

シクロヘキセ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：0358

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TABLE 1 EXPERIMENTAL DESIGN AND MATERIALS AND METHODS
IN THE 2-WEEK INHALATION STUDY OF CYCLOHEXENE

<Method of Administration>	Inhalation
<Number of Groups>	Male 6, Female 6
<Size of Groups>	5 males and 5 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, 600, 1200, 2400, 4800 or 9600ppm
<Duration of Dosing>	6 h/d, 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 : 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 Before the exposure : 1-2, 1-4, 1-7, 2-3 and 2-7 (wk-d) During the exposure : First day(0.5, 1.5 and 3.5 hour) Observed 1 or 2 per day for mortality
	Body Weight Weighed 0-0, 1-2, 1-4, 1-7, 2-3 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 STUDY OF CYCLOHEXENE

<Hematology>

Hematological examination performed on all 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, Reticulocyte,
Prothrombin time (PT),
Activated partial thromboplastin time (APTT),
White blood cell (WBC), Differential WBC.

<Biochemistry>

Biochemistrical examination performed on all 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,
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 five animals per sex per groups.
(schedule 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 per sex groups.
(dead animals and schedule sacrificed 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 2-WEEK INHALATION STUDY OF CYCLOHEXENE

Week-Day on Study	Oppm		600ppm		1200ppm		2400ppm		4800ppm		9600ppm								
	Av.Wt.	No.of Surviv. <5>	Av.Wt.	% of cont. <5>	No.of Surviv. <5>	Av.Wt.	% of cont. <5>	No.of Surviv. <5>	Av.Wt.	% of cont. <5>	No.of Surviv. <5>	Av.Wt.	% of cont. <5>	No.of Surviv. <5>					
0-0	111	(5)	5/5	111	(5)	100	5/5	111	(5)	100	5/5	111	(5)	100	5/5	111	(5)	100	5/5
1-1	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	—	0/5
1-2	117	(5)	5/5	115	(5)	98	5/5	116	(5)	99	5/5	112	(5)	96	5/5	110	(5)	94	5/5
1-3	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	—	0/5
1-4	120	(5)	5/5	117	(5)	98	5/5	119	(5)	99	5/5	111	(5)	93	5/5	106	(5)	88	5/5
1-5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	—	0/5
1-6	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	—	0/5
1-7	130	(5)	5/5	128	(5)	98	5/5	132	(5)	102	5/5	121	(5)	93	5/5	116	(5)	89	5/5
2-1	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	—	0/5
2-2	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	—	0/5
2-3	140	(5)	5/5	136	(5)	97	5/5	142	(5)	101	5/5	125	(5)	89	5/5	113	(5)	81	5/5
2-4	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	—	0/5
2-5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	—	0/5
2-6	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	—	0/5
2-7	155	(5)	5/5	152	(5)	98	5/5	160	(5)	103	5/5	140	(5)	90	5/5	128	(4)	83	4/5

< > : 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 2-WEEK INHALATION STUDY OF CYCLOHEXENE

Week-Day on Study	Oppm		600ppm		1200ppm		2400ppm		4800ppm		9600ppm								
	Av.Wt.	No.of Surviv. <5>	Av.Wt.	% of cont. <5>	No.of Surviv. <5>	Av.Wt.	% of cont. <5>	No.of Surviv. <5>	Av.Wt.	% of cont. <5>	No.of Surviv. <5>	Av.Wt.	% of cont. <5>	No.of Surviv. <5>					
0-0	95	(5)	5/5	95	(5)	100	5/5	95	(5)	100	5/5	95	(5)	100	5/5	95	(5)	100	5/5
1-1	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	—	0/5
1-2	99	(5)	5/5	98	(5)	99	5/5	98	(5)	99	5/5	94	(5)	95	5/5	93	(5)	94	5/5
1-3	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	—	0/5
1-4	101	(5)	5/5	101	(5)	100	5/5	99	(5)	98	5/5	94	(5)	93	5/5	91	(5)	90	5/5
1-5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	—	0/5
1-6	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	—	0/5
1-7	107	(5)	5/5	108	(5)	101	5/5	107	(5)	100	5/5	101	(5)	94	5/5	97	(5)	91	5/5
2-1	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	—	0/5
2-2	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	—	0/5
2-3	111	(5)	5/5	111	(5)	100	5/5	110	(5)	99	5/5	102	(5)	92	5/5	96	(5)	86	5/5
2-4	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	—	0/5
2-5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	—	0/5
2-6	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	5/5	—	—	—	0/5
2-7	117	(5)	5/5	118	(5)	101	5/5	120	(5)	103	5/5	110	(5)	94	5/5	104	(5)	89	5/5

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

TABLE 4 CLINICAL OBSERVATION FIRST DAY DURING EXPOSURE OF MALE RATS IN THE 2-WEEK INHALATION STUDY OF CYCLOHEXENE

Group name	First day during exposure		
	0.5hour	1.5hour	3.5hour
9600ppm	Lacrymation Ataxic gait Tachypnea	Lacrymation Lateral Deep breathing	Death
4800ppm	Lacrymation Ataxic gait Tachypnea	Lacrymation Tachypnea	Lacrymation Ataxic gait Tachypnea
2400ppm	Lacrymation	Lacrymation	Lacrymation
1200ppm ~ 0ppm	Non remarkable	Non remarkable	Non remarkable

TABLE 5 CLINICAL OBSERVATION FIRST DAY DURING EXPOSURE OF FEMALE RATS IN THE 2-WEEK INHALATION STUDY OF CYCLOHEXENE

Group name	First day during exposure		
	0.5hour	1.5hour	3.5hour
9600ppm	Lacrymation Ataxic gait Tachypnea	Lacrymation Lateral Deep breathing	Death
4800ppm	Lacrymation Ataxic gait Tachypnea	Lacrymation Tachypnea	Lacrymation Tachypnea
2400ppm	Lacrymation	Lacrymation	Lacrymation
1200ppm ~ 0ppm	Non remarkable	Non remarkable	Non remarkable

TABLE 6 FOOD CONSUMPTION CHANGES OF MALE RATS IN THE 2-WEEK INHALATION STUDY OF CYCLOHEXENE

Week-Day on Study	0ppm		600ppm		1200ppm		2400ppm		4800ppm		9600ppm						
	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.			
		<5>		<5>		<5>		<5>		<5>		<5>		<5>			
1-7	13.8 (5)	5/5	14.0 (5)	101	5/5	14.1 (5)	102	5/5	13.4 (5)	97	5/5	10.7 (5)	78	5/5	- (-)	-	0/5
2-7	13.8 (5)	5/5	14.1 (5)	102	5/5	14.9 (5)	108	5/5	14.1 (5)	102	5/5	11.6 (4)	84	4/5	- (-)	-	0/5

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

TABLE 7 FOOD CONSUMPTION CHANGES OF FEMALE RATS IN THE 2-WEEK INHALATION STUDY OF CYCLOHEXENE

Week-Day on Study	0ppm		600ppm		1200ppm		2400ppm		4800ppm		9600ppm						
	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.			
		<5>		<5>		<5>		<5>		<5>		<5>		<5>			
1-7	11.5 (5)	5/5	11.7 (5)	102	5/5	11.2 (5)	97	5/5	10.5 (5)	91	5/5	9.7 (5)	84	5/5	- (-)	-	0/5
2-7	10.6 (5)	5/5	10.8 (5)	102	5/5	11.1 (5)	105	5/5	9.8 (5)	92	5/5	10.3 (5)	97	5/5	- (-)	-	0/5

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