

ジクロロメタンのラットを用いた
吸入による2週間毒性試験報告書

試験番号：0229

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TABLE 1 EXPERIMENTAL DESIGN AND MATERIALS AND METHODS
IN THE 2-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 8 wk
<Doses>	Male and Female 0, 1000, 2000, 4000, 8000 or 16000ppm
<Duration of Dosing>	5 d/wk for 2 wk
<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 Available <i>ad libitum</i>
	Animal per Cage Single (stainless steel wire)
	Animal Room Environment Barrier system Temperature : 21 \pm 2 $^{\circ}$ C Humidity : 60 \pm 10% Fluorescent light 12 h/d 15~17 room air changes /h
	Chamber Environment Barrier system Temperature : 20~24 $^{\circ}$ C Humidity : 30~70% 12 \pm 1 chamber air changes /h
<Type and Frequency of Observation>	Clinical Sign Observed 2 per d (1 per d without Exposure day)
	Body Weight Weighed 0-0, 1-1, 1-7, and 2-7(wk-d)
	Food Consumption Weighed 1-7 and 2-7(wk-d)

TABLE 1 EXPERIMENTAL DESIGN AND MATERIALS AND METHODS
(Continued) IN THE 2-WEEK INHALATION STUDIES OF DICHLOROMETHANE

<Hematology>

Hematological examination performed on five animals per sex per groups.
(schedule 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, Reticulocyte,
Prothrombin time (PT),
Activated partial thromboplastin time (APTT).

<Biochemistry>

Biochemistrical examination performed on five animals per sex per groups.
(schedule sacrificed animals)

The following measurement parameters were examined;

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

<Necropsy>

Necropsy performed on all animals.

<Organ Weight>

Organ weight measurement performed on five animals per sex per groups.
(schedule 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, hardierian gland, muscle, bone.

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

Week-Day on Study	Control			1000ppm			2000ppm			4000ppm			8000ppm			16000ppm		
	Au.Wt.	No.of Surviv. <10>		Au.Wt.	% of cont. <10>	No.of Surviv.	Au.Wt.	% of cont. <10>	No.of Surviv.	Au.Wt.	% of cont. <10>	No.of Surviv.	Au.Wt.	% of cont. <10>	No.of Surviv.	Au.Wt.	% of cont. <10>	No.of Surviv.
0-0	113 (10)	10/10		114 (10)	101	10/10	114 (10)	101	10/10	114 (10)	101	10/10	113 (10)	100	10/10	113 (10)	100	1/10
1-1	116 (10)	10/10		116 (10)	100	10/10	117 (10)	101	10/10	115 (10)	99	10/10	110 (10)	95	10/10	104 (1)	90	1/10
1-7	134 (10)	10/10		138 (10)	103	10/10	135 (10)	101	10/10	134 (10)	100	10/10	120 (10)	90	10/10	- (-)	-	0/10
2-7	157 (10)	10/10		167 (10)	106	10/10	159 (10)	101	10/10	161 (10)	103	10/10	138 (10)	88	10/10	- (-)	-	0/10
< >:No.of effective animals,():No.of measured animals Au.Wt.: g																		

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

Week-Day on Study	Control			1000ppm			2000ppm			4000ppm			8000ppm			16000ppm		
	Au.Wt.	No.of Surviv. <10>		Au.Wt.	% of cont. <10>	No.of Surviv.	Au.Wt.	% of cont. <10>	No.of Surviv.	Au.Wt.	% of cont. <10>	No.of Surviv.	Au.Wt.	% of cont. <10>	No.of Surviv.	Au.Wt.	% of cont. <10>	No.of Surviv.
0-0	101 (10)	10/10		99 (10)	98	10/10	100 (10)	99	10/10	100 (10)	99	10/10	99 (10)	98	10/10	99 (10)	98	3/10
1-1	102 (10)	10/10		100 (10)	98	10/10	101 (10)	99	10/10	101 (10)	99	10/10	95 (10)	93	10/10	100 (3)	98	1/10
1-7	111 (10)	10/10		110 (10)	99	10/10	112 (10)	101	10/10	111 (10)	100	10/10	98 (10)	88	10/10	- (-)	-	0/10
2-7	125 (10)	10/10		122 (10)	98	10/10	125 (10)	100	10/10	125 (10)	100	10/10	110 (10)	88	10/10	- (-)	-	0/10
< >:No.of effective animals,():No.of measured animals Au.Wt.: g																		

TABLE 4 FOOD CONSUMPTION CHANGES OF MALE RATS IN THE 2-WEEK INHALATION STUDY OF DICHLOROMETHANE

Week-Day on Study	Control		1000ppm			2000ppm			4000ppm			8000ppm			16000ppm		
	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	13.8 (10)	10/10	14.0 (10)	101	10/10	13.8 (10)	100	10/10	13.6 (10)	99	10/10	10.2 (10)	74	10/10	7.2 (1)	52	0/10
2-7	14.2 (10)	10/10	15.3 (10)	108	10/10	14.4 (10)	101	10/10	14.3 (10)	101	10/10	11.9 (10)	84	10/10	- (-)	-	0/10
< >:No.of effective animals,():No.of measured animals Av.FC.: g																	

TABLE 5 FOOD CONSUMPTION CHANGES OF FEMALE RATS IN THE 2-WEEK INHALATION STUDY OF DICHLOROMETHANE

Week-Day on Study	Control		1000ppm			2000ppm			4000ppm			8000ppm			16000ppm		
	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	11.4 (10)	98	10/10	11.5 (10)	99	10/10	11.6 (10)	100	10/10	8.2 (10)	71	10/10	7.2 (1)	62	0/10
2-7	11.8 (10)	10/10	11.5 (10)	97	10/10	11.6 (10)	98	10/10	11.7 (10)	99	10/10	9.6 (10)	81	10/10	- (-)	-	0/10
< >:No.of effective animals,():No.of measured animals Av.FC.: g																	