ジクロロメタンのラットを用いた
吸入による 13 週間毒性試験報告書

試験番号：0257

TABLES

TABLES

TABLE 1 EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE 13-WEEK INHALATION STUDIES OF DICHLOROMETHANE

<Method of Administration>
Inhalation
<Number of Groups>
Male 6, Female 6
<Size of Groups>
10 males and 10 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
19 wk
<Doses>
Male and Female
0, 500, 1000, 2000, 4000 or 8000ppm
<Duration of Dosing>
5 d/wk for 13 wk
<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
Available *ad libitum*
Animal per Cage
Single (stainless steel wire)
Animal Room Environment
Barrier system
Temperature : 21±2℃
Humidity : 60±10%
Fluorescent light 12 h/d
15~17 room air changes /h
Chamber Environment
Barrier system
Temperature : 20~24℃
Humidity : 30~70%
12±1 chamber air changes /h
<Type and Frequency of Observation>
Clinical Sign
Observed 2 per d
Body Weight
Weighed 1 per wk
Food Consumption
Weighed 1 per wk

TABLE 1 (Continued) EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE 13-WEEK INHALATION STUDIES OF DICHLOROMETHANE

<Hematology>
Hematological examination performed on scheduld 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,
Prothrombin time(PT),
Activated partial thromboplastin time(APTT).

<Biochemistry>
Biochemistrical examination performed on scheduld sacrificed animals.
The following measurement parameters were examined;
Total protein, Albumin, A/G/ ratio,
Total bilirubin, Glucose, Total cholesterol,
Phospholipid, Triglyceride,
Glutamic oxaloacetic transaminase (GOT),
Glutamic pyruvic transaminase (GPT),
Alkaline phosphatase(ALP),
Lactate dehydrogenase (LDH),
γ -Glutamyl transpeptidase(G-GPT),
Creatine phosphokinase (CPK),
Urea nitrogen, Creatinine, 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, 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, thymus.

<Histopathologic Examination>
Histopathologic examination performed on at least two animals per sex per groups.
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, prostate, ovary, uterus, vagina,
mammary gland, brain, spinal cord, peripheral nerve,
eye, harderian gland, muscle, bone.

TABLE 2 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF MALE RATS IN THE 13-WEEK INHALATION STUDY OF DICHLOROMETHANE

Week-Day on Study	Control		500 ppm			1000 ppm			2000 ppm			4000 ppm			8000 ppm		
	Av.Wt.	No.of Surviv. <10>	Av.Wt.	% of cont. <10>	No.of Surviv.	Av.Wt.	% of cont. <10>	No.of Surviv.	Av.Wt.	% of cont. <10>	No.of Surviv.	Av.Wt.	% of cont. <10>	No.of Surviv.	Av.Wt.	% of cont. <10>	No.of Surviv.
0-0	120 (10)	10/10	120 (10)	100	10/10	120 (10)	100	10/10	119 (10)	99	10/10	119 (10)	99	10/10	119 (10)	99	10/10
1-7	144 (10)	10/10	148 (10)	103	10/10	144 (10)	100	10/10	142 (10)	99	10/10	140 (10)	97	10/10	119 (10)	83	10/10
2-7	171 (10)	10/10	176 (10)	103	10/10	167 (10)	98	10/10	165 (10)	96	10/10	163 (10)	95	10/10	129 (10)	75	10/10
3-7	199 (10)	10/10	201 (10)	101	10/10	188 (10)	94	10/10	188 (10)	94	10/10	185 (10)	93	10/10	143 (10)	72	10/10
4-7	224 (10)	10/10	221 (10)	99	10/10	207 (10)	92	10/10	206 (10)	92	10/10	203 (10)	91	10/10	156 (10)	70	10/10
5-7	238 (10)	10/10	241 (10)	101	10/10	226 (10)	95	10/10	224 (10)	94	10/10	221 (10)	93	10/10	170 (10)	71	10/10
6-7	251 (10)	10/10	256 (10)	102	10/10	239 (10)	95	10/10	238 (10)	95	10/10	234 (10)	93	10/10	180 (10)	72	10/10
7-7	265 (10)	10/10	271 (10)	102	10/10	254 (10)	96	10/10	251 (10)	95	10/10	248 (10)	94	10/10	189 (10)	71	10/10
8-7	279 (10)	10/10	286 (10)	103	10/10	266 (10)	95	10/10	263 (10)	94	10/10	260 (10)	93	10/10	198 (10)	71	10/10
9-7	289 (10)	10/10	296 (10)	102	10/10	278 (10)	96	10/10	275 (10)	95	10/10	270 (10)	93	10/10	210 (10)	73	10/10
10-7	300 (10)	10/10	306 (10)	102	10/10	285 (10)	95	10/10	283 (10)	94	10/10	279 (10)	93	10/10	215 (10)	72	10/10
11-7	309 (10)	10/10	314 (10)	102	10/10	295 (10)	95	10/10	290 (10)	94	10/10	286 (10)	93	10/10	220 (10)	71	10/10
12-7	319 (10)	10/10	320 (10)	100	10/10	304 (10)	95	10/10	298 (10)	93	10/10	294 (10)	92	10/10	226 (10)	71	10/10
13-6	325 (10)	10/10	328 (10)	101	10/10	309 (10)	95	10/10	304 (10)	94	10/10	303 (10)	93	10/10	231 (10)	71	10/10

< >: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 13-WEEK INHALATION STUDY OF DICHLOROMETHANE

Week-Day on Study	Control		500 ppm			1000 ppm			2000 ppm			4000 ppm			8000 ppm		
	Av.Wt.	No.of Surviv. <10>	Av.Wt.	% of cont. <10>	No.of Surviv.	Av.Wt.	% of cont. <10>	No.of Surviv.	Av.Wt.	% of cont. <10>	No.of Surviv.	Av.Wt.	% of cont. <10>	No.of Surviv.	Av.Wt.	% of cont. <10>	No.of Surviv.
0-0	100 (10)	10/10	100 (10)	100	10/10	99 (10)	99	10/10	99 (10)	99	10/10	100 (10)	100	10/10	100 (10)	100	10/10
1-7	114 (10)	10/10	115 (10)	101	10/10	114 (10)	100	10/10	114 (10)	100	10/10	109 (10)	96	10/10	99 (10)	87	10/10
2-7	128 (10)	10/10	129 (10)	101	10/10	128 (10)	100	10/10	127 (10)	99	10/10	121 (10)	95	10/10	106 (10)	83	10/10
3-7	139 (10)	10/10	138 (10)	99	10/10	136 (10)	98	10/10	135 (10)	97	10/10	132 (10)	95	10/10	117 (10)	84	10/10
4-7	148 (10)	10/10	145 (10)	98	10/10	146 (10)	99	10/10	143 (10)	97	10/10	141 (10)	95	10/10	126 (10)	85	10/10
5-7	153 (10)	10/10	154 (10)	101	10/10	152 (10)	99	10/10	151 (10)	99	10/10	147 (10)	96	10/10	132 (10)	86	10/10
6-7	158 (10)	10/10	160 (10)	101	10/10	158 (10)	100	10/10	156 (10)	99	10/10	151 (10)	96	10/10	138 (10)	87	10/10
7-7	164 (10)	10/10	165 (10)	101	10/10	162 (10)	99	10/10	161 (10)	98	10/10	157 (10)	96	10/10	143 (10)	87	10/10
8-7	170 (10)	10/10	170 (10)	100	10/10	168 (10)	99	10/10	163 (10)	96	10/10	159 (10)	94	10/10	148 (10)	87	10/10
9-7	173 (10)	10/10	176 (10)	102	10/10	171 (10)	99	10/10	168 (10)	97	10/10	163 (10)	94	10/10	153 (10)	88	10/10
10-7	177 (10)	10/10	180 (10)	102	10/10	175 (10)	99	10/10	171 (10)	97	10/10	166 (10)	94	10/10	156 (10)	88	10/10
11-7	182 (10)	10/10	183 (10)	101	10/10	179 (10)	98	10/10	176 (10)	97	10/10	170 (10)	93	10/10	160 (10)	88	10/10
12-7	185 (10)	10/10	185 (10)	100	10/10	180 (10)	97	10/10	178 (10)	96	10/10	171 (10)	92	10/10	163 (10)	88	10/10
13-6	188 (10)	10/10	190 (10)	101	10/10	184 (10)	98	10/10	181 (10)	96	10/10	173 (10)	92	10/10	166 (10)	88	10/10

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

TABLE 4 FOOD CONSUMPTION CHANGES OF MALE RATS IN THE 13-WEEK INHALATION STUDY OF DICHLOROMETHANE

Week-Day on Study	Control		500 ppm			1000 ppm			2000 ppm			4000 ppm			8000 ppm		
	Av.FC.	No.of Surviv. <10>	Av.FC.	% of cont. <10>	No.of Surviv.	Av.FC.	% of cont. <10>	No.of Surviv.	Av.FC.	% of cont. <10>	No.of Surviv.	Av.FC.	% of cont. <10>	No.of Surviv.	Av.FC.	% of cont. <10>	No.of Surviv.
1-7	14.0 (10)	10/10	14.4 (10)	103	10/10	13.6 (10)	97	10/10	14.0 (10)	100	10/10	13.0 (10)	93	10/10	8.8 (10)	63	10/10
2-7	14.8 (10)	10/10	15.5 (10)	105	10/10	15.0 (10)	101	10/10	14.5 (10)	98	10/10	14.2 (10)	96	10/10	10.2 (10)	69	10/10
3-7	16.5 (10)	10/10	16.8 (10)	102	10/10	15.4 (10)	93	10/10	16.0 (10)	97	10/10	15.7 (10)	95	10/10	12.0 (10)	73	10/10
4-7	17.6 (10)	10/10	17.7 (10)	101	10/10	16.0 (10)	91	10/10	16.1 (10)	91	10/10	16.6 (10)	94	10/10	13.4 (10)	76	10/10
5-7	16.8 (10)	10/10	17.8 (10)	106	10/10	15.5 (10)	92	10/10	15.9 (10)	95	10/10	16.2 (10)	96	10/10	14.3 (10)	85	10/10
6-7	16.8 (10)	10/10	17.3 (10)	103	10/10	15.5 (10)	92	10/10	16.1 (10)	96	10/10	15.9 (10)	95	10/10	14.7 (10)	88	10/10
7-7	17.2 (10)	10/10	17.6 (10)	102	10/10	16.0 (10)	93	10/10	16.5 (10)	96	10/10	16.4 (10)	95	10/10	15.2 (10)	88	10/10
8-7	17.3 (10)	10/10	17.9 (10)	103	10/10	16.0 (10)	92	10/10	16.0 (10)	92	10/10	16.4 (10)	95	10/10	15.8 (10)	91	10/10
9-7	16.9 (10)	10/10	17.3 (10)	102	10/10	16.6 (10)	98	10/10	16.3 (10)	96	10/10	16.3 (10)	96	10/10	16.2 (10)	96	10/10
10-7	17.1 (10)	10/10	17.4 (10)	102	10/10	16.0 (10)	94	10/10	16.2 (10)	95	10/10	16.0 (10)	94	10/10	14.7 (10)	86	10/10
11-7	17.7 (10)	10/10	17.6 (10)	99	10/10	16.8 (10)	95	10/10	16.1 (10)	91	10/10	16.6 (10)	94	10/10	15.6 (10)	88	10/10
12-7	17.5 (10)	10/10	17.2 (10)	98	10/10	16.5 (10)	94	10/10	15.8 (10)	90	10/10	16.4 (10)	94	10/10	16.5 (10)	94	10/10
13-6	17.6 (10)	10/10	17.8 (10)	101	10/10	16.9 (10)	96	10/10	16.4 (10)	93	10/10	17.3 (10)	98	10/10	16.9 (10)	96	10/10

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

TABLE 5 FOOD CONSUMPTION CHANGES OF FEMALE RATS IN THE 13-WEEK INHALATION STUDY OF DICHLOROMETHANE

Week-Day on Study	Control		500 ppm			1000 ppm			2000 ppm			4000 ppm			8000 ppm		
	Av.FC.	No.of Surviv. <10>	Av.FC.	% of cont. <10>	No.of Surviv.	Av.FC.	% of cont. <10>	No.of Surviv.	Av.FC.	% of cont. <10>	No.of Surviv.	Av.FC.	% of cont. <10>	No.of Surviv.	Av.FC.	% of cont. <10>	No.of Surviv.
1-7	11.6 (10)	10/10	12.0 (10)	103	10/10	11.8 (10)	102	10/10	11.8 (10)	102	10/10	10.3 (10)	89	10/10	7.8 (10)	67	10/10
2-7	12.3 (10)	10/10	13.0 (10)	106	10/10	12.8 (10)	104	10/10	12.7 (10)	103	10/10	11.4 (10)	93	10/10	9.0 (10)	73	10/10
3-7	12.7 (10)	10/10	12.6 (10)	99	10/10	12.2 (10)	96	10/10	12.6 (10)	99	10/10	12.2 (10)	96	10/10	10.4 (10)	82	10/10
4-7	13.2 (10)	10/10	13.0 (10)	98	10/10	12.9 (10)	98	10/10	13.0 (10)	98	10/10	12.5 (10)	95	10/10	11.8 (10)	89	10/10
5-7	12.4 (10)	10/10	13.0 (10)	105	10/10	12.5 (10)	101	10/10	12.6 (10)	102	10/10	12.1 (10)	98	10/10	11.8 (10)	95	10/10
6-7	12.3 (10)	10/10	12.1 (10)	98	10/10	12.0 (10)	98	10/10	12.2 (10)	99	10/10	11.5 (10)	93	10/10	12.0 (10)	98	10/10
7-7	12.7 (10)	10/10	11.7 (10)	92	10/10	12.1 (10)	95	10/10	11.7 (10)	92	10/10	11.6 (10)	91	10/10	12.4 (10)	98	10/10
8-7	12.4 (10)	10/10	12.0 (10)	97	10/10	12.0 (10)	97	10/10	11.3 (10)	91	10/10	11.3 (10)	91	10/10	12.7 (10)	102	10/10
9-7	12.1 (10)	10/10	12.6 (10)	104	10/10	12.1 (10)	100	10/10	11.5 (10)	95	10/10	11.0 (10)	91	10/10	12.6 (10)	104	10/10
10-7	12.3 (10)	10/10	12.1 (10)	98	10/10	11.8 (10)	96	10/10	12.0 (10)	98	10/10	11.4 (10)	93	10/10	12.1 (10)	98	10/10
11-7	12.2 (10)	10/10	11.5 (10)	94	10/10	12.1 (10)	99	10/10	11.7 (10)	96	10/10	11.2 (10)	92	10/10	12.9 (10)	106	10/10
12-7	12.1 (10)	10/10	11.7 (10)	97	10/10	11.8 (10)	98	10/10	11.7 (10)	97	10/10	11.5 (10)	95	10/10	13.4 (10)	111	10/10
13-6	12.3 (10)	10/10	12.6 (10)	102	10/10	12.1 (10)	98	10/10	12.0 (10)	98	10/10	11.5 (10)	93	10/10	14.0 (10)	114	10/10

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