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 13 週間毒性試験(混水試験)報告書

試験番号：０３５２

APPENDIXES

APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7
SMALL STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	1	0	0	0	0	0	0	0	0	0	0	0

APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1 13
SEX : FEMALE

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

Clinical sign	Group Name	Administration week-day												
		1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7
Abnormal sign	0 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0

APPENDIX B 1

BODY WEIGHT CHANGES :SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 0	1	2	3	4	5	6
Control	23.8± 0.7	24.5± 0.8	25.2± 0.8	26.3± 1.1	26.8± 1.1	27.4± 1.2	28.3± 1.5
500 ppm	23.8± 0.7	24.5± 1.1	25.3± 0.9	25.9± 0.9	26.6± 1.1	27.5± 1.3	28.1± 1.4
1000 ppm	23.8± 0.8	24.1± 0.7	24.9± 0.9	25.3± 0.7	26.0± 1.0	26.6± 1.0	27.2± 0.9
2000 ppm	23.8± 0.7	23.2± 0.7	24.2± 0.7	25.1± 0.9*	25.6± 0.8*	26.1± 0.7*	26.5± 0.7**
4000 ppm	23.8± 0.8	20.4± 1.7**	22.8± 0.9**	23.6± 0.9**	24.1± 1.0**	24.9± 0.8**	25.2± 1.2**
5000 ppm	23.8± 0.7	19.2± 1.7**	20.5± 2.4**	22.2± 1.2**	23.2± 0.8**	23.9± 1.1**	24.4± 1.0**

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

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 7	8	9	10	11	12	13
Control	29.1± 1.7	29.6± 1.4	29.8± 1.7	31.8± 1.8	32.5± 1.9	33.1± 2.2	34.0± 2.3
500 ppm	28.7± 1.5	29.1± 1.5	29.3± 2.1	31.1± 1.9	31.6± 2.3	31.9± 2.3	32.5± 2.2
1000 ppm	27.9± 1.0	28.1± 1.3*	28.3± 1.3	30.1± 1.4	30.4± 1.8*	31.0± 1.7*	30.9± 2.0**
2000 ppm	27.1± 0.8**	27.3± 1.1**	27.3± 1.1**	28.7± 1.1*	28.9± 1.3**	29.2± 1.4**	29.4± 1.5**
4000 ppm	25.5± 1.4**	25.4± 1.5**	25.4± 1.3**	26.4± 1.3**	26.3± 1.4**	26.5± 1.5**	26.7± 1.6**
5000 ppm	24.7± 1.0**	24.8± 0.9**	24.6± 0.9**	25.5± 0.5**	25.3± 0.8**	25.7± 1.1**	25.8± 1.1**

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

APPENDIX B 2

BODY WEIGHT CHANGES : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 0	1	2	3	4	5	6
Control	19.5± 0.6	20.3± 0.8	20.8± 0.8	21.6± 1.1	21.6± 0.7	22.1± 1.1	22.4± 0.7
500 ppm	19.5± 0.6	20.3± 0.7	20.7± 0.7	21.1± 0.7	21.4± 0.6	22.0± 0.8	22.2± 0.7
1000 ppm	19.5± 0.6	20.0± 0.6	21.0± 1.1	21.1± 0.8	21.5± 0.9	21.9± 0.6	22.6± 1.0
2000 ppm	19.5± 0.6	19.5± 0.8	20.2± 0.5	20.7± 0.9	20.9± 0.9	21.7± 0.8	21.8± 0.7
4000 ppm	19.5± 0.6	17.2± 0.7**	19.4± 0.9*	20.2± 0.5**	20.4± 0.8**	20.9± 0.8*	21.3± 0.8*
5000 ppm	19.5± 0.6	14.5± 1.2**	17.3± 1.8**	19.1± 1.1**	19.7± 0.9**	20.7± 1.0**	20.9± 1.2**

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

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 7	8	9	10	11	12	13
Control	22.9± 1.2	23.2± 1.8	22.9± 0.8	24.1± 1.0	24.4± 1.4	24.6± 2.2	24.7± 1.9
500 ppm	22.7± 1.5	22.9± 1.0	22.5± 1.0	23.8± 0.7	23.9± 0.8	24.6± 1.3	24.0± 1.1
1000 ppm	21.8± 0.7	22.6± 1.0	22.5± 0.8	24.2± 0.7	23.9± 1.2	24.5± 1.4	24.4± 1.0
2000 ppm	22.3± 1.1	22.5± 0.8	22.2± 0.8	23.1± 1.1	23.4± 0.9	23.8± 1.4	23.7± 0.7
4000 ppm	21.2± 0.8**	21.6± 0.9*	21.4± 0.8**	22.3± 0.8**	22.6± 0.8**	22.9± 0.9	23.0± 0.9**
5000 ppm	20.9± 1.2**	21.2± 1.1**	21.2± 1.2**	22.1± 1.6**	22.3± 1.4**	22.7± 1.2*	22.6± 1.2**

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

APPENDIX C 1

WATER CONSUMPTION CHANGES : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 1	2	3	4	5	6	7
Control	4.9± 1.2	4.7± 0.9	4.4± 0.9	4.2± 0.8	4.0± 0.7	4.1± 0.8	4.0± 0.9
500 ppm	3.9± 0.5	3.8± 0.4	3.8± 0.4	3.7± 0.3	3.5± 0.3	3.6± 0.3	3.4± 0.3
1000 ppm	2.9± 0.2	2.8± 0.2*	2.7± 0.3	2.7± 0.2	2.6± 0.2	2.7± 0.3	2.6± 0.2
2000 ppm	2.3± 0.2**	2.2± 0.3**	2.3± 0.3**	2.2± 0.2**	2.3± 0.2**	2.4± 0.3**	2.2± 0.2**
4000 ppm	1.4± 0.3**	1.8± 0.2**	1.8± 0.2**	1.8± 0.2**	1.8± 0.1**	1.9± 0.1**	1.8± 0.2**
5000 ppm	1.1± 0.4**	1.5± 0.2**	1.7± 0.3**	1.6± 0.2**	1.6± 0.2**	1.8± 0.2**	1.7± 0.2**

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

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 8	9	10	11	12	13
Control	3.8± 1.0	4.1± 0.9	3.8± 0.8	3.5± 0.3	3.7± 0.7	3.7± 0.8
500 ppm	3.3± 0.3	3.4± 0.3	3.3± 0.3	3.2± 0.3	3.3± 0.4	3.2± 0.2
1000 ppm	2.6± 0.2*	2.7± 0.2*	2.6± 0.1	2.5± 0.2**	2.7± 0.1	2.6± 0.3*
2000 ppm	2.3± 0.2**	2.4± 0.2**	2.2± 0.2**	2.3± 0.3**	2.3± 0.2**	2.3± 0.2**
4000 ppm	1.8± 0.2**	2.0± 0.1**	1.8± 0.2**	1.8± 0.1**	1.9± 0.1**	1.9± 0.2**
5000 ppm	1.8± 0.3**	1.8± 0.2**	1.6± 0.2**	1.6± 0.3**	1.7± 0.2**	1.7± 0.2**

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

APPENDIX C 2

WATER CONSUMPTION CHANGES : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 1	2	3	4	5	6	7
Control	4.3± 0.4	4.3± 0.4	4.2± 0.3	4.1± 0.3	3.9± 0.4	4.2± 0.2	4.0± 0.3
500 ppm	4.2± 0.4	4.1± 0.4	4.2± 0.5	4.4± 0.7	4.1± 0.3	4.4± 0.4	4.1± 0.4
1000 ppm	3.4± 0.2**	3.3± 0.2**	3.5± 0.4	3.4± 0.4	3.4± 0.4**	3.7± 0.3**	3.5± 0.2**
2000 ppm	2.2± 0.3**	2.2± 0.3**	2.5± 0.2**	2.5± 0.2*	2.6± 0.3**	2.8± 0.2**	2.7± 0.3**
4000 ppm	1.6± 0.2**	1.8± 0.2**	1.9± 0.2**	1.8± 0.2**	1.9± 0.2**	2.0± 0.2**	2.0± 0.2**
5000 ppm	1.0± 0.2**	1.8± 0.2**	1.8± 0.2**	1.8± 0.2**	1.9± 0.2**	2.0± 0.3**	2.0± 0.2**

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

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 8	9	10	11	12	13
Control	4.2± 0.3	4.2± 0.2	4.1± 0.2	3.9± 0.2	4.4± 0.3	4.2± 0.4
500 ppm	4.2± 0.4	4.3± 0.5	4.1± 0.5	3.9± 0.4	4.2± 0.4	4.1± 0.5
1000 ppm	3.5± 0.3**	3.6± 0.4	3.3± 0.3**	3.4± 0.3**	3.5± 0.3**	3.5± 0.2
2000 ppm	2.7± 0.3**	2.7± 0.3**	2.5± 0.3**	2.6± 0.3**	2.7± 0.3**	2.9± 0.3**
4000 ppm	2.0± 0.3**	2.0± 0.2**	1.9± 0.2**	1.9± 0.2**	1.9± 0.1**	2.1± 0.3**
5000 ppm	2.0± 0.1**	2.1± 0.2**	2.0± 0.3**	2.0± 0.3**	2.2± 0.2**	2.2± 0.2**

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

APPENDIX D 1

FOOD CONSUMPTION CHANGES : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 1	2	3	4	5	6	7
Control	3.9± 0.3	3.7± 0.3	3.8± 0.3	3.8± 0.2	3.8± 0.2	3.8± 0.2	4.0± 0.3
500 ppm	3.7± 0.3	3.6± 0.2	3.7± 0.1	3.7± 0.1	3.8± 0.3	3.7± 0.2	3.9± 0.3
1000 ppm	3.5± 0.1*	3.5± 0.2	3.5± 0.2*	3.5± 0.2	3.6± 0.1	3.5± 0.1**	3.7± 0.2*
2000 ppm	3.3± 0.2**	3.6± 0.2	3.6± 0.2	3.5± 0.1	3.6± 0.2	3.5± 0.2**	3.7± 0.2**
4000 ppm	2.5± 0.3**	3.5± 0.3	3.6± 0.2	3.4± 0.2*	3.4± 0.2**	3.4± 0.2**	3.5± 0.2**
5000 ppm	2.3± 0.3**	3.0± 0.6**	3.5± 0.3*	3.4± 0.5*	3.4± 0.3**	3.3± 0.2**	3.3± 0.2**

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

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 8	9	10	11	12	13
Control	4.0± 0.2	4.1± 0.2	4.2± 0.2	4.3± 0.5	4.1± 0.2	4.2± 0.3
500 ppm	3.8± 0.1*	3.9± 0.3	4.0± 0.3	4.0± 0.3	3.9± 0.2*	4.0± 0.2
1000 ppm	3.6± 0.2**	3.8± 0.2**	3.9± 0.2**	3.8± 0.2	3.8± 0.3**	3.9± 0.3**
2000 ppm	3.6± 0.2**	3.7± 0.2**	3.9± 0.2**	3.8± 0.2	3.8± 0.2**	3.8± 0.2**
4000 ppm	3.5± 0.2**	3.5± 0.2**	3.6± 0.2**	3.5± 0.3**	3.5± 0.2**	3.6± 0.3**
5000 ppm	3.4± 0.2**	3.4± 0.2**	3.5± 0.2**	3.3± 0.2**	3.5± 0.2**	3.5± 0.3**

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

APPENDIX D 2

FOOD CONSUMPTION CHANGES : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 1	2	3	4	5	6	7
Control	3.5± 0.3	3.1± 0.5	3.5± 0.2	3.4± 0.2	3.6± 0.3	3.5± 0.2	3.7± 0.2
500 ppm	3.3± 0.2	3.2± 0.2	3.4± 0.3	3.4± 0.2	3.6± 0.2	3.5± 0.2	3.7± 0.4
1000 ppm	3.3± 0.2	3.4± 0.3	3.5± 0.2	3.5± 0.3	3.7± 0.2	3.7± 0.3	3.7± 0.3
2000 ppm	3.0± 0.2**	3.2± 0.2	3.4± 0.2	3.3± 0.2	3.5± 0.2	3.4± 0.2	3.6± 0.2
4000 ppm	2.4± 0.3**	3.1± 0.4	3.3± 0.2	3.2± 0.3	3.2± 0.3*	3.3± 0.3	3.3± 0.3*
5000 ppm	2.0± 0.2**	2.9± 0.5	3.4± 0.3	3.3± 0.2	3.3± 0.3	3.2± 0.3*	3.3± 0.3*

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

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 8	9	10	11	12	13
Control	3.8± 0.3	3.9± 0.2	4.0± 0.2	3.8± 0.2	4.0± 0.4	3.9± 0.4
500 ppm	3.7± 0.2	3.8± 0.2	3.9± 0.1	3.7± 0.2	3.9± 0.1	3.8± 0.2
1000 ppm	3.9± 0.2	3.9± 0.3	4.0± 0.3	3.8± 0.2	3.9± 0.3	3.8± 0.3
2000 ppm	3.7± 0.1	3.7± 0.2	3.7± 0.2	3.6± 0.2	3.8± 0.4	3.8± 0.2
4000 ppm	3.4± 0.3**	3.5± 0.3**	3.6± 0.4*	3.4± 0.2*	3.5± 0.3**	3.7± 0.3
5000 ppm	3.4± 0.2**	3.5± 0.3**	3.6± 0.4*	3.4± 0.3**	3.5± 0.3**	3.6± 0.3

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

APPENDIX E 1

CHEMICAL INTAKE CHANGES : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
UNIT : g／kg／d a y
REPORT TYPE : A1 13
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2	3	4	5	6	7
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
500 ppm	0.080± 0.008	0.075± 0.007	0.074± 0.009	0.070± 0.007	0.064± 0.005	0.064± 0.006	0.059± 0.005
1000 ppm	0.122± 0.010	0.111± 0.011	0.108± 0.011	0.104± 0.006	0.097± 0.008	0.101± 0.011	0.093± 0.007
2000 ppm	0.199± 0.020	0.185± 0.027	0.187± 0.027	0.173± 0.020	0.177± 0.020	0.178± 0.023	0.161± 0.016
4000 ppm	0.275± 0.054	0.321± 0.044	0.304± 0.033	0.293± 0.037	0.288± 0.023	0.294± 0.019	0.290± 0.034
5000 ppm	0.289± 0.074	0.355± 0.035	0.381± 0.081	0.343± 0.053	0.344± 0.051	0.362± 0.053	0.350± 0.046

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
UNIT : g／kg／d a y
REPORT TYPE : A1 13
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 8	9	10	11	12	13
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
500 ppm	0.057± 0.005	0.059± 0.005	0.053± 0.006	0.051± 0.006	0.052± 0.008	0.050± 0.004
1000 ppm	0.093± 0.008	0.096± 0.008	0.085± 0.005	0.083± 0.007	0.086± 0.006	0.084± 0.008
2000 ppm	0.170± 0.019	0.177± 0.015	0.155± 0.020	0.158± 0.022	0.158± 0.015	0.155± 0.013
4000 ppm	0.284± 0.032	0.312± 0.029	0.265± 0.038	0.271± 0.021	0.280± 0.023	0.291± 0.031
5000 ppm	0.370± 0.059	0.367± 0.045	0.304± 0.045	0.324± 0.048	0.336± 0.035	0.335± 0.036

APPENDIX E 2

CHEMICAL INTAKE CHANGES : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
UNIT : g／kg／d a y
REPORT TYPE : A1 13
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2	3	4	5	6	7
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
500 ppm	0.103± 0.009	0.099± 0.011	0.099± 0.011	0.103± 0.016	0.094± 0.006	0.100± 0.008	0.091± 0.008
1000 ppm	0.171± 0.014	0.159± 0.011	0.164± 0.015	0.161± 0.020	0.154± 0.016	0.163± 0.018	0.161± 0.013
2000 ppm	0.228± 0.020	0.216± 0.030	0.244± 0.029	0.237± 0.013	0.235± 0.023	0.255± 0.028	0.242± 0.026
4000 ppm	0.371± 0.046	0.378± 0.037	0.368± 0.031	0.360± 0.029	0.363± 0.031	0.369± 0.038	0.374± 0.027
5000 ppm	0.325± 0.047	0.507± 0.048	0.484± 0.065	0.468± 0.062	0.464± 0.048	0.469± 0.055	0.483± 0.049

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
UNIT : g／kg／d a y
REPORT TYPE : A1 13
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 8	9	10	11	12	13
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
500 ppm	0.092± 0.008	0.096± 0.010	0.086± 0.011	0.082± 0.007	0.086± 0.011	0.085± 0.010
1000 ppm	0.155± 0.017	0.160± 0.017	0.137± 0.011	0.142± 0.015	0.142± 0.015	0.145± 0.011
2000 ppm	0.237± 0.027	0.240± 0.028	0.220± 0.032	0.221± 0.023	0.228± 0.029	0.245± 0.033
4000 ppm	0.362± 0.041	0.373± 0.028	0.332± 0.027	0.336± 0.043	0.335± 0.022	0.362± 0.045
5000 ppm	0.472± 0.029	0.491± 0.051	0.442± 0.060	0.458± 0.052	0.478± 0.051	0.483± 0.038

APPENDIX F 1

HEMATOLOGY : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV fℓ	MCH pg	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	9	10.79± 0.27	15.7± 0.4	51.4± 1.2	47.6± 0.4	14.5± 0.2	30.5± 0.4	1376± 54
500 ppm	10	10.88± 0.35	15.7± 0.5	51.7± 1.5	47.5± 0.6	14.5± 0.1	30.4± 0.3	1460± 85
1000 ppm	8	10.62± 0.35	15.6± 0.3	50.8± 1.5	47.9± 0.6	14.7± 0.3	30.6± 0.7	1507± 65*
2000 ppm	9	10.61± 0.22	15.4± 0.4	50.9± 0.9	48.0± 0.4	14.5± 0.2	30.3± 0.3	1530± 106**
4000 ppm	9	10.44± 0.39	15.2± 0.4*	50.2± 1.5	48.1± 0.6	14.5± 0.3	30.2± 0.4	1602± 234**
5000 ppm	10	10.50± 0.26	15.2± 0.4	50.5± 1.4	48.0± 0.6	14.5± 0.2	30.2± 0.3	1532± 79**

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

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHERS
Control	9	1.56± 0.69	0± 0	15± 3	1± 1	0± 0	2± 2	81± 3	0± 0
500 ppm	10	1.44± 0.57	0± 1	16± 4	1± 1	0± 0	3± 1	81± 4	0± 0
1000 ppm	8	1.64± 0.40	0± 0	19± 3	1± 1	0± 0	2± 1	78± 3	0± 0
2000 ppm	9	1.62± 0.72	0± 1	20± 7	1± 2	0± 0	2± 1	77± 7	0± 1
4000 ppm	9	0.95± 0.56	0± 0	23± 10	0± 1	0± 0	3± 2	74± 9	0± 0
5000 ppm	10	2.10± 0.91	0± 0	18± 5	1± 1	0± 0	2± 1	79± 5	0± 0

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

APPENDIX F 2

HEMATOLOGY : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

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	10	10.74± 0.38	15.9± 0.6	51.4± 1.8	47.8± 0.4	14.8± 0.2	31.0± 0.5	1213± 137
500 ppm	10	10.53± 0.33	15.6± 0.5	51.0± 1.5	48.5± 0.6	14.8± 0.2	30.6± 0.3	1349± 90
1000 ppm	10	10.59± 0.26	15.8± 0.4	51.9± 1.0	48.9± 0.8**	14.9± 0.2	30.4± 0.4*	1334± 78
2000 ppm	10	10.36± 0.42	15.5± 0.7	50.5± 2.3	48.7± 0.8*	15.0± 0.1	30.7± 0.6	1320± 150
4000 ppm	10	10.21± 0.44**	15.3± 0.6*	50.2± 1.8	49.2± 0.6**	15.0± 0.2	30.4± 0.3*	1333± 74
5000 ppm	10	10.03± 0.21**	15.1± 0.3**	49.5± 0.8*	49.4± 0.6**	15.1± 0.2*	30.5± 0.3	1325± 65

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

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	WBC $10^3/\mu l$		Differential WBC (%) N-BAND		N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHERS	
Control	10	0.95±	0.55	0±	1	15±	6	1±	1	0±	0	2±	1	82±	6	0±	0
500 ppm	10	1.40±	0.78	1±	2	23±	11	1±	1	0±	0	2±	1	74±	12	0±	0
1000 ppm	10	1.34±	0.71	0±	1	24±	8*	1±	1	0±	0	2±	2	73±	9*	0±	1
2000 ppm	10	1.10±	0.60	0±	0	22±	3**	0±	0	0±	0	2±	1	75±	3*	0±	0
4000 ppm	10	1.27±	0.75	0±	0	19±	4	1±	1	0±	0	1±	1	79±	4	0±	0
5000 ppm	10	1.07±	1.12	0±	0	24±	11	0±	0	0±	0	2±	1	74±	11	0±	0

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

APPENDIX G 1

BIOCHEMISTRY : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

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	TRIGLYCERIDE mg/dl
Control	9	5.0± 0.2	2.8± 0.1	1.3± 0.1	0.14± 0.01	195± 36	84± 6	33± 9
500 ppm	10	5.1± 0.1	2.9± 0.1	1.3± 0.1	0.15± 0.01	206± 35	85± 6	38± 14
1000 ppm	8	5.0± 0.1	2.9± 0.1	1.4± 0.1	0.14± 0.01	219± 35	80± 6	34± 13
2000 ppm	10	5.0± 0.2	2.9± 0.1	1.4± 0.1	0.15± 0.03	240± 46	83± 6	33± 16
4000 ppm	9	5.0± 0.1	2.9± 0.2	1.3± 0.2	0.14± 0.02	186± 41	81± 8	20± 9
5000 ppm	10	4.9± 0.1	2.9± 0.1	1.4± 0.1	0.14± 0.02	184± 30	81± 6	19± 8

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

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	PHOSPHOLIPID mg/dl	GOT IU/l	GPT IU/l	LDH IU/l	ALP IU/l	G-GTP IU/l	CPK IU/l
Control	9	171± 14	47± 9	19± 3	204± 63	135± 11	1± 1	81± 48
500 ppm	10	171± 13	43± 3	18± 2	183± 25	137± 10	0± 1	57± 20
1000 ppm	8	164± 8	40± 4	16± 1	165± 16	133± 10	1± 1	45± 8
2000 ppm	10	168± 12	38± 4*	17± 4	179± 60	143± 11	1± 1	50± 18
4000 ppm	9	151± 26	49± 17	18± 3	205± 54	151± 15*	1± 1	71± 33
5000 ppm	10	159± 14	42± 10	22± 10	185± 80	149± 10*	1± 1	57± 26

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

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	UREA NITROGEN mg/dl	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dl	INORGANIC PHOSPHORUS mg/dl
Control	9	25.8± 6.1	152± 1	4.5± 0.6	123± 2	8.7± 0.3	7.1± 0.6
500 ppm	10	24.3± 3.7	151± 1	4.4± 0.4	123± 2	8.8± 0.2	6.5± 0.5
1000 ppm	8	23.8± 4.3	151± 1	4.4± 0.3	122± 2	8.7± 0.2	7.0± 1.1
2000 ppm	10	25.8± 3.8	151± 2	4.4± 0.5	122± 3	8.7± 0.4	7.2± 1.3
4000 ppm	9	28.0± 4.7	153± 2	4.2± 0.3	123± 2	8.7± 0.2	7.5± 1.5
5000 ppm	10	25.7± 2.4	152± 2	4.2± 0.5	122± 2	8.7± 0.2	7.1± 1.2

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

APPENDIX G 2

BIOCHEMISTRY : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

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	TRIGLYCERIDE mg/dl
Control	10	5.2± 0.1	3.1± 0.1	1.6± 0.1	0.13± 0.01	150± 23	74± 8	19± 5
500 ppm	10	5.0± 0.1	3.0± 0.1	1.5± 0.1	0.14± 0.01	154± 22	76± 10	19± 6
1000 ppm	10	5.1± 0.1	3.1± 0.1	1.6± 0.1	0.13± 0.01	159± 24	80± 11	18± 8
2000 ppm	10	5.1± 0.2	3.1± 0.2	1.5± 0.1	0.14± 0.04	171± 21	82± 9	19± 13
4000 ppm	10	4.9± 0.2**	3.0± 0.1	1.6± 0.1	0.13± 0.01	159± 23	88± 8**	17± 6
5000 ppm	10	4.9± 0.1**	3.0± 0.1	1.6± 0.1	0.14± 0.02	169± 29	93± 10**	19± 5

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

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	PHOSPHOLIPID mg/dl	GOT IU/l	GPT IU/l	LDH IU/l	ALP IU/l	G-GTP IU/l	CPK IU/l
Control	10	148± 18	55± 8	21± 3	196± 37	228± 24	1± 1	67± 43
500 ppm	10	151± 21	59± 9	24± 6	262± 55	207± 11	1± 1	191± 184
1000 ppm	10	156± 24	58± 7	20± 4	201± 43	228± 28	1± 1	104± 74
2000 ppm	10	157± 20	56± 8	23± 8	245± 77	205± 11	1± 1	150± 154
4000 ppm	10	163± 19	54± 9	23± 7	212± 64	203± 19	1± 1	101± 36
5000 ppm	10	168± 18	60± 11	22± 2	248± 71	199± 25*	1± 1	113± 56

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

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	UREA NITROGEN mg/dl		SODIUM mEq/ℓ		POTASSIUM mEq/ℓ		CHLORIDE mEq/ℓ		CALCIUM mg/dl		INORGANIC PHOSPHORUS mg/dl	
Control	10	17.8±	2.5	151±	1	4.8±	0.3	121±	2	8.8±	0.2	6.9±	0.6
500 ppm	10	19.4±	2.5	151±	1	4.6±	0.4	123±	1	8.7±	0.2	6.7±	0.7
1000 ppm	10	22.3±	3.2**	152±	2	4.6±	0.2	123±	2*	8.8±	0.2	7.4±	1.4
2000 ppm	10	22.5±	2.1**	152±	2	4.4±	0.3	123±	1	8.6±	0.3	6.6±	0.6
4000 ppm	10	21.6±	3.3*	151±	1	4.1±	0.3**	121±	2	8.7±	0.2	7.1±	0.9
5000 ppm	10	25.1±	2.9**	153±	3	4.2±	0.5**	122±	2	8.7±	0.2	7.4±	0.7

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

APPENDIX H 1

URINALYSIS : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0352 URINALYSIS
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	±	+	2+	3+	4+	CHI	Occult blood −	±	+	2+	3+	CHI
Control	10	0	0	0	1	5	2	2		0	0	7	3	0	0		10	0	0	0	0	0		1	8	1	0	0	0		10	0	0	0	0	
500 ppm	10	0	0	1	1	2	4	2		0	0	6	3	0	1		10	0	0	0	0	0		2	6	2	0	0	0		10	0	0	0	0	
1000 ppm	10	0	0	0	4	6	0	0		0	0	2	8	0	0	*	10	0	0	0	0	0		3	5	2	0	0	0		10	0	0	0	0	
2000 ppm	10	0	0	4	3	2	1	0		0	0	2	8	0	0	*	10	0	0	0	0	0		3	3	4	0	0	0		10	0	0	0	0	
4000 ppm	10	0	0	8	0	2	0	0	**	0	0	1	8	1	0	*	10	0	0	0	0	0		3	3	3	1	0	0		10	0	0	0	0	
5000 ppm	10	0	2	6	2	0	0	0	**	0	0	4	6	0	0		10	0	0	0	0	0		4	1	4	1	0	0	*	10	0	0	0	0	

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

STUDY NO. : 0352 URINALYSIS
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

Group Name	NO. of Animals	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0	
500 ppm	10	10	0	0	0	0	
1000 ppm	10	10	0	0	0	0	
2000 ppm	10	10	0	0	0	0	
4000 ppm	10	10	0	0	0	0	
5000 ppm	10	10	0	0	0	0	

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

APPENDIX H 2

URINALYSIS : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0352 URINALYSIS
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	±	+	2+	3+	4+	CHI	Occult blood −	±	+	2+	3+	CHI
Control	10	0	0	0	0	6	4	0		0	0	5	5	0	0		10	0	0	0	0	0		5	5	0	0	0	0		10	0	0	0	0	
500 ppm	10	0	0	1	2	2	5	0		0	0	8	2	0	0		10	0	0	0	0	0		2	8	0	0	0	0		10	0	0	0	0	
1000 ppm	10	0	2	3	2	1	2	0	*	0	0	2	8	0	0		10	0	0	0	0	0		1	7	2	0	0	0		10	0	0	0	0	
2000 ppm	10	0	1	4	5	0	0	0	**	0	0	1	9	0	0		10	0	0	0	0	0		0	7	3	0	0	0	*	10	0	0	0	0	
4000 ppm	10	0	0	9	1	0	0	0	**	0	0	0	10	0	0	**	10	0	0	0	0	0		0	8	2	0	0	0	*	10	0	0	0	0	
5000 ppm	10	0	1	4	4	1	0	0	**	0	0	1	9	0	0		10	0	0	0	0	0		1	7	2	0	0	0		10	0	0	0	0	

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

STUDY NO. : 0352 URINALYSIS
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

Group Name	NO. of Animals	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0	
500 ppm	10	10	0	0	0	0	
1000 ppm	10	10	0	0	0	0	
2000 ppm	10	10	0	0	0	0	
4000 ppm	10	10	0	0	0	0	
5000 ppm	10	10	0	0	0	0	

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

APPENDIX I 1

GROSS FINDINGS : SUMMARY, MOUSE : MALE ALL ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
ALL ANIMALS (0- 14W)

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	500 ppm 10 (%)	1000 ppm 10 (%)	2000 ppm 10 (%)
spleen	black zone		0 (0)	1 (10)	0 (0)	1 (10)
kidney	hydronephrosis		0 (0)	1 (10)	0 (0)	0 (0)

Organ	Findings	Group Name NO. of Animals	4000 ppm 10 (%)	5000 ppm 10 (%)
spleen	black zone		0 (0)	1 (10)
kidney	hydronephrosis		0 (0)	0 (0)

APPENDIX I 2

GROSS FINDINGS : SUMMARY, MOUSE : FEMALE ALL ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
ALL ANIMALS (0- 14W)

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	500 ppm 10 (%)	1000 ppm 10 (%)	2000 ppm 10 (%)
spleen	black zone		1 (10)	0 (0)	1 (10)	0 (0)
ovary	cyst		0 (0)	1 (10)	1 (10)	2 (20)

Organ	Findings	Group Name	4000 ppm	5000 ppm
		NO. of Animals	10 (%)	10 (%)
spleen	black zone		0 (0)	0 (0)
ovary	cyst		0 (0)	0 (0)

APPENDIX J 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (14W)

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	30.8± 2.1	0.038± 0.007	0.011± 0.002	0.209± 0.040	0.151± 0.013	0.168± 0.019
500 ppm	10	29.4± 2.3	0.037± 0.007	0.011± 0.002	0.220± 0.044	0.149± 0.008	0.164± 0.009
1000 ppm	10	28.1± 1.8**	0.034± 0.006	0.010± 0.003	0.231± 0.022	0.149± 0.014	0.158± 0.008
2000 ppm	10	26.8± 1.4**	0.034± 0.004	0.010± 0.003	0.226± 0.020	0.143± 0.004	0.157± 0.010
4000 ppm	10	24.3± 1.7**	0.030± 0.007*	0.010± 0.002	0.216± 0.023	0.145± 0.013	0.150± 0.008*
5000 ppm	10	23.8± 0.9**	0.031± 0.003	0.010± 0.002	0.179± 0.045	0.135± 0.012	0.152± 0.008

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

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (14W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.420± 0.023	0.048± 0.005	1.184± 0.044	0.442± 0.009
500 ppm	10	0.460± 0.141	0.048± 0.005	1.149± 0.069	0.431± 0.014
1000 ppm	10	0.402± 0.030	0.047± 0.003	1.167± 0.089	0.428± 0.018
2000 ppm	10	0.415± 0.021	0.046± 0.008	1.187± 0.060	0.438± 0.011
4000 ppm	10	0.422± 0.019	0.046± 0.008	1.179± 0.126	0.433± 0.019
5000 ppm	10	0.421± 0.015	0.044± 0.007	1.213± 0.054	0.427± 0.014

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

APPENDIX J 2

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (14W)

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	21.6± 1.7	0.038± 0.004	0.014± 0.001	0.032± 0.006	0.126± 0.009	0.157± 0.009
500 ppm	10	21.3± 0.8	0.037± 0.005	0.013± 0.001	0.030± 0.009	0.132± 0.010	0.156± 0.008
1000 ppm	10	21.3± 1.1	0.041± 0.007	0.013± 0.001	0.033± 0.010	0.128± 0.006	0.159± 0.009
2000 ppm	10	21.1± 0.8	0.041± 0.007	0.013± 0.002	0.031± 0.007	0.128± 0.009	0.155± 0.017
4000 ppm	10	20.9± 0.8	0.040± 0.007	0.013± 0.002	0.026± 0.007	0.119± 0.008	0.149± 0.010
5000 ppm	10	20.5± 1.0	0.039± 0.005	0.012± 0.002	0.025± 0.007	0.121± 0.011	0.144± 0.010*

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

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (14W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.281± 0.014	0.057± 0.008	0.927± 0.090	0.462± 0.015
500 ppm	10	0.287± 0.015	0.052± 0.005	0.941± 0.057	0.458± 0.017
1000 ppm	10	0.309± 0.010	0.054± 0.005	0.946± 0.048	0.460± 0.012
2000 ppm	10	0.319± 0.013**	0.052± 0.006	0.982± 0.056	0.457± 0.017
4000 ppm	10	0.334± 0.028**	0.049± 0.004*	1.000± 0.044*	0.439± 0.017*
5000 ppm	10	0.334± 0.026**	0.048± 0.006**	1.044± 0.064**	0.429± 0.027**

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

APPENDIX K 1

ORGAN WEIGHT, RELATIVE : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (14W)

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	30.8± 2.1	0.122± 0.020	0.034± 0.007	0.677± 0.116	0.493± 0.065	0.546± 0.064
500 ppm	10	29.4± 2.3	0.125± 0.019	0.036± 0.006	0.750± 0.150	0.509± 0.040	0.560± 0.047
1000 ppm	10	28.1± 1.8**	0.120± 0.022	0.036± 0.012	0.827± 0.103	0.529± 0.029	0.564± 0.031
2000 ppm	10	26.8± 1.4**	0.125± 0.013	0.039± 0.010	0.848± 0.101*	0.533± 0.023	0.587± 0.037
4000 ppm	10	24.3± 1.7**	0.120± 0.023	0.040± 0.009	0.888± 0.093**	0.598± 0.056**	0.619± 0.038**
5000 ppm	10	23.8± 0.9**	0.130± 0.012	0.042± 0.010	0.754± 0.196	0.569± 0.050**	0.640± 0.036**

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

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (14W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.368± 0.092	0.157± 0.018	3.857± 0.232	1.441± 0.116
500 ppm	10	1.601± 0.652	0.165± 0.019	3.924± 0.216	1.475± 0.141
1000 ppm	10	1.432± 0.081	0.166± 0.013	4.152± 0.144**	1.527± 0.080
2000 ppm	10	1.553± 0.096**	0.172± 0.029	4.437± 0.147**	1.639± 0.094**
4000 ppm	10	1.740± 0.117**	0.190± 0.046	4.835± 0.246**	1.786± 0.112**
5000 ppm	10	1.770± 0.100**	0.184± 0.028	5.092± 0.193**	1.795± 0.079**

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

APPENDIX K 2

ORGAN WEIGHT, RELATIVE : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (14W)

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	21.6± 1.7	0.178± 0.018	0.063± 0.006	0.147± 0.027	0.587± 0.052	0.730± 0.059
500 ppm	10	21.3± 0.8	0.173± 0.021	0.062± 0.006	0.142± 0.039	0.620± 0.042	0.732± 0.039
1000 ppm	10	21.3± 1.1	0.193± 0.024	0.061± 0.007	0.153± 0.050	0.604± 0.046	0.750± 0.048
2000 ppm	10	21.1± 0.8	0.193± 0.030	0.061± 0.011	0.147± 0.031	0.608± 0.041	0.736± 0.081
4000 ppm	10	20.9± 0.8	0.191± 0.027	0.060± 0.010	0.123± 0.030	0.569± 0.036	0.710± 0.035
5000 ppm	10	20.5± 1.0	0.190± 0.026	0.060± 0.007	0.119± 0.033	0.591± 0.041	0.701± 0.041

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

STUDY NO. : 0352
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (14W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.308± 0.091	0.262± 0.026	4.291± 0.119	2.152± 0.157
500 ppm	10	1.351± 0.072	0.244± 0.021	4.424± 0.214	2.153± 0.105
1000 ppm	10	1.455± 0.096**	0.253± 0.015	4.448± 0.156	2.166± 0.134
2000 ppm	10	1.510± 0.062**	0.247± 0.024	4.651± 0.201**	2.167± 0.118
4000 ppm	10	1.594± 0.126**	0.233± 0.021*	4.774± 0.107**	2.096± 0.075
5000 ppm	10	1.630± 0.089**	0.234± 0.024*	5.095± 0.205**	2.094± 0.084

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

APPENDIX L 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : MALE : ALL ANIMALS

(13-WEEK STUDY)

Organ	Findings	Group Name	Control				500 ppm				1000 ppm				2000 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
{Respiratory system}																		
lung			<10>				<10>				<10>				<10>			
	granulation		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}																		
bone marrow			< 9>				< 9>				<10>				<10>			
	hyperplasia:vascular		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(11)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thymus			<10>				<10>				<10>				<10>			
	atrophy		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)	(10)	(0)	(0)	(0)
spleen			<10>				<10>				<10>				<10>			
	deposit of melanin		0	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)
{Digestive system}																		
liver			<10>				<10>				<10>				<10>			
	granulation		2	0	0	0	5	0	0	0	2	0	0	0	1	0	0	0
			(20)	(0)	(0)	(0)	(50)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(10)	(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				5000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
lung			<10>				<10>			
	granulation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}										
bone marrow			<10>				<10>			
	hyperplasia:vascular		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thymus			<10>				<10>			
	atrophy		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen			<10>				<10>			
	deposit of melanin		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Digestive system}										
liver			<10>				<10>			
	granulation		3	0	0	0	2	0	0	0
			(30)	(0)	(0)	(0)	(20)	(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	Control				500 ppm				1000 ppm				2000 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
pancreas			<10>				<10>				<10>				<10>			
	necrosis:focal		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)	(10)	(0)	(0)	(0)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	basophilic change		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hydronephrosis		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:papilla		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
ureter			<10>				<10>				<10>				<10>			
	inflammatory polyp		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Reproductive system}																		
testis			<10>				<10>				<10>				<10>			
	atrophy		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(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				5000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
pancreas			<10>				<10>			
	necrosis:focal		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Urinary system}										
kidney			<10>				<10>			
	basophilic change		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hydronephrosis		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:papilla		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
ureter			<10>				<10>			
	inflammatory polyp		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Reproductive system}										
testis			<10>				<10>			
	atrophy		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(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	Control				500 ppm				1000 ppm				2000 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Nervous system}																		
spinal cord			<10>				<10>				<10>				<10>			
	epidermal cyst		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(10)	(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				5000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Nervous system}										
spinal cord			<10>				< 9>			
	epidermal cyst		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

APPENDIX L 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : FEMALE: ALL ANIMALS

(13-WEEK STUDY)

Organ	Findings	Group Name	Control				500 ppm				1000 ppm				2000 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}																		
spleen			<10>				<10>				<10>				<10>			
	deposit of melanin		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}																		
liver			<10>				<10>				<10>				<10>			
	granulation		6	0	0	0	3	0	0	0	6	0	0	0	4	0	0	0
			(60)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(60)	(0)	(0)	(0)	(40)	(0)	(0)	(0)
	perivascular inflammation		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)	(10)	(0)	(0)	(0)
{Endocrine system}																		
parathyroid			< 9>				<10>				<10>				< 8>			
	cyst		1	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0
			(11)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Nervous system}																		
spinal cord			<10>				<10>				<10>				<10>			
	epidermal cyst		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				5000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
spleen			<10>				<10>			
	deposit of melanin		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}										
liver			<10>				<10>			
	granulation		5	0	0	0	7	0	0	0
			(50)	(0)	(0)	(0)	(70)	(0)	(0)	(0)
	perivascular inflammation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Endocrine system}										
parathyroid			< 7>				< 8>			
	cyst		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Nervous system}										
spinal cord			<10>				<10>			
	epidermal cyst		1	0	0	0	0	0	0	0
			(10)	(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

APPENDIX M 1

IDENTITY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE IN THE 13-WEEK DRINKING WATER STUDY

IDENTITY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE IN THE 13-WEEK DRINKING WATER STUDY

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

Lot No. : WTE0491

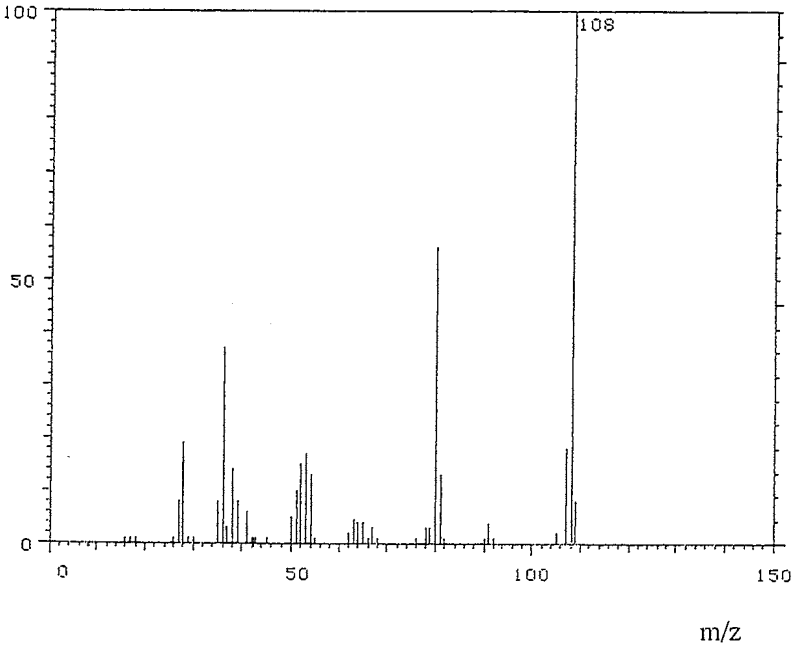
1. Spectral Data

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 $(NH_2C_6H_4NH_2 \cdot 2HCl) - (2HCl)$

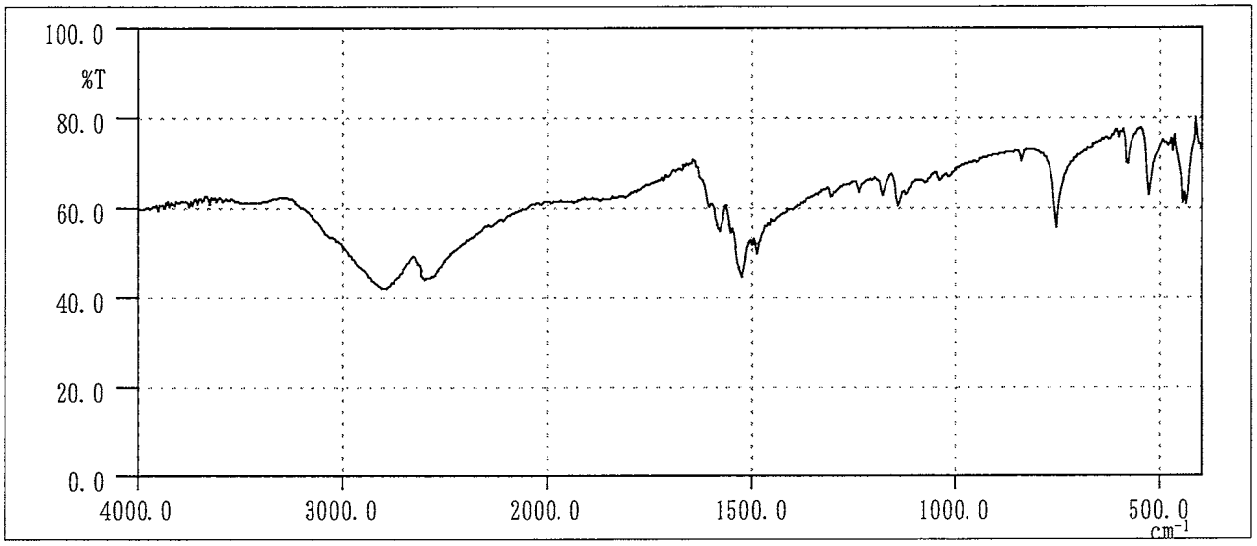
Results: The mass spectrum was consistent with calculated spectrum.

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 M 2

STABILITY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE IN THE 13-WEEK DRINKING WATER STUDY

STABILITY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE IN THE 13-WEEK DRINKING WATER STUDY

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

Lot No. : WTE0491

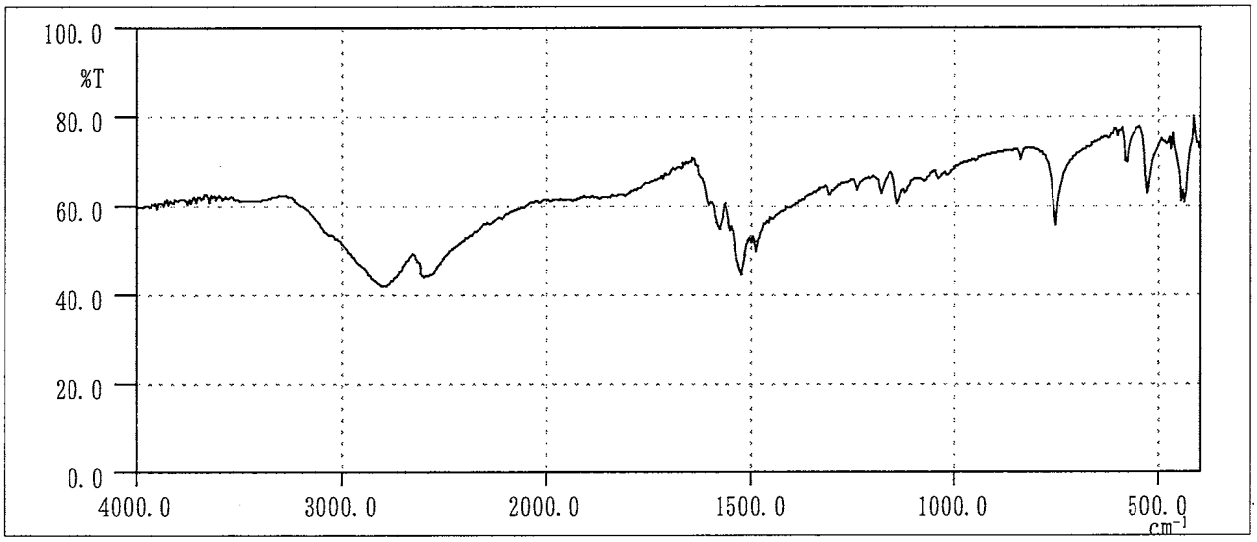
1. Sample : This lot was used from 1998.3.2 to 1998.6.3. Test substance was stored in cold storage in a dark place.

2. Infrared Spectrometry

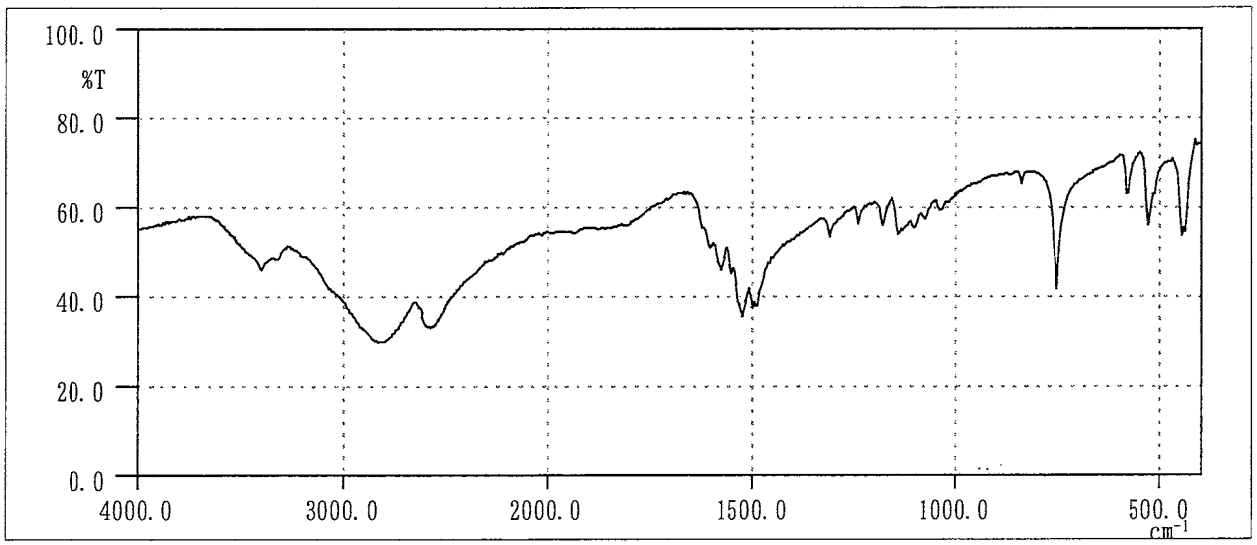
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr

Resolution : 2 cm^{-1}



Infrared Spectrum of Test Substance (date analyzed : 1998.02.18)



Infrared Spectrum of Test Substance (date analyzed : 1998.06.10)

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 (%)
1998.02.18	1	3.022	100
1998.06.10	1	2.917	100

Results: High performance liquid chromatography indicated one major peak (peak No.1) analyzed on 1998.2.18 and one major peak (peak No.1) analyzed on 1998.6.10. No new trace impurity peak in the test substance analyzed on 1998.6.10 was detected.

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

APPENDIX M 3

CONCENTMOUSEION OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE IN FORMULATED WATER IN THE 13-WEEK DRINKING WATER STUDY

CONCENTRATION OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE IN FORMULATED WATER IN THE 13-WEEK DRINKING WATER STUDY

	Target Concentration				
Date Analyzed	500[a]	1000	2000	4000	5000
1998.03.02	495 (99.0)[b]	989 (98.9)	1960 (98.0)	3920 (98.0)	4890 (97.8)

[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 $\times$ 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 M 4

STABILITY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE IN FORMULATED WATER IN THE 13-WEEK DRINKING WATER STUDY

STABILITY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE IN FORMULATED WATER IN THE 13-WEEK DRINKING WATER STUDY

		Target Concentration	
Date Prepared	Date Analyzed	500[a]	5000
1998.02.09	1998.02.09	503 (100)[b]	4900 (100)
	1998.02.13[c]	485 (96.4)	4850 (99.0)

[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

METHODS FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE

METHODS FOR HEMATOLOGY,BIOCHEMISTRY AND URINALYSIS IN THE 13-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]
Triglyceride	Enzymatic method (LPL･GK･GPO･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]
Alkaline phosphatase (ALP)	GSCC 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]
Urinalysis	
pH,Protein,Glucose,Ketone body,Occult Blood, Urobilinogen	Urinalysis reagent paper method [4]

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.)

4) Ames reagent strips for urinalysis (Uro-Labstix : Bayer-Sankyo Co.,Ltd.)

APPENDIX O 1

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-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
Triglyceride	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
Alkaline phosphatase (ALP)	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