

シクロヘキセ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：0363

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TABLE 1 EXPERIMENTAL DESIGN AND MATERIALS AND METHODS
IN THE 13-WEEK INHALATION STUDY OF CYCLOHEXENE

<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, 150, 300, 600, 1200 or 2400ppm
<Duration of Dosing>	6 h/d, 5 d/wk for 13 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 : 55 \pm 15% 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 air changes /h
<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
	Food Consumption Weighed 1 per wk

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

<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.

<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, Reticulocyte,
Prothrombin time (PT),
Activated partial thromboplastin time (APTT),
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, Phospholipid,
Glutamic oxaloacetic transaminase (GOT),
Glutamic pyruvic transaminase (GPT),
Lactate dehydrogenase (LDH),
Alkaline phosphatase (ALP),
 γ -Glutamyl transpeptidase (γ -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 scheduled sacrificed animals.

The following organs were weighed;

thymus, adrenal, testis, ovary, heart, lung, kidney, spleen, liver, brain.

<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, 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.

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

Week-Day on Study	0ppm		150ppm			300ppm			600ppm			1200ppm			2400ppm		
	Av.Wt.	No.of Surviv.	Av.Wt.	% of cont.	No.of Surviv.	Av.Wt.	% of cont.	No.of Surviv.	Av.Wt.	% of cont.	No.of Surviv.	Av.Wt.	% of cont.	No.of Surviv.	Av.Wt.	% of cont.	No.of Surviv.
		<10>		<10>			<10>			<10>			<10>			<10>	
0-0	115 (10)	10/10	115 (10)	100	10/10	115 (10)	100	10/10	115 (10)	100	10/10	115 (10)	100	10/10	115 (10)	100	10/10
1-7	139 (10)	10/10	142 (10)	102	10/10	143 (10)	103	10/10	140 (10)	101	10/10	134 (10)	96	10/10	137 (10)	99	10/10
2-7	166 (10)	10/10	165 (10)	99	10/10	171 (10)	103	10/10	166 (10)	100	10/10	156 (10)	94	10/10	163 (10)	98	10/10
3-7	189 (10)	10/10	188 (10)	99	10/10	192 (10)	102	10/10	189 (10)	100	10/10	178 (10)	94	10/10	178 (10)	94	10/10
4-7	211 (10)	10/10	210 (10)	100	10/10	214 (10)	101	10/10	210 (10)	100	10/10	196 (10)	93	10/10	197 (10)	93	10/10
5-7	225 (10)	10/10	224 (10)	100	10/10	228 (10)	101	10/10	226 (10)	100	10/10	209 (10)	93	10/10	211 (10)	94	10/10
6-7	239 (10)	10/10	237 (10)	99	10/10	242 (10)	101	10/10	242 (10)	101	10/10	223 (10)	93	10/10	224 (10)	94	10/10
7-7	251 (10)	10/10	250 (10)	100	10/10	258 (10)	103	10/10	255 (10)	102	10/10	235 (10)	94	10/10	238 (10)	95	10/10
8-7	263 (10)	10/10	262 (10)	100	10/10	270 (10)	103	10/10	265 (10)	101	10/10	246 (10)	94	10/10	251 (10)	95	10/10
9-7	273 (10)	10/10	273 (10)	100	10/10	278 (10)	102	10/10	277 (10)	101	10/10	258 (10)	95	10/10	263 (10)	96	10/10
10-7	282 (10)	10/10	282 (10)	100	10/10	286 (10)	101	10/10	286 (10)	101	10/10	267 (10)	95	10/10	272 (10)	96	10/10
11-7	289 (10)	10/10	290 (10)	100	10/10	293 (10)	101	10/10	292 (10)	101	10/10	273 (10)	94	10/10	280 (10)	97	10/10
12-7	295 (10)	10/10	296 (10)	100	10/10	300 (10)	102	10/10	298 (10)	101	10/10	279 (10)	95	10/10	288 (10)	98	10/10
13-7	300 (10)	10/10	302 (10)	101	10/10	305 (10)	102	10/10	301 (10)	100	10/10	284 (10)	95	10/10	292 (10)	97	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 CYCLOHEXENE

Week-Day on Study	0ppm		150ppm			300ppm			600ppm			1200ppm			2400ppm		
	Av.Wt.	No.of Surviv.	Av.Wt.	% of cont.	No.of Surviv.	Av.Wt.	% of cont.	No.of Surviv.	Av.Wt.	% of cont.	No.of Surviv.	Av.Wt.	% of cont.	No.of Surviv.	Av.Wt.	% of cont.	No.of Surviv.
	<10>	<10>	<10>	<10>	<10>	<10>	<10>	<10>	<10>	<10>	<10>	<10>	<10>	<10>	<10>	<10>	<10>
0-0	95 (10)	10/10	95 (10)	100	10/10	95 (10)	100	10/10	95 (10)	100	10/10	95 (10)	100	10/10	95 (10)	100	10/10
1-7	108 (10)	10/10	108 (10)	100	10/10	111 (10)	103	10/10	107 (10)	99	10/10	106 (10)	98	10/10	107 (10)	99	10/10
2-7	119 (10)	10/10	118 (10)	99	10/10	123 (10)	103	10/10	118 (10)	99	10/10	117 (10)	98	10/10	117 (10)	98	10/10
3-7	126 (10)	10/10	127 (10)	101	10/10	129 (10)	102	10/10	128 (10)	102	10/10	125 (10)	99	10/10	123 (10)	98	10/10
4-7	134 (10)	10/10	136 (10)	101	10/10	139 (10)	104	10/10	138 (10)	103	10/10	133 (10)	99	10/10	130 (10)	97	10/10
5-7	140 (10)	10/10	140 (10)	100	10/10	143 (10)	102	10/10	143 (10)	102	10/10	138 (10)	99	10/10	135 (10)	96	10/10
6-7	147 (10)	10/10	148 (10)	101	10/10	149 (10)	101	10/10	148 (10)	101	10/10	140 (10)	95	10/10	140 (10)	95	10/10
7-7	148 (10)	10/10	150 (10)	101	10/10	153 (10)	103	10/10	151 (10)	102	10/10	145 (10)	98	10/10	143 (10)	97	10/10
8-7	155 (10)	10/10	157 (10)	101	10/10	156 (10)	101	10/10	156 (10)	101	10/10	148 (10)	95	10/10	149 (10)	96	10/10
9-7	159 (10)	10/10	160 (10)	101	10/10	161 (10)	101	10/10	159 (10)	100	10/10	152 (10)	96	10/10	152 (10)	96	10/10
10-7	161 (10)	10/10	165 (10)	102	10/10	165 (10)	102	10/10	164 (10)	102	10/10	157 (10)	98	10/10	156 (10)	97	10/10
11-7	165 (10)	10/10	169 (10)	102	10/10	170 (10)	103	10/10	168 (10)	102	10/10	159 (10)	96	10/10	157 (10)	95	10/10
12-7	166 (10)	10/10	169 (10)	102	10/10	170 (10)	102	10/10	169 (10)	102	10/10	161 (10)	97	10/10	160 (10)	96	10/10
13-7	167 (10)	10/10	172 (10)	103	10/10	172 (10)	103	10/10	171 (10)	102	10/10	161 (10)	96	10/10	161 (10)	96	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 CYCLOHEXENE

Week-Day on Study	0ppm		150ppm		300ppm		600ppm		1200ppm		2400ppm						
	Av.FC.	No.of Surviv.	Av.FC.	% of cont.	No.of Surviv.	Av.FC.	% of cont.	No.of Surviv.	Av.FC.	% of cont.	No.of Surviv.	Av.FC.	% of cont.	No.of Surviv.			
	<10>	<10>	<10>	<10>	<10>	<10>	<10>	<10>	<10>	<10>	<10>	<10>	<10>	<10>			
1-7	13.5 (10)	10/10	13.7 (10)	101	10/10	13.1 (10)	97	10/10	13.0 (10)	96	10/10	12.6 (10)	93	10/10	12.3 (10)	91	10/10
2-7	14.1 (10)	10/10	14.2 (10)	101	10/10	15.0 (10)	106	10/10	14.4 (10)	102	10/10	14.0 (10)	99	10/10	14.5 (10)	103	10/10
3-7	15.1 (10)	10/10	14.5 (10)	96	10/10	15.8 (10)	105	10/10	15.1 (10)	100	10/10	14.7 (10)	97	10/10	15.8 (10)	105	10/10
4-7	16.0 (10)	10/10	15.5 (10)	97	10/10	15.8 (10)	99	10/10	15.8 (10)	99	10/10	15.9 (10)	99	10/10	15.7 (10)	98	10/10
5-7	16.0 (10)	10/10	15.2 (10)	95	10/10	16.1 (10)	101	10/10	15.6 (10)	98	10/10	15.1 (10)	94	10/10	15.4 (10)	96	10/10
6-7	15.4 (10)	10/10	15.5 (10)	101	10/10	16.1 (10)	105	10/10	15.6 (10)	101	10/10	15.6 (10)	101	10/10	15.7 (10)	102	10/10
7-7	15.3 (10)	10/10	15.2 (10)	99	10/10	15.4 (10)	101	10/10	15.6 (10)	102	10/10	15.2 (10)	99	10/10	15.5 (10)	101	10/10
8-7	15.3 (10)	10/10	15.3 (10)	100	10/10	15.7 (10)	103	10/10	15.8 (10)	103	10/10	15.3 (10)	100	10/10	16.1 (10)	105	10/10
9-7	15.3 (10)	10/10	15.4 (10)	101	10/10	15.4 (10)	101	10/10	15.6 (10)	102	10/10	15.2 (10)	99	10/10	16.0 (10)	105	10/10
10-7	15.2 (10)	10/10	15.6 (10)	103	10/10	15.4 (10)	101	10/10	15.8 (10)	104	10/10	15.2 (10)	100	10/10	15.8 (10)	104	10/10
11-7	15.4 (10)	10/10	15.4 (10)	100	10/10	15.4 (10)	100	10/10	15.4 (10)	100	10/10	15.2 (10)	99	10/10	15.8 (10)	103	10/10
12-7	15.6 (10)	10/10	15.7 (10)	101	10/10	15.6 (10)	100	10/10	15.6 (10)	100	10/10	15.5 (10)	99	10/10	16.1 (10)	103	10/10
13-7	15.2 (10)	10/10	15.1 (10)	99	10/10	15.8 (10)	104	10/10	15.5 (10)	102	10/10	14.9 (10)	98	10/10	15.8 (10)	104	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 CYCLOHEXENE

Week-Day on Study	0ppm		150ppm		300ppm		600ppm		1200ppm		2400ppm						
	Av.FC.	No.of Surviv.	Av.FC.	% of cont.	No.of Surviv.	Av.FC.	% of cont.	No.of Surviv.	Av.FC.	% of cont.	No.of Surviv.	Av.FC.	% of cont.	No.of Surviv.			
	<10>	<10>	<10>	<10>	<10>	<10>	<10>	<10>	<10>	<10>	<10>	<10>	<10>	<10>			
1-7	10.3 (10)	10/10	10.6 (10)	103	10/10	10.9 (10)	106	10/10	10.8 (10)	105	10/10	10.2 (10)	99	10/10	9.9 (10)	96	10/10
2-7	10.3 (10)	10/10	10.2 (10)	99	10/10	11.2 (10)	109	10/10	10.8 (10)	105	10/10	10.1 (10)	98	10/10	10.5 (10)	102	10/10
3-7	10.1 (10)	10/10	10.5 (10)	104	10/10	11.3 (10)	112	10/10	11.3 (10)	112	10/10	10.5 (10)	104	10/10	10.9 (10)	108	10/10
4-7	10.5 (10)	10/10	10.7 (10)	102	10/10	11.3 (10)	108	10/10	11.3 (10)	108	10/10	11.0 (10)	105	10/10	10.8 (10)	103	10/10
5-7	10.3 (10)	10/10	10.5 (10)	102	10/10	10.6 (10)	103	10/10	10.8 (10)	105	10/10	10.1 (10)	98	10/10	10.4 (10)	101	10/10
6-7	10.3 (10)	10/10	10.5 (10)	102	10/10	10.9 (10)	106	10/10	10.9 (10)	106	10/10	10.4 (10)	101	10/10	10.3 (10)	100	10/10
7-7	10.0 (10)	10/10	10.3 (10)	103	10/10	10.5 (10)	105	10/10	10.5 (10)	105	10/10	9.9 (10)	99	10/10	9.9 (10)	99	10/10
8-7	9.9 (10)	10/10	10.4 (10)	105	10/10	10.2 (10)	103	10/10	10.5 (10)	106	10/10	9.9 (10)	100	10/10	10.1 (10)	102	10/10
9-7	10.2 (10)	10/10	10.4 (10)	102	10/10	10.6 (10)	104	10/10	10.4 (10)	102	10/10	10.0 (10)	98	10/10	9.9 (10)	97	10/10
10-7	10.1 (10)	10/10	10.5 (10)	104	10/10	10.4 (10)	103	10/10	10.3 (10)	102	10/10	9.9 (10)	98	10/10	9.9 (10)	98	10/10
11-7	10.3 (10)	10/10	11.4 (10)	111	10/10	11.1 (10)	108	10/10	10.8 (10)	105	10/10	10.2 (10)	99	10/10	9.8 (10)	95	10/10
12-7	10.0 (10)	10/10	10.5 (10)	105	10/10	10.6 (10)	106	10/10	11.0 (10)	110	10/10	10.1 (10)	101	10/10	10.0 (10)	100	10/10
13-7	10.0 (10)	10/10	10.4 (10)	104	10/10	10.5 (10)	105	10/10	10.6 (10)	106	10/10	9.9 (10)	99	10/10	9.9 (10)	99	10/10

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