アリルクロリドのマウスを用いた 吸入による 2 週間毒性試験報告書

試験番号:0333

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INHALATION STUDY OF ALLYL CHLORIDE

INHALATION STUDY OF ALLYL CHLORIDE

TABLE 7

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

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<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
               Crj:BDF1 mouse
     Animal Source
               Charles River Japan, Inc.
     Duration Held Before Study
               2 wk
     Age When Placed on Study
               6 wk
     Age When Killed
               8 \text{ 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 \gamma-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 .
                                   : 21±2°C
               Temperature
               Humidity
                                   : 55±10%
               Fluorescent light 12 h/d
               15~17 room air changes /h
     Chamber Environment
               Barrier system
               Temperature
                                   : 20~24°C
                                   : 30~70%
               Humidity
               12±1 air changes /h
<Type and Frequency of Observation>
     Clinical Sign
               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
                         During the exposure: 1-1(3 and 5.5 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)
```

<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.

<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,

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, gall bladder, 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 MICE IN THE 2-WEEK INHALATION STUDY OF ALLYL CHLORIDE

		First day during exposure									
Group name.	3hour	5.5hour	after exposure	after exposure							
		Locomotor movement decrease	Diarrhea								
1000	Non remarkable	Diarrhea	Loose stool	Almandar Dand							
1000ppm	Non remarkable	Loose stool	Soiled perianus	Already Dead							
		Crouching position									
		Diarrhea	Diarrhea	Locomotion movement decrease							
500ppm	Non remarkable	Loose stool	Loose stool	Piloerection							
			Soiled perianus	Subnomal temp							
250	Non remarkable	Non remarkable	Diarrhea	Non remarkable							
250ppm	Non remarkable	Non remarkable	Loose stool	Non remarkable							
125 ppm \sim 0ppm	Non remarkable	Non remarkable	Non remarkable	Non remarkable							

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

		2th day						
Group name.	3hour	5.5hour	after exposure	after exposure				
		Locomotor movement decrease	Diarrhea	Locomotor movement decrease				
		Diarrhea	Loose stool	Piloerection				
1000	Non remarkable	Loose stool	Soiled perianus	Subnomal temp				
1000ppm	non remarkable	Crouching position		Hematuria(2505)				
				Dead(2507)				
				Dead(2509)				
		Diarrhea	Diarrhea					
500ppm	Non remarkable	Loose stool	Loose stool	Non remarkable				
			Soiled perianus					
050	Non remarkable	Non remarkable	Diarrhea	Non managhabla				
250ppm	non remarkable	Non remarkable	Loose stool	Non remarkable				
125ppm ∼	Non remarkable	Non remarkable	Non remarkable	Non remarkable				
0ppm	14011 1emai kabie	140H Temarkable	Tron remarkable	Non remarkable				

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

		0ppm		62.5p	pm		125.0	opm		250.0ppm			500.0p	pm	1000.0ppm			
Week-Day on Study	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	22.6 (10)	10/10	22.6 (10)	100	10/10	22.6 (10)	100	10/10	22.6 (10)	100	10/10	22.5 (10)	100	10/10	22.6 (10)	100	10/10	
1-2	23.2 (10)	10/10	22.7 (10)	98	10/10	22.9 (10)	99	10/10	22.3 (10)	96	10/10	20.2 (8)	87	8/10	- (-)	_	0/10	
1-4	23.9 (10)	10/10	23.1 (10)	97	10/10	23.2 (10)	97	10/10	22.9 (10)	96	10/10	19.2 (3)	80	3/10	- (-)		0/10	
1-7	24.5 (10)	10/10	23.5 (10)	96	10/10	23.1 (10)	94	10/10	23.9 (10)	98	10/10	17.7 (2)	72	2/10	- (-)	_	0/10	
2-3	24.7 (10)	10/10	23.5 (10)	95	10/10	23.3 (10)	94	10/10	25.3 (10)	102	10/10	- (-)	_	0/10	- (-)		0/10	
2-7	25.2 (10)	10/10	23.9 (10)	95	10/10	23.3 (10)	92	10/10	25.7 (10)	102	10/10	- (-)	_	0/10	- (-)	_	0/10	

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

		0ppm	62.5ppm			125.0ppm				250.0ppm			500.0ppm			1000.0ppm			
Week-Day on Study	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.		% of cont. <10>	No.of Surviv.		
0-0	18.6 (10)	10/10	18.6 (10)	100	10/10	18.6 (10)	100	10/10	18.5 (10)	99	10/10	18.5 (10)	99	10/10	18.6 (10)	100	10/10		
1-2	18.9 (10)	10/10	18.1 (10)	96	10/10	18.6 (10)	98	10/10	18.2 (10)	96	10/10	17.6 (10)	93	10/10	16.8 (6)	89	4/10		
1-4	19.5 (10)	10/10	18.9 (10)	97	10/10	19.1 (10)	98	10/10	19.2 (10)	98	10/10	17.4 (10)	89	10/10	15.1 (1)	77	1/10		
1-7	19.8 (10)	10/10	19.6 (10)	99	10/10	19.4 (10)	98	10/10	20.2 (10)	102	10/10	17.6 (10)	89	10/10	- (-)	-	0/10		
2-3	20.1 (10)	10/10	19.9 (10)	99	10/10	19.6 (10)	98	10/10	21.5 (10)	107	10/10	- (-)	. –	0/10	- (-)	_	0/10		
2-7	20.2 (10)	10/10	19.9 (10)	99	10/10	20.4 (10)	101	10/10	21.0 (10)	104	10/10	- (-)	_	0/10	- (-)	-	0/10		

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

	Оррг			62.5ppm			125.0ppm			250.0ppm			500.0	opm	1000.0ppm			
Week-Day on Study	Av.FC.	No.of Surviv. <10>	Av.FC.		No.of Surviv.	Av.FC.		No.of Surviv.	Av.FC.		No.of Surviv.	Av.FC.		No.of Surviv.	Av.FC.		No.of Surviv.	
1-7 2-7	4.7 (5) 4.2 (10)	10/10 10/10	4.3 (10) 3.9 (10)			4.3 (10) 4.2 (10)		10/10 10/10	4.0 (10) 4.8 (10)		10/10 10/10	1.5 (2)		2/10 0/10	- (-) - (-)	- -	0/10 0/10	
	< >	· : No.of e	ffective	animal	s, () : N	lo.of mea	sured a	animals	Av.FC	. : g			·····	***				

TABLE 7 FOOD CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-WEEK INHALATION STUDY OF ALLYL CHLORIDE

		0ppm	62.5ppm			125.0ppm			250.0ppm				500.0	opm	1000.0ppm			
Week-Day on Study	Av.FC.	No.of Surviv. <10>	Av.FC.		No.of Surviv.	Av.FC.		No.of Surviv.	Av.FC.		No.of Surviv.	Av.FC.	% of cont. <10>	No.of Surviv.	Av.FC.		No.of Surviv.	
1-7	3.8 (10)	10/10	3.8 (10)	100	10/10	3.8 (10)	100	10/10	4.0 (10)	105	10/10	3.0 (10)	79	10/10	- (-)	_	0/10	
2-7	3.6 (10)	10/10	3.4 (10)	94	10/10	3.6 (10)	100	10/10	4.2 (10)	117	10/10	- (-)	-	0/10	- (-)	_	0/10	