o-フェニレンジアミン二塩酸塩のラットを用いた
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：０３５１

APPENDIXES

APPENDIXES

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
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
SOILED PERI GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	250 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	1	1	1	1	1	1	1	1	1	1	1
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	7	3	4	5	3	4	1	2	2	2	2
EXOPHTHALMOS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	500 ppm	0	1	1	1	1	1	1	1	1	1	1	1	1
	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
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
EYE OPACITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	500 ppm	0	1	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
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
CORNEAL OPACITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	500 ppm	0	1	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
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
NOSE HEMORRHAGIC DISCHA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	250 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
	3000 ppm	1	1	0	0	0	0	0	0	0	0	0	0	0
RED URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	250 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	1	1	1	1	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0

APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

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
DEATH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	250 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
	3000 ppm	1	2	2	2	2	2	2	2	2	2	2	2	2
HUNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	250 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
	3000 ppm	0	0	0	0	0	0	1	1	1	1	1	0	0
SOILED PERI GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	250 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	1	0	0	1	1	1
	2000 ppm	0	0	4	4	4	6	4	6	6	6	6	6	7
	3000 ppm	9	8	8	8	8	8	8	8	8	8	8	8	8
NOSE HEMORRHAGIC DISCHA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	250 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
	3000 ppm	9	8	0	0	0	0	0	0	0	0	0	0	0
SMALL STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	250 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
	3000 ppm	0	0	0	0	0	0	0	0	2	2	1	0	0

APPENDIX B 1

BODY WEIGHT CHANGES :SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
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	122± 3	151± 5	182± 7	207± 10	226± 11	244± 11	257± 12
250 ppm	122± 3	152± 5	185± 7	211± 8	232± 10	247± 10	260± 11
500 ppm	122± 3	151± 5	182± 7	205± 6	226± 7	241± 8	254± 8
1000 ppm	122± 3	146± 5	174± 7	198± 8	217± 10	232± 10*	242± 11*
2000 ppm	122± 4	138± 2**	167± 4**	189± 6**	206± 7**	219± 7**	230± 8**
3000 ppm	122± 3	124± 9**	147± 13**	166± 13**	182± 13**	196± 15**	205± 15**

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

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
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	269± 13	281± 14	290± 14	299± 15	306± 13	313± 14	316± 14
250 ppm	272± 11	284± 12	293± 12	301± 13	308± 14	313± 15	317± 17
500 ppm	266± 8	277± 9	287± 10	294± 10	301± 9	307± 10	310± 10
1000 ppm	253± 12*	263± 12**	271± 13*	277± 13**	282± 13**	287± 14**	291± 14**
2000 ppm	237± 10**	246± 11**	254± 13**	260± 12**	265± 13**	268± 14**	271± 15**
3000 ppm	214± 16**	222± 17**	229± 18**	236± 18**	239± 19**	243± 18**	246± 18**

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

APPENDIX B 2

BODY WEIGHT CHANGES : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
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	99± 3	115± 6	129± 4	137± 5	146± 5	153± 6	158± 7
250 ppm	99± 2	115± 3	126± 3	135± 3	143± 4	149± 4	154± 5
500 ppm	99± 3	112± 2	123± 2	133± 4	140± 4*	145± 6*	150± 7
1000 ppm	99± 3	108± 3*	120± 4**	128± 5**	136± 6**	141± 7**	145± 7**
2000 ppm	99± 3	103± 3**	113± 4**	121± 4**	125± 4**	130± 5**	131± 6**
3000 ppm	99± 3	76± 8**	87± 8**	100± 5**	106± 5**	108± 8**	108± 8**

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

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
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	163± 7	168± 8	172± 8	178± 8	179± 8	182± 8	183± 8
250 ppm	157± 5	161± 5	164± 5	168± 5	171± 4	172± 7*	175± 6
500 ppm	156± 8	158± 8	162± 9*	166± 10*	168± 10*	170± 9**	170± 9**
1000 ppm	149± 7**	151± 8**	156± 7**	158± 8**	160± 7**	163± 8**	163± 7**
2000 ppm	135± 6**	135± 9**	139± 8**	142± 8**	145± 7**	146± 8**	148± 8**
3000 ppm	109± 11**	112± 11**	113± 10**	114± 14**	120± 11**	121± 8**	122± 8**

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

APPENDIX C 1

WATER CONSUMPTION CHANGES : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
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	17.2± 0.9	19.2± 1.4	19.7± 1.5	20.0± 1.3	19.0± 1.4	19.2± 1.6	18.0± 1.4
250 ppm	17.0± 1.2	19.7± 1.7	19.0± 1.5	19.8± 1.5	19.2± 2.0	19.2± 1.9	17.8± 1.4
500 ppm	14.9± 0.9	16.1± 0.9	16.6± 0.7	17.4± 0.6**	17.1± 0.9	17.1± 0.9	16.5± 0.9
1000 ppm	14.4± 3.3*	15.7± 3.7*	16.1± 4.0**	15.9± 0.7**	16.4± 3.7*	16.1± 3.9*	15.5± 4.3*
2000 ppm	12.4± 0.6**	13.4± 0.8**	14.3± 0.8**	14.9± 1.0**	13.7± 1.1**	13.8± 1.0**	13.5± 1.3**
3000 ppm	9.8± 2.0**	11.6± 1.0**	12.4± 1.2**	13.2± 1.2**	12.8± 1.4**	12.6± 1.3**	12.3± 1.2**

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

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
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	18.4± 1.6	18.2± 1.0	18.4± 1.7	17.7± 1.1	17.5± 1.2	17.2± 1.4
250 ppm	18.1± 1.8	17.9± 1.5	17.7± 1.5	17.7± 1.5	17.1± 1.5	17.6± 1.2
500 ppm	16.0± 1.0	16.0± 0.8	15.8± 0.8	15.4± 0.7	15.6± 0.8	15.4± 0.9
1000 ppm	15.7± 3.9*	15.6± 4.2*	15.4± 4.6*	14.6± 4.1*	14.3± 4.1**	15.0± 4.1*
2000 ppm	12.9± 1.2**	12.8± 1.0**	12.7± 1.0**	12.2± 0.9**	12.2± 1.1**	12.6± 0.6**
3000 ppm	11.8± 1.4**	13.3± 3.8**	14.5± 5.0**	11.5± 1.5**	11.6± 1.3**	11.8± 1.1**

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

APPENDIX C 2

WATER CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
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	14.9± 1.7	16.0± 1.5	16.2± 2.0	15.7± 1.6	17.8± 4.8	17.0± 3.5	17.1± 4.0
250 ppm	15.2± 0.8	15.3± 1.1	15.8± 1.7	16.1± 4.3	16.6± 4.5	15.1± 1.9	16.9± 5.5
500 ppm	14.2± 3.5	13.4± 1.0**	13.4± 1.0	14.1± 2.5	16.4± 10.4	13.7± 2.5	13.3± 1.8
1000 ppm	11.0± 0.8*	11.3± 0.9**	11.2± 1.3**	11.4± 1.1**	11.1± 0.9**	10.7± 0.8**	10.6± 0.6**
2000 ppm	9.8± 0.5**	9.7± 0.6**	9.7± 0.4**	9.7± 0.7**	9.5± 0.4**	9.1± 0.7**	9.0± 0.5**
3000 ppm	3.8± 1.7**	8.0± 1.4**	7.8± 0.7**	7.9± 0.9**	6.9± 0.7**	7.0± 0.4**	6.5± 0.6**

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

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
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	19.1± 7.8	18.7± 7.1	23.3± 13.4	16.9± 5.1	19.9± 9.1	18.7± 8.3
250 ppm	18.3± 9.2	16.8± 4.7	17.5± 6.0	18.9± 8.8	15.4± 3.4	16.1± 4.2
500 ppm	12.4± 1.4	12.1± 0.8	12.7± 0.8	12.4± 0.6	12.4± 1.2	12.0± 0.5
1000 ppm	9.8± 0.8**	10.1± 0.8**	10.1± 1.0**	9.9± 1.0**	10.2± 1.0**	10.3± 1.1**
2000 ppm	8.2± 0.4**	9.8± 3.4**	8.9± 0.8**	8.4± 0.7**	8.6± 0.6**	8.7± 0.9**
3000 ppm	6.2± 0.5**	6.3± 1.1**	6.3± 1.0**	7.1± 0.6**	6.8± 0.8**	6.8± 0.5**

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

APPENDIX D 1

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
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	13.8± 0.4	15.7± 0.9	15.5± 1.0	16.3± 0.9	16.0± 0.6	15.6± 0.8	15.7± 1.0
250 ppm	13.4± 0.5	15.4± 0.6	15.4± 0.9	16.4± 0.9	15.7± 0.6	15.7± 1.0	15.7± 1.2
500 ppm	13.0± 0.5	14.7± 0.7*	14.9± 0.4	15.6± 0.6	15.4± 0.6	15.2± 0.5	15.6± 0.8
1000 ppm	12.4± 0.8*	14.1± 0.6**	14.8± 1.0	15.6± 1.2	15.2± 0.9	14.8± 0.9	15.0± 1.1
2000 ppm	11.0± 0.3**	13.3± 0.5**	14.2± 0.6**	14.7± 0.9**	14.6± 0.8**	14.4± 0.8*	14.3± 1.1*
3000 ppm	9.1± 1.1**	11.7± 1.1**	12.8± 0.8**	13.6± 0.9**	14.0± 1.2**	13.9± 1.2**	14.2± 1.2*

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

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
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	15.8± 1.3	15.9± 1.2	15.9± 1.0	15.8± 1.0	15.5± 0.8	15.4± 1.0
250 ppm	16.0± 1.0	15.7± 1.2	15.6± 1.4	15.7± 1.1	15.0± 1.1	15.0± 1.1
500 ppm	15.6± 0.6	15.5± 0.7	15.2± 0.7	15.3± 0.6	15.0± 0.5	14.7± 0.5
1000 ppm	15.0± 0.9	15.2± 0.9	15.1± 1.1	14.8± 1.0	14.4± 1.1	14.6± 1.1
2000 ppm	14.7± 1.3	14.4± 1.3*	14.3± 1.0**	14.3± 1.3**	14.2± 1.2*	14.1± 1.1
3000 ppm	14.2± 1.1**	14.3± 1.4**	14.6± 1.1*	14.1± 1.0**	14.3± 1.1*	14.5± 1.0

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

APPENDIX D 2

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
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	11.2± 0.7	11.6± 0.6	10.8± 0.6	11.2± 0.5	11.1± 0.6	10.9± 0.6	11.1± 0.6
250 ppm	11.2± 0.5	11.0± 0.4	11.1± 0.3	11.0± 0.3	10.6± 0.4	10.3± 0.6	10.5± 0.4
500 ppm	10.5± 0.3	10.8± 0.4	10.8± 0.7	10.8± 0.6	10.5± 0.8	10.5± 0.6	10.3± 0.8*
1000 ppm	9.8± 0.5*	10.3± 0.7*	10.4± 1.0	10.2± 1.0**	10.2± 1.0*	9.8± 0.8**	9.9± 0.7**
2000 ppm	8.3± 0.7**	9.3± 0.5**	9.6± 0.5*	9.3± 0.5**	9.5± 0.5**	8.8± 0.6**	9.1± 0.5**
3000 ppm	4.5± 1.2**	7.1± 1.0**	8.5± 0.4**	8.4± 0.7**	7.7± 1.0**	7.5± 0.7**	7.8± 0.9**

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

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
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	11.0± 0.7	11.1± 0.6	11.4± 0.7	11.0± 0.6	11.0± 0.5	10.9± 0.7
250 ppm	10.4± 0.6	10.5± 0.6	10.5± 0.5*	10.6± 0.5	10.2± 0.5*	10.4± 0.5
500 ppm	10.4± 0.7	10.4± 0.8	10.4± 0.7**	10.3± 0.5*	10.1± 0.4**	9.9± 0.3**
1000 ppm	9.9± 0.6**	10.0± 0.6**	9.8± 0.8**	9.8± 0.7**	9.7± 0.6**	9.7± 0.6**
2000 ppm	8.9± 0.6**	9.4± 0.4**	9.3± 0.4**	9.4± 0.4**	9.4± 0.5**	9.6± 0.4**
3000 ppm	8.2± 0.8**	8.4± 0.5**	8.1± 1.1**	8.9± 0.6**	8.7± 0.9**	8.6± 0.4**

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

APPENDIX E 1

CHEMICAL INTAKE CHANGES : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
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
250 ppm	0.028± 0.001	0.027± 0.002	0.022± 0.001	0.021± 0.001	0.019± 0.001	0.018± 0.001	0.016± 0.001
500 ppm	0.049± 0.003	0.045± 0.003	0.041± 0.002	0.039± 0.002	0.035± 0.002	0.034± 0.002	0.031± 0.002
1000 ppm	0.098± 0.024	0.090± 0.023	0.082± 0.021	0.073± 0.003	0.071± 0.018	0.067± 0.018	0.061± 0.018
2000 ppm	0.180± 0.007	0.161± 0.008	0.152± 0.008	0.145± 0.011	0.126± 0.009	0.120± 0.007	0.113± 0.008
3000 ppm	0.235± 0.038	0.238± 0.011	0.224± 0.013	0.218± 0.014	0.196± 0.010	0.184± 0.011	0.173± 0.008

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
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
250 ppm	0.016± 0.001	0.015± 0.001	0.015± 0.001	0.014± 0.001	0.014± 0.001	0.014± 0.001
500 ppm	0.029± 0.002	0.028± 0.001	0.027± 0.002	0.026± 0.002	0.026± 0.001	0.025± 0.001
1000 ppm	0.060± 0.016	0.058± 0.017	0.056± 0.017	0.052± 0.015	0.050± 0.015	0.052± 0.015
2000 ppm	0.104± 0.006	0.101± 0.004	0.098± 0.005	0.092± 0.004	0.091± 0.005	0.093± 0.004
3000 ppm	0.160± 0.010	0.174± 0.048	0.186± 0.068	0.144± 0.013	0.143± 0.009	0.144± 0.008

APPENDIX E 2

CHEMICAL INTAKE CHANGES : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
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
250 ppm	0.033± 0.002	0.031± 0.002	0.029± 0.003	0.029± 0.008	0.028± 0.008	0.025± 0.003	0.027± 0.009
500 ppm	0.064± 0.015	0.054± 0.004	0.051± 0.003	0.050± 0.008	0.056± 0.034	0.046± 0.007	0.043± 0.005
1000 ppm	0.102± 0.008	0.094± 0.006	0.087± 0.007	0.084± 0.006	0.079± 0.004	0.074± 0.005	0.071± 0.003
2000 ppm	0.191± 0.011	0.172± 0.009	0.161± 0.004	0.155± 0.013	0.147± 0.010	0.139± 0.011	0.134± 0.010
3000 ppm	0.145± 0.057	0.278± 0.059	0.235± 0.020	0.221± 0.019	0.191± 0.013	0.196± 0.018	0.179± 0.011

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
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
250 ppm	0.029± 0.015	0.025± 0.007	0.026± 0.009	0.027± 0.013	0.022± 0.005	0.023± 0.006
500 ppm	0.039± 0.004	0.038± 0.002	0.038± 0.003	0.037± 0.002	0.037± 0.004	0.035± 0.001
1000 ppm	0.065± 0.004	0.065± 0.005	0.064± 0.005	0.062± 0.005	0.062± 0.005	0.063± 0.006
2000 ppm	0.122± 0.007	0.141± 0.046	0.126± 0.019	0.117± 0.010	0.118± 0.010	0.118± 0.010
3000 ppm	0.166± 0.013	0.169± 0.039	0.167± 0.016	0.179± 0.026	0.169± 0.029	0.168± 0.017

APPENDIX F 1

HEMATOLOGY : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
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 f ℓ	MCH p g	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	10	9.42± 0.29	15.8± 0.5	46.9± 1.4	49.8± 0.7	16.7± 0.2	33.6± 0.5	687± 41
250 ppm	10	9.34± 0.25	15.7± 0.3	46.4± 0.9	49.6± 0.8	16.8± 0.1	33.8± 0.5	661± 38
500 ppm	10	9.16± 0.22	15.5± 0.4	45.7± 1.2	49.9± 0.7	16.9± 0.3	33.9± 0.7	660± 39
1000 ppm	10	9.14± 0.25	15.4± 0.6	45.7± 1.2	50.0± 0.9	16.9± 0.3	33.7± 0.6	650± 65
2000 ppm	10	8.83± 0.28**	15.2± 0.5	44.9± 1.4**	50.8± 0.8*	17.3± 0.4**	34.0± 0.4	647± 52
3000 ppm	10	8.75± 0.28**	15.3± 0.4	45.1± 1.0**	51.6± 1.0**	17.5± 0.3**	33.9± 0.4	644± 64

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

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RETICULOCYTE ‰	PROTHROMBIN TIME sec	APTT sec
Control	10	28± 7	12.1± 0.8	23.5± 1.5
250 ppm	10	28± 5	12.4± 0.9	23.5± 2.7
500 ppm	10	27± 6	12.0± 0.6	22.6± 3.1
1000 ppm	10	29± 6	12.0± 0.8	23.1± 2.0
2000 ppm	10	26± 7	12.0± 0.6	23.0± 2.4
3000 ppm	10	27± 5	11.8± 0.7	22.5± 1.2

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

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
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	10	4.15±	2.25	0±	0	33±	10	1±	1	0±	0	3±	2	62±	10	1±	1
250 ppm	10	4.15±	2.39	0±	0	32±	10	1±	1	0±	0	4±	1	62±	10	1±	1
500 ppm	10	3.28±	1.91	0±	0	30±	9	1±	1	0±	0	4±	2	63±	9	1±	1
1000 ppm	10	3.68±	2.52	0±	0	36±	12	1±	1	0±	0	3±	1	59±	12	1±	1
2000 ppm	10	4.39±	2.06	0±	0	29±	7	1±	1	0±	0	4±	1	64±	7	1±	1
3000 ppm	10	5.28±	3.26	0±	0	29±	7	1±	1	0±	0	5±	1	64±	8	1±	1

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

APPENDIX F 2

HEMATOLOGY : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
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 fℓ	MCH pg	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	10	8.52± 0.30	15.6± 0.5	44.8± 1.4	52.6± 0.5	18.3± 0.2	34.8± 0.6	716± 83
250 ppm	10	8.69± 0.26	15.7± 0.4	45.5± 1.3	52.3± 0.8	18.1± 0.2	34.5± 0.7	714± 54
500 ppm	10	8.56± 0.26	15.5± 0.5	44.6± 1.5	52.1± 0.5	18.1± 0.1	34.7± 0.6	711± 81
1000 ppm	10	8.42± 0.25	15.4± 0.5	44.3± 1.5	52.6± 0.6	18.3± 0.1	34.8± 0.4	682± 80
2000 ppm	10	8.22± 0.23	15.4± 0.5	44.4± 1.0	54.1± 0.9**	18.7± 0.2**	34.6± 0.6	630± 78*
3000 ppm	8	8.14± 0.37*	15.4± 0.6	44.5± 1.7	54.7± 0.7**	18.9± 0.3**	34.6± 0.6	505± 62**

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

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RETICULOCYTE ‰	PROTHROMBIN TIME sec	APTT sec
Control	10	21± 7	10.7± 0.2	18.3± 1.5
250 ppm	10	24± 4	10.9± 0.3	18.0± 1.0
500 ppm	10	22± 5	10.8± 0.4	18.7± 1.1
1000 ppm	10	24± 6	11.1± 0.4	19.6± 1.5
2000 ppm	10	24± 6	11.4± 0.4**	19.3± 1.4
3000 ppm	8	19± 4	11.6± 0.3**	19.4± 1.6

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

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE 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	10	2.28±	1.49	0±	0	33±	12	1±	1	0±	0	3±	2	63±	12	0±	0
250 ppm	10	1.91±	1.25	0±	1	31±	11	2±	1	0±	0	3±	2	64±	11	1±	1
500 ppm	10	1.96±	1.02	0±	0	29±	9	1±	1	0±	0	5±	2	64±	12	1±	2
1000 ppm	10	2.56±	1.80	1±	1	27±	9	2±	1	0±	0	4±	2	66±	12	1±	1
2000 ppm	10	2.66±	1.84	0±	0	29±	9	2±	1	0±	0	4±	2	65±	11	1±	1
3000 ppm	8	2.07±	1.34	1±	1	33±	9	1±	1	0±	0	4±	2	59±	10	2±	1**

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

APPENDIX G 1

BIOCHEMISTRY : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
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	10	6.3±	0.2	3.9±	0.1	1.6±	0.1	0.13±	0.01	170±	12	64±	5	65±	32
250 ppm	10	6.4±	0.1	3.9±	0.1	1.6±	0.1	0.12±	0.01	171±	12	66±	5	72±	33
500 ppm	10	6.3±	0.2	3.8±	0.1	1.6±	0.1	0.13±	0.01	174±	9	64±	3	68±	20
1000 ppm	10	6.2±	0.1	3.8±	0.1	1.6±	0.1	0.13±	0.01	171±	8	68±	2	87±	33
2000 ppm	10	6.2±	0.2	3.8±	0.1**	1.6±	0.1	0.13±	0.01	165±	7	70±	5*	82±	33
3000 ppm	10	6.1±	0.3**	3.7±	0.1**	1.6±	0.1	0.13±	0.01	159±	11	69±	5	82±	17

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

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
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	10	115± 10	76± 13	43± 5	176± 32	238± 17	1± 1	101± 9
250 ppm	10	121± 10	92± 34	50± 14	203± 70	237± 19	1± 1	95± 8
500 ppm	10	118± 5	75± 10	42± 3	176± 28	229± 15	1± 1	101± 13
1000 ppm	10	126± 7*	74± 10	41± 6	178± 27	228± 15	2± 1	96± 7
2000 ppm	10	129± 8**	63± 9	34± 3**	160± 38	221± 16	2± 1	98± 18
3000 ppm	10	128± 8**	64± 5	33± 3**	157± 36	226± 17	1± 1	106± 12

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

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	UREA NITROGEN mg/dl	CREATININE mg/dl	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dl	INORGANIC PHOSPHORUS mg/dl
Control	10	18.2± 1.4	0.5± 0.0	142± 1	4.3± 0.5	107± 1	10.3± 0.2	6.1± 0.7
250 ppm	10	18.2± 1.0	0.5± 0.0	142± 1	4.3± 0.4	107± 1	10.3± 0.2	6.0± 0.6
500 ppm	10	19.2± 1.8	0.5± 0.0	141± 1	4.3± 0.3	107± 1	10.2± 0.2	5.9± 0.6
1000 ppm	10	19.7± 3.7	0.5± 0.1	140± 1**	4.5± 0.3	105± 1	10.2± 0.2	6.0± 0.5
2000 ppm	10	21.7± 3.0*	0.5± 0.1	140± 1**	4.5± 0.3	106± 1	10.2± 0.2	6.0± 0.6
3000 ppm	10	24.4± 3.9**	0.5± 0.1	140± 1**	4.6± 0.4	106± 1	10.1± 0.2	6.1± 0.5

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

APPENDIX G 2

BIOCHEMISTRY : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
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	6.1± 0.2	3.8± 0.1	1.6± 0.1	0.14± 0.01	135± 10	71± 5	18± 3
250 ppm	10	6.1± 0.1	3.8± 0.1	1.6± 0.1	0.14± 0.02	133± 12	68± 5	16± 3
500 ppm	10	5.9± 0.1**	3.6± 0.2	1.6± 0.1	0.14± 0.01	137± 11	65± 5*	18± 3
1000 ppm	10	5.8± 0.2**	3.6± 0.1	1.7± 0.1	0.14± 0.01	133± 9	63± 5**	19± 4
2000 ppm	10	5.6± 0.2**	3.5± 0.1**	1.6± 0.1	0.14± 0.01	134± 8	55± 5**	21± 5
3000 ppm	8	5.5± 0.1**	3.4± 0.1**	1.7± 0.1	0.15± 0.01	139± 12	54± 6**	16± 2

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

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
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	132± 7	67± 16	36± 14	221± 77	163± 10	2± 1	111± 23
250 ppm	10	128± 9	72± 15	38± 11	285± 154	172± 16	2± 1	124± 40
500 ppm	10	121± 8*	71± 9	34± 4	289± 77	160± 10	2± 1	121± 19
1000 ppm	10	120± 11*	64± 7	31± 3	230± 74	165± 18	1± 1	118± 28
2000 ppm	10	108± 7**	72± 12	30± 4	273± 116	179± 24	2± 1	141± 40
3000 ppm	8	103± 12**	88± 5**	36± 3	299± 59	242± 30**	3± 1	147± 19

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

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	UREA NITROGEN mg/dl	CREATININE mg/dl	SODIUM mEq/l	POTASSIUM mEq/l	CHLORIDE mEq/l	CALCIUM mg/dl	INORGANIC PHOSPHORUS mg/dl
Control	10	18.5± 1.6	0.5± 0.0	141± 1	4.2± 0.4	107± 1	10.0± 0.1	5.5± 1.2
250 ppm	10	19.1± 1.8	0.5± 0.1	140± 1	4.4± 0.3	108± 2	10.0± 0.2	5.6± 1.2
500 ppm	10	18.5± 2.5	0.5± 0.1	140± 1	4.4± 0.4	108± 1	9.8± 0.2	5.4± 1.0
1000 ppm	10	19.8± 3.3	0.5± 0.0	139± 1*	4.5± 0.4	108± 1	9.8± 0.2	5.7± 0.8
2000 ppm	10	26.5± 7.4**	0.5± 0.1	139± 1**	4.6± 0.5	108± 2	9.7± 0.2	5.7± 0.5
3000 ppm	8	31.5± 4.0**	0.5± 0.0	140± 1	4.4± 0.5	110± 1**	9.5± 0.3**	5.8± 0.5

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

APPENDIX H 1

URINALYSIS : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0351 URINALYSIS
ANIMAL : RAT F344/DuCrj
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	Bilirubin −	+	2+	3+	CHI
Control	10	0	0	0	0	0	6	4		0	0	4	6	0	0		10	0	0	0	0	0		0	5	5	0	0	0		10	0	0	0	
250 ppm	10	0	0	0	0	0	7	3		0	0	7	3	0	0		10	0	0	0	0	0		0	7	3	0	0	0		10	0	0	0	
500 ppm	10	0	0	0	0	0	9	1		0	0	4	6	0	0		10	0	0	0	0	0		0	9	1	0	0	0		10	0	0	0	
1000 ppm	10	0	0	0	0	0	8	2		0	0	4	6	0	0		10	0	0	0	0	0		1	6	3	0	0	0		10	0	0	0	
2000 ppm	10	0	0	0	0	0	6	4		0	0	1	9	0	0		10	0	0	0	0	0		0	6	4	0	0	0		10	0	0	0	
3000 ppm	10	0	0	0	0	1	7	2		0	0	4	5	1	0		10	0	0	0	0	0		0	9	1	0	0	0		10	0	0	0	

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

STUDY NO. : 0351 URINALYSIS
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

Group Name	NO. of Animals	Occult blood −	±	+	2+	3+	CHI	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0		10	0	0	0	0	
250 ppm	10	10	0	0	0	0		10	0	0	0	0	
500 ppm	10	10	0	0	0	0		10	0	0	0	0	
1000 ppm	10	9	0	0	0	1		10	0	0	0	0	
2000 ppm	10	10	0	0	0	0		10	0	0	0	0	
3000 ppm	10	9	0	0	0	1		10	0	0	0	0	

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

APPENDIX H 2

URINALYSIS : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0351 URINALYSIS
ANIMAL : RAT F344/DuCrj
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	Bilirubin −	+	2+	3+	CHI
Control	10	0	0	0	0	0	7	3		0	1	7	2	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
250 ppm	10	0	0	0	0	0	6	4		0	1	8	1	0	0		10	0	0	0	0	0		9	1	0	0	0	0		10	0	0	0	
500 ppm	10	0	0	0	0	2	6	2		0	0	7	3	0	0		10	0	0	0	0	0		9	1	0	0	0	0		10	0	0	0	
1000 ppm	10	0	0	0	0	0	9	1		0	0	7	3	0	0		10	0	0	0	0	0		7	3	0	0	0	0		10	0	0	0	
2000 ppm	10	0	0	0	2	2	5	1		0	0	3	7	0	0		10	0	0	0	0	0		5	5	0	0	0	0	**	10	0	0	0	
3000 ppm	8	0	0	2	0	4	2	0	**	0	0	2	6	0	0		8	0	0	0	0	0		2	6	0	0	0	0	**	8	0	0	0	

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

STUDY NO. : 0351 URINALYSIS
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

Group Name	NO. of Animals	Occult blood −	±	+	2+	3+	CHI	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0		10	0	0	0	0	
250 ppm	10	10	0	0	0	0		10	0	0	0	0	
500 ppm	10	10	0	0	0	0		10	0	0	0	0	
1000 ppm	10	10	0	0	0	0		10	0	0	0	0	
2000 ppm	10	10	0	0	0	0		10	0	0	0	0	
3000 ppm	8	8	0	0	0	0		8	0	0	0	0	

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

APPENDIX I 1

GROSS FINDINGS : SUMMARY, RAT : MALE ALL ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	250 ppm 10 (%)	500 ppm 10 (%)	1000 ppm 10 (%)
liver	herniation		1 (10)	1 (10)	1 (10)	0 (0)
kidney	hydronephrosis		0 (0)	0 (0)	0 (0)	1 (10)

Organ	Findings	Group Name / NO. of Animals	2000 ppm 10 (%)	3000 ppm 10 (%)
liver	herniation		1 (10)	2 (20)
kidney	hydronephrosis		0 (0)	0 (0)

APPENDIX I 2

GROSS FINDINGS : SUMMARY, RAT : FEMALE ALL ANIMALS

(13-WEEK STUDY)

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	250 ppm 10 (%)	500 ppm 10 (%)	1000 ppm 10 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)
gl stomach	erosion		0 (0)	0 (0)	0 (0)	0 (0)
liver	herniation		1 (10)	0 (0)	1 (10)	1 (10)
kidney	nodule		1 (10)	0 (0)	0 (0)	0 (0)
ovary	cyst		1 (10)	0 (0)	0 (0)	0 (0)

Organ	Findings	Group Name NO. of Animals	2000 ppm 10 (%)	3000 ppm 10 (%)
thymus	atrophic		0 (0)	1 (10)
gl stomach	erosion		0 (0)	1 (10)
liver	herniation		3 (30)	1 (10)
kidney	nodule		0 (0)	0 (0)
ovary	cyst		0 (0)	0 (0)

APPENDIX I 3

GROSS FINDINGS : SUMMARY, RAT : FEMALE : SACRIFICED ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	250 ppm 10 (%)	500 ppm 10 (%)	1000 ppm 10 (%)
liver	herniation		1 (10)	0 (0)	1 (10)	1 (10)
kidney	nodule		1 (10)	0 (0)	0 (0)	0 (0)
ovary	cyst		1 (10)	0 (0)	0 (0)	0 (0)

Organ	Findings	Group Name NO. of Animals	2000 ppm 10 (%)	3000 ppm 8 (%)
liver	herniation		3 (30)	1 (13)
kidney	nodule		0 (0)	0 (0)
ovary	cyst		0 (0)	0 (0)

APPENDIX I 4

GROSS FINDINGS : SUMMARY, RAT : FEMALE

DEAD AND MORIBUND ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 14W)

Organ	Findings	Group Name NO. of Animals	Control 0 (%)	250 ppm 0 (%)	500 ppm 0 (%)	1000 ppm 0 (%)
thymus	atrophic		- (-)	- (-)	- (-)	- (-)
gl stomach	erosion		- (-)	- (-)	- (-)	- (-)

Organ	Findings	Group Name NO. of Animals	2000 ppm 0 (%)	3000 ppm 2 (%)
thymus	atrophic		- (-)	1 (50)
gl stomach	erosion		- (-)	1 (50)

APPENDIX J 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
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	294± 13	0.251± 0.038	0.053± 0.007	3.129± 0.111	0.917± 0.056	1.043± 0.029
250 ppm	10	296± 15	0.266± 0.032	0.060± 0.011	3.139± 0.103	0.911± 0.064	1.019± 0.044
500 ppm	10	290± 10	0.259± 0.042	0.052± 0.008	3.020± 0.218	0.911± 0.062	1.026± 0.046
1000 ppm	10	276± 14*	0.238± 0.032	0.054± 0.011	3.035± 0.071	0.890± 0.066	0.984± 0.022**
2000 ppm	10	256± 14**	0.204± 0.022**	0.052± 0.006	3.021± 0.114	0.818± 0.074**	0.956± 0.035**
3000 ppm	10	232± 17**	0.178± 0.021**	0.048± 0.007	2.951± 0.151*	0.772± 0.078**	0.925± 0.057**

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

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
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	1.827± 0.090	0.567± 0.024	7.468± 0.389	1.881± 0.056
250 ppm	10	1.805± 0.112	0.571± 0.032	7.617± 0.490	1.883± 0.040
500 ppm	10	1.782± 0.066	0.579± 0.035	7.503± 0.356	1.894± 0.043
1000 ppm	10	2.176± 1.188	0.549± 0.025	7.554± 0.534	1.855± 0.047
2000 ppm	10	1.754± 0.071	0.509± 0.037**	7.386± 0.736	1.824± 0.054*
3000 ppm	10	1.673± 0.114**	0.475± 0.032**	7.035± 0.670	1.766± 0.050**

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

APPENDIX J 2

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
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	169± 8	0.213± 0.022	0.059± 0.008	0.116± 0.019	0.628± 0.052	0.776± 0.049
250 ppm	10	161± 5	0.202± 0.029	0.059± 0.007	0.109± 0.010	0.609± 0.037	0.763± 0.032
500 ppm	10	158± 9**	0.187± 0.018*	0.057± 0.005	0.109± 0.016	0.593± 0.044	0.731± 0.034*
1000 ppm	10	153± 7**	0.187± 0.020*	0.055± 0.006	0.102± 0.011	0.568± 0.035**	0.730± 0.024*
2000 ppm	10	139± 8**	0.162± 0.013**	0.051± 0.004*	0.090± 0.007**	0.533± 0.033**	0.690± 0.029**
3000 ppm	8	114± 9**	0.108± 0.015**	0.047± 0.006**	0.064± 0.009**	0.452± 0.043**	0.603± 0.028**

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

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
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	1.215± 0.129	0.392± 0.031	4.118± 0.230	1.765± 0.050
250 ppm	10	1.134± 0.038	0.376± 0.020	3.893± 0.145	1.718± 0.051
500 ppm	10	1.148± 0.067	0.372± 0.020	3.832± 0.143	1.723± 0.033
1000 ppm	10	1.162± 0.029	0.361± 0.015*	3.756± 0.123*	1.708± 0.066
2000 ppm	10	1.181± 0.039	0.324± 0.020**	3.589± 0.175**	1.656± 0.035**
3000 ppm	8	1.075± 0.055**	0.255± 0.029**	3.062± 0.377**	1.612± 0.053**

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

APPENDIX K 1

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
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	294± 13	0.085± 0.011	0.018± 0.003	1.064± 0.033	0.311± 0.013	0.355± 0.016
250 ppm	10	296± 15	0.090± 0.010	0.020± 0.004	1.060± 0.038	0.307± 0.015	0.344± 0.018
500 ppm	10	290± 10	0.089± 0.014	0.018± 0.002	1.042± 0.079	0.314± 0.017	0.354± 0.013
1000 ppm	10	276± 14*	0.086± 0.008	0.020± 0.004	1.103± 0.046	0.323± 0.014	0.358± 0.016
2000 ppm	10	256± 14**	0.080± 0.007	0.021± 0.002	1.184± 0.070**	0.319± 0.017	0.375± 0.015*
3000 ppm	10	232± 17**	0.077± 0.009	0.021± 0.002	1.273± 0.061**	0.332± 0.020*	0.399± 0.016**

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

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.621± 0.018	0.193± 0.009	2.537± 0.053	0.640± 0.029
250 ppm	10	0.609± 0.021	0.193± 0.011	2.569± 0.070	0.636± 0.025
500 ppm	10	0.615± 0.025	0.199± 0.009	2.585± 0.060	0.653± 0.031
1000 ppm	10	0.797± 0.464**	0.199± 0.007	2.740± 0.106**	0.675± 0.032
2000 ppm	10	0.686± 0.029**	0.199± 0.010	2.882± 0.155**	0.715± 0.050**
3000 ppm	10	0.720± 0.019**	0.205± 0.006*	3.023± 0.118**	0.763± 0.041**

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

APPENDIX K 2

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
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	169± 8	0.126± 0.013	0.035± 0.004	0.068± 0.012	0.371± 0.029	0.459± 0.016
250 ppm	10	161± 5	0.125± 0.017	0.036± 0.004	0.068± 0.005	0.377± 0.024	0.473± 0.013
500 ppm	10	158± 9**	0.118± 0.010	0.036± 0.003	0.069± 0.010	0.376± 0.023	0.464± 0.024
1000 ppm	10	153± 7**	0.123± 0.012	0.036± 0.004	0.067± 0.009	0.372± 0.029	0.478± 0.016
2000 ppm	10	139± 8**	0.117± 0.012	0.037± 0.004	0.065± 0.004	0.385± 0.024	0.500± 0.039**
3000 ppm	8	114± 9**	0.095± 0.010**	0.041± 0.003**	0.057± 0.007*	0.398± 0.016	0.533± 0.033**

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

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.718± 0.067	0.231± 0.012	2.433± 0.051	1.045± 0.044
250 ppm	10	0.702± 0.018	0.233± 0.007	2.412± 0.042	1.065± 0.043
500 ppm	10	0.727± 0.022	0.236± 0.010	2.428± 0.065	1.093± 0.059
1000 ppm	10	0.761± 0.030**	0.236± 0.009	2.459± 0.084	1.118± 0.038**
2000 ppm	10	0.854± 0.030**	0.234± 0.010	2.593± 0.067**	1.199± 0.057**
3000 ppm	8	0.948± 0.048**	0.224± 0.011	2.690± 0.169**	1.426± 0.110**

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

APPENDIX L 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : ALL ANIMALS

(13-WEEK STUDY)

Organ	Findings	Group Name	Control				250 ppm				500 ppm				1000 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}																		
nasal cavit			<10>				<10>				<10>				<10>			
	inflammation:respiratory epithelium		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)
	duct ectasia:olfactory gland		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)
	necrosis:olfactory epithelium		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)
lung			<10>				<10>				<10>				<10>			
	accumulation of foamy cells		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)
{Circulatory system}																		
heart			<10>				<10>				<10>				<10>			
	inflammatory cell nest		1	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Digestive system}																		
liver			<10>				<10>				<10>				<10>			
	herniation		1	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(10)	(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	2000 ppm				3000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			<10>				<10>			
	inflammation:respiratory epithelium		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	duct ectasia:olfactory gland		1	0	0	0	7	0	0	0 **
			(10)	(0)	(0)	(0)	(70)	(0)	(0)	(0)
	necrosis:olfactory epithelium		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
lung			<10>				<10>			
	accumulation of foamy cells		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Circulatory system}										
heart			<10>				<10>			
	inflammatory cell nest		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}										
liver			<10>				<10>			
	herniation		1	0	0	0	2	0	0	0
			(10)	(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				250 ppm				500 ppm				1000 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}																		
liver			<10>				<10>				<10>				<10>			
	granulation		0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	perivascular inflammation		2	0	0	0	3	0	0	0	1	0	0	0	3	0	0	0
			(20)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(30)	(0)	(0)	(0)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	basophilic change		0	0	0	0	2	0	0	0	0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	eosinophilic body		2	8	0	0	1	9	0	0	7	3	0	0	4	5	0	0
			(20)	(80)	(0)	(0)	(10)	(90)	(0)	(0)	(70)	(30)	(0)	(0)	(40)	(50)	(0)	(0)
	hydronephrosis		0	0	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)
	mineralization:papilla		0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	degeneration:papilla		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	2000 ppm				3000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Digestive system)										
liver			<10>				<10>			
	granulation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	perivascular inflammation		3	0	0	0	1	0	0	0
			(30)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
(Urinary system)										
kidney			<10>				<10>			
	basophilic change		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	eosinophilic body		8	2	0	0 *	8	1	0	0 **
			(80)	(20)	(0)	(0)	(80)	(10)	(0)	(0)
	hydronephrosis		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:papilla		1	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	degeneration:papilla		1	0	0	0	2	0	0	0
			(10)	(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				250 ppm				500 ppm				1000 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}																		
urin bladd			<10>				<10>				<10>				<10>			
	simple hyperplasia:transitional epithelium		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)
	nodular hyperplasia:transitional epithelium		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)
{Endocrine system}																		
thyroid			<10>				<10>				<10>				<10>			
	ultimobranchial body remanet		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)
{Reproductive system}																		
testis			<10>				<10>				<10>				<10>			
	atrophy		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)	(0)	(0)	(0)
{Special sense organs/appendage}																		
Harder gl			<10>				<10>				<10>				<10>			
	inflammation		1	0	0	0	0	0	0	0	1	0	0	0	4	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(40)	(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	2000 ppm				3000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}										
urin bladd			<10>				<10>			
	simple hyperplasia:transitional epithelium		1	1	0	0	1	2	0	0
			(10)	(10)	(0)	(0)	(10)	(20)	(0)	(0)
	nodular hyperplasia:transitional epithelium		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
{Endocrine system}										
thyroid			<10>				<10>			
	ultimobranchial body remanet		2	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Reproductive system}										
testis			<10>				<10>			
	atrophy		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Special sense organs/appendage}										
Harder gl			<10>				<10>			
	inflammation		3	1	0	0	3	2	0	0
			(30)	(10)	(0)	(0)	(30)	(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 L 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE: ALL ANIMALS

(13-WEEK STUDY)

Organ	Findings	Group Name	Control				250 ppm				500 ppm				1000 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}																		
nasal cavit			<10>				<10>				<10>				<10>			
	inflammation:respiratory epithelium		0	0	0	0	2	0	0	0	1	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(30)	(0)	(0)	(0)
	duct ectasia:olfactory gland		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)
	necrosis:olfactory epithelium		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)
lung			<10>				<10>				<10>				<10>			
	perivascular inflammation		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)
	accumulation of foamy cells		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)
{Hematopoietic system}																		
bone marrow			<10>				<10>				<10>				<10>			
	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)

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	2000 ppm				3000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			<10>				<10>			
	inflammation:respiratory epithelium		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	duct ectasia:olfactory gland		0	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(30)	(0)	(0)	(0)
	necrosis:olfactory epithelium		1	0	0	0	6	0	0	0 *
			(10)	(0)	(0)	(0)	(60)	(0)	(0)	(0)
lung			<10>				<10>			
	perivascular inflammation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	accumulation of foamy cells		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}										
bone marrow			<10>				<10>			
	congestion		0	0	0	0	0	2	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

Organ	Findings	Group Name	Control				250 ppm				500 ppm				1000 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}																		
bone marrow			<10>				<10>				<10>				<10>			
	granulation		0	1	0	0	1	3	0	0	0	2	0	0	0	1	0	0
			(0)	(10)	(0)	(0)	(10)	(30)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(10)	(0)	(0)
thymus			<10>				<10>				<10>				< 9>			
	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)
{Circulatory system}																		
heart			<10>				<10>				<10>				<10>			
	inflammatory cell nest		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)
{Digestive system}																		
liver			<10>				<10>				<10>				<10>			
	herniation		1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	granulation		1	0	0	0	2	0	0	0	1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(20)	(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	2000 ppm				3000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
bone marrow			<10>				<10>			
	granulation		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	1	1	0
			(0)	(0)	(0)	(0)	(0)	(10)	(10)	(0)
{Circulatory system}										
heart			<10>				<10>			
	inflammatory cell nest		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}										
liver			<10>				<10>			
	herniation		3	0	0	0	1	0	0	0
			(30)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	granulation		0	0	0	0	2	0	0	0
			(0)	(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				250 ppm				500 ppm				1000 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}																		
liver			<10>				<10>				<10>				<10>			
	perivascular inflammation		3	0	0	0	3	0	0	0	4	0	0	0	1	0	0	0
			(30)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(40)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	mineralization:cortico-medullary junction		2	0	0	0	6	0	0	0	3	0	0	0	2	0	0	0
			(20)	(0)	(0)	(0)	(60)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	mineralization:papilla		4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(40)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	degeneration:papilla		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)
{Endocrine system}																		
thyroid			<10>				<10>				<10>				<10>			
	ultimobranchial body remanet		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)

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	2000 ppm				3000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
liver			<10>				<10>			
	perivascular inflammation		5	0	0	0	1	0	0	0
			(50)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Urinary system}										
kidney			<10>				<10>			
	mineralization:cortico-medullary junction		2	0	0	0	1	0	0	0
			(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	mineralization:papilla		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	degeneration:papilla		5	0	0	0 *	6	0	0	0 *
			(50)	(0)	(0)	(0)	(60)	(0)	(0)	(0)
{Endocrine system}										
thyroid			<10>				<10>			
	ultimobranchial 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
Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				250 ppm				500 ppm				1000 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Special sense organs/appendage}																		
Harder gl			<10>				<10>				<10>				<10>			
	inflammation		3	1	0	0	1	2	0	0	1	1	1	0	2	1	1	0
			(30)	(10)	(0)	(0)	(10)	(20)	(0)	(0)	(10)	(10)	(10)	(0)	(20)	(10)	(10)	(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	2000 ppm				3000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Special sense organs/appendage}										
Harder gl			<10>				<10>			
	inflammation		3	3	1	0	3	5	0	0
			(30)	(30)	(10)	(0)	(30)	(50)	(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 3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : SACRIFICED ANIMALS

(13-WEEK STUDY)

Organ	Findings	Group Name	Control				250 ppm				500 ppm				1000 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}																		
nasal cavit			<10>				<10>				<10>				<10>			
	inflammation:respiratory epithelium		0	0	0	0	2	0	0	0	1	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(30)	(0)	(0)	(0)
	duct ectasia:olfactory gland		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)
	necrosis:olfactory epithelium		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)
lung			<10>				<10>				<10>				<10>			
	perivascular inflammation		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)
	accumulation of foamy cells		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)
{Hematopoietic system}																		
bone marrow			<10>				<10>				<10>				<10>			
	granulation		0	1	0	0	1	3	0	0	0	2	0	0	0	1	0	0
			(0)	(10)	(0)	(0)	(10)	(30)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(10)	(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	2000 ppm				3000 ppm			
		No. of Animals on Study	10				8			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			<10>				< 8>			
	inflammation:respiratory epithelium		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	duct ectasia:olfactory gland		0	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(38)	(0)	(0)	(0)
	necrosis:olfactory epithelium		1	0	0	0	6	0	0	0 **
			(10)	(0)	(0)	(0)	(75)	(0)	(0)	(0)
lung			<10>				< 8>			
	perivascular inflammation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	accumulation of foamy cells		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}										
bone marrow			<10>				< 8>			
	granulation		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	Control				250 ppm				500 ppm				1000 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Circulatory system}																		
heart			<10>				<10>				<10>				<10>			
	inflammatory cell nest		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)
{Digestive system}																		
liver			<10>				<10>				<10>				<10>			
	herniation		1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	granulation		1	0	0	0	2	0	0	0	1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	perivascular inflammation		3	0	0	0	3	0	0	0	4	0	0	0	1	0	0	0
			(30)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(40)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	mineralization:cortico-medullary junction		2	0	0	0	6	0	0	0	3	0	0	0	2	0	0	0
			(20)	(0)	(0)	(0)	(60)	(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	2000 ppm				3000 ppm			
		No. of Animals on Study	10				8			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Circulatory system}										
heart			<10>				< 8>			
	inflammatory cell nest		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}										
liver			<10>				< 8>			
	herniation		3	0	0	0	1	0	0	0
			(30)	(0)	(0)	(0)	(13)	(0)	(0)	(0)
	granulation		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(25)	(0)	(0)	(0)
	perivascular inflammation		5	0	0	0	1	0	0	0
			(50)	(0)	(0)	(0)	(13)	(0)	(0)	(0)
{Urinary system}										
kidney			<10>				< 8>			
	mineralization:cortico-medullary junction		2	0	0	0	1	0	0	0
			(20)	(0)	(0)	(0)	(13)	(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				250 ppm				500 ppm				1000 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	mineralization:papilla		4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(40)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	degeneration:papilla		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)
{Endocrine system}																		
thyroid			<10>				<10>				<10>				<10>			
	ultimobranchial body remanet		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)
{Special sense organs/appendage}																		
Harder gl			<10>				<10>				<10>				<10>			
	inflammation		3	1	0	0	1	2	0	0	1	1	1	0	2	1	1	0
			(30)	(10)	(0)	(0)	(10)	(20)	(0)	(0)	(10)	(10)	(10)	(0)	(20)	(10)	(10)	(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	2000 ppm				3000 ppm			
		No. of Animals on Study	10				8			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}										
kidney			<10>				< 8>			
	mineralization:papilla		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	degeneration:papilla		5	0	0	0 *	6	0	0	0 **
			(50)	(0)	(0)	(0)	(75)	(0)	(0)	(0)
{Endocrine system}										
thyroid			<10>				< 8>			
	ultimobranchial body remanet		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Special sense organs/appendage}										
Harder gl			<10>				< 8>			
	inflammation		3	3	1	0	3	5	0	0 *
			(30)	(30)	(10)	(0)	(38)	(63)	(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 4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : DEAD AND MORIBUND ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0351
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 14W)

Organ	Findings	Group Name	Control				250 ppm				500 ppm				1000 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		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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	2000 ppm				3000 ppm			
		No. of Animals on Study	0				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
bone marrow			< 0>				< 2>			
	congestion		-	-	-	-	0	2	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
thymus			< 0>				< 2>			
	atrophy		-	-	-	-	0	1	1	0
			(-)	(-)	(-)	(-)	(0)	(50)	(50)	(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 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

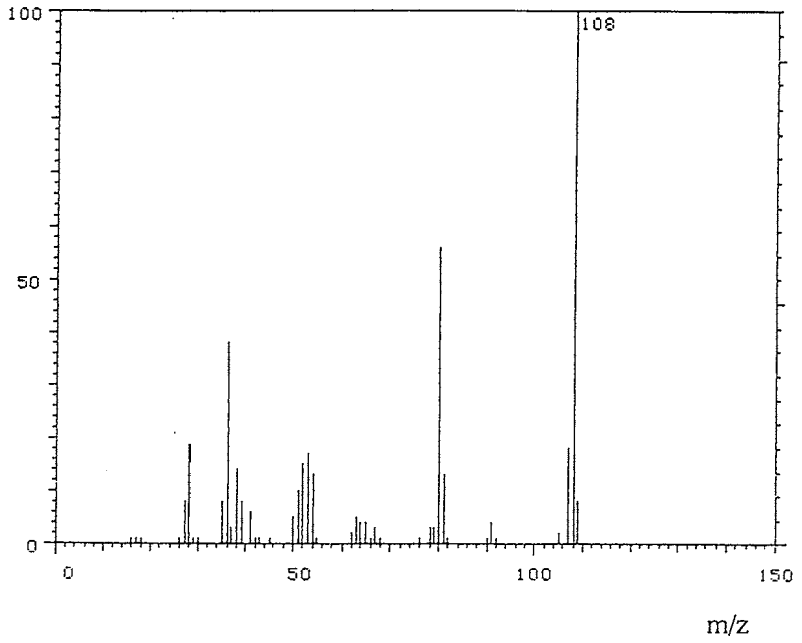
1. Spectral Data

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

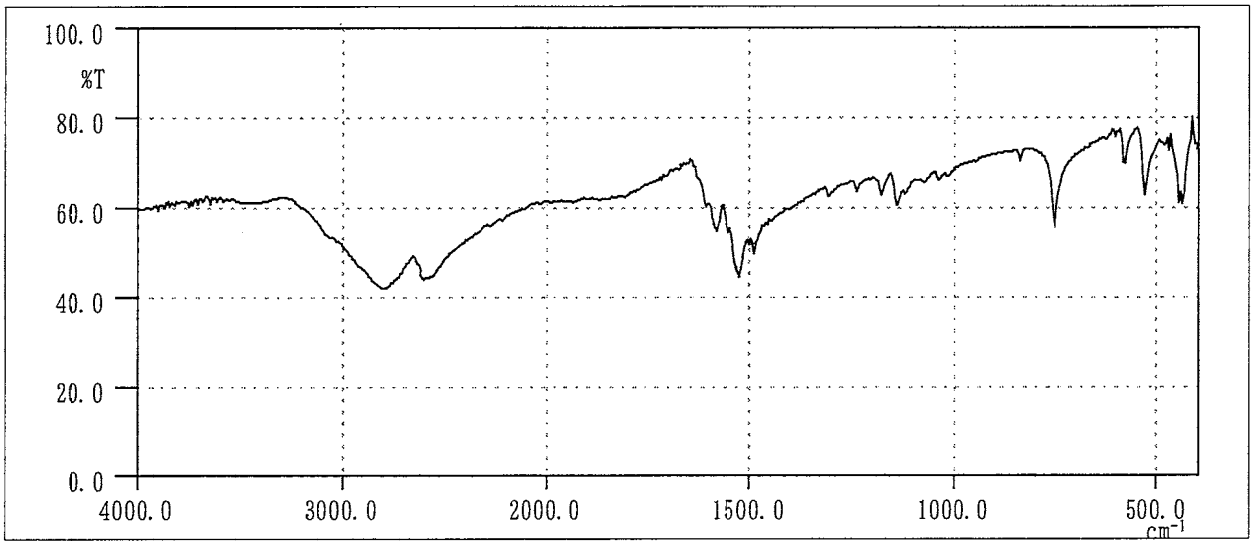
Results: The mass spectrum was consistent with calculated spectrum.

Infrared Spectrometry

Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr

Resolution : 2 cm^{-1}



Infrared Spectrum of Test Substance

Determined Values	Literature Values*
Wave Number (cm^{-1})	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

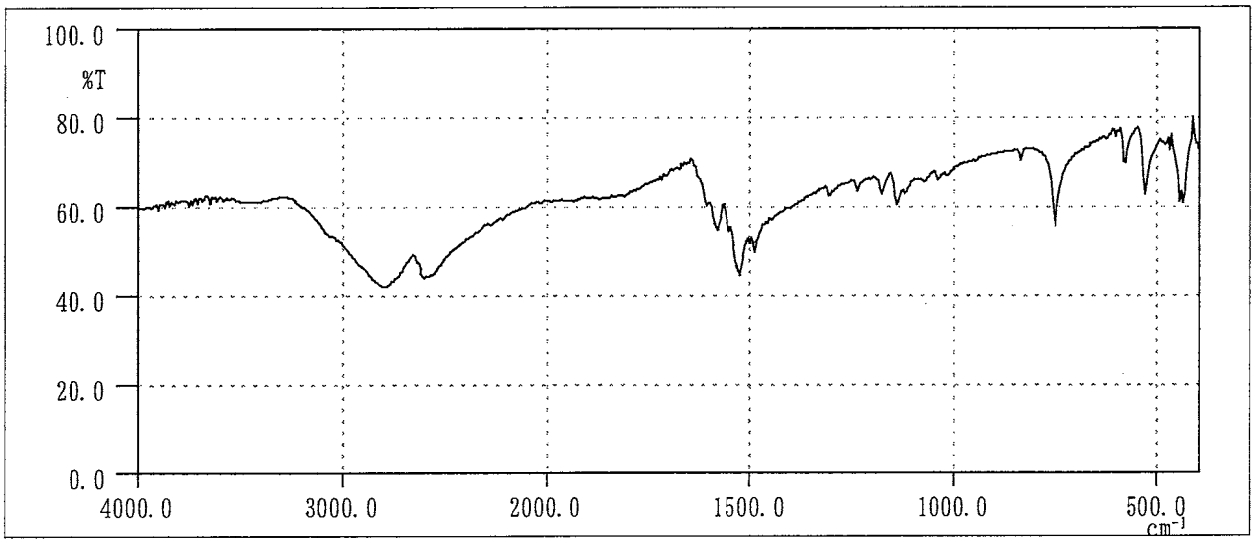
1. Sample : This lot was used from 1998.2.23 to 1998.5.27. Test substance was stored in cold storage in a dark place.

2. Infrared Spectrometry

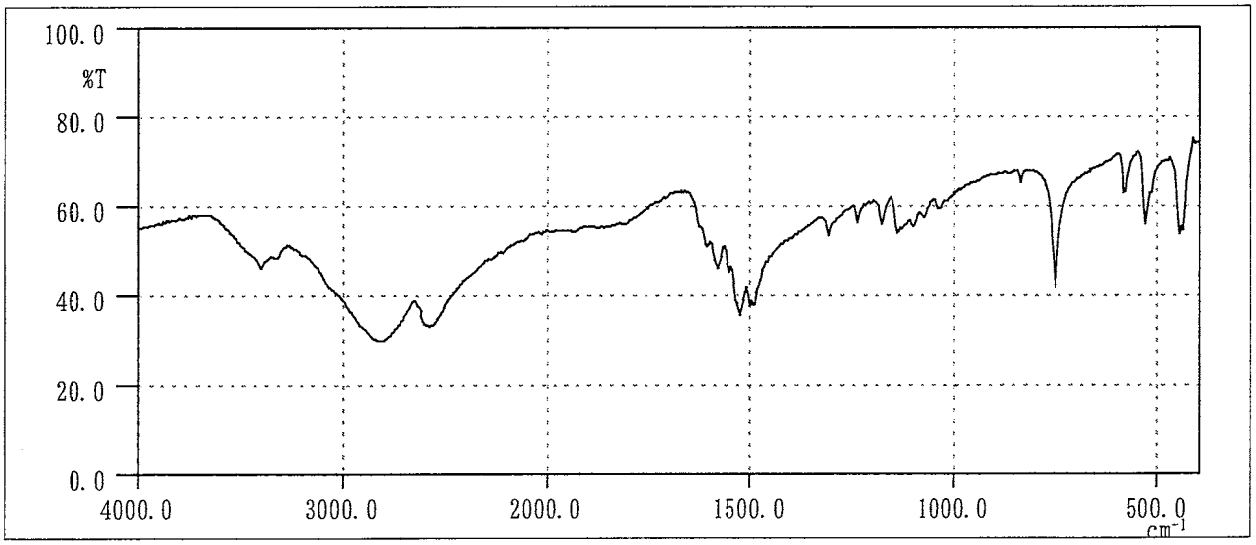
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

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

CONCENTRATION 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	250[a]	500	1000	2000	3000
1998.02.23	248 (99.2)[b]	488 (97.6)	1010 (101)	2030 (102)	2990 (99.7)

[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	250[a]	3000
1998.02.09	1998.02.09	251 (100)[b]	2970 (100)
	1998.02.13[c]	238 (94.8)	2880 (97.0)

[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]
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]
Triglyceride	Enzymatic method (LPL･GK･GPO･POD) [4]
Phospholipid	Enzymatic method (PLD･COD･POD) [4]
Glutamic oxaloacetic transaminase (GOT)	IFCC method [4]
Glutamic pyruvic transaminase (GPT)	IFCC method [4]
Lactate dehydrogenase (LDH)	Wroblewski-LaDue method [4]
Alkaline phosphatase (ALP)	p-Nitrophenylphosphate method [4]
γ-Glutamyl transpeptidase (γ-GTP)	L-γ-Glutamyl-p-nitroanilide method [4]
Creatine phosphokinase (CPK)	GSCC 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]
Urinalysis	
pH,Protein,Glucose,Ketone body,Bilirubin,Occult Blood, Urobilinogen	Urinalysis reagent paper method [5]

1) Automatic blood cell analyzer (Technicon H･1 : Technicon Instruments Corporation)
2) Automatic coagulometer (Sysmex CA-5000 : Toa Medical Electronics Co.,Ltd.)
3) Automatic blood cell differential analyzer (Hitachi 8200 : Hitachi,Ltd.)
4) Automatic analyzer (Hitachi 7070 : Hitachi,Ltd.)
5) Ames reagent strips for urinalysis (Multistix : 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
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
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
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