キノリンのラット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：０２８２

APPENDIX

APPENDIXES

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 1-1	1-3	1-7	2-3	2-7
		1	1	1	1	1
DEATH	Control	0	0	0	0	0
	77 ppm	0	0	0	0	0
	192 ppm	0	0	0	0	0
	480 ppm	0	0	0	0	0
	1200 ppm	0	0	0	0	0
	3000 ppm	0	0	0	0	9
LOCOMOTOR MOVEMENT DECR	Control	0	0	0	0	0
	77 ppm	0	0	0	0	0
	192 ppm	0	0	0	0	0
	480 ppm	0	0	0	0	0
	1200 ppm	0	0	0	0	0
	3000 ppm	0	0	0	1	1
HUNCHBACK POSITION	Control	0	0	0	0	0
	77 ppm	0	0	0	0	0
	192 ppm	0	0	0	0	0
	480 ppm	0	0	0	0	0
	1200 ppm	0	0	0	1	1
	3000 ppm	0	0	0	10	1
PILOERECTION	Control	0	0	0	0	0
	77 ppm	0	0	0	0	0
	192 ppm	0	0	0	0	0
	480 ppm	0	0	0	0	0
	1200 ppm	0	0	0	2	2
	3000 ppm	0	0	0	10	1
IRREGULAR BREATHING	Control	0	0	0	0	0
	77 ppm	0	0	0	0	0
	192 ppm	0	0	0	0	0
	480 ppm	0	0	0	0	0
	1200 ppm	0	0	0	0	0
	3000 ppm	0	0	0	0	1
ABNORMAL RESPIRATION	Control	0	0	0	0	0
	77 ppm	0	0	0	0	0
	192 ppm	0	0	0	0	0
	480 ppm	0	0	0	0	0
	1200 ppm	0	0	0	0	0
	3000 ppm	0	0	0	0	1

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 1-1 1	1-3 1	1-7 1	2-3 1	2-7 1
SMALL STOOL	Control	0	0	0	0	0
	77 ppm	0	0	0	0	0
	192 ppm	0	0	0	0	0
	480 ppm	0	0	0	0	0
	1200 ppm	0	0	0	2	2
	3000 ppm	0	0	10	10	1
OLIGO-STOOL	Control	0	0	0	0	0
	77 ppm	0	0	0	0	0
	192 ppm	0	0	0	0	0
	480 ppm	0	0	0	0	0
	1200 ppm	0	0	0	0	0
	3000 ppm	0	0	0	10	1

APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

Clinical sign	Group Name	Administration Week-day 1-1	1-3	1-7	2-3	2-7
		1	1	1	1	1
DEATH	Control	0	0	0	0	0
	77 ppm	0	0	0	0	0
	192 ppm	0	0	0	0	0
	480 ppm	0	0	0	0	0
	1200 ppm	0	0	1	3	3
	3000 ppm	0	0	1	10	-
HUNCHBACK POSITION	Control	0	0	0	0	0
	77 ppm	0	0	0	0	0
	192 ppm	0	0	0	0	0
	480 ppm	0	0	0	0	0
	1200 ppm	0	0	8	6	6
	3000 ppm	0	0	9	0	-
PILOERECTION	Control	0	0	0	0	0
	77 ppm	0	0	0	0	0
	192 ppm	0	0	0	0	0
	480 ppm	0	0	0	0	0
	1200 ppm	0	0	0	6	6
	3000 ppm	0	0	0	0	-
IRREGULAR BREATHING	Control	0	0	0	0	0
	77 ppm	0	0	0	0	0
	192 ppm	0	0	0	0	0
	480 ppm	0	0	0	0	0
	1200 ppm	0	0	0	0	0
	3000 ppm	0	0	1	0	-
ABNORMAL RESPIRATION	Control	0	0	0	0	0
	77 ppm	0	0	0	0	0
	192 ppm	0	0	0	0	0
	480 ppm	0	0	0	0	0
	1200 ppm	0	0	0	0	0
	3000 ppm	0	0	1	0	-
SMALL STOOL	Control	0	0	0	0	0
	77 ppm	0	0	0	0	0
	192 ppm	0	0	0	0	0
	480 ppm	0	0	0	0	0
	1200 ppm	0	0	9	7	7
	3000 ppm	0	0	9	0	-

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

Clinical sign	Group Name	Administration Week-day 1-1	1-3	1-7	2-3	2-7
		1	1	1	1	1
OLIGO-STOOL	Control	0	0	0	0	0
	77 ppm	0	0	0	0	0
	192 ppm	0	0	0	0	0
	480 ppm	0	0	0	0	0
	1200 ppm	0	0	0	0	0
	3000 ppm	0	0	2	0	-

APPENDIX B 1

BODY WEIGHT CHANGES :SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-1	1-3	1-7	2-3	2-7
Control	124± 4	125± 6	132± 6	150± 9	162± 10	179± 12
77 ppm	124± 4	125± 4	132± 5	149± 6	161± 8	178± 11
192 ppm	124± 4	124± 4	132± 4	148± 5	161± 6	178± 8
480 ppm	124± 4	120± 4*	126± 5*	140± 6	152± 7	167± 10
1200 ppm	124± 4	113± 4**	106± 4**	102± 11**	107± 17**	122± 20**
3000 ppm	124± 4	111± 4**	98± 3**	79± 3**	68± 3**	63± 0 ?

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX B 2

BODY WEIGHT CHANGES : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0		1-1		1-3		1-7		2-3		2-7	
Control	100±	3	101±	3	105±	3	115±	4	122±	4	132±	5
77 ppm	100±	2	100±	2	105±	3	114±	3	121±	3	131±	4
192 ppm	100±	2	98±	3	103±	3	113±	4	120±	4	130±	5
480 ppm	100±	2	95±	3**	96±	3**	105±	4**	113±	4**	122±	4**
1200 ppm	100±	3	90±	2**	80±	2**	66±	5**	70±	6**	78±	7**
3000 ppm	100±	2	88±	2**	78±	2**	60±	3**	-		-	

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX C 1

WATER CONSUMPTION CHANGES : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-3(3)	1-7(4)	2-3(3)	2-7(4)
Control	17.5± 1.2	17.4± 1.4	17.9± 1.4	17.8± 1.4
77 ppm	16.5± 0.8	16.4± 1.0	17.2± 1.4	17.0± 1.5
192 ppm	15.8± 1.4	15.7± 1.3	15.9± 0.8	15.8± 1.1**
480 ppm	11.6± 0.9**	12.4± 0.6**	13.0± 0.8**	12.6± 1.1**
1200 ppm	4.1± 1.0**	4.6± 2.2**	7.1± 2.9**	8.9± 1.8**
3000 ppm	1.4± 0.2**	1.1± 0.2**	1.3± 0.4**	1.4± 0.0 ?

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX C 2

WATER CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-3(3)	1-7(4)	2-3(3)	2-7(4)
Control	16.1± 0.9	15.7± 1.2	15.9± 1.3	16.3± 1.3
77 ppm	14.8± 0.9	14.8± 1.1	15.2± 1.5	14.9± 1.9
192 ppm	13.6± 1.3	13.1± 1.0	13.2± 1.6	13.3± 1.5
480 ppm	7.8± 1.2**	9.7± 0.6**	9.7± 0.7**	9.7± 0.3**
1200 ppm	2.3± 0.5**	2.1± 0.8**	4.6± 2.1**	6.2± 0.8**
3000 ppm	1.4± 0.3**	1.0± 0.3**	1.0± 0.0 ?	-

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX D 1

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(7)	2-7(7)
Control	13.7± 1.2	14.6± 1.2
77 ppm	13.2± 0.6	14.4± 1.1
192 ppm	12.9± 0.6	14.2± 0.7
480 ppm	12.0± 0.6*	13.4± 1.3
1200 ppm	6.2± 1.3**	9.2± 2.1**
3000 ppm	3.8± 0.5**	3.1± 0.0 ?

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX D 2

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration 1-7(7)	week-day(effective) 2-7(7)
Control	10.9± 0.7	11.0± 0.7
77 ppm	10.8± 0.4	11.1± 0.6
192 ppm	10.5± 0.8	11.4± 0.8
480 ppm	8.9± 0.6**	10.5± 0.5
1200 ppm	3.3± 0.6**	6.2± 1.3**
3000 ppm	2.8± 0.9**	-

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX E 1

CHEMICAL INTAKE CHANGES : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
UNIT : g/kg/day
REPORT TYPE : A1 2
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2
Control	0.000± 0.000	0.000± 0.000
77 ppm	0.009± 0.001	0.007± 0.000
192 ppm	0.020± 0.002	0.017± 0.001
480 ppm	0.042± 0.001	0.036± 0.002
1200 ppm	0.052± 0.021	0.087± 0.009
3000 ppm	0.040± 0.006	0.067± 0.000

APPENDIX E 2

CHEMICAL INTAKE CHANGES : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
UNIT : g/kg/day
REPORT TYPE : A1 2
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2
Control	0.000± 0.000	0.000± 0.000
77 ppm	0.010± 0.001	0.009± 0.001
192 ppm	0.022± 0.002	0.020± 0.002
480 ppm	0.044± 0.002	0.038± 0.001
1200 ppm	0.039± 0.012	0.095± 0.007
3000 ppm	0.050± 0.017	-

APPENDIX F 1

HEMATOLOGY : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV f ℓ	MCH p g	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	5	7.93± 0.18	14.8± 0.4	43.6± 1.4	55.0± 0.5	18.7± 0.2	34.0± 0.4	819± 59
77 ppm	5	7.64± 0.21	14.7± 0.2	42.0± 1.5	54.9± 0.8	19.3± 0.7	35.1± 1.6	817± 120
192 ppm	5	7.80± 0.39	14.6± 0.7	42.8± 2.0	54.9± 0.2	18.7± 0.1	34.1± 0.3	891± 42
480 ppm	5	7.82± 0.22	14.4± 0.3	42.8± 1.3	54.8± 0.5	18.5± 0.2	33.7± 0.5	902± 73
1200 ppm	5	8.01± 0.40	14.9± 0.7	43.5± 2.5	54.3± 0.9	18.6± 0.2	34.2± 0.4	832± 97
3000 ppm	0	-	-	-	-	-	-	-

Significant difference ; * : $P \leqq 0.05$ ** : $P \leqq 0.01$ Test of Dunnett

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	RETICULOCYTE ‰		PROTHROMBIN TIME sec		APTT sec	
Control	5	46±	5	12.8±	0.5	19.6±	4.6
77 ppm	5	53±	7	12.7±	0.1	17.5±	0.7
192 ppm	5	48±	17	12.5±	0.4	16.6±	3.8
480 ppm	5	51±	10	12.7±	0.3	17.2±	2.4
1200 ppm	5	28±	10*	13.5±	0.7	23.6±	13.0
3000 ppm	0	-		-		-	

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHERS
Control	5	4.21± 0.97	0± 0	20± 4	1± 1	0± 0	4± 2	76± 5	0± 0
77 ppm	5	4.92± 1.34	0± 0	19± 3	0± 0	0± 0	4± 2	76± 4	0± 0
192 ppm	5	4.13± 1.42	0± 0	15± 2	0± 0	0± 0	3± 1	82± 3	0± 0
480 ppm	5	3.66± 0.85	0± 0	17± 5	1± 1	0± 0	4± 2	78± 2	0± 0
1200 ppm	5	3.16± 0.42	1± 1	26± 11	1± 1	0± 0	3± 1	69± 10	0± 0
3000 ppm	0	-	-	-	-	-	-	-	-

Significant difference ; * : $P \leqq 0.05$ ** : $P \leqq 0.01$ Test of Dunnett

APPENDIX F 2

HEMATOLOGY : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV f ℓ	MCH p g	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	5	8.20± 0.23	15.5± 0.4	44.5± 1.4	54.3± 0.5	18.9± 0.3	34.8± 0.4	831± 78
77 ppm	5	8.02± 0.15	15.1± 0.3	43.6± 0.7	54.3± 0.6	18.9± 0.0	34.7± 0.4	828± 57
192 ppm	5	8.12± 0.22	15.3± 0.5	44.2± 1.1	54.4± 0.1	18.8± 0.2	34.5± 0.4	890± 39
480 ppm	5	8.10± 0.22	15.2± 0.3	44.0± 0.9	54.3± 1.1	18.8± 0.4	34.7± 0.3	800± 116
1200 ppm	5	8.95± 0.54**	17.0± 1.1	48.7± 3.1	54.4± 0.4	18.9± 0.2	34.8± 0.3	635± 109**
3000 ppm	0	-	-	-	-	-	-	-

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	RETICULOCYTE ‰		PROTHROMBIN TIME sec		APTT sec	
Control	5	41±	5	13.0±	0.4	19.8±	5.4
77 ppm	5	33±	6	12.9±	0.1	18.2±	3.4
192 ppm	5	34±	6	13.2±	0.7	23.9±	16.3
480 ppm	5	38±	8	13.0±	0.3	14.9±	2.5
1200 ppm	5	18±	6**	14.1±	1.1	18.6±	8.4
3000 ppm	0	-		-		-	

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHERS
Control	5	4.05± 0.66	0± 0	19± 6	1± 1	0± 0	3± 1	77± 6	0± 0
77 ppm	5	3.92± 0.51	0± 0	19± 7	1± 0	0± 0	3± 2	77± 8	0± 0
192 ppm	5	4.65± 0.82	0± 0	18± 4	1± 1	0± 0	3± 1	77± 3	0± 0
480 ppm	5	4.24± 0.40	0± 0	17± 5	2± 1	0± 0	3± 1	78± 5	0± 0
1200 ppm	5	3.61± 0.14	1± 1	31± 13	1± 1	0± 0	5± 2	62± 12*	0± 0
3000 ppm	0	-	-	-	-	-	-	-	-

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX G 1

BIOCHEMISTRY : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	TOTAL PROTEIN g/dℓ		ALBUMIN g/dℓ		A/G RATIO		T-BILIRUBIN mg/dℓ		GLUCOSE mg/dℓ		T-CHOLESTEROL mg/dℓ		PHOSPHOLIPID mg/dℓ	
Control	5	5.7±	0.1	3.4±	0.0	1.5±	0.0	0.15±	0.00	196±	7	59±	3	118±	4
77 ppm	5	5.6±	0.1	3.4±	0.1	1.5±	0.1	0.16±	0.01	191±	6	67±	4	132±	7
192 ppm	5	5.7±	0.1	3.4±	0.1	1.5±	0.1	0.16±	0.02	188±	5	73±	3	149±	6**
480 ppm	5	5.6±	0.1	3.3±	0.0	1.5±	0.1	0.16±	0.01	180±	4*	80±	3**	157±	6**
1200 ppm	5	5.5±	0.1	3.3±	0.1*	1.5±	0.0	0.17±	0.01	164±	15**	116±	12**	225±	17**
3000 ppm	0	-		-		-		-		-		-		-	

Significant defference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	GOT IU/ℓ		GPT IU/ℓ		LDH IU/ℓ		G-GTP IU/ℓ		CPK IU/ℓ		UREA NITROGEN mg/dℓ		CREATININE mg/dℓ	
Control	5	63±	3	33±	2	191±	57	2±	1	217±	71	15.6±	1.6	0.5±	0.0
77 ppm	5	62±	3	34±	2	177±	52	2±	0	184±	36	16.2±	2.4	0.4±	0.1
192 ppm	5	59±	3	33±	2	160±	35	3±	1	179±	29	18.1±	2.6	0.4±	0.0
480 ppm	5	59±	3	30±	2	188±	22	2±	3	188±	22	17.5±	1.5	0.4±	0.0
1200 ppm	5	66±	7	33±	6	270±	84	2±	1	213±	56	18.9±	2.2	0.4±	0.0
3000 ppm	0	-		-		-		-		-		-		-	

Significant defference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	SODIUM mEq／ℓ		POTASSIUM mEq／ℓ		CHLORIDE mEq／ℓ		CALCIUM mg／dℓ		INORGANIC PHOSPHORUS mg／dℓ	
Control	5	142±	1	3.8±	0.4	105±	1	11.0±	0.2	8.1±	1.1
77 ppm	5	141±	1	4.1±	0.3	105±	1	11.0±	0.2	7.9±	1.1
192 ppm	5	140±	1	4.3±	0.1	104±	1	11.1±	0.1	7.9±	1.1
480 ppm	5	140±	1	4.1±	0.3	105±	1	11.2±	0.1	7.1±	1.0
1200 ppm	5	141±	2	4.3±	0.3	106±	2	11.4±	0.3**	6.8±	0.8
3000 ppm	0	-		-		-		-		-	

Significant defference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX G 2

BIOCHEMISTRY : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	TOTAL PROTEIN g/dℓ		ALBUMIN g/dℓ		A/G RATIO		T-BILIRUBIN mg/dℓ		GLUCOSE mg/dℓ		T-CHOLESTEROL mg/dℓ		PHOSPHOLIPID mg/dℓ	
Control	5	5.7±	0.1	3.4±	0.1	1.5±	0.1	0.16±	0.01	187±	7	77±	2	135±	6
77 ppm	5	5.5±	0.1	3.4±	0.1	1.6±	0.1	0.15±	0.01	189±	10	79±	4	140±	7
192 ppm	5	5.5±	0.1	3.3±	0.0	1.6±	0.1	0.17±	0.01	181±	4	82±	4	155±	8
480 ppm	5	5.3±	0.2**	3.2±	0.1**	1.5±	0.0	0.17±	0.01	174±	6	93±	6*	173±	11**
1200 ppm	5	5.2±	0.2**	3.2±	0.1**	1.6±	0.1	0.20±	0.02**	144±	14**	110±	22**	202±	39**
3000 ppm	0	-		-		-		-		-		-		-	

Significant defference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	GOT IU/ℓ		GPT IU/ℓ		LDH IU/ℓ		G-GTP IU/ℓ		CPK IU/ℓ		UREA NITROGEN mg/dℓ		CREATININE mg/dℓ	
Control	5	63±	4	32±	1	181±	51	2±	0	183±	30	17.6±	1.5	0.4±	0.1
77 ppm	5	60±	4	30±	4	197±	47	2±	1	190±	33	16.8±	2.7	0.5±	0.1
192 ppm	5	61±	4	31±	3	166±	27	1±	4	162±	27	17.1±	1.9	0.5±	0.1
480 ppm	5	64±	3	30±	2	277±	150	3±	2	197±	40	18.6±	2.1	0.4±	0.0
1200 ppm	5	83±	15*	40±	10	292±	78	5±	1*	202±	16	23.6±	4.2**	0.4±	0.1
3000 ppm	0	-		-		-		-		-		-		-	

Significant defference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	SODIUM mEq／ℓ		POTASSIUM mEq／ℓ		CHLORIDE mEq／ℓ		CALCIUM mg／dℓ		INORGANIC PHOSPHORUS mg／dℓ	
Control	5	141±	1	4.0±	0.2	107±	3	10.8±	0.3	7.6±	1.5
77 ppm	5	140±	1	3.8±	0.3	107±	2	10.7±	0.3	7.5±	1.1
192 ppm	5	140±	2	3.9±	0.3	106±	3	10.8±	0.1	7.1±	0.8
480 ppm	5	140±	1	4.1±	0.2	107±	2	10.6±	0.3	6.5±	1.0
1200 ppm	5	147±	3**	3.7±	0.3	112±	3*	11.5±	0.1**	4.9±	1.0**
3000 ppm	0	-		-		-		-		-	

Significant defference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX H 1

GROSS FINDINGS : SUMMARY, RAT : MALE ALL ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
ALL ANIMALS (0- 2W)

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	77 ppm 10 (%)	192 ppm 10 (%)	480 ppm 10 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)

Organ	Findings	Group Name / NO. of Animals	1200 ppm 10 (%)	3000 ppm 10 (%)
thymus	atrophic		1 (10)	10 (100)

APPENDIX H 2

GROSS FINDINGS : SUMMARY, RAT : FEMALE ALL ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
ALL ANIMALS (0- 2W)

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	77 ppm 10 (%)	192 ppm 10 (%)	480 ppm 10 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)
liver	herniation		1 (10)	0 (0)	1 (10)	0 (0)

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
ALL ANIMALS (0- 2W)

Organ	Findings	Group Name NO. of Animals	1200 ppm 10 (%)	3000 ppm 10 (%)
thymus	atrophic		6 (60)	10 (100)
liver	herniation		1 (10)	0 (0)

APPENDIX H 3

GROSS FINDINGS : SUMMARY, RAT : MALE

DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name NO. of Animals	Control 0 (%)	77 ppm 0 (%)	192 ppm 0 (%)	480 ppm 0 (%)
thymus	atrophic		- (-)	- (-)	- (-)	- (-)

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name NO. of Animals	1200 ppm 0 (%)	3000 ppm 9 (%)
thymus	atrophic		- (-)	9 (100)

APPENDIX H 4

GROSS FINDINGS : SUMMARY, RAT : FEMALE

DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name NO. of Animals	Control 0 (%)	77 ppm 0 (%)	192 ppm 0 (%)	480 ppm 0 (%)
thymus	atrophic		- (-)	- (-)	- (-)	- (-)

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name	1200 ppm	3000 ppm
		NO. of Animals	3 (%)	10 (%)
thymus	atrophic		3 (100)	10 (100)

APPENDIX H 5

GROSS FINDINGS : SUMMARY, RAT : MALE : SACRIFICED ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	77 ppm 10 (%)	192 ppm 10 (%)	480 ppm 10 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name / NO. of Animals	1200 ppm 10 (%)	3000 ppm 1 (%)
thymus	atrophic		1 (10)	1 (100)

APPENDIX H 6

GROSS FINDINGS : SUMMARY, RAT : FEMALE : SACRIFICED ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	77 ppm 10 (%)	192 ppm 10 (%)	480 ppm 10 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)
liver	herniation		1 (10)	0 (0)	1 (10)	0 (0)

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name NO. of Animals	1200 ppm 7 (%)	3000 ppm 0 (%)
thymus	atrophic		3 (43)	- (-)
liver	herniation		1 (14)	- (-)

APPENDIX I 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	5	175± 4	0.369± 0.022	0.039± 0.005	2.020± 0.164	0.609± 0.039	0.774± 0.012
77 ppm	5	174± 11	0.375± 0.031	0.039± 0.003	1.943± 0.157	0.627± 0.039	0.792± 0.046
192 ppm	5	181± 9	0.386± 0.016	0.042± 0.004	2.028± 0.089	0.654± 0.056	0.811± 0.043
480 ppm	5	169± 12	0.389± 0.035	0.045± 0.007	1.701± 0.398	0.598± 0.058	0.784± 0.068
1200 ppm	5	129± 16**	0.229± 0.066**	0.038± 0.004	1.634± 0.362	0.462± 0.028**	0.648± 0.037**
3000 ppm	1	63± 0 ?	0.020± 0.000 ?	0.033± 0.000 ?	0.631± 0.000 ?	0.287± 0.000 ?	0.511± 0.000 ?

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

? : Significant test is not applied,because No. of data in this group is less than 3.

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	1.281± 0.051	0.403± 0.021	6.587± 0.343	1.764± 0.012
77 ppm	5	1.291± 0.077	0.420± 0.045	6.724± 0.736	1.756± 0.059
192 ppm	5	1.351± 0.104	0.411± 0.029	7.077± 0.762	1.769± 0.036
480 ppm	5	1.312± 0.117	0.404± 0.027	7.078± 0.639	1.725± 0.057
1200 ppm	5	1.183± 0.105	0.320± 0.032**	6.645± 1.060	1.671± 0.027**
3000 ppm	1	0.831± 0.000 ?	0.057± 0.000 ?	1.834± 0.000 ?	1.548± 0.000 ?

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX I 2

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	Body Weight		THYMUS		ADRENALS		OVARIES		HEART		LUNGS	
Control	5	131±	5	0.305±	0.018	0.047±	0.004	0.080±	0.010	0.500±	0.067	0.649±	0.031
77 ppm	5	134±	3	0.330±	0.026	0.047±	0.003	0.093±	0.014	0.528±	0.045	0.657±	0.033
192 ppm	5	131±	3	0.298±	0.014	0.051±	0.006	0.089±	0.009	0.502±	0.027	0.681±	0.058
480 ppm	5	120±	4**	0.311±	0.015	0.044±	0.005	0.068±	0.013	0.468±	0.047	0.623±	0.037
1200 ppm	5	80±	7**	0.104±	0.043**	0.034±	0.004**	0.057±	0.008*	0.329±	0.033**	0.531±	0.048**
3000 ppm	0	-		-		-		-		-		-	

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	0.997± 0.049	0.321± 0.016	4.676± 0.501	1.658± 0.032
77 ppm	5	1.035± 0.040	0.338± 0.018	4.981± 0.353	1.634± 0.035
192 ppm	5	1.054± 0.029	0.338± 0.014	5.113± 0.426	1.617± 0.051
480 ppm	5	1.063± 0.034	0.320± 0.033	4.590± 0.238	1.620± 0.030
1200 ppm	5	0.847± 0.045**	0.196± 0.026**	3.662± 0.554**	1.548± 0.020**
3000 ppm	0	-	-	-	-

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX J 1

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	5	175± 4	0.211± 0.009	0.023± 0.003	1.152± 0.075	0.348± 0.017	0.442± 0.010
77 ppm	5	174± 11	0.215± 0.017	0.023± 0.002	1.115± 0.041	0.360± 0.021	0.456± 0.029
192 ppm	5	181± 9	0.213± 0.012	0.023± 0.003	1.122± 0.055	0.361± 0.014	0.449± 0.029
480 ppm	5	169± 12	0.230± 0.012	0.027± 0.004	0.998± 0.174	0.353± 0.020	0.463± 0.023
1200 ppm	5	129± 16**	0.175± 0.034*	0.030± 0.003**	1.268± 0.249	0.361± 0.030	0.506± 0.040**
3000 ppm	1	63± 0 ?	0.032± 0.000 ?	0.052± 0.000 ?	1.002± 0.000 ?	0.456± 0.000 ?	0.811± 0.000 ?

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

? : Significant test is not applied,because No. of data in this group is less than 3.

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	0.731± 0.039	0.230± 0.010	3.759± 0.168	1.007± 0.019
77 ppm	5	0.741± 0.020	0.241± 0.014	3.853± 0.221	1.011± 0.062
192 ppm	5	0.745± 0.028	0.227± 0.008	3.902± 0.248	0.978± 0.030
480 ppm	5	0.774± 0.020	0.239± 0.007	4.175± 0.094*	1.021± 0.058
1200 ppm	5	0.921± 0.039**	0.248± 0.010*	5.134± 0.237**	1.311± 0.166*
3000 ppm	1	1.319± 0.000 ?	0.090± 0.000 ?	2.911± 0.000 ?	2.457± 0.000 ?

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX J 2

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	5	131± 5	0.233± 0.018	0.035± 0.002	0.061± 0.005	0.381± 0.037	0.497± 0.035
77 ppm	5	134± 3	0.246± 0.016	0.035± 0.002	0.069± 0.010	0.394± 0.030	0.491± 0.017
192 ppm	5	131± 3	0.228± 0.008	0.039± 0.004	0.068± 0.005	0.385± 0.018	0.521± 0.038
480 ppm	5	120± 4**	0.260± 0.011	0.037± 0.005	0.057± 0.011	0.391± 0.029	0.521± 0.022
1200 ppm	5	80± 7**	0.127± 0.041	0.043± 0.005*	0.071± 0.012	0.411± 0.029	0.662± 0.018**
3000 ppm	0	-	-	-	-	-	-

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	0.761± 0.018	0.245± 0.012	3.563± 0.275	1.267± 0.054
77 ppm	5	0.773± 0.022	0.253± 0.014	3.721± 0.215	1.222± 0.025
192 ppm	5	0.808± 0.025	0.259± 0.015	3.913± 0.259	1.239± 0.041
480 ppm	5	0.890± 0.044**	0.267± 0.024	3.841± 0.235	1.355± 0.045
1200 ppm	5	1.060± 0.060**	0.244± 0.011	4.551± 0.321**	1.945± 0.199*
3000 ppm	0	-	-	-	-

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX K 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : ALL ANIMALS

(2-WEEK STUDY)

Organ	Findings	Group Name	Control				77 ppm				192 ppm				480 ppm			
		No. of Animals on Study	2				2				2				2			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
[Hematopoietic system]																		
bone marrow			< 2>				< 2>				< 2>				< 2>			
	decreased hematopoiesis		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thymus			< 2>				< 2>				< 2>				< 2>			
	atrophy		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen			< 2>				< 2>				< 2>				< 2>			
	atrophy		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]																		
stomach			< 2>				< 2>				< 2>				< 2>			
	erosion:glandular stomach		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hemorrhage:glandular stomach		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
liver			< 2>				< 2>				< 2>				< 2>			
	herniation		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	1200 ppm				3000 ppm			
		No. of Animals on Study	2				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]										
bone marrow			< 2>				< 2>			
	decreased hematopoiesis		1	1	0	0	0	0	2	0
			(50)	(50)	(0)	(0)	(0)	(0)	(100)	(0)
thymus			< 2>				< 2>			
	atrophy		0	0	0	0	0	0	2	0
			(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)
spleen			< 2>				< 2>			
	atrophy		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
[Digestive system]										
stomach			< 2>				< 2>			
	erosion:glandular stomach		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
	hemorrhage:glandular stomach		0	0	0	0	0	2	0	0
			(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
liver			< 2>				< 2>			
	herniation		1	0	0	0	0	0	0	0
			(50)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	Control				77 ppm				192 ppm				480 ppm			
		No. of Animals on Study	2				2				2				2			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																		
kidney			< 2>				< 2>				< 2>				< 2>			
	basophilic change		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(50)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Endocrine system]																		
pituitary			< 2>				< 2>				< 2>				< 2>			
	Rathke pouch		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thyroid			< 2>				< 2>				< 2>				< 2>			
	ultimibranchial body remanet		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	1200 ppm				3000 ppm			
		No. of Animals on Study	2				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]										
kidney			< 2>				< 2>			
	basophilic change		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Endocrine system]										
pituitary			< 2>				< 2>			
	Rathke pouch		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thyroid			< 2>				< 1>			
	ultimibranchial body remanet		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

APPENDIX K 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE: ALL ANIMALS

(2-WEEK STUDY)

Organ	Findings	Group Name	Control				77 ppm				192 ppm				480 ppm			
		No. of Animals on Study	2				2				2				2			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
[Hematopoietic system]																		
bone marrow			< 2>				< 2>				< 2>				< 2>			
	decreased hematopoiesis		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
thymus			< 2>				< 2>				< 2>				< 2>			
	atrophy		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen			< 2>				< 2>				< 2>				< 2>			
	atrophy		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]																		
stomach			< 2>				< 2>				< 2>				< 2>			
	hemorrhage:glandular stomach		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
liver			< 2>				< 2>				< 2>				< 2>			
	herniation		1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(50)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Urinary system]																		
kidney			< 2>				< 2>				< 2>				< 2>			
	mineralization:cortico-medullary junction		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	1200 ppm				3000 ppm			
		No. of Animals on Study	3				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]										
bone marrow			< 3>				< 2>			
	decreased hematopoiesis		0	3	0	0	0	1	1	0
			(0)	(100)	(0)	(0)	(0)	(50)	(50)	(0)
thymus			< 3>				< 2>			
	atrophy		0	0	1	0	0	0	2	0
			(0)	(0)	(33)	(0)	(0)	(0)	(100)	(0)
spleen			< 3>				< 2>			
	atrophy		1	0	0	0	2	0	0	0
			(33)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
[Digestive system]										
stomach			< 3>				< 2>			
	hemorrhage:glandular stomach		1	0	0	0	1	0	0	0
			(33)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
liver			< 3>				< 2>			
	herniation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Urinary system]										
kidney			< 3>				< 2>			
	mineralization:cortico-medullary junction		1	0	0	0	0	0	0	0
			(33)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	Control				77 ppm				192 ppm				480 ppm			
		No. of Animals on Study	2				2				2				2			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
[Endocrine system]																		
adrenal			< 2>				< 2>				< 2>				< 2>			
	hemorrhage		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	1200 ppm				3000 ppm			
		No. of Animals on Study	3				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]										
adrenal			< 3>				< 2>			
	hemorrhage		0	1	0	0	2	0	0	0
			(0)	(33)	(0)	(0)	(100)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

APPENDIX K 3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name	Control				77 ppm				192 ppm				480 ppm			
		No. of Animals on Study	0				0				0				0			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Hematopoietic system]																		
bone marrow			< 0>				< 0>				< 0>				< 0>			
	decreased hematopoiesis		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
thymus			< 0>				< 0>				< 0>				< 0>			
	atrophy		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
spleen			< 0>				< 0>				< 0>				< 0>			
	atrophy		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
[Digestive system]																		
stomach			< 0>				< 0>				< 0>				< 0>			
	erosion:glandular stomach		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
	hemorrhage:glandular stomach		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	1200 ppm				3000 ppm			
		No. of Animals on Study	0				1			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]										
bone marrow			< 0>				< 1>			
	decreased hematopoiesis		-	-	-	-	0	0	1	0
			(-)	(-)	(-)	(-)	(0)	(0)	(100)	(0)
thymus			< 0>				< 1>			
	atrophy		-	-	-	-	0	0	1	0
			(-)	(-)	(-)	(-)	(0)	(0)	(100)	(0)
spleen			< 0>				< 1>			
	atrophy		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
[Digestive system]										
stomach			< 0>				< 1>			
	erosion:glandular stomach		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
	hemorrhage:glandular stomach		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

APPENDIX K 4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

Organ	Findings	Group Name	Control				77 ppm				192 ppm				480 ppm			
		No. of Animals on Study	0				0				0				0			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
bone marrow			< 0>				< 0>				< 0>				< 0>			
	decreased hematopoiesis		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
thymus			< 0>				< 0>				< 0>				< 0>			
	atrophy		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
spleen			< 0>				< 0>				< 0>				< 0>			
	atrophy		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Digestive system]																		
stomach			< 0>				< 0>				< 0>				< 0>			
	hemorrhage:glandular stomach		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Urinary system]																		
kidney			< 0>				< 0>				< 0>				< 0>			
	mineralization:cortico-medullary junction		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	1200 ppm				3000 ppm			
		No. of Animals on Study	1				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]										
bone marrow			< 1>				< 2>			
	decreased hematopoiesis		0	1	0	0	0	1	1	0
			(0)	(100)	(0)	(0)	(0)	(50)	(50)	(0)
thymus			< 1>				< 2>			
	atrophy		0	0	1	0	0	0	2	0
			(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)
spleen			< 1>				< 2>			
	atrophy		1	0	0	0	2	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
[Digestive system]										
stomach			< 1>				< 2>			
	hemorrhage:glandular stomach		1	0	0	0	1	0	0	0
			(100)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
[Urinary system]										
kidney			< 1>				< 2>			
	mineralization:cortico-medullary junction		1	0	0	0	0	0	0	0
			(100)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	Control				77 ppm				192 ppm				480 ppm			
		No. of Animals on Study	0				0				0				0			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]																		
adrenal			< 0>				< 0>				< 0>				< 0>			
	hemorrhage		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name	1200 ppm				3000 ppm			
		No. of Animals on Study	1				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]										
adrenal			< 1>				< 2>			
	hemorrhage		0	1	0	0	2	0	0	0
			(0)	(100)	(0)	(0)	(100)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

APPENDIX K 5

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : SACRIFICED ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0282
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name	Control				77 ppm				192 ppm				480 ppm			
		No. of Animals on Study	2				2				2				2			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
bone marrow			< 2>				< 2>				< 2>				< 2>			
	decreased hematopoiesis		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thymus			< 2>				< 2>				< 2>				< 2>			
	atrophy		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen			< 2>				< 2>				< 2>				< 2>			
	atrophy		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]																		
stomach			< 2>				< 2>				< 2>				< 2>			
	hemorrhage:glandular stomach		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
liver			< 2>				< 2>				< 2>				< 2>			
	herniation		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Urinary system]																		
kidney			< 2>				< 2>				< 2>				< 2>			
	basophilic change		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(50)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	1200 ppm				3000 ppm			
		No. of Animals on Study	2				1			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]										
bone marrow			< 2>				< 1>			
	decreased hematopoiesis		1	1	0	0	0	0	1	0
			(50)	(50)	(0)	(0)	(0)	(0)	(100)	(0)
thymus			< 2>				< 1>			
	atrophy		0	0	0	0	0	0	1	0
			(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)
spleen			< 2>				< 1>			
	atrophy		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
[Digestive system]										
stomach			< 2>				< 1>			
	hemorrhage:glandular stomach		0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
liver			< 2>				< 1>			
	herniation		1	0	0	0	0	0	0	0
			(50)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Urinary system]										
kidney			< 2>				< 1>			
	basophilic change		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	Control				77 ppm				192 ppm				480 ppm			
		No. of Animals on Study	2				2				2				2			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]																		
pituitary			< 2>				< 2>				< 2>				< 2>			
	Rathke pouch		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thyroid			< 2>				< 2>				< 2>				< 2>			
	ultimibranchial body remanet		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	1200 ppm				3000 ppm			
		No. of Animals on Study	2				1			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]										
pituitary				< 2>				< 1>		
	Rathke pouch		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thyroid				< 2>				< 0>		
	ultimibranchial body remanet		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

APPENDIX K 6

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : SACRIFICED ANIMALS

(2-WEEK STUDY)

Organ	Findings	Group Name	Control				77 ppm				192 ppm				480 ppm			
		No. of Animals on Study	2				2				2				2			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
bone marrow			< 2>				< 2>				< 2>				< 2>			
	decreased hematopoiesis		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
[Digestive system]																		
liver			< 2>				< 2>				< 2>				< 2>			
	herniation		1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(50)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Urinary system]																		
kidney			< 2>				< 2>				< 2>				< 2>			
	mineralization:cortico-medullary junction		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	1200 ppm				3000 ppm			
		No. of Animals on Study	2				0			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]										
bone marrow			< 2>				< 0>			
	decreased hematopoiesis		0	2	0	0	-	-	-	-
			(0)	(100)	(0)	(0)	(-)	(-)	(-)	(-)
[Digestive system]										
liver			< 2>				< 0>			
	herniation		0	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
[Urinary system]										
kidney			< 2>				< 0>			
	mineralization:cortico-medullary junction		0	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

APPENDIX L 1

IDENTITY AND IMPURITY OF QUINOLINE IN THE 2-WEEK DRINKING WATER STUDY

IDENTITY AND IMPURITY OF QUINOLINE IN THE 2-WEEK DRINKING WATER STUDY

Test Substance : Quinoline (Tokyo Kasei Kogyo Co., Ltd.)

Lot No. : FHD03

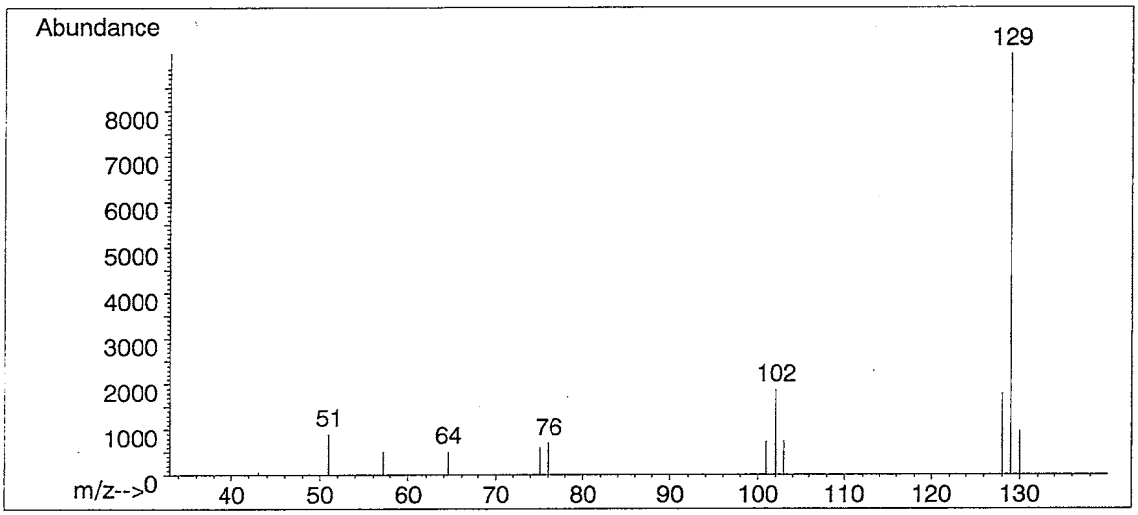
1. Spectral Data

Mass Spectrometry

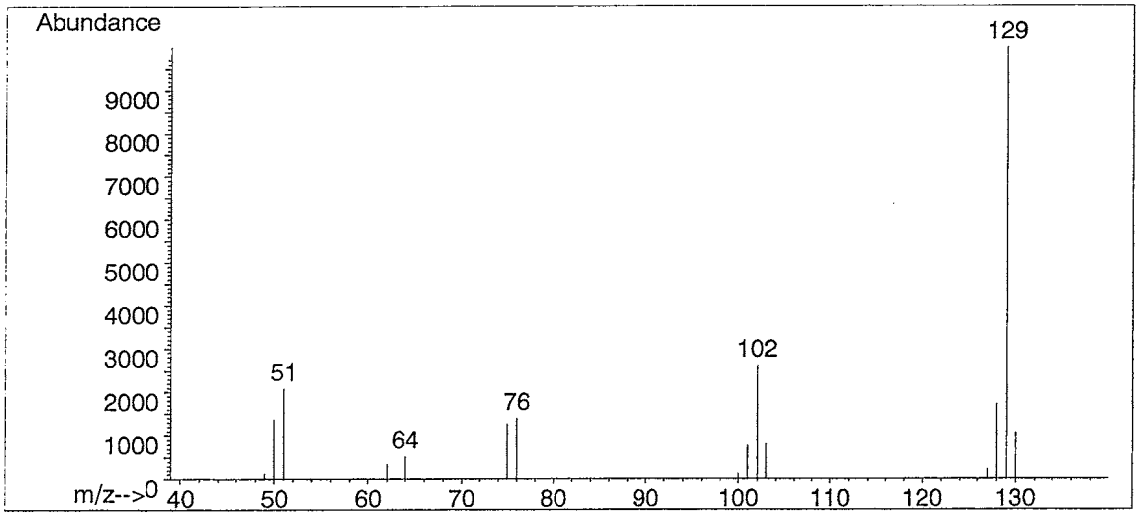
Instrument : Hewlett Packard 5989B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance



Mass Spectrum of Literature Data*

Results: The mass spectrum was consistent with literature spectrum.

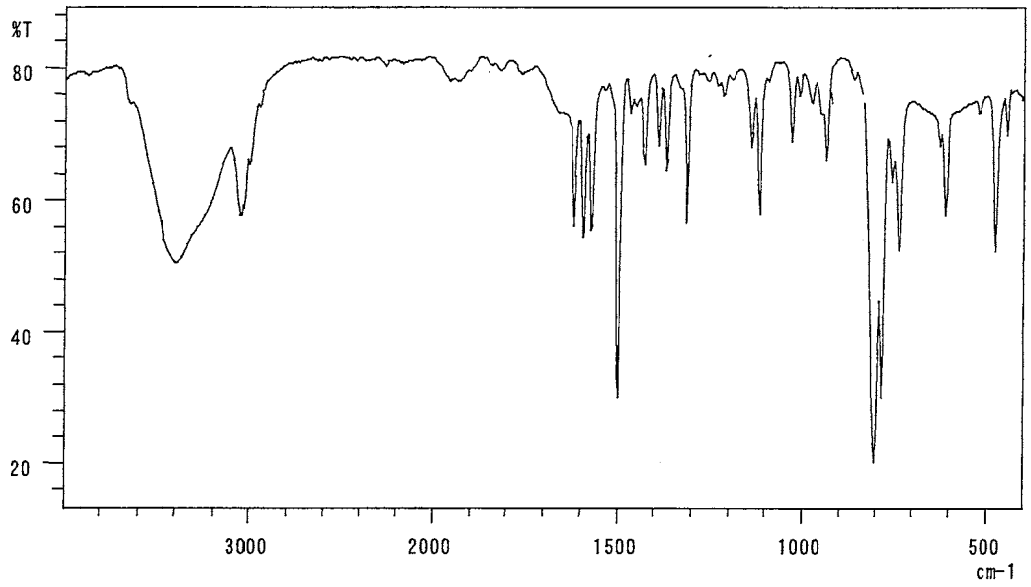
(*Fred W. McLafferty (1994) Wiley Registry of Mass Spectral Data, 6th edition. John Wiley and Sons, Inc. (U.S.), Entry Number 6221)

Infrared Spectrometry

Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 4 cm^{-1}



Infrared Spectrum of Test Substance

Determined Values	Literature Values*
Wave Number (cm^{-1})	Wave Number (cm^{-1})
440～ 460	440～ 460
460～ 500	460～ 500
600～ 640	600～ 640
720～ 760	720～ 760
760～ 800	760～ 800
800～ 840	800～ 840
920～ 960	920～ 960
1020～1040	1020～1040
1100～1130	1100～1130
1130～1160	1130～1160
1300～1320	1300～1320
1340～1380	1340～1380
1380～1400	1380～1400
1400～1440	1400～1440
1480～1520	1480～1520
1560～1580	1560～1580
1580～1600	1580～1600
1600～1640	1600～1640
2890～3120	
3120～3720	3120～3720

Results: The infrared spectrum was consistent with literature spectrum.
(*William W. Simons (1978) The Sadtler Handbook of Infrared Spectra. Sadtler Research Laboratories, Inc. (U.K.), p.218)

2. Impurity

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : INNOWAX (0.2 mmϕ $\times$50 m)

Column Temperature : 190° C

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μL

Sample Name	Peak No.	Area (%)	Peak Name
Test Substance	1	0.166	2-Methyl Naphthalene
	2	99.686	Quinoline
	3	0.148	Isoquinoline

Results: Gas chromatography indicated one major peak (peak No.2) and two impurities. It was identified only by comparing its gas chromatograph with that of 2-methyl naphthalene (peak No.1) and isoquinoline (peak No.3) in the quinoline, the amount in the test substance were 0.166%, and 0.148%.

3. Conclusions: The test substance was identified as quinoline by the mass spectrum and the infrared spectrum. Gas chromatography indicated one major peak (peak No.2) and two impurities. It was identified only by comparing its gas chromatograph with that of 2-methyl naphthalene and isoquinoline, the amount in the test substance were 0.166% and 0.148%.

APPENDIX L 2

STABILITY OF QUINOLINE IN THE 2-WEEK DRINKING WATER STUDY

STABILITY OF QUINOLINE IN THE 2-WEEK DRINKING WATER STUDY

Test Substance : Quinoline (Tokyo Kasei Kogyo Co., Ltd.)

Lot No. : FHD03

1. Sample Storage : This lot was used from 1995.2.6 to 1995.2.20. Test substance was stored in a dark place at room temperature.

2. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : INNOWAX (0.2 mmϕ × 50 m)

Column Temperature : 190° C

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μL

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
1995.01.30	1	5.402	0.166
	2	6.354	99.686
	3	6.780	0.148
1995.02.27	1	5.399	0.166
	2	6.353	99.685
	3	6.778	0.149

Results: Gas chromatography indicated one major peak (peak No.2) and two impurities (peaks No.1 and No.3 < 0.4% of total area) analyzed on 1995.1.30 and one major peak (peak No.2) and two impurities (peaks No.1 and No.3 < 0.4% of total area) analyzed on 1995.2.27. No new trace impurity peak in the test substance analyzed on 1995.2.27 was detected.

3. Conclusions: The test substance was stable for about 1 month in a dark place at room temperature.

APPENDIX L 3

CONCENTRATION OF QUINOLINE IN FORMULATED WATER IN THE 2-WEEK DRINKING WATER STUDY

CONCENTRATION OF QUINOLINE IN FORMULATED WATER IN THE 2-WEEK DRINKING WATER STUDY

	Target Concentration				
Date Analyzed	77[a]	192	480	1200	3000
1995.02.06	66.0(85.7)[b]	178.6(93.0)	478.8(99.8)	1250.6(104.2)	3172.3(105.7)

[a] ppm
[b] %

Analytical Method : The samples were analyzed by gas chromatography.

Instrument : Hewlett Packard 5890A
Column : INNOWAX (0.2 mmϕ $\times$50 m)
Column Temperature : 190℃
Injection Volume : 1 μL
Detector : FID (Flame Ionization Detector)
Injection Volume : 1 μL

APPENDIX L 4

STABILITY OF QUINOLINE IN FORMULATED WATER

IN THE 2-WEEK DRINKING WATER STUDY

STABILITY OF QUINOLINE IN FORMULATED WATER IN THE 2-WEEK DRINKING WATER STUDY

		Target Concentration				
Date Prepare	Date Analyzed	77[a]	192	480	1200	3000
1995.02.06	1995.02.06	66.0(100)[b]	178.6(100)	478.8(100)	1250.6(100)	3172.3(100)
	1995.02.13[c]	67.5(102.3)	163.6(91.6)	436.3(91.1)	1150.4(92.0)	2689.8(84.8)

[a] ppm
[b] %(Percentage was based on the concentration on date of preparation.)
[c] animal room samples

Analytical Method : The samples were analyzed by gas chromatography.

Instrument : Hewlett Packard 5890A
Column : HP INNOWAX (0.2 mmϕ $\times$ 50 m)
Column Temperature : 190℃
Flow Rate : 1 mL/min
Detector : FID (Flame Ionization Detector)
Injection Volume : 1 μL

APPENDIX M 1

METHODS FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK DRINKING WATER STUDY OF QUINOLINE

METHODS FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK DRINKING WATER STUDY OF QUINOLINE

Item	Method
Hematology	
Red blood cell (RBC)	Light scattering method [1]
Hemoglobin (Hgb)	Cyanmethemoglobin method [1]
Hematocrit (Hct)	Calculated as RBC × MCV/10 [1]
Mean corpuscular volume (MCV)	Light scattering method [1]
Mean corpuscular hemoglobin (MCH)	Calculated as Hgb/RBC × 10 [1]
Mean corpuscular hemoglobin concentration (MCHC)	Calculated as Hgb/Hct × 100 [1]
Platelet	Light scattering method [1]
Reticulocyte	Pattern recognition method [3] (New methyleneblue staining)
Prothrombin time	Quick one stage method [2]
Activated partial thromboplastin time (APTT)	Ellagic acid activaterd method [2]
White blood cell (WBC)	Light scattering method [1]
Differential WBC	Pattern recognition method [3] (May-Grunwald-Giemsa staining)
Biochemistry	
Total protein (TP)	Biuret method [4]
Albumin (Alb)	BCG method [4]
A/G ratio	Calculated as Alb/(TP－Alb) [4]
T-bilirubin	Alkaline azobilirubin method [4]
Glucose	Enzymatic method (GLK･G-6-PDH) [4]
T-cholesterol	Enzymatic method (CE･COD･POD) [4]
Phospholipid	Enzymatic method (PLD･COD･POD) [4]
Glutamic oxaloacetic transaminase (GOT)	UV･Rate method [4]
Glutamic pyruvic transaminase (GPT)	UV･Rate method [4]
Lactate dehydrogenase (LDH)	UV･Rate method [4]
γ-Glutamyl transpeptidase (γ-GTP)	L-γ-Glutamyl-p-nitroanilide method [4]
Creatine phosphokinase (CPK)	UV･Rate method [4]
Urea nitrogen	Enzymatic method (Urease･GLDH) [4]
Creatinine	Jaffe method [4]
Sodium	Ion selective electrode method [4]
Potassium	Ion selective electrode method [4]
Chloride	Ion selective electrode method [4]
Calcium	OCPC method [4]
Inorganic phosphorus	Enzymatic method (PNP･XOD･POD) [4]

1) Automatic blood cell analyzer (Technicon H･1 : Technicon Instruments Corporation,USA)

2) Automatic coagulometer (Sysmex CA-5000 : Toa Medical Electronics Co.,Ltd.,Japan)

3) Automatic blood cell differential analyzer (Hitachi 8200 : Hitachi,Ltd.,Japan)

4) Automatic analyzer (Hitachi 7070 : Hitachi,Ltd.,Japan)

APPENDIX N 1

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK DRINKING WATER STUDY OF QUINOLINE

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK DRINKING WATER STUDY OF QUINOLINE

Item	Unit	Decimal Place
Hematology		
Red blood cell (RBC)	$\times 10^6/\mu L$	2
Hemoglobin	g/dL	1
Hematocrit	%	1
Mean corpuscular volume (MCV)	fL	1
Mean corpuscular hemoglobin (MCH)	pg	1
Mean corpuscular hemoglobin concentration (MCHC)	g/dL	1
Platelet	$\times 10^3/\mu L$	0
Reticulocyte	‰	0
Prothrombin time	sec	1
Activated partial thromboplastin time (APTT)	sec	1
White blood cell (WBC)	$\times 10^3/\mu L$	2
Differential WBC	%	0
Biochemistry		
Total protein	g/dL	1
Albumin	g/dL	1
A/G ratio	–	1
T-bilirubin	mg/dL	2
Glucose	mg/dL	0
T-cholesterol	mg/dL	0
Phospholipid	mg/dL	0
Glutamic oxaloacetic transminase (GOT)	IU/L	0
Glutamic pyruvic transaminase (GPT)	IU/L	0
Lactate dehydrogenase (LDH)	IU/L	0
γ-Glutamyl transpeptidase (γ-GTP)	IU/L	0
Creatine phosphokinase (CPK)	IU/L	0
Urea nitrogen	mg/dL	1
Creatinine	mg/dL	1
Sodium	mEq/L	0
Potassium	mEq/L	1
Chloride	mEq/L	0
Calcium	mg/dL	1
Inorganic phosphorus	mg/dL	1