o-フェニレンジアミン二塩酸塩のマウスを用いた
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：０３３７

APPENDIXES

APPENDIXES

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
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
PILOERECTION	0 ppm	0	0	0	0	0
	500 ppm	0	0	0	0	0
	1000 ppm	0	0	1	0	0
	2000 ppm	0	0	0	0	0
	4000 ppm	0	0	0	0	0
	6000 ppm	0	0	0	0	0
SOILED PERI GENITALIA	0 ppm	0	0	0	0	0
	500 ppm	0	0	0	0	0
	1000 ppm	0	0	0	0	0
	2000 ppm	0	0	0	0	0
	4000 ppm	0	0	0	0	0
	6000 ppm	0	0	0	2	3
SMALL STOOL	0 ppm	0	0	0	0	0
	500 ppm	0	0	0	0	0
	1000 ppm	0	0	0	0	0
	2000 ppm	0	0	0	0	0
	4000 ppm	0	0	0	0	0
	6000 ppm	0	0	0	4	4
OLIGO-STOOL	0 ppm	0	0	0	0	0
	500 ppm	0	1	1	1	1
	1000 ppm	0	0	1	0	0
	2000 ppm	0	0	1	1	1
	4000 ppm	0	0	0	0	0
	6000 ppm	0	0	0	0	0

APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
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
DEATH	0 ppm	0	0	0	0	0
	500 ppm	0	0	0	0	0
	1000 ppm	0	0	0	0	0
	2000 ppm	0	0	0	0	0
	4000 ppm	0	0	0	0	0
	6000 ppm	0	0	0	1	1
PILOERECTION	0 ppm	0	0	0	0	0
	500 ppm	0	0	0	0	0
	1000 ppm	0	0	0	0	0
	2000 ppm	0	0	0	0	0
	4000 ppm	0	0	0	0	0
	6000 ppm	0	0	0	1	1
SMALL STOOL	0 ppm	0	0	0	0	0
	500 ppm	0	0	0	0	0
	1000 ppm	0	0	0	0	0
	2000 ppm	0	0	0	0	0
	4000 ppm	0	0	0	0	0
	6000 ppm	0	0	0	1	1

APPENDIX B 1

BODY WEIGHT CHANGES :SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
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
0 ppm	22.8± 0.6	22.4± 0.8	23.2± 1.1	23.5± 1.3	23.5± 1.5	24.1± 1.0
500 ppm	22.8± 0.6	21.4± 1.3	22.0± 2.0	22.5± 2.2	22.7± 2.9	23.0± 3.1
1000 ppm	22.8± 1.0	22.0± 0.9	22.1± 1.5	22.1± 3.1	22.8± 1.9	23.6± 2.2
2000 ppm	22.9± 0.4	21.0± 0.6	20.9± 2.0	21.4± 3.3	21.6± 2.3	23.3± 1.9
4000 ppm	22.8± 0.8	19.9± 0.6**	18.4± 0.6**	19.4± 1.5*	19.8± 0.9*	21.5± 0.9
6000 ppm	22.8± 0.7	20.0± 0.6**	17.9± 0.6**	15.5± 1.2**	15.4± 2.4**	15.7± 3.4**

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

APPENDIX B 2

BODY WEIGHT CHANGES : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
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
0 ppm	19.3± 0.7	18.6± 1.2	19.4± 0.4	20.1± 0.8	20.9± 0.9	20.7± 0.6
500 ppm	19.3± 0.7	19.1± 0.2	19.8± 0.6	20.3± 0.4	20.8± 1.2	21.2± 0.3
1000 ppm	19.3± 0.6	18.5± 0.5	19.3± 0.9	19.7± 0.5	19.8± 0.8	20.1± 0.7
2000 ppm	19.3± 0.6	17.8± 0.5	18.6± 0.9	19.3± 0.5	20.5± 0.7	20.4± 0.7
4000 ppm	19.3± 0.6	16.8± 0.5**	15.4± 0.4**	16.5± 1.9*	17.7± 2.2**	19.4± 1.3
6000 ppm	19.3± 0.6	16.3± 0.7**	14.7± 1.0**	13.1± 1.5**	13.6± 2.2**	14.8± 3.1*

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

APPENDIX C 1

WATER CONSUMPTION CHANGES : SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
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)
0 ppm	4.2± 0.1	4.0± 0.3	3.8± 0.3	4.0± 0.8
500 ppm	3.2± 1.1	3.8± 0.6	3.7± 1.0	3.5± 0.7
1000 ppm	3.2± 0.8	3.1± 1.4	3.1± 0.8	3.1± 0.9
2000 ppm	1.8± 0.7*	2.1± 0.5	1.8± 0.6**	2.2± 0.2**
4000 ppm	0.9± 0.2**	1.6± 0.3*	1.7± 0.5**	1.9± 0.3**
6000 ppm	0.6± 0.1**	0.6± 0.2**	0.9± 0.6**	1.2± 0.5**

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

APPENDIX C 2

WATER CONSUMPTION CHANGES : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
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)
0 ppm	4.8± 0.8	4.8± 0.5	4.3± 0.4	4.3± 1.8
500 ppm	4.2± 0.3	4.0± 0.4*	4.2± 0.4	4.0± 0.2
1000 ppm	3.2± 0.5	3.0± 0.6**	2.9± 0.5**	3.1± 0.5
2000 ppm	2.2± 0.3	2.2± 0.2**	2.1± 0.1**	2.2± 0.2
4000 ppm	1.0± 0.2**	1.5± 0.4**	1.9± 0.5**	1.9± 0.2*
6000 ppm	0.7± 0.1**	0.7± 0.3**	1.0± 0.3**	1.6± 0.4**

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

APPENDIX D 1

FOOD CONSUMPTION CHANGES : SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration 1-7(7)	week-day(effective) 2-7(7)
0 ppm	3.8± 0.4	3.9± 0.2
500 ppm	3.6± 0.6	3.9± 0.5
1000 ppm	3.5± 0.6	4.0± 0.1
2000 ppm	3.4± 0.9	4.4± 0.4
4000 ppm	2.8± 0.2*	3.9± 0.2
6000 ppm	2.2± 0.3**	2.9± 0.6

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

APPENDIX D 2

FOOD CONSUMPTION CHANGES : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(7)	2-7(7)
0 ppm	3.4± 0.2	3.5± 0.3
500 ppm	3.5± 0.1	3.6± 0.1
1000 ppm	3.4± 0.3	3.6± 0.3
2000 ppm	3.3± 0.2	3.6± 0.2
4000 ppm	2.4± 0.2**	3.8± 0.2
6000 ppm	1.8± 0.4**	2.6± 0.6

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

APPENDIX E 1

CHEMICAL INTAKE CHANGES : SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0337 CHEMICAL INTAKE CHANGES (SUMMARY)
ANIMAL : MOUSE Crj:BDF1 ALL ANIMALS
UNIT : g/kgBW/day
SEX : MALE

Group Name	Administration week-day			
	1-3	1-7	2-3	2-7
Control	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000
500ppm	0.071 ± 0.020	0.084 ± 0.010	0.080 ± 0.014	0.076 ± 0.009
1000ppm	0.143 ± 0.037	0.135 ± 0.056	0.138 ± 0.035	0.133 ± 0.036
2000ppm	0.164 ± 0.055	0.190 ± 0.024	0.169 ± 0.062	0.191 ± 0.016
4000ppm	0.187 ± 0.034	0.336 ± 0.043	0.346 ± 0.095	0.361 ± 0.060
6000ppm	0.201 ± 0.038	0.230 ± 0.056	0.351 ± 0.153	0.438 ± 0.246

APPENDIX E 2

CHEMICAL INTAKE CHANGES : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
UNIT : g/kgBW/day
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day			
	1-3	1-7	2-3	2-7
Control	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000
500ppm	0.106 ± 0.009	0.099 ± 0.010	0.102 ± 0.012	0.094 ± 0.004
1000ppm	0.169 ± 0.029	0.154 ± 0.032	0.145 ± 0.028	0.152 ± 0.029
2000ppm	0.232 ± 0.024	0.228 ± 0.018	0.207 ± 0.005	0.211 ± 0.019
4000ppm	0.270 ± 0.043	0.353 ± 0.056	0.423 ± 0.105	0.389 ± 0.057
6000ppm	0.268 ± 0.032	0.323 ± 0.103	0.445 ± 0.082	0.635 ± 0.043

APPENDIX F 1

HEMATOLOGY : SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
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 fℓ	MCH pg	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
0 ppm	3	9.98± 0.68	16.1± 0.8	50.2± 3.5	50.4± 2.4	16.2± 2.0	32.2± 3.3	1069± 532
500 ppm	5	9.81± 0.47	15.2± 0.9	48.3± 3.1	49.1± 1.3	15.5± 0.9	31.4± 1.8	1269± 333
1000 ppm	5	9.90± 0.39	15.4± 0.3	50.2± 1.9	50.7± 1.3	15.6± 0.8	30.7± 1.4	1243± 358
2000 ppm	5	10.02± 0.64	15.3± 0.8	49.9± 3.3	49.7± 0.3	15.3± 0.9	30.8± 1.7	1148± 175
4000 ppm	4	10.19± 0.46	15.2± 0.4	50.4± 2.1	49.5± 0.8	15.0± 0.3	30.2± 0.4	1324± 239
6000 ppm	4	10.81± 0.50	16.7± 0.8	53.6± 2.4	49.6± 0.4	15.4± 0.2	31.1± 0.6	1284± 338

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
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
0 ppm	3	1.96± 0.48	0± 0	23± 14	2± 3	0± 0	1± 0	74± 17	0± 0
500 ppm	5	1.62± 0.67	0± 0	22± 18	1± 1	0± 0	2± 1	76± 17	0± 0
1000 ppm	5	2.07± 1.27	0± 0	20± 10	1± 1	0± 0	2± 2	77± 12	0± 0
2000 ppm	5	1.78± 0.45	0± 1	21± 12	1± 1	0± 0	2± 1	75± 12	0± 0
4000 ppm	4	1.88± 0.34	1± 1	16± 3	2± 1	0± 0	2± 2	79± 2	0± 0
6000 ppm	4	0.60± 0.54	2± 2	43± 19	1± 1	0± 0	3± 2	53± 21	0± 0

APPENDIX F 2

HEMATOLOGY : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
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 fℓ	MCH pg	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
0 ppm	5	9.49± 1.11	15.2± 0.6	47.0± 5.6	49.5± 0.4	16.1± 1.6	32.6± 3.5	1013± 139
500 ppm	5	9.83± 0.47	14.6± 0.7	49.0± 2.9	49.8± 1.0	14.8± 0.2	29.9± 0.8	1116± 110
1000 ppm	4	9.93± 0.31	15.1± 0.2	49.3± 1.8	49.6± 1.5	15.2± 0.3	30.7± 0.8	1104± 60
2000 ppm	5	9.98± 0.32	15.0± 0.5	48.8± 1.4	49.0± 0.9	15.0± 0.2	30.6± 0.6	1118± 79
4000 ppm	5	10.26± 0.33	15.4± 0.6	50.8± 1.8	49.5± 0.4	15.0± 0.2	30.3± 0.7	1174± 131
6000 ppm	4	10.14± 0.16	15.5± 0.3	49.2± 1.3	48.6± 0.6	15.2± 0.1	31.3± 0.3	1369± 92**

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

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
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	
0 ppm	5	2.32±	0.71	0±	0	16±	7	2±	1	0±	0	2±	1	79±	6	1±	1
500 ppm	5	2.67±	1.30	1±	1	11±	3	2±	1	0±	0	2±	1	84±	2	0±	1
1000 ppm	4	2.38±	0.72	0±	0	13±	1	2±	1	0±	0	3±	1	83±	3	0±	0
2000 ppm	5	2.58±	0.72	1±	1	12±	4	2±	1	0±	0	1±	0	84±	4	0±	0
4000 ppm	5	2.52±	1.09	0±	1	17±	4	2±	1	0±	0	2±	0	78±	3	0±	1
6000 ppm	4	1.31±	1.11	0±	1	40±	14	1±	1	0±	0	2±	1	58±	14	0±	0

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

APPENDIX G 1

BIOCHEMISTRY : SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
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
0 ppm	3	5.4± 0.2	2.9± 0.2	1.2± 0.1	0.23± 0.04	178± 144	99± 8	201± 15
500 ppm	5	5.0± 0.4	2.8± 0.1	1.3± 0.1	0.18± 0.01	280± 82	97± 28	193± 12
1000 ppm	5	5.0± 0.3	2.7± 0.1	1.2± 0.1	0.24± 0.08	294± 56	93± 21	194± 25
2000 ppm	5	4.8± 0.4	2.7± 0.3	1.3± 0.2	0.21± 0.02	300± 51	92± 20	193± 32
4000 ppm	4	4.9± 0.1	2.8± 0.1	1.4± 0.1	0.22± 0.03	310± 37	87± 6	183± 15
6000 ppm	4	5.6± 0.3	3.2± 0.3	1.4± 0.1	0.36± 0.11	141± 112	92± 28	162± 76

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
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	SODIUM mEq/ℓ
0 ppm	3	43± 9	43± 9	517± 273	3± 1	297± 207	29.2± 7.3	152± 0
500 ppm	5	38± 9	26± 1	264± 132	2± 1	204± 119	38.4± 24.1	151± 6
1000 ppm	5	38± 6	29± 4	321± 138	2± 2	204± 83	28.6± 4.6	150± 2
2000 ppm	5	34± 4	25± 8	272± 108	2± 1	194± 82	31.0± 6.5	149± 2
4000 ppm	4	36± 3	25± 6	208± 55	2± 1	126± 51	29.2± 4.7	149± 1
6000 ppm	4	148± 124	43± 12	607± 577	5± 2	741± 1101	61.3± 26.0	168± 15

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	POTASSIUM mEq/ℓ		CHLORIDE mEq/ℓ		CALCIUM mg/dℓ		INORGANIC PHOSPHORUS mg/dℓ	
0 ppm	3	5.2±	0.9	114±	2	9.5±	0.3	10.3±	2.9
500 ppm	5	5.8±	1.2	123±	5	9.5±	0.6	9.4±	2.5
1000 ppm	5	5.2±	1.0	121±	3	9.3±	0.3	9.9±	2.0
2000 ppm	5	5.3±	0.3	121±	2	8.9±	0.6	9.1±	0.8
4000 ppm	4	4.7±	0.6	119±	1	9.2±	0.3	9.0±	1.4
6000 ppm	4	5.6±	1.0	137±	14	8.9±	1.1	10.8±	2.5

APPENDIX G 2

BIOCHEMISTRY : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
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
0 ppm	5	4.9± 0.3	3.0± 0.1	1.5± 0.1	0.19± 0.02	252± 40	79± 15	164± 31
500 ppm	5	4.8± 0.3	2.9± 0.2	1.5± 0.2	0.22± 0.08	270± 14	78± 9	167± 20
1000 ppm	4	4.9± 0.2	2.9± 0.2	1.4± 0.2	0.20± 0.02	265± 41	76± 11	156± 22
2000 ppm	5	4.8± 0.2	2.9± 0.1	1.6± 0.1	0.21± 0.05	296± 30	76± 5	167± 14
4000 ppm	5	4.9± 0.3	3.0± 0.2	1.5± 0.1	0.20± 0.02	290± 34	89± 12	181± 24
6000 ppm	4	5.5± 0.4	3.4± 0.2**	1.7± 0.1	0.23± 0.04	170± 96	105± 8**	186± 26

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

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
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		SODIUM mEq/ℓ	
0 ppm	5	44±	5	29±	3	284±	87	2±	1	192±	65	23.1±	3.0	149±	2
500 ppm	5	39±	5	35±	13	249±	87	2±	1	183±	85	22.3±	5.1	148±	4
1000 ppm	4	41±	7	30±	7	228±	52	2±	1	194±	99	21.5±	4.6	147±	3
2000 ppm	5	37±	2	29±	8	226±	53	3±	1	130±	62	28.9±	5.7	146±	2
4000 ppm	5	46±	14	30±	11	267±	51	2±	1	249±	93	30.0±	5.7	147±	1
6000 ppm	4	75±	53	38±	13	322±	54	2±	1	259±	118	46.0±	17.4*	158±	9

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

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	POTASSIUM mEq／ℓ	CHLORIDE mEq／ℓ	CALCIUM mg／dℓ	INORGANIC PHOSPHORUS mg／dℓ
0 ppm	5	5.0± 0.8	121± 3	9.4± 0.9	8.8± 0.8
500 ppm	5	5.7± 0.4	120± 4	9.2± 0.7	9.2± 1.1
1000 ppm	4	5.7± 0.4	121± 3	8.8± 0.7	9.7± 2.7
2000 ppm	5	5.2± 0.5	119± 5	9.0± 0.2	8.3± 1.1
4000 ppm	5	5.3± 0.5	119± 1	9.0± 0.7	9.0± 2.1
6000 ppm	4	5.7± 0.5	128± 8	9.3± 0.7	8.3± 1.6

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

APPENDIX H 1

GROSS FINDINGS : SUMMARY, MOUSE : MALE ALL ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name NO. of Animals	0 ppm 5 (%)	500 ppm 5 (%)	1000 ppm 5 (%)	2000 ppm 5 (%)
spleen	black zone		0 (0)	1 (20)	0 (0)	0 (0)
kidney	hydronephrosis		1 (20)	1 (20)	1 (20)	1 (20)

Organ	Findings	Group Name NO. of Animals	4000 ppm 5 (%)	6000 ppm 5 (%)
spleen	black zone		0 (0)	0 (0)
kidney	hydronephrosis		0 (0)	0 (0)

APPENDIX H 2

GROSS FINDINGS : SUMMARY, MOUSE : FEMALE ALL ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name NO. of Animals	0 ppm 5 (%)	500 ppm 5 (%)	1000 ppm 5 (%)	2000 ppm 5 (%)
spleen	black zone		0 (0)	0 (0)	1 (20)	1 (20)
kidney	hydronephrosis		1 (20)	0 (0)	0 (0)	0 (0)

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name NO. of Animals	4000 ppm 5 (%)	6000 ppm 5 (%)
spleen	black zone		0 (0)	0 (0)
kidney	hydronephrosis		0 (0)	0 (0)

APPENDIX H 3

GROSS FINDINGS : SUMMARY, MOUSE : FEMALE : SACRIFICED ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name NO. of Animals	0 ppm 5 (%)	500 ppm 5 (%)	1000 ppm 5 (%)	2000 ppm 5 (%)
spleen	black zone		0 (0)	0 (0)	1 (20)	1 (20)
kidney	hydronephrosis		1 (20)	0 (0)	0 (0)	0 (0)

Organ	Findings	Group Name	4000 ppm	6000 ppm
		NO. of Animals	5 (%)	4 (%)
spleen	black zone		0 (0)	0 (0)
kidney	hydronephrosis		0 (0)	0 (0)

APPENDIX H 4

GROSS FINDINGS : SUMMARY, MOUSE : FEMALE : DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

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

Organ _____	Findings _____	Group Name	0 ppm	500 ppm	1000 ppm	2000 ppm
		No. of Animals	0 (%)	0 (%)	0 (%)	0 (%)
			- (-)	- (-)	- (-)	- (-)

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

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

		Group Name	4000 ppm	6000 ppm
Organ	Findings	No. of Animals	0 (%)	1 (%)
			- (-)	Non remarkable

APPENDIX I 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
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
0 ppm	5	24.1± 1.0	0.046± 0.010	0.009± 0.001	0.182± 0.031	0.128± 0.006	0.134± 0.008
500 ppm	5	23.0± 3.1	0.043± 0.017	0.008± 0.002	0.179± 0.014	0.121± 0.012	0.136± 0.005
1000 ppm	5	23.6± 2.2	0.046± 0.016	0.010± 0.003	0.161± 0.033	0.127± 0.013	0.145± 0.010
2000 ppm	5	23.3± 1.9	0.043± 0.016	0.009± 0.002	0.173± 0.040	0.121± 0.014	0.150± 0.012
4000 ppm	5	21.5± 0.9	0.032± 0.008	0.010± 0.003	0.161± 0.022	0.112± 0.007	0.140± 0.011
6000 ppm	5	15.7± 3.4**	0.011± 0.008**	0.007± 0.002	0.156± 0.017	0.088± 0.010**	0.132± 0.015

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

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
0 ppm	5	0.376± 0.032	0.060± 0.023	1.218± 0.085	0.434± 0.005
500 ppm	5	0.428± 0.143	0.049± 0.004	1.212± 0.272	0.425± 0.013
1000 ppm	5	0.417± 0.103	0.054± 0.007	1.365± 0.178	0.427± 0.004
2000 ppm	5	0.386± 0.017	0.045± 0.004	1.307± 0.119	0.431± 0.015
4000 ppm	5	0.358± 0.010	0.039± 0.004*	1.279± 0.104	0.417± 0.007*
6000 ppm	5	0.275± 0.054*	0.017± 0.010**	0.760± 0.283**	0.400± 0.021**

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

APPENDIX I 2

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
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
0 ppm	5	20.7± 0.6	0.068± 0.007	0.011± 0.002	0.030± 0.008	0.118± 0.006	0.146± 0.006
500 ppm	5	21.2± 0.3	0.077± 0.008	0.012± 0.003	0.026± 0.006	0.118± 0.008	0.152± 0.010
1000 ppm	5	20.1± 0.7	0.075± 0.007	0.012± 0.001	0.027± 0.003	0.112± 0.007	0.149± 0.010
2000 ppm	5	20.4± 0.7	0.075± 0.009	0.010± 0.003	0.029± 0.005	0.112± 0.008	0.149± 0.008
4000 ppm	5	19.4± 1.3	0.060± 0.020	0.012± 0.001	0.023± 0.005	0.101± 0.009*	0.142± 0.006
6000 ppm	4	14.8± 3.1*	0.016± 0.011**	0.010± 0.002	0.017± 0.006**	0.085± 0.019**	0.136± 0.018

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

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
0 ppm	5	0.327± 0.160	0.060± 0.009	1.010± 0.030	0.446± 0.008
500 ppm	5	0.259± 0.006	0.057± 0.006	1.118± 0.033	0.450± 0.014
1000 ppm	5	0.275± 0.010	0.057± 0.006	1.091± 0.093	0.444± 0.017
2000 ppm	5	0.290± 0.009	0.056± 0.003	1.155± 0.101	0.439± 0.003
4000 ppm	5	0.286± 0.019	0.050± 0.009	1.215± 0.093*	0.429± 0.010
6000 ppm	4	0.260± 0.037	0.025± 0.011**	0.836± 0.283	0.410± 0.023*

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

APPENDIX J 1

ORGAN WEIGHT, RELATIVE : SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
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
0 ppm	5	24.1± 1.0	0.189± 0.039	0.037± 0.006	0.752± 0.105	0.532± 0.034	0.559± 0.036
500 ppm	5	23.0± 3.1	0.182± 0.058	0.037± 0.010	0.786± 0.096	0.533± 0.063	0.602± 0.079
1000 ppm	5	23.6± 2.2	0.192± 0.056	0.042± 0.013	0.679± 0.096	0.540± 0.024	0.617± 0.059
2000 ppm	5	23.3± 1.9	0.182± 0.059	0.037± 0.009	0.743± 0.155	0.521± 0.054	0.649± 0.061
4000 ppm	5	21.5± 0.9	0.150± 0.036	0.047± 0.012	0.746± 0.089	0.519± 0.033	0.647± 0.027
6000 ppm	5	15.7± 3.4**	0.069± 0.033**	0.047± 0.012	1.025± 0.225*	0.568± 0.059	0.851± 0.086**

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

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
0 ppm	5	1.567± 0.186	0.254± 0.111	5.074± 0.477	1.807± 0.077
500 ppm	5	1.972± 1.062	0.219± 0.039	5.218± 0.622	1.876± 0.246
1000 ppm	5	1.809± 0.638	0.230± 0.045	5.772± 0.312	1.824± 0.169
2000 ppm	5	1.673± 0.216	0.193± 0.020	5.620± 0.250	1.862± 0.121
4000 ppm	5	1.664± 0.058	0.182± 0.021	5.941± 0.482	1.937± 0.074
6000 ppm	5	1.769± 0.305	0.101± 0.033**	4.722± 0.782	2.609± 0.406**

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

APPENDIX J 2

ORGAN WEIGHT, RELATIVE : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
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
0 ppm	5	20.7± 0.6	0.328± 0.028	0.055± 0.010	0.144± 0.036	0.572± 0.037	0.707± 0.032
500 ppm	5	21.2± 0.3	0.363± 0.038	0.056± 0.013	0.124± 0.029	0.555± 0.042	0.717± 0.039
1000 ppm	5	20.1± 0.7	0.371± 0.026	0.061± 0.005	0.134± 0.016	0.557± 0.031	0.743± 0.066
2000 ppm	5	20.4± 0.7	0.364± 0.032	0.050± 0.013	0.142± 0.023	0.548± 0.041	0.731± 0.050
4000 ppm	5	19.4± 1.3	0.303± 0.092	0.061± 0.009	0.121± 0.024	0.520± 0.035	0.731± 0.049
6000 ppm	4	14.8± 3.1**	0.102± 0.053**	0.065± 0.011	0.109± 0.021	0.575± 0.039	0.926± 0.090**

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

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
0 ppm	5	1.586± 0.794	0.290± 0.042	4.881± 0.086	2.156± 0.056
500 ppm	5	1.220± 0.041	0.269± 0.026	5.263± 0.170	2.120± 0.070
1000 ppm	5	1.370± 0.066	0.284± 0.027	5.422± 0.350*	2.212± 0.079
2000 ppm	5	1.422± 0.077	0.276± 0.010	5.646± 0.410**	2.151± 0.086
4000 ppm	5	1.472± 0.055*	0.254± 0.031	6.252± 0.219**	2.215± 0.126
6000 ppm	4	1.774± 0.119**	0.159± 0.046**	5.519± 0.790*	2.832± 0.438*

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

APPENDIX K 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : MALE : ALL ANIMALS

(2-WEEK STUDY)

Organ	Findings	Group Name / No. of Animals on Study / Grade	0 ppm 5				500 ppm 5				1000 ppm 5				2000 ppm 5			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Hematopoietic system}																		
thymus		< 5>																
	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		< 5>																
	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)
	deposit of melanin		0 (0)	0 (0)	0 (0)	0 (0)	1 (20)	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		< 5>																
	inflammatory polyp		0 (0)	1 (20)	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)
	hydronephrosis		0 (0)	1 (20)	0 (0)	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)
{Musculoskeletal system}																		
muscle		< 5>																
	necrosis		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
Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	4000 ppm				6000 ppm			
		No. of Animals on Study	5				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
thymus			< 5>				< 4>			
	atrophy		0	0	0	0	1	3	0	0 *
			(0)	(0)	(0)	(0)	(25)	(75)	(0)	(0)
spleen			< 5>				< 5>			
	atrophy		0	0	0	0	0	3	0	0
			(0)	(0)	(0)	(0)	(0)	(60)	(0)	(0)
	deposit of melanin		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Urinary system}										
kidney			< 5>				< 5>			
	inflammatory polyp		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hydronephrosis		0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)
{Musculoskeletal system}										
muscle			< 5>				< 5>			
	necrosis		0	0	0	0	2	1	0	0
			(0)	(0)	(0)	(0)	(40)	(20)	(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
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

APPENDIX K 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : FEMALE: ALL ANIMALS

(2-WEEK STUDY)

Organ	Findings	Group Name / No. of Animals on Study / Grade	0 ppm 5				500 ppm 5				1000 ppm 5				2000 ppm 5			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Hematopoietic system}																		
bone marrow		< 5>																
	congestion		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		< 5>																
	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		< 5>																
	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)
	deposit of melanin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)
{Circulatory system}																		
heart		< 5>																
	inflammatory infiltration		1 (20)	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		< 5>																
	hydronephrosis		0 (0)	1 (20)	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
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	4000 ppm				6000 ppm			
		No. of Animals on Study	5				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
bone marrow			< 5>				< 5>			
	congestion		0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)
thymus			< 5>				< 5>			
	atrophy		0	0	0	0	1	3	0	0 *
			(0)	(0)	(0)	(0)	(20)	(60)	(0)	(0)
spleen			< 5>				< 5>			
	atrophy		0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)
	deposit of melanin		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
{Circulatory system}										
heart			< 5>				< 5>			
	inflammatory infiltration		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Urinary system}										
kidney			< 5>				< 5>			
	hydronephrosis		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
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	0 ppm				500 ppm				1000 ppm				2000 ppm			
		No. of Animals on Study	5				5				5				5			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Musculoskeletal system}																		
muscle			< 5>				< 5>				< 5>				< 5>			
	necrosis		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
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	4000 ppm				6000 ppm			
		No. of Animals on Study	5				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Musculoskeletal system}										
muscle			< 5>				< 5>			
	necrosis		0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(20)	(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
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

APPENDIX K 3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : FEMALE : SACRIFICED ANIMALS

(2-WEEK STUDY)

Organ	Findings	Group Name	0 ppm				500 ppm				1000 ppm				2000 ppm			
		No. of Animals on Study	5				5				5				5			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}																		
thymus			< 5>				< 5>				< 5>				< 5>			
	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			< 5>				< 5>				< 5>				< 5>			
	deposit of melanin		0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
{Circulatory system}																		
heart			< 5>				< 5>				< 5>				< 5>			
	inflammatory infiltration		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Urinary system}																		
kidney			< 5>				< 5>				< 5>				< 5>			
	hydronephrosis		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Musculoskeletal system}																		
muscle			< 5>				< 5>				< 5>				< 5>			
	necrosis		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
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	4000 ppm				6000 ppm			
		No. of Animals on Study	5				4			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
thymus			< 5>				< 4>			
	atrophy		0	0	0	0	1	2	0	0
			(0)	(0)	(0)	(0)	(25)	(50)	(0)	(0)
spleen			< 5>				< 4>			
	deposit of melanin		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(25)	(0)	(0)	(0)
{Circulatory system}										
heart			< 5>				< 4>			
	inflammatory infiltration		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Urinary system}										
kidney			< 5>				< 4>			
	hydronephrosis		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Musculoskeletal system}										
muscle			< 5>				< 4>			
	necrosis		0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(25)	(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
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

APPENDIX K 4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : FEMALE : DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0337
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name	0 ppm				500 ppm				1000 ppm				2000 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>			
	congestion		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
thymus			< 0>				< 0>				< 0>				< 0>			
	atrophy		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
spleen			< 0>				< 0>				< 0>				< 0>			
	atrophy		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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	4000 ppm				6000 ppm			
		No. of Animals on Study	0				1			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
bone marrow			< 0>				< 1>			
	congestion		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
thymus			< 0>				< 1>			
	atrophy		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
spleen			< 0>				< 1>			
	atrophy		-	-	-	-	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 L 1

IDENTITY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE IN THE 2-WEEK DRINKING WATER STUDY

IDENTITY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE IN THE 2-WEEK DRINKING WATER STUDY

Test Substance : *o*-Phenylenediamine Dihydrochloride (Wako Pure Chemical Industries, Ltd.)

Lot No. : WTM0491

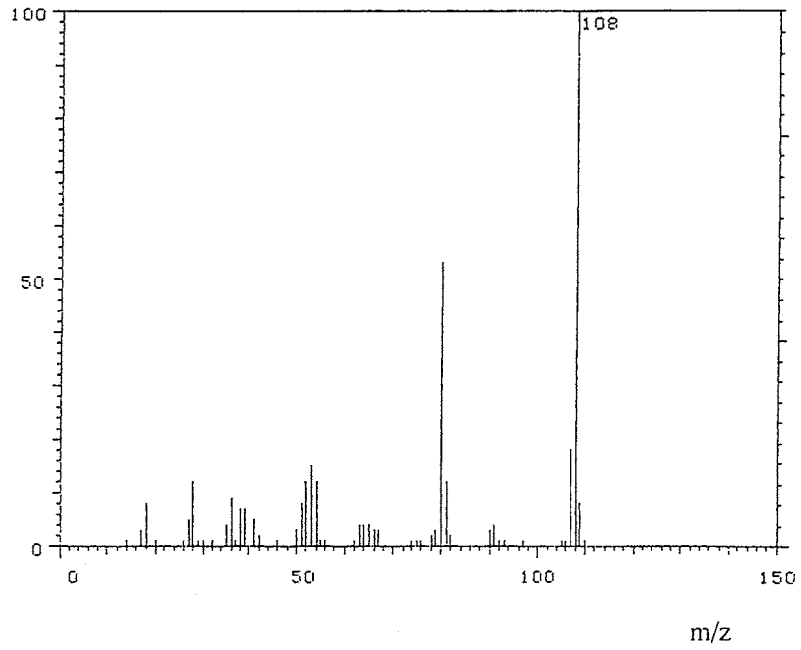
1. Spectral Data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Determined Value Fragment Peak (m/z)	Calculated Value Fragment Peak (m/z)
108	108 $(NH_2C_6H_4NH_2 \cdot 2HCl) - (2HCl)$

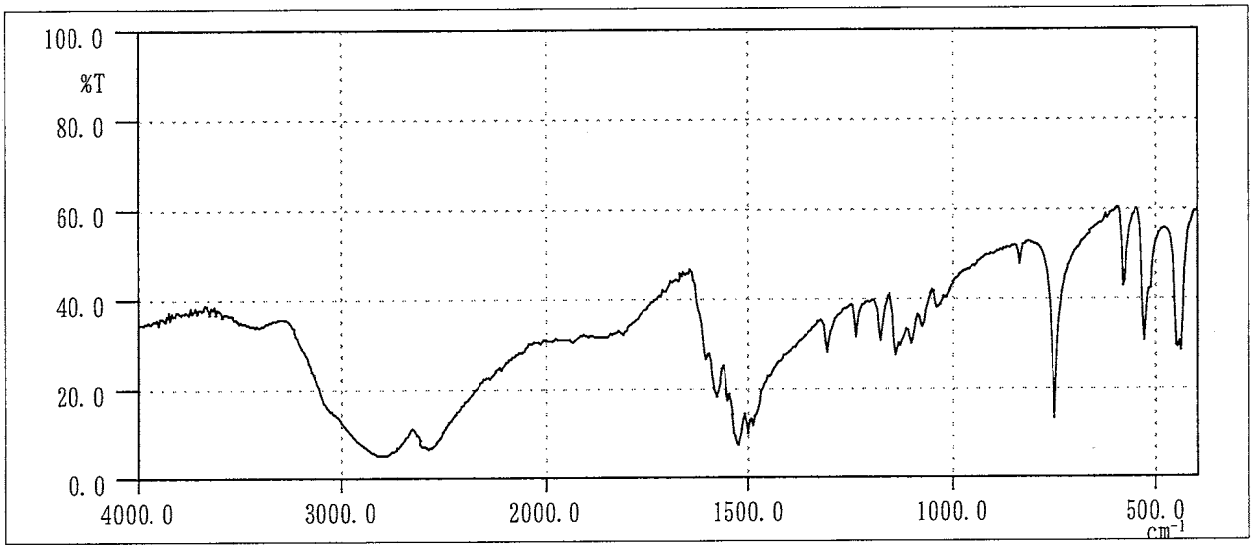
Results: The mass spectrum was consistent with calculated spectrum.

Infrared Spectrometry

Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr

Resolution : 2 cm^{-1}



Infrared Spectrum of Test Substance

Determined Values Wave Number (cm^{-1})	Literature Values* Wave Number (cm^{-1})
410～ 480	410～ 480
480～ 550	480～ 550
550～ 600	550～ 600
680～ 800	680～ 800
820～ 850	820～ 850
1010～1050	1010～1050
1050～1160	1050～1160
1160～1200	1160～1200
1250～1280	1250～1280
1280～1330	1280～1330
1330～1640	1330～1640
2100～3200	2100～3200

Results: The infrared spectrum was consistent with literature spectrum.
(*Performed by Wako Pure Chemical Industries, Ltd.)

2. Conclusions: The test substance was identified as *o*-phenylenediamine dihydrochloride by the mass spectrum and the infrared spectrum.

APPENDIX L 2

STABILITY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE IN THE 2-WEEK DRINKING WATER STUDY

STABILITY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE IN THE 2-WEEK DRINKING WATER STUDY

Test Substance : *o*-Phenylenediamine Dihydrochloride (Wako Pure Chemical Industries, Ltd.)

Lot No. : WTM0491

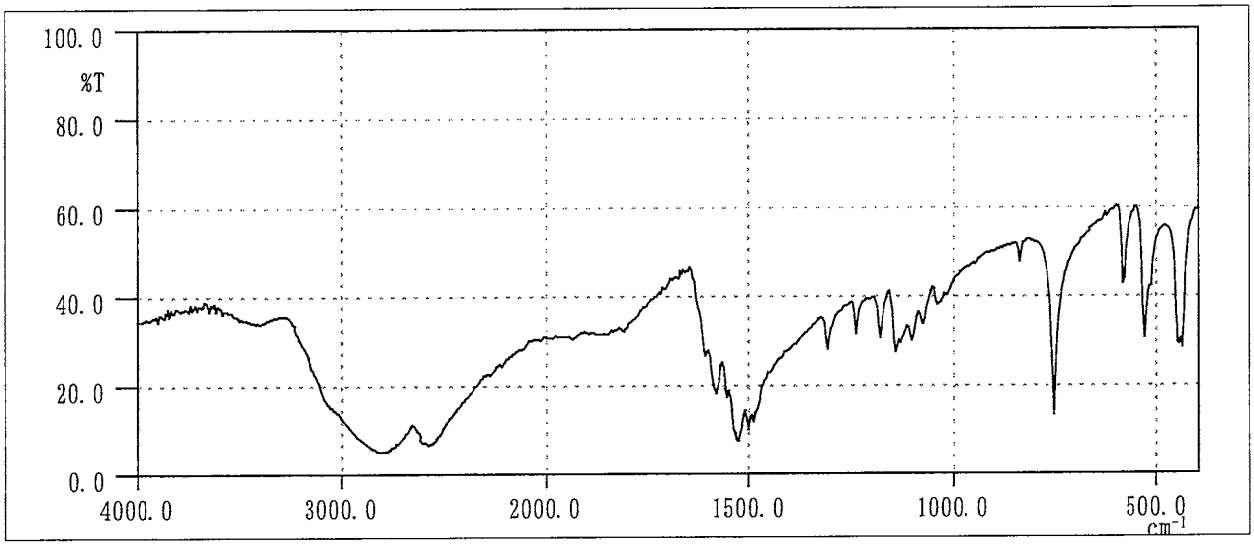
1. Sample : This lot was used from 1997.9.15 to 1997.9.29. Test substance was stored in cold storage in a dark place.

2. Infrared Spectrometry

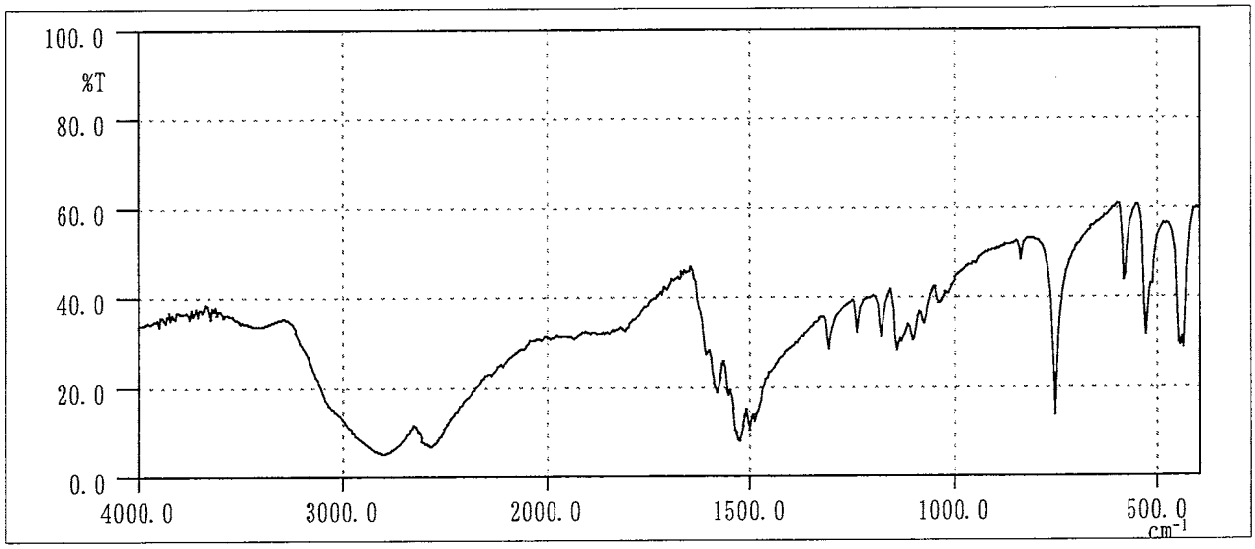
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr

Resolution : 2 cm^{-1}



Infrared Spectrum of Test Substance (date analyzed : 1997.09.09)



Infrared Spectrum of Test Substance (date analyzed : 1997.09.30)

Results: The results of infrared spectrum did not change before and after the study.

3. High Performance Liquid Chromatography

Instrument : Hewlett Packard 1090 High Performance Liquid Chromatograph

Column : TSK GEL ODS-80TM (4.6 mϕ × 15 cm)

Column Temperature : Room Temperature

Flow Rate : 1 mL/min

Mobile Phase : Distilled Water (10mM Potassium Dihydrogenphosphate, 5mM 1-Hexanesulfonic Acid Sodium Salt) : Acetonitrile = 80 : 20

Detector : UV (290 nm)

Injection Volume : 20 μL

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
1997.09.09	1	3.267	100
1997.09.30	1	3.229	100

Results: High performance liquid chromatography indicated one major peak (peak No.1) analyzed on 1997.9.09 and one major peak (peak No.1) analyzed on 1997.9.30. No new trace impurity peak in the test substance analyzed on 1997.9.30 was detected.

4. Conclusions: The test substance was stable for about 1 month in cold storage in a dark place.

APPENDIX L 3

CONCENTMOUSEION OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE IN FORMULATED WATER IN THE 2-WEEK DRINKING WATER STUDY

CONCENTRATION OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE IN FORMULATED WATER IN THE 2-WEEK DRINKING WATER STUDY

	Target Concentration				
Date Analyzed	500[a]	1000	2000	4000	6000
1997.09.15	497 (99.4)[b]	988 (98.8)	2050 (103)	3960 (99.0)	5840 (97.3)

[a] ppm
[b] %

Analytical Method : The samples were analyzed by high performance liquid chromatography.

Instrument : Hewlett Packard 1090 High Performance Liquid Chromatograph
Column : TSK GEL ODS-80TM (4.6 mmϕ × 15 cm)
Column Temperature : Room Temperature
Flow Rate : 1 mL/min
Mobile Phase : Distilled Water (10mM Potassium Dihydrogenphosphate, 5mM 1-Hexanesulfonic Acid Sodium Salt) : Acetonitrile = 80 : 20
Detector : UV (290 nm)
Injection Volume : 20 µL

APPENDIX L 4

STABILITY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE IN FORMULATED WATER IN THE 2-WEEK DRINKING WATER STUDY

STABILITY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE IN FORMULATED WATER IN THE 2-WEEK DRINKING WATER STUDY

		Target Concentration	
Date Prepared	Date Analyzed	500[a]	6000
1997.09.01	1997.09.01	477 (100)[b]	5790 (100)
	1997.09.05[c]	474 (99.4)	5920 (102)

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

Analytical Method : The samples were analyzed by high performance liquid chromatography.

Instrument : Hewlett Packard 1090 High Performance Liquid Chromatograph
Column : TSK GEL ODS-80TM (4.6 mmϕ $\times$ 15 cm)
Column Temperature : Room Temperature
Flow Rate : 1 mL/min
Mobile Phase : Distilled Water (10mM Potassium Dihydrogenphosphate, 5mM 1-Hexanesulfonic Acid Sodium Salt) : Acetonitrile = 80 : 20
Detector : UV (290 nm)
Injection Volume : 20 µL

APPENDIX N 1

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE

METHODS FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE

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]
White blood cell (WBC)	Light scattering method [1]
Differential WBC	Pattern recognition method [2] (May-Grunwald-Giemsa staining)
Biochemistry	
Total protein (TP)	Biuret method [3]
Albumin (Alb)	BCG method [3]
A/G ratio	Calculated as Alb/(TP－Alb) [3]
T-bilirubin	Alkaline azobilirubin method [3]
Glucose	Enzymatic method (GLK・G-6-PDH) [3]
T-cholesterol	Enzymatic method (CE・COD・POD) [3]
Phospholipid	Enzymatic method (PLD・COD・POD) [3]
Glutamic oxaloacetic transaminase (GOT)	IFCC method [3]
Glutamic pyruvic transaminase (GPT)	IFCC method [3]
Lactate dehydrogenase (LDH)	Wroblewski-LaDue method [3]
γ-Glutamyl transpeptidase (γ-GTP)	L-γ-Glutamyl-p-nitroanilide method [3]
Creatine phosphokinase (CPK)	GSCC method [3]
Urea nitrogen	Enzymatic method (Urease・GLDH) [3]
Sodium	Ion selective electrode method [3]
Potassium	Ion selective electrode method [3]
Chloride	Ion selective electrode method [3]
Calcium	OCPC method [3]
Inorganic phosphorus	Enzymatic method (PNP・XOD・POD) [3]

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

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

3) Automatic analyzer (Hitachi 7070 : Hitachi,Ltd.)

APPENDIX M 1

METHODS FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE

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
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 transaminase (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
Sodium	mEq/L	0
Potassium	mEq/L	1
Chloride	mEq/L	0
Calcium	mg/dL	1
Inorganic phosphorus	mg/dL	1