68	41/50
104	49.2 (37)	37/50	42.6 (33)	87	33/50	38.2 (38)	78	37/49	34.5 (40)	70	40/50

< > : 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 *N,N*-DIMETHYLFORMAMIDE

Week on Study	Control		200ppm			400ppm			800ppm		
	Av.Wt.	No.of Surviv. <49>	Av.Wt.	% of cont. <50>	No.of Surviv.	Av.Wt.	% of cont. <50>	No.of Surviv.	Av.Wt.	% of cont. <49>	No.of Surviv.
0	18.8 (49)	50/50	18.8 (50)	100	50/50	18.8 (50)	100	50/50	18.8 (49)	100	50/50
1	19.4 (49)	50/50	19.2 (50)	99	50/50	19.6 (50)	101	50/50	19.1 (49)	98	50/50
2	20.3 (49)	50/50	20.3 (50)	100	50/50	20.5 (50)	101	50/50	19.9 (49)	98	50/50
3	20.9 (49)	50/50	20.8 (50)	100	50/50	21.8 (50)	104	50/50	20.5 (49)	98	50/50
4	21.6 (49)	50/50	21.6 (50)	100	50/50	22.3 (50)	103	50/50	21.0 (49)	97	50/50
5	22.2 (49)	50/50	21.7 (50)	98	50/50	22.7 (50)	102	50/50	21.2 (49)	95	50/50
6	22.8 (49)	50/50	22.6 (50)	99	50/50	23.0 (50)	101	50/50	21.6 (49)	95	50/50
7	22.8 (49)	50/50	22.9 (50)	100	50/50	23.0 (50)	101	50/50	21.3 (49)	93	50/50
8	23.6 (49)	50/50	23.3 (50)	99	50/50	24.1 (50)	102	50/50	23.1 (49)	98	49/49
9	24.1 (49)	50/50	24.0 (50)	100	50/50	24.4 (50)	101	50/50	23.2 (49)	96	49/49
10	24.3 (49)	50/50	23.9 (50)	98	50/50	24.8 (50)	102	50/50	23.7 (49)	98	49/49
11	24.3 (49)	50/50	24.1 (50)	99	50/50	24.8 (50)	102	50/50	23.7 (49)	98	49/49
12	24.7 (49)	50/50	24.3 (50)	98	50/50	25.3 (50)	102	50/50	23.3 (49)	94	49/49
13	24.7 (49)	50/50	24.6 (50)	100	50/50	25.2 (50)	102	50/50	24.1 (49)	98	49/49
14	25.0 (49)	50/50	24.7 (50)	99	50/50	25.2 (50)	101	50/50	24.3 (49)	97	49/49
18	26.5 (49)	50/50	26.2 (50)	99	50/50	26.5 (50)	100	50/50	25.4 (49)	96	49/49
22	27.8 (49)	50/50	27.2 (50)	98	50/50	27.3 (50)	98	50/50	26.3 (49)	95	49/49
26	28.6 (49)	50/50	27.7 (50)	97	50/50	27.7 (50)	97	50/50	26.4 (49)	92	49/49
30	29.4 (49)	49/49	28.5 (50)	97	50/50	28.4 (50)	97	50/50	27.4 (49)	93	49/49
34	30.2 (48)	48/49	29.2 (50)	97	50/50	28.7 (50)	95	50/50	27.9 (49)	92	49/49
38	30.7 (48)	48/49	29.4 (50)	96	50/50	29.1 (50)	95	50/50	28.0 (49)	91	49/49
42	31.4 (48)	48/49	29.7 (50)	95	50/50	29.3 (50)	93	50/50	28.3 (49)	90	49/49
46	31.7 (47)	47/49	30.1 (50)	95	50/50	29.8 (50)	94	50/50	28.6 (49)	90	49/49
50	31.6 (47)	47/49	30.1 (50)	95	50/50	30.1 (50)	95	50/50	28.9 (49)	91	49/49
54	31.8 (47)	47/49	30.1 (50)	95	50/50	30.1 (50)	95	50/50	28.8 (48)	91	48/49
58	32.0 (47)	47/49	30.4 (50)	95	50/50	30.2 (50)	94	50/50	28.9 (48)	90	48/49
62	32.2 (46)	46/49	30.5 (48)	95	48/50	30.6 (50)	95	50/50	28.6 (48)	89	48/49
66	33.0 (45)	45/49	30.8 (47)	93	47/50	31.2 (50)	95	50/50	29.0 (48)	88	48/49
70	33.7 (45)	45/49	31.8 (47)	94	47/50	31.7 (49)	94	49/50	29.4 (48)	87	48/49
74	34.3 (44)	44/49	32.3 (46)	94	46/50	31.8 (49)	93	49/50	29.2 (48)	85	48/49
78	34.2 (43)	43/49	32.8 (45)	96	45/50	32.2 (47)	94	46/50	29.1 (46)	85	45/49
82	34.4 (40)	40/49	32.7 (42)	95	42/50	33.0 (46)	96	45/50	28.9 (44)	84	44/49
86	34.7 (39)	39/49	32.9 (40)	95	40/50	32.7 (39)	94	39/50	28.3 (39)	82	39/49
90	34.1 (38)	38/49	32.8 (39)	96	39/50	33.1 (37)	97	37/50	28.1 (37)	82	37/49
94	33.8 (36)	35/49	33.4 (37)	99	37/50	33.1 (32)	98	32/50	27.8 (35)	82	35/49
98	34.2 (33)	33/49	33.7 (35)	99	35/50	33.4 (27)	98	27/50	27.8 (32)	81	32/49
102	34.4 (30)	30/49	33.8 (34)	98	34/50	32.0 (22)	93	22/50	27.1 (24)	79	24/49
104	33.7 (30)	29/49	33.6 (31)	100	30/50	32.0 (21)	95	21/50	27.3 (22)	81	22/49

< > : 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 *N*,*N*-DIMETHYLFORMAMIDE

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	0/50	1/49	1/46	1/42	2/50(1/13)
	200ppm	0/50	0/50	0/50	0/50	0/50	1/50	3/47	2/44	4/50(2/17)
	400ppm	0/49	0/49	0/49	1/49	1/49	2/49	3/48	2/45	3/49(3/13)
	800ppm	0/50	0/49	0/49	0/49	0/49	1/48	3/46	4/44	5/50(2/10)
Internal mass										
	Control	0/50	0/50	1/50	1/50	1/50	3/49	4/46	7/42	10/50(5/13)
	200ppm	0/50	0/50	0/50	0/50	0/50	3/50	8/47	13/44	17/50(8/17)
	400ppm	0/49	0/49	0/49	0/49	1/49	3/49	14/48	34/45	38/49(9/13)
	800ppm	0/50	1/49	1/49	1/49	4/49	6/48	24/46	39/44	44/50(7/10)

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 *N*,*N*-DIMETHYLFORMAMIDE

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	0/49	0/49	0/49	1/48	1/47	1/45	1/43	2/37	2/49(1/21)
	200ppm	0/50	0/50	0/50	0/50	0/50	0/47	1/44	5/38	5/50(0/20)
	400ppm	0/50	0/50	0/50	0/50	0/50	1/50	1/46	1/35	2/50(1/29)
	800ppm	0/49	0/49	0/49	0/49	1/48	2/48	1/44	0/36	2/49(2/28)
Internal mass										
	Control	0/49	0/49	0/49	0/48	1/47	2/45	4/43	9/37	12/49(7/21)
	200ppm	0/50	0/50	0/50	0/50	1/50	5/47	23/44	30/38	37/50(13/20)
	400ppm	0/50	0/50	0/50	0/50	2/50	6/50	37/46	35/35	46/50(25/29)
	800ppm	0/49	0/49	0/49	0/49	1/48	13/48	33/44	35/36	44/49(22/28)

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 *N,N*-DIMETHYLFORMAMIDE

Week on Study	Control Av.FC.	Control No.of Surviv. <50>	200ppm Av.FC.	200ppm % of cont.	200ppm No.of Surviv. <50>	400ppm Av.FC.	400ppm % of cont.	400ppm No.of Surviv. <49>	800ppm Av.FC.	800ppm % of cont.	800ppm No.of Surviv. <50>
1	4.1 (50)	50/50	3.8 (50)	93	50/50	3.8 (49)	93	50/50	3.5 (50)	85	50/50
2	4.0 (50)	50/50	4.1 (50)	103	50/50	4.2 (49)	105	50/50	3.8 (50)	95	50/50
3	4.1 (50)	50/50	4.1 (50)	100	50/50	4.4 (49)	107	50/50	3.9 (50)	95	50/50
4	4.2 (50)	50/50	4.3 (50)	102	50/50	4.4 (49)	105	50/50	4.1 (50)	98	50/50
5	4.2 (50)	50/50	4.3 (50)	102	50/50	4.3 (49)	102	50/50	4.0 (50)	95	50/50
6	4.2 (50)	50/50	4.3 (50)	102	50/50	4.3 (49)	102	50/50	4.0 (50)	95	50/50
7	4.2 (50)	50/50	4.4 (50)	105	50/50	4.3 (49)	102	49/49	3.9 (50)	93	50/50
8	4.3 (50)	50/50	4.3 (50)	100	50/50	4.4 (49)	102	49/49	4.1 (49)	95	49/50
9	4.4 (50)	50/50	4.4 (50)	100	50/50	4.3 (48)	98	49/49	3.8 (49)	86	49/50
10	4.4 (50)	50/50	4.5 (50)	102	50/50	4.3 (49)	98	49/49	4.0 (49)	91	49/50
11	4.4 (50)	50/50	4.4 (50)	100	50/50	4.2 (49)	95	49/49	4.0 (49)	91	49/50
12	4.5 (50)	50/50	4.5 (50)	100	50/50	4.3 (49)	96	49/49	4.0 (49)	89	49/50
13	4.4 (50)	50/50	4.5 (50)	102	50/50	4.5 (49)	102	49/49	4.2 (49)	95	49/50
14	4.4 (50)	50/50	4.6 (50)	105	50/50	4.4 (49)	100	49/49	4.0 (49)	91	49/50
18	4.7 (50)	50/50	4.8 (50)	102	50/50	4.6 (49)	98	49/49	4.1 (49)	87	49/50
22	4.8 (50)	50/50	4.9 (50)	102	50/50	4.6 (49)	96	49/49	4.2 (49)	88	49/50
26	4.8 (50)	50/50	4.9 (50)	102	50/50	4.6 (49)	96	49/49	4.2 (49)	88	49/50
30	4.8 (50)	50/50	4.9 (50)	102	50/50	4.7 (49)	98	49/49	4.2 (49)	88	49/50
34	4.9 (50)	50/50	4.9 (50)	100	50/50	4.7 (49)	96	49/49	4.3 (49)	88	49/50
38	4.9 (50)	50/50	5.0 (50)	102	50/50	4.9 (49)	100	49/49	4.5 (49)	92	49/50
42	4.9 (50)	50/50	4.9 (50)	100	50/50	4.8 (49)	98	49/49	4.3 (49)	88	49/50
46	5.1 (50)	50/50	5.1 (50)	100	50/50	4.8 (49)	94	49/49	4.4 (49)	86	49/50
50	5.2 (50)	50/50	5.2 (50)	100	50/50	5.0 (49)	96	49/49	4.5 (49)	87	49/50
54	5.0 (50)	50/50	5.0 (50)	100	50/50	4.8 (49)	96	49/49	4.4 (49)	88	49/50
58	5.1 (50)	50/50	5.2 (50)	102	50/50	4.9 (49)	96	49/49	4.5 (49)	88	49/50
62	5.2 (49)	49/50	5.2 (50)	100	50/50	5.1 (49)	98	49/49	4.9 (49)	94	49/50
66	5.2 (49)	49/50	5.2 (50)	100	50/50	5.0 (49)	96	49/49	4.8 (48)	92	48/50
70	5.3 (48)	48/50	5.2 (49)	98	49/50	4.9 (48)	92	48/49	4.7 (47)	89	47/50
74	5.4 (45)	46/50	5.4 (48)	100	48/50	5.1 (48)	94	48/49	4.9 (47)	91	47/50
78	5.4 (46)	46/50	5.5 (47)	102	47/50	5.4 (48)	100	48/49	5.1 (46)	94	46/50
82	5.3 (44)	44/50	5.3 (47)	100	47/50	5.2 (46)	98	46/49	5.1 (46)	96	46/50
86	5.3 (43)	43/50	5.4 (46)	102	46/50	5.2 (45)	98	45/49	5.3 (45)	100	45/50
90	5.6 (42)	42/50	5.4 (44)	96	44/50	5.5 (45)	98	45/49	5.7 (45)	102	45/50
94	5.6 (42)	42/50	5.3 (43)	95	43/50	5.5 (45)	98	45/49	5.8 (44)	104	44/50
98	5.4 (40)	40/50	5.5 (39)	102	39/50	5.4 (44)	100	44/49	5.5 (44)	102	44/50
102	5.3 (37)	37/50	5.3 (33)	100	33/50	5.3 (38)	100	38/49	5.2 (41)	98	41/50
104	5.1 (37)	37/50	5.3 (33)	104	33/50	5.4 (38)	106	37/49	5.1 (37)	100	40/50

< > : 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 *N,N*-DIMETHYLFORMAMIDE

Week on Study	Control Av.FC.	Control No.of Surviv. <49>	200ppm Av.FC.	200ppm % of cont. <50>	200ppm No.of Surviv.	400ppm Av.FC.	400ppm % of cont. <50>	400ppm No.of Surviv.	800ppm Av.FC.	800ppm % of cont. <49>	800ppm No.of Surviv.
1	3.5 (49)	50/50	3.1 (50)	89	50/50	3.1 (50)	89	50/50	3.0 (49)	86	50/50
2	3.6 (49)	50/50	3.6 (50)	100	50/50	3.5 (50)	97	50/50	3.5 (49)	97	50/50
3	3.7 (49)	50/50	3.8 (50)	103	50/50	4.1 (50)	111	50/50	3.6 (49)	97	50/50
4	4.0 (49)	50/50	4.0 (50)	100	50/50	4.1 (50)	103	50/50	3.8 (49)	95	50/50
5	4.1 (49)	50/50	4.0 (50)	98	50/50	4.2 (50)	102	50/50	3.7 (49)	90	50/50
6	4.1 (49)	50/50	4.2 (50)	102	50/50	4.2 (50)	102	50/50	3.8 (49)	93	50/50
7	4.2 (49)	50/50	4.3 (50)	102	50/50	4.3 (50)	102	50/50	4.0 (49)	95	49/49
8	4.2 (49)	50/50	4.2 (50)	100	50/50	4.5 (50)	107	50/50	4.1 (49)	98	49/49
9	4.3 (49)	50/50	4.4 (50)	102	50/50	4.6 (50)	107	50/50	3.9 (49)	91	49/49
10	4.2 (49)	50/50	4.3 (50)	102	50/50	4.4 (50)	105	50/50	4.0 (49)	95	49/49
11	4.2 (49)	50/50	4.3 (49)	102	50/50	4.3 (50)	102	50/50	4.0 (49)	95	49/49
12	4.3 (49)	50/50	4.4 (50)	102	50/50	4.7 (50)	109	50/50	4.0 (49)	93	49/49
13	4.4 (49)	50/50	4.4 (50)	100	50/50	4.4 (50)	100	50/50	4.1 (49)	93	49/49
14	4.2 (49)	50/50	4.4 (50)	105	50/50	4.4 (50)	105	50/50	4.1 (49)	98	49/49
18	4.6 (49)	50/50	4.6 (50)	100	50/50	4.8 (50)	104	50/50	4.2 (49)	91	49/49
22	4.7 (49)	50/50	4.8 (50)	102	50/50	4.8 (50)	102	50/50	4.3 (49)	91	49/49
26	4.7 (49)	50/50	4.7 (50)	100	50/50	4.7 (50)	100	50/50	4.3 (49)	91	49/49
30	4.7 (49)	49/49	4.8 (50)	102	50/50	4.6 (50)	98	50/50	4.3 (49)	91	49/49
34	4.5 (48)	48/49	4.7 (50)	104	50/50	4.7 (50)	104	50/50	4.5 (49)	100	49/49
38	4.7 (48)	48/49	4.8 (50)	102	50/50	4.8 (50)	102	50/50	4.6 (49)	98	49/49
42	4.5 (48)	48/49	4.7 (50)	104	50/50	4.7 (50)	104	50/50	4.4 (49)	98	49/49
46	4.6 (47)	47/49	4.8 (50)	104	50/50	4.7 (50)	102	50/50	4.5 (49)	98	49/49
50	4.7 (47)	47/49	4.8 (50)	102	50/50	4.8 (50)	102	50/50	4.5 (49)	96	49/49
54	4.6 (47)	47/49	4.6 (50)	100	50/50	4.7 (50)	102	50/50	4.5 (48)	98	48/49
58	4.5 (47)	47/49	4.7 (50)	104	50/50	4.5 (50)	100	50/50	4.4 (48)	98	48/49
62	4.7 (46)	46/49	4.8 (48)	102	48/50	4.8 (50)	102	50/50	4.7 (48)	100	48/49
66	4.9 (45)	45/49	4.8 (47)	98	47/50	4.9 (50)	100	50/50	4.7 (48)	96	48/49
70	4.7 (45)	45/49	4.8 (47)	102	47/50	5.1 (49)	109	49/50	4.8 (48)	102	48/49
74	4.9 (44)	44/49	4.8 (46)	98	46/50	5.5 (49)	112	49/50	5.0 (48)	102	48/49
78	4.8 (43)	43/49	4.9 (45)	102	45/50	5.5 (47)	115	46/50	4.9 (46)	102	45/49
82	4.6 (40)	40/49	4.8 (42)	104	42/50	5.6 (46)	122	45/50	4.7 (44)	102	44/49
86	4.8 (39)	39/49	5.2 (40)	108	40/50	5.9 (39)	123	39/50	4.8 (39)	100	39/49
90	4.9 (38)	38/49	5.3 (39)	108	39/50	6.0 (37)	122	37/50	4.8 (37)	98	37/49
94	5.1 (36)	35/49	5.6 (37)	110	37/50	6.1 (32)	120	32/50	4.9 (35)	96	35/49
98	5.2 (33)	33/49	5.6 (35)	108	35/50	5.9 (27)	113	27/50	4.7 (32)	90	32/49
102	5.1 (30)	30/49	5.5 (34)	108	34/50	5.4 (22)	106	22/50	4.3 (24)	84	24/49
104	5.0 (30)	29/49	5.5 (30)	110	30/50	5.3 (21)	106	21/50	4.3 (22)	86	22/49

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

TABLE 8 NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS IN MALE MICE IN THE 2-YEAR INHALATION STUDY OF *N,N*-DIMETHYLFORMAMIDE

Group Name	Control	200ppm	400ppm	800ppm
SITE : liver				
TUMOR : hepatocellular adenoma				
Tumor rate				
Overall rates(a)	6/50(12.0)	36/50(72.0)	41/49(83.7)	41/50(82.0)
Adjusted rates(b)	14.63	90.91	90.91	93.18
Terminal rates(c)	5/37(13.5)	30/33(90.9)	33/37(89.2)	37/40(92.5)
Statistical analysis				
Peto test				
Standard method(d)	P=0.6009			
Prevalence method(d)	P<0.0001**			
Combined analysis (d)	P<0.0001**			
Cochran-Armitage test(e)	P<0.0001**			
Fisher Exact test(e)		P<0.0001**	P<0.0001**	P<0.0001**
SITE : liver				
TUMOR : hepatocellular carcinoma				
Tumor rate				
Overall rates(a)	2/50(4.0)	12/50(24.0)	16/49(32.7)	16/50(32.0)
Adjusted rates(b)	2.70	20.45	32.56	33.33
Terminal rates(c)	1/37(2.7)	6/33(18.2)	12/37(32.4)	12/40(30.0)
Statistical analysis				
Peto test				
Standard method(d)	P=0.4283			
Prevalence method(d)	P=0.0011**			
Combined analysis (d)	P=0.0026**			
Cochran-Armitage test(e)	P=0.0018**			
Fisher Exact test(e)		P=0.0038**	P=0.0002**	P=0.0002**
SITE : liver				
TUMOR : hepatoblastoma				
Tumor rate				
Overall rates(a)	0/50(0.0)	13/50(26.0)	7/49(14.3)	4/50(8.0)
Adjusted rates(b)	0.0	33.33	7.89	10.00
Terminal rates(c)	0/37(0.0)	11/33(33.3)	2/37(5.4)	4/40(10.0)
Statistical analysis				
Peto test				
Standard method(d)	P=0.3799			
Prevalence method(d)	P=0.5378			
Combined analysis (d)	P=0.4857			
Cochran-Armitage test(e)	P=0.8798			
Fisher Exact test(e)		P<0.0001**	P=0.0058**	P=0.0587
SITE : liver				
TUMOR : hepatocellular adenoma, hepatocellular carcinoma, hepatoblastoma				
Tumor rate				
Overall rates(a)	8/50(16.0)	42/50(84.0)	46/49(93.9)	44/50(88.0)
Adjusted rates(b)	17.07	93.94	95.12	97.67
Terminal rates(c)	6/37(16.2)	31/33(93.9)	35/37(94.6)	39/40(97.5)
Statistical analysis				
Peto test				
Standard method(d)	P=0.4412			
Prevalence method(d)	P<0.0001**			
Combined analysis (d)	P<0.0001**			
Cochran-Armitage test(e)	P<0.0001**			
Fisher Exact test(e)		P<0.0001**	P<0.0001**	P<0.0001**

TABLE 8 NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS IN MALE MICE IN THE 2-YEAR INHALATION STUDY OF *N,N*-DIMETHYLFORMAMIDE (continued)

Group Name	Control	200ppm	400ppm	800ppm
SITE : lung				
TUMOR : bronchiolar-alveolar carcinoma				
Tumor rate				
Overall rates(a)	8/50(16.0)	6/50(12.0)	3/49(6.1)	2/50(4.0)
Adjusted rates(b)	17.50	15.15	6.52	2.22
Terminal rates(c)	6/37(16.2)	5/33(15.2)	1/37(2.7)	0/40(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P=0.5409			
Prevalence method(d)	P=0.9932			
Combined analysis (d)	P=0.9889			
Cochran-Armitage test(e)	P=0.0314*			
Fisher Exact test(e)		P=0.3871	P=0.1061	P=0.0458*

(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.
? :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 IN FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF *N,N*-DIMETHYLFORMAMIDE

Group Name	Control	200ppm	400ppm	800ppm
SITE : liver				
TUMOR : hepatocellular adenoma				
Tumor rate				
Overall rates(a)	1/49(2.0)	42/50(84.0)	47/50(94.0)	48/49(98.0)
Adjusted rates(b)	3.45	93.55	100.00	100.00
Terminal rates(c)	1/29(3.4)	28/30(93.3)	21/21(100.0)	22/22(100.0)
Statistical analysis				
Peto test				
Standard method(d)	P=0.5980			
Prevalence method(d)	P<0.0001**			
Combined analysis (d)	P<0.0001**			
Cochran-Armitage test(e)	P<0.0001**			
Fisher Exact test(e)		P<0.0001**	P<0.0001**	P<0.0001**
SITE : liver				
TUMOR : hepatocellular carcinoma				
Tumor rate				
Overall rates(a)	3/49(6.1)	25/50(50.0)	32/50(64.0)	35/49(71.4)
Adjusted rates(b)	10.34	57.58	72.73	72.00
Terminal rates(c)	3/29(10.3)	17/30(56.7)	15/21(71.4)	15/22(68.2)
Statistical analysis				
Peto test				
Standard method(d)	P<0.0001**			
Prevalence method(d)	P<0.0001**			
Combined analysis (d)	P<0.0001**?			
Cochran-Armitage test(e)	P<0.0001**			
Fisher Exact test(e)		P<0.0001**	P<0.0001**	P<0.0001**
SITE : liver				
TUMOR : hepatoblastoma				
Tumor rate				
Overall rates(a)	0/49(0.0)	0/50(0.0)	4/50(8.0)	0/49(0.0)
Adjusted rates(b)	0.0	0.0	4.76	0.0
Terminal rates(c)	0/29(0.0)	0/30(0.0)	1/21(4.8)	0/22(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P=0.3491			
Prevalence method(d)	P=0.3476			
Combined analysis (d)	P=0.3156			
Cochran-Armitage test(e)	P=0.7290			
Fisher Exact test(e)		P=0.5000	P=0.0612	P=0.5000
SITE : liver				
TUMOR : hepatocellular adenoma,hepatocellular carcinoma,hepatoblastoma				
Tumor rate				
Overall rates(a)	3/49(6.1)	45/50(90.0)	49/50 (98.0)	49/49(100.0)
Adjusted rates(b)	10.34	97.30	100.00	100.00
Terminal rates(c)	3/29(10.3)	29/30(96.7)	21/21(100.0)	22/22(100.0)
Statistical analysis				
Peto test				
Standard method(d)	P<0.0001**			
Prevalence method(d)	P<0.0001**			
Combined analysis (d)	P<0.0001**			
Cochran-Armitage test(e)	P<0.0001**			
Fisher Exact test(e)		P<0.0001**	P<0.0001**	P<0.0001**

TABLE 9 NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS IN FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF *N,N*-DIMETHYLFORMAMIDE (continued)

Group Name	Control	200ppm	400ppm	800ppm
SITE : pititary gland				
TUMOR : adenoma				
Tumor rate				
Overall rates(a)	7/49(14.3)	9/50(18.0)	6/49(12.2)	0/49(0.0)
Adjusted rates(b)	20.69	23.68	23.81	0.0
Terminal rates(c)	6/29(20.7)	7/30(23.3)	5/21(23.8)	0/22(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P=0.4109			
Prevalence method(d)	P=0.9958			
Combined analysis (d)	P=0.9941			
Cochran-Armitage test(e)	P=0.0076**			
Fisher Exact test(e)		P=0.4101	P=0.5000	P=0.0062**
SITE : lymph node				
TUMOR : malignant lymphoma				
Tumor rate				
Overall rates(a)	13/49(26.5)	9/50(18.0)	7/50(14.0)	3/49(6.1)
Adjusted rates(b)	27.59	13.33	4.76	9.09
Terminal rates(c)	8/29(27.6)	4/30(13.3)	1/21(4.8)	2/22(9.1)
Statistical analysis				
Peto test				
Standard method(d)	P=0.9073			
Prevalence method(d)	P=0.9706			
Combined analysis (d)	P=0.9880			
Cochran-Armitage test(e)	P=0.0061**			
Fisher Exact test(e)		P=0.2182	P=0.0961	P=0.0060**
SITE : ALL SITE				
TUMOR : malignant lymphoma				
Tumor rate				
Overall rates(a)	15/49(30.6)	12/50(24.0)	9/50(18.0)	3/49(6.1)
Adjusted rates(b)	31.03	20.00	9.52	9.09
Terminal rates(c)	9/29(31.0)	6/30(20.0)	2/21(9.5)	2/22(9.1)
Statistical analysis				
Peto test				
Standard method(d)	P=0.9424			
Prevalence method(d)	P=0.9835			
Combined analysis (d)	P=0.9955			
Cochran-Armitage test(e)	P=0.0015**			
Fisher Exact test(e)		P=0.3042	P=0.1093	P=0.0016**

(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.
? :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 SELECTED NON NEOPLASTIC LESIONS OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF *N*,*N*-DIMETHYLFORMAMIDE

Group Name		Control				200 ppm				400 ppm				800 ppm			
No. of Animals		50				50				49				50			
Organ	Findings Grade a)	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
nasal cavit		<50>				<50>				<49>				<50>			
	eosinophilic change: olfactory epithelium	29	1	0	0	13	0	0	0**	2	1	0	0**	4	0	0	0**
	respiratory metaplasia: olfactory epithelium	11	0	0	0	21	0	0	0	17	0	0	0	11	37	0	0**
	respiratory metaplasia: gland	4	2	0	0	16	10	0	0**	2	0	0	0	14	0	0	0*
	thickening of bone	0	0	0	0	0	0	0	0	0	0	0	0	41	3	0	0**
lung		<50>				<50>				<49>				<50>			
	accumulation of foamy cells	0	1	0	0	0	0	0	0	1	0	0	0	7	2	0	0*
spleen		<50>				<50>				<49>				<50>			
	extramedullary hematopoiesis	2	0	1	0	9	6	3	0**	4	5	3	0*	10	4	2	0**
liver		<50>				<50>				<49>				<50>			
	necrosis:focal	6	1	1	0	14	3	0	0	2	5	2	0	0	0	0	0*
	necrosis:single cell	11	1	0	0	23	15	0	0**	13	30	0	0**	6	42	0	0**
	inflammatory cell nest	15	0	0	0	37	0	0	0**	42	0	0	0**	47	1	0	0**
	clear cell focus	0	2	2	0	4	16	1	0**	2	10	1	0*	5	12	0	0**
	acidophilic cell focus	1	0	0	0	3	15	20	0**	1	18	22	0**	1	22	19	0**
	swelling:central	0	0	0	0	27	12	0	0**	10	31	0	0**	4	43	1	0**
	nuclear atypia:central	0	0	0	0	28	5	0	0**	16	26	0	0**	25	20	0	0**
kidney		<50>				<50>				<49>				<50>			
	hyaline droplet	0	1	0	0	1	1	0	0	5	0	0	0*	5	0	0	0*
adrenal		<50>				<50>				<49>				<50>			
	hyperplasia:cortical cell	9	0	0	0	5	1	0	0	3	4	0	0*	0	0	0	0**

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

Significant difference ; * : $P \leqq 0.05$ ** : $P \leqq 0.01$ Test of Chi Square

TABLE 11 SELECTED NON NEOPLASTIC LESIONS OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF *N,N*-DIMETHYLFORMAMIDE

Organ	Findings	Group Name / No. of Animals / Grade a)	Control 49				200 ppm 50				400 ppm 50				800 ppm 49			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
nasal cavit			<49>				<49>				<50>				<49>			
	eosinophilic change: olfactory epithelium		8	0	1	0	11	0	0	0	11	1	0	0	34	0	0	0 **
	eosinophilic change: respiratory epithelium		20	17	3	0	28	17	0	0	30	8	1	0	32	16	0	0 **
	respiratory metaplasia: olfactory epithelium		1	0	0	0	12	0	0	0 **	16	0	0	0 **	5	44	0	0 **
	respiratory metaplasia: gland		5	0	0	0	4	1	0	0	5	0	0	0	20	0	0	0 **
	thickening of bone		0	0	0	0	0	0	0	0	0	0	0	0	44	2	0	0 **
lung			<49>				<50>				<50>				<49>			
	inflammatory infiltration		5	1	0	0	0	1	0	0	3	1	0	0	0	0	0	0 *
spleen			<49>				<50>				<50>				<49>			
	extramedullary hematopoiesis		4	6	4	0	8	9	1	0	10	10	8	0 *	11	11	0	0 *
liver			<49>				<50>				<50>				<49>			
	necrosis:single cell		13	9	0	0	9	4	0	0	4	2	0	0 **	13	6	0	0
	inflammatory cell nest		24	0	0	0	13	0	0	0 *	4	0	0	0 **	17	1	1	0
	acidophilic cell focus		0	1	0	0	0	6	37	0 **	1	3	39	0 **	0	3	45	0 **
	swelling:central		2	0	0	0	9	2	0	0 *	4	1	0	0	7	9	0	0 **
	nuclear atypia:central		2	0	0	0	6	1	0	0	2	1	0	0	10	6	0	0 **
pituitary			<49>				<50>				<49>				<49>			
	hyperplasia		14	2	0	0	12	6	0	0	7	4	0	0	4	1	0	0 *
adrenal			<49>				<50>				<50>				<49>			
	spindle-cell hyperplasia		32	12	0	0	48	1	0	0 **	45	1	0	0 **	47	0	0	0 **
ovary			<49>				<49>				<49>				<49>			
	cyst		11	0	0	0	6	0	0	0	4	2	0	0	1	5	0	0 **
uterus			<49>				<50>				<50>				<49>			
	cystc endometrial hyperplasia		28	6	0	0	24	10	1	0	29	4	0	0	13	0	0	0 *

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

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

TABLE 12 CAUSE OF DEATH OF MICE IN THE 2-YEAR INHALATION STUDY OF *N,N*-DIMETHYLFORMAMIDE

	Male				Female			
Group	Control	200ppm	400ppm	800ppm	Control	200ppm	400ppm	800ppm
Number of dead or moribund animals	13	17	12	10	20	20	29	27
No microscopical confirmation	1	0	0	0	1	1	0	1
Integumentary system lesion	0	1	0	0	0	0	0	0
Hepatic lesion	0	1	0	1	0	0	0	0
Urinary system lesion	0	0	0	1	0	0	0	0
Renal lesion	0	0	0	0	1	0	0	0
Urinary retention	1	1	1	0	1	0	0	0
Arteritis	1	0	0	0	1	0	0	0
Hydronephrosis	1	0	0	0	1	0	0	1
Peritonitis	1	0	0	0	0	0	0	0
Tumor death : leukemia	2	3	2	1	6	6	7	1
subcutis	0	0	0	0	0	0	0	1
lung	1	1	0	1	0	1	0	0
spleen	2	0	0	0	0	1	2	1
heart	0	0	1	0	0	0	0	0
stomach	0	1	0	0	0	0	0	0
small intestine	0	1	0	0	0	0	0	0
liver	3	6	8	3	1	5	11	15
pituitary gland	0	0	0	0	0	0	1	0
thyroid	0	0	0	1	0	0	0	0
uterus	-	-	-	-	7	6	8	5
mammary gland	0	0	0	0	1	0	0	0
preputial/clitoral gland	0	1	0	0	0	0	0	0
brain	0	0	0	0	0	0	0	1
peripheral nerves	0	1	0	0	0	0	0	0
bone	0	0	0	0	0	0	0	1
peritoneum	0	0	0	2	0	0	0	0