アリルクロリドのラットを用いた
吸入による２週間毒性試験報告書

試験番号：０３３２

TABLES

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

<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, 62.5, 125, 250, 500 or 1000ppm
<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 *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 : 55±10%
Fluorescent light 12 h/d
15~17 room air changes /h
Chamber Environment
Barrier system
Temperature : 20~24℃
Humidity : 30~70%
12±1 air changes /h
<Type and Frequency of Observation>
Clinical Sign
Before the exposure : 1-1, 1-2, 1-4, 1-7, 2-3 and 2-7
After the exposure : 1-1, 1-2, 1-3 and 1-4
During the exposure : 1-1(1, 3 and 6 hours)
Observed 1 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 (Continued) EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE 2-WEEK INHALATION STUDY OF ALLYL CHLORIDE

<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, Reticulocyte,
Prothrombin time (PT),
Activated partial thromboplastin time (APTT),
White blood cell (WBC),Differential WBC.

<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,
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 two animals per sex per schedule sacrificed groups and three animals per sex per all dead groups before schedule sacrificed.
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 CLINICAL OBSERVATION DURING AND AFTER EXPOSURE OF MALE RATS IN THE 2-WEEK INHALATION STUDY OF ALLYL CHLORIDE

Group name	First day during exposure			First day
	1hour	3hour	6hour	after exposure
1000ppm	Non remarkable	Locomotor movement decrease Sound-response decreased Lacrymation Crouching position	Locomotor movement decrease Sound-response decreased Lacrymation Crouching position	Lacrymation Diarrhea Loose stool Soiled perianus
500ppm	Non remarkable	Locomotor movement decrease Sound-response decreased Crouching position	Locomotor movement decrease Sound-response decreased Crouching position	Lacrymational trace Loose stool Soiled perianus
250ppm ～ 0ppm	Non remarkable	Non remarkable	Non remarkable	Non remarkable

Group name	2th day	3th day	4th day
	after exposure	after exposure	after exposure
1000ppm	Piloerection Lacrymation Nose hemorrhagic dischage Diarrhea Loose stool Soiled perianus	Locomotor movement decrease Piloerection Lacrymation Nose hemorrhagic dischage Diarrhea Loose stool Soiled perianus	Locomotor movement decrease Hunchback position Piloerection Lacrymation Nose hemorrhagic dischage Diarrhea Loose stool Soiled perianus Tremor(1508) Irregular breathing(1508) Salivation(1508) Hypersensitivity(1508)
500ppm	Lacrymation	Non remarkable	Non remarkable
250ppm ～ 0ppm	Non remarkable	Non remarkable	Non remarkable

TABLE 3 CLINICAL OBSERVATION DURING AND AFTER EXPOSURE OF FEMALE RATS IN THE 2-WEEK INHALATION STUDY OF ALLYL CHLORIDE

Group name	First day during exposure			First day
	1hour	3hour	6hour	after exposure
1000ppm	Non remarkable	Locomotor movement decrease Sound-response decreased Lacrymation Crouching position	Locomotor movement decrease Sound-response decreased Lacrymation Crouching position	Lacrymation Diarrhea Loose stool Soiled perianus
500ppm	Non remarkable	Locomotor movement decrease Sound-response decreased Crouching position	Locomotor movement decrease Sound-response decreased Crouching position	Lacrymational trace Loose stool Soiled perianus
250ppm ～ 0ppm	Non remarkable	Non remarkable	Non remarkable	Non remarkable

Group name	2th day	3th day	4th day
	after exposure	after exposure	after exposure
1000ppm	Piloerection Lacrymation Nose hemorrhagic dischage Diarrhea Loose stool Soiled perianus	Locomotor movement decrease Prone Weakness Piloerection Lacrymation Nose hemorrhagic dischage Irregular breathing Deep breathing Diarrhea Loose stool Black-brown stool Soiled perianus Subnomal temp Dead(2502), Dead(2503), Dead(2507), Dead(2509), Dead(2510)	Locomotor movement decrease Hunchback position Piloerection Lacrymation Nose hemorrhagic dischage Diarrhea Loose stool Soiled perianus Dead(2501) Dead(2505)
500ppm	Lacrymation	Non remarkable	Non remarkable
250ppm ～ 0ppm	Non remarkable	Non remarkable	Non remarkable

TABLE 4 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF MALE RATS IN THE 2-WEEK INHALATION STUDY OF ALLYL CHLORIDE

Week-Day on Study	0ppm Av.Wt.	0ppm No.of Surviv. <10>	62.5ppm Av.Wt.	62.5ppm % of cont. <10>	62.5ppm No.of Surviv.	125.0ppm Av.Wt.	125.0ppm % of cont. <10>	125.0ppm No.of Surviv.	250.0ppm Av.Wt.	250.0ppm % of cont. <10>	250.0ppm No.of Surviv.	500.0ppm Av.Wt.	500.0ppm % of cont. <10>	500.0ppm No.of Surviv.	1000.0ppm Av.Wt.	1000.0ppm % of cont. <10>	1000.0ppm No.of Surviv.
0-0	116 (10)	10/10	116 (10)	100	10/10	116 (10)	100	10/10	116 (10)	100	10/10	116 (10)	100	10/10	116 (10)	100	10/10
1-2	122 (10)	10/10	122 (10)	100	10/10	122 (10)	100	10/10	121 (10)	99	10/10	118 (10)	97	10/10	103 (10)	84	10/10
1-4	127 (10)	10/10	127 (10)	100	10/10	128 (10)	101	10/10	128 (10)	101	10/10	120 (10)	94	10/10	92 (10)	72	10/10
1-7	136 (10)	10/10	136 (10)	100	10/10	139 (10)	102	10/10	138 (10)	101	10/10	132 (10)	97	10/10	94 (8)	69	8/10
2-3	146 (10)	10/10	145 (10)	99	10/10	151 (10)	103	10/10	148 (10)	101	10/10	139 (10)	95	10/10	84 (4)	58	4/10
2-7	158 (10)	10/10	158 (10)	100	10/10	168 (10)	106	10/10	163 (10)	103	10/10	145 (10)	92	10/10	- (-)	-	0/10

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

TABLE 5 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF FEMALE RATS IN THE 2-WEEK INHALATION STUDY OF ALLYL CHLORIDE

Week-Day on Study	0ppm Av.Wt.	0ppm No.of Surviv. <10>	62.5ppm Av.Wt.	62.5ppm % of cont. <10>	62.5ppm No.of Surviv.	125.0ppm Av.Wt.	125.0ppm % of cont. <10>	125.0ppm No.of Surviv.	250.0ppm Av.Wt.	250.0ppm % of cont. <10>	250.0ppm No.of Surviv.	500.0ppm Av.Wt.	500.0ppm % of cont. <10>	500.0ppm No.of Surviv.	1000.0ppm Av.Wt.	1000.0ppm % of cont. <10>	1000.0ppm No.of Surviv.
0-0	93 (10)	10/10	93 (10)	100	10/10	93 (10)	100	10/10	93 (10)	100	10/10	93 (10)	100	10/10	93 (10)	100	10/10
1-2	97 (10)	10/10	96 (10)	99	10/10	95 (10)	98	10/10	94 (10)	97	10/10	93 (10)	96	10/10	85 (10)	88	10/10
1-4	100 (10)	10/10	100 (10)	100	10/10	100 (10)	100	10/10	99 (10)	99	10/10	95 (10)	95	10/10	76 (2)	76	0/10
1-7	105 (10)	10/10	106 (10)	101	10/10	107 (10)	102	10/10	105 (10)	100	10/10	102 (10)	97	10/10	- (-)	-	0/10
2-3	109 (10)	10/10	111 (10)	102	10/10	112 (10)	103	10/10	109 (10)	100	10/10	107 (10)	98	10/10	- (-)	-	0/10
2-7	114 (10)	10/10	117 (10)	103	10/10	118 (10)	104	10/10	116 (10)	102	10/10	111 (10)	97	10/10	- (-)	-	0/10

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

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

Week-Day on Study	0ppm		62.5ppm			125.0ppm			250.0ppm			500.0ppm			1000.0ppm		
	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	12.7 (10)	10/10	15.0 (10)	118	10/10	15.0 (10)	118	10/10	15.9 (10)	125	10/10	14.8 (10)	117	10/10	5.0 (8)	39	8/10
2-7	14.1 (10)	10/10	14.7 (10)	104	10/10	15.7 (10)	111	10/10	16.3 (10)	116	10/10	15.6 (10)	111	10/10	- (-)	-	0/10

< > : 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 ALLYL CHLORIDE

Week-Day on Study	0ppm		62.5ppm			125.0ppm			250.0ppm			500.0ppm			1000.0ppm		
	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	12.9 (10)	10/10	11.6 (10)	90	10/10	12.0 (10)	93	10/10	11.8 (10)	91	10/10	11.8 (10)	91	10/10	- (-)	-	0/10
2-7	10.5 (10)	10/10	11.5 (10)	110	10/10	11.6 (10)	110	10/10	11.3 (10)	108	10/10	12.3 (10)	117	10/10	- (-)	-	0/10

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