

キノリンのマウスを用いた経口投与による
2週間毒性試験(混水試験)報告書

試験番号：0283

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TABLE 1 EXPERIMENTAL DESIGN AND MATERIALS AND METHODS
IN THE 2-WEEK DRINKING STUDY OF QUINOLINE

2-week study	
<Method of Administration>	Drinking Water
<Number of Groups>	Male 6, Female 6
<Size of Groups>	10 males and 10 females of each group
<Animals>	Strain and Species Crj:BDF ₁ mouse
	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> 0, 77, 192, 480, 1200 or 3000 ppm <Female> 0, 77, 192, 480, 1200 or 3000 ppm
<Duration of Dosing>	7d/wk for 2wk
<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 in duration of quarantine Glass bottle in duration of acclimation and administration Available <i>ad libitum</i>
	Animal per Cage Single (stainless steel wire)
	Animal Room Environment Barrier system Temperature : $24 \pm 2^\circ\text{C}$ Humidity : $55 \pm 10\%$ Fluorescent light 12h/d 15~17 room air changes /h
<Type and Frequency of Observation>	Clinical Sign Observed 1 per d
	Body Weight Weighed 0-0, 1-1, 1-3, 1-7, 2-3, and 2-7 (wk-d)
	Food Consumption Weighed 1-7, and 2-7 (wk-d)
	Water Consumption Weighed 1-3, 2-7, 2-3, and 2-7 (wk-d)

TABLE 1 EXPERIMENTAL DESIGN AND MATERIALS AND METHODS
(Continued) IN THE 2-WEEK DRINKING STUDY OF QUINOLINE

2-week study	
<Hematology>	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>	Total protein, Albumin, A/G ratio, Total bilirubin, Glucose, Total cholesterol Phospholipid, Glutamic oxaloacetic transaminase (GOT), Glutamic pyruvic transaminase (GPT), Lactate dehydrogenase (LDH), Creatine phosphokinase (CPK), Urea nitrogen, Sodium, Potassium, Chloride, Calcium, Inorganic phosphorus.
<Urinalysis>	None
<Necropsy>	Necropsy performed on all animals.
<Organ Weight>	Organ weight measurement performed on at least five animals per sex per group at sacrifice The following organs were weighed; thymus, adrenal, testis, ovary, heart, lung, kidney, spleen, liver, and brain.
<Histopathologic Examination>	Histopathologic examination performed on at least two animals per sex per group. 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, other organs/tissues with gross lesions.

TABLE 2 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF MALE MICE IN THE 2-WEEK DRINKING WATER STUDY OF QUINOLINE

Week-Day on Study	Control		77ppm			192ppm			480ppm			1200ppm			3000ppm		
	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	24.3(10)	10/10	24.3(10)	100	10/10	24.3(10)	100	10/10	24.3(10)	100	10/10	24.3(10)	100	10/10	24.3(10)	100	10/10
1-1	23.5(10)	10/10	23.3(10)	99	10/10	23.4(10)	100	10/10	23.3(10)	99	10/10	21.8(10)	93	10/10	21.2(10)	90	10/10
1-3	24.3(10)	10/10	24.2(10)	100	10/10	24.3(10)	100	10/10	24.0(10)	99	10/10	22.6(10)	93	10/10	19.3(10)	79	10/10
1-7	24.5(10)	10/10	25.2(10)	103	10/10	24.2(10)	99	10/10	24.7(10)	101	10/10	23.7(10)	97	10/10	16.2(10)	66	10/10
2-3	25.3(10)	10/10	25.2(10)	100	10/10	25.2(10)	100	10/10	24.9(10)	98	10/10	22.7(10)	90	10/10	15.2(8)	60	8/10
2-7	26.1(10)	10/10	26.0(10)	100	10/10	26.2(10)	100	10/10	25.8(10)	99	10/10	23.6(10)	90	10/10	13.3(2)	51	4/10
< >:No. of effective animals, ():No. of measurement animals Av.Wt.:g																	

TABLE 3 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF FEMALE MICE IN THE 2-WEEK DRINKING WATER STUDY OF QUINOLINE

Week-Day on Study	Control		77ppm			192ppm			480ppm			1200ppm			3000ppm		
	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	20.0(10)	10/10	20.0(10)	100	10/10	20.0(10)	100	10/10	20.0(10)	100	10/10	20.0(10)	100	10/10	20.0(10)	100	10/10
1-1	18.7(10)	10/10	18.8(10)	101	10/10	18.6(10)	99	10/10	18.6(10)	99	10/10	17.4(10)	93	10/10	16.7(10)	89	10/10
1-3	19.4(10)	10/10	19.3(10)	99	10/10	19.3(10)	99	10/10	19.0(10)	98	10/10	17.1(10)	88	10/10	14.9(10)	77	10/10
1-7	19.9(10)	10/10	20.0(10)	101	10/10	20.0(10)	101	10/10	20.0(10)	101	10/10	18.8(10)	94	10/10	12.3(10)	62	10/10
2-3	19.8(10)	10/10	20.0(10)	101	10/10	19.9(10)	101	10/10	20.0(10)	101	10/10	19.0(10)	96	10/10	11.1(8)	56	8/10
2-7	21.0(10)	10/10	21.4(10)	102	10/10	21.0(10)	100	10/10	21.0(10)	100	10/10	20.2(10)	96	10/10	- (-)	-	0/10
< >:No. of effective animals, ():No. of measurement animals Av.Wt.:g																	

TABLE 4 WATER CONSUMPTION CHANGES OF MALE MICE IN THE 2-WEEK DRINKING WATER STUDY OF QUINOLINE

Week-Day on Study	Control		77ppm			192ppm			480ppm			1200ppm			3000ppm		
	Av.Wc. <10>	No. of Surviv. 10/10	Av.Wc. <10>	% of cont. <10>	No. of Surviv. 10/10	Av.Wc. <10>	% of cont. <10>	No. of Surviv. 10/10	Av.Wc. <10>	% of cont. <10>	No. of Surviv. 10/10	Av.Wc. <10>	% of cont. <10>	No. of Surviv. 10/10	Av.Wc. <10>	% of cont. <10>	No. of Surviv. 10/10
1-3	4.5(10)	10/10	4.1(10)	91	10/10	4.1(10)	91	10/10	3.5(10)	78	10/10	1.8(10)	40	10/10	0.6(10)	13	10/10
1-7	3.6(10)	10/10	3.9(10)	108	10/10	4.0(10)	111	10/10	3.4(10)	94	10/10	1.9(10)	53	10/10	0.4(10)	11	10/10
2-3	4.9(10)	10/10	4.3(10)	88	10/10	4.5(10)	92	10/10	3.6(10)	73	10/10	1.3(10)	27	10/10	0.3(9)	6	8/10
2-7	4.3(10)	10/10	4.3(10)	100	10/10	4.2(10)	98	10/10	3.4(10)	79	10/10	1.4(10)	33	10/10	0.3(4)	7	4/10
< >:No. of effective animals, ():No. of measurement animals									Av.Wc.:g								

TABLE 5 WATER CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-WEEK DRINKING WATER STUDY OF QUINOLINE

Week-Day on Study	Control		77ppm			192ppm			480ppm			1200ppm			3000ppm		
	Av.Wc. <10>	No. of Surviv. 10/10	Av.Wc. <10>	% of cont. <10>	No. of Surviv. 10/10	Av.Wc. <10>	% of cont. <10>	No. of Surviv. 10/10	Av.Wc. <10>	% of cont. <10>	No. of Surviv. 10/10	Av.Wc. <10>	% of cont. <10>	No. of Surviv. 10/10	Av.Wc. <10>	% of cont. <10>	No. of Surviv. 10/10
1-3	4.0(10)	10/10	4.2(10)	105	10/10	3.9(10)	98	10/10	3.3(10)	83	10/10	1.3(10)	33	10/10	0.5(10)	13	10/10
1-7	3.7(10)	10/10	4.2(10)	114	10/10	4.2(10)	114	10/10	3.5(10)	95	10/10	1.8(10)	49	10/10	0.4(10)	11	10/10
2-3	4.3(10)	10/10	4.7(10)	109	10/10	4.4(10)	102	10/10	3.4(10)	79	10/10	1.5(10)	35	10/10	0.4(9)	9	8/10
2-7	4.1(10)	10/10	4.3(10)	105	10/10	4.2(10)	102	10/10	3.3(10)	80	10/10	1.7(9)	41	10/10	- (-)	-	0/10
< >:No. of effective animals, ():No. of measurement animals									Av.Wc.:g								

TABLE 6

FOOD CONSUMPTION CHANGES OF MALE MICE IN THE 2-WEEK DRINKING WATER STUDY OF QUINOLINE

Week on Study	Control		77ppm			192ppm			480ppm			1200ppm			3000ppm		
	Av.Fc. <10>	No. of Surviv. 10/10	Av.Fc. <10>	% of cont. 100	No. of Surviv. 10/10	Av.Fc. <10>	% of cont. 97	No. of Surviv. 10/10	Av.Fc. <10>	% of cont. 94	No. of Surviv. 10/10	Av.Fc. <10>	% of cont. 89	No. of Surviv. 10/10	Av.Fc. <10>	% of cont. 47	No. of Surviv. 10/10
1	3.6(10)	10/10	3.6(10)	100	10/10	3.5(10)	97	10/10	3.4(10)	94	10/10	3.2(10)	89	10/10	1.7(10)	47	10/10
2	3.7(10)	10/10	3.6(10)	97	10/10	3.7(10)	100	10/10	3.5(10)	95	10/10	3.1(10)	84	10/10	1.3(4)	35	4/10
< >:No. of effective animals, ():No. of measurement animals Av.Fc.:g																	

TABLE 7

FOOD CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-WEEK DRINKING WATER STUDY OF QUINOLINE

Week on Study	Control		77ppm			192ppm			480ppm			1200ppm			3000ppm		
	Av.Fc. <10>	No. of Surviv. 10/10	Av.Fc. <10>	% of cont. 103	No. of Surviv. 10/10	Av.Fc. <10>	% of cont. 103	No. of Surviv. 10/10	Av.Fc. <10>	% of cont. 103	No. of Surviv. 10/10	Av.Fc. <10>	% of cont. 83	No. of Surviv. 10/10	Av.Fc. <10>	% of cont. 43	No. of Surviv. 10/10
1	3.0(10)	10/10	3.1(10)	103	10/10	3.1(10)	103	10/10	3.1(10)	103	10/10	2.5(10)	83	10/10	1.3(10)	43	10/10
2	3.2(10)	10/10	3.2(10)	100	10/10	3.1(10)	97	10/10	3.1(10)	97	10/10	2.8(10)	88	10/10	- (-)	-	0/10
< >:No. of effective animals, ():No. of measurement animals Av.Fc.:g																	