2－フェノキシエタノール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：　０４５９

APPENDICES

APPENDICES

APPENDICES (CONTINUED)

APPENDICES (CONTINUED)

APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0459
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
DEATH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 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
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	1
HUNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 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
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	1	0
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 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
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	1	1
SOILED PERI GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	1	1	1	2	2	2	2	2
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	1	2
	20000 ppm	1	5	3	2	2	7	9	9	9	10	10	10	9
NON REMARKABLE	Control	10	10	10	10	10	10	10	10	10	10	10	10	10
	1250 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	2500 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	5000 ppm	10	10	10	10	10	9	9	9	8	8	8	8	8
	10000 ppm	10	10	10	10	10	10	10	10	10	10	10	9	8
	20000 ppm	9	5	7	8	8	3	1	1	1	0	0	0	0

APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0459
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
SOILED	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 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
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	2	0	0	0	0	0	0	0	0	0	0	0	0
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 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
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	5	5	3	1	0	0	0	0	0	0	0	0	0
SOILED PERI GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	0	2	1	1	0	0	0	0	0	0	0	1	1
	2500 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	1	1	1	1
	10000 ppm	0	3	0	0	0	0	1	1	3	4	3	4	4
	20000 ppm	6	7	6	6	5	9	8	8	8	10	10	10	10
SMALL STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 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
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	3	0	0	0	0	0	0	0	0	0	0	0	0
OLIGO-STOOL	Control	0	0	1	0	0	0	0	0	0	0	0	0	0
	1250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 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
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	2	0	0	0	0	0	0	0	0	0	0	0	0
NON REMARKABLE	Control	10	10	9	10	10	10	10	10	10	10	10	10	10
	1250 ppm	10	8	9	9	10	10	10	10	10	10	10	9	9
	2500 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	5000 ppm	10	10	10	10	10	10	10	10	10	9	9	9	9
	10000 ppm	10	7	10	10	10	10	9	9	7	6	7	6	6
	20000 ppm	4	2	4	4	5	1	2	2	2	0	0	0	0

APPENDIX B 1

BODY WEIGHT CHANGES : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0459
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7
Control	126± 4	154± 5	182± 8	204± 8	224± 9	240± 9	253± 11
1250 ppm	126± 4	155± 7	182± 9	204± 12	223± 13	240± 14	252± 16
2500 ppm	126± 4	153± 6	177± 8	197± 11	216± 13	232± 15	246± 16
5000 ppm	125± 5	153± 6	177± 9	198± 11	216± 12	234± 11	246± 12
10000 ppm	126± 4	149± 6	174± 10	195± 14	215± 16	233± 17	245± 18
20000 ppm	126± 4	136± 7**	161± 8**	181± 9**	199± 10**	213± 12**	223± 13**

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

STUDY NO. : 0459
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 7-7	8-7	9-7	10-7	11-7	12-7	13-7
Control	265± 12	279± 13	287± 14	295± 16	300± 16	308± 18	312± 18
1250 ppm	263± 16	276± 17	284± 17	292± 18	298± 18	306± 19	311± 18
2500 ppm	258± 17	270± 17	279± 17	285± 17	290± 16	297± 15	302± 16
5000 ppm	259± 15	271± 15	280± 16	290± 16	295± 18	300± 19	307± 20
10000 ppm	257± 20	270± 22	281± 23	287± 24	292± 23	299± 26	306± 27
20000 ppm	235± 13**	245± 13**	248± 18**	251± 23**	247± 29**	242± 37**	251± 28**

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. : 0459
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7
Control	99± 3	112± 2	124± 3	131± 6	140± 4	149± 4	154± 4
1250 ppm	99± 3	112± 4	124± 6	130± 7	138± 7	147± 9	151± 10
2500 ppm	99± 3	112± 3	122± 4	129± 4	133± 6	142± 6	146± 7
5000 ppm	99± 3	113± 4	122± 4	128± 6	135± 6	143± 6	148± 7
10000 ppm	99± 3	107± 3*	116± 5**	123± 5*	129± 6**	137± 7**	141± 8**
20000 ppm	99± 3	95± 11**	110± 9**	118± 8**	123± 9**	129± 11**	131± 13**

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

STUDY NO. : 0459
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 7-7	8-7	9-7	10-7	11-7	12-7	13-7
Control	157± 5	162± 5	165± 6	169± 6	171± 6	175± 7	176± 8
1250 ppm	154± 11	158± 12	160± 12	165± 13	166± 12	169± 13	170± 15
2500 ppm	148± 8	150± 7*	155± 7	157± 7	161± 7	165± 9	165± 9
5000 ppm	150± 6	153± 6	157± 8	159± 8	163± 7	164± 10	167± 9
10000 ppm	145± 9*	148± 9**	152± 10*	154± 11**	159± 12*	160± 12*	161± 12*
20000 ppm	134± 12**	138± 13**	141± 13**	141± 13**	144± 12**	143± 12**	144± 13**

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. : 0459
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(3)	2-7(3)	3-7(3)	4-7(3)	5-7(3)	6-7(3)	7-7(3)
Control	18.2± 1.3	19.0± 1.3	19.9± 1.7	21.7± 4.1	19.9± 2.0	19.2± 2.2	18.5± 2.0
1250 ppm	17.9± 1.4	18.7± 1.5	19.1± 1.2	20.0± 0.9	18.5± 1.3	18.1± 1.2	17.6± 1.3
2500 ppm	16.9± 1.2	17.7± 1.3	17.9± 1.6	18.5± 1.0	17.8± 2.1	17.3± 0.8	16.6± 1.1*
5000 ppm	15.8± 0.7**	16.8± 0.8**	17.7± 1.9*	18.2± 1.4	17.9± 1.5	17.7± 1.3	17.2± 1.1
10000 ppm	14.1± 1.5**	14.9± 1.3**	15.5± 1.7**	16.8± 1.7**	18.8± 7.6	16.4± 2.9**	15.5± 1.6**
20000 ppm	16.2± 1.9*	14.0± 1.3**	14.2± 2.1**	15.6± 1.8**	15.1± 2.3**	15.4± 1.9**	15.4± 1.9**

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

STUDY NO. : 0459
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(3)	9-7(3)	10-7(3)	11-7(3)	12-7(3)	13-7(3)
Control	19.4± 2.0	18.4± 1.8	18.6± 2.9	19.0± 4.3	18.9± 3.8	20.5± 5.2
1250 ppm	18.2± 1.0	18.3± 1.3	17.9± 1.5	18.8± 1.5	19.7± 3.8	18.5± 1.5
2500 ppm	17.6± 1.0	17.2± 1.2	17.1± 1.1	17.3± 1.0	17.9± 1.0	17.6± 1.0
5000 ppm	18.4± 1.2	17.7± 1.3	17.9± 1.1	17.8± 1.1	17.6± 1.5	18.3± 1.3
10000 ppm	16.8± 2.2	16.7± 2.1	16.1± 1.9*	17.0± 3.3	17.0± 1.8	17.4± 2.7
20000 ppm	17.2± 2.9	15.4± 2.4**	16.3± 3.0	17.5± 2.5	17.5± 3.3	18.2± 4.3

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. : 0459
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(3)	2-7(3)	3-7(3)	4-7(3)	5-7(3)	6-7(3)	7-7(3)
Control	15.4± 1.5	16.3± 3.3	17.7± 4.5	19.6± 5.6	17.5± 4.0	16.8± 2.7	16.8± 4.4
1250 ppm	15.0± 1.2	18.4± 6.7	19.2± 11.0	19.2± 5.9	21.1± 9.6	20.1± 9.0	21.0± 9.3
2500 ppm	14.1± 1.0	14.2± 1.2	17.0± 5.5	18.8± 9.1	16.8± 7.0	15.2± 2.9	23.5± 16.3
5000 ppm	16.2± 4.7	17.0± 6.6	15.5± 2.7	17.7± 5.8	19.4± 9.0	21.0± 8.1	20.7± 7.8
10000 ppm	12.8± 4.3**	12.8± 2.8*	11.8± 1.1**	12.3± 1.4**	13.3± 3.5*	13.1± 2.4	13.3± 5.3
20000 ppm	11.5± 2.1**	10.9± 0.8**	10.2± 1.5**	11.0± 1.7**	10.3± 2.1**	10.5± 0.9**	9.3± 1.3**

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

STUDY NO. : 0459
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(3)	9-7(3)	10-7(3)	11-7(3)	12-7(3)	13-7(3)
Control	20.1± 6.8	22.7± 13.8	21.2± 8.0	19.1± 5.7	22.9± 11.6	21.1± 6.8
1250 ppm	20.9± 6.7	18.9± 8.4	20.1± 6.3	17.2± 4.5	18.3± 6.1	21.0± 6.4
2500 ppm	17.6± 7.1	23.3± 10.2	16.5± 5.1	17.4± 5.6	23.0± 13.4	19.9± 12.0
5000 ppm	20.9± 6.2	15.9± 2.7	17.6± 4.5	19.0± 5.5	23.8± 13.4	20.9± 6.5
10000 ppm	13.3± 3.8*	14.7± 8.6	14.6± 9.2*	16.3± 9.1	18.6± 9.1	15.4± 5.8*
20000 ppm	10.7± 1.4**	10.7± 2.1**	11.0± 2.8**	11.7± 2.5**	11.6± 2.3**	13.0± 2.6**

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. : 0459
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(7)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	14.0± 0.8	14.9± 1.0	15.6± 0.9	15.6± 0.8	16.2± 0.9	14.9± 1.0	14.5± 1.1
1250 ppm	13.6± 0.8	14.7± 0.9	15.4± 1.1	15.2± 1.0	15.8± 1.1	14.6± 1.1	14.0± 0.9
2500 ppm	13.7± 0.7	14.4± 1.1	15.1± 1.2	14.9± 1.0	15.4± 1.4	14.5± 0.9	13.9± 0.9
5000 ppm	13.5± 0.8	14.4± 1.0	15.0± 1.2	15.0± 1.0	15.8± 1.1	14.6± 1.1	14.6± 1.0
10000 ppm	12.3± 0.6**	13.7± 0.8*	14.4± 1.2	15.0± 1.1	15.4± 1.2	14.4± 1.1	14.2± 1.0
20000 ppm	10.3± 0.8**	12.9± 0.7**	13.4± 0.9**	13.7± 0.8**	13.6± 0.8**	12.8± 0.7**	13.2± 0.6*

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. : 0459
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(7)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	10.7± 0.6	10.7± 0.5	10.7± 0.6	10.6± 0.7	10.9± 0.6	10.0± 0.7	10.0± 0.6
1250 ppm	10.4± 0.7	10.5± 0.8	10.5± 0.7	10.1± 0.8	10.7± 0.7	10.1± 0.9	9.8± 0.9
2500 ppm	10.7± 0.5	10.2± 0.7	10.5± 0.7	10.1± 0.8	10.4± 0.8	9.7± 0.8	9.5± 0.8
5000 ppm	10.4± 0.4	10.3± 0.6	10.4± 0.8	10.3± 0.7	10.6± 0.7	10.2± 0.7	9.5± 0.8
10000 ppm	9.4± 0.5**	9.3± 0.8**	9.3± 0.8**	9.3± 0.6**	9.8± 0.7**	9.3± 0.7	9.2± 0.7
20000 ppm	7.1± 1.6**	9.6± 0.7**	9.3± 0.7**	8.8± 0.8**	8.8± 1.0**	8.3± 1.0**	8.2± 0.9**

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

STUDY NO. : 0459
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)
Control	15.0± 0.8	15.0± 1.1	14.6± 1.2	14.6± 0.9	14.4± 1.1	14.3± 1.1
1250 ppm	14.5± 0.9	14.4± 1.0	14.1± 0.8	14.5± 0.9	14.4± 0.8	14.3± 0.8
2500 ppm	14.2± 0.9	14.3± 1.1	13.9± 0.9	13.6± 0.8	13.7± 0.4	13.9± 0.7
5000 ppm	14.7± 0.9	14.7± 1.0	14.6± 1.0	14.5± 1.0	14.2± 1.0	14.4± 1.1
10000 ppm	14.1± 1.1	14.6± 1.2	14.1± 1.0	14.0± 0.9	14.1± 1.2	14.1± 1.0
20000 ppm	13.2± 0.7**	12.6± 1.4**	12.4± 1.5**	11.7± 2.0**	10.7± 2.4**	11.4± 2.0**

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

STUDY NO. : 0459
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)
Control	9.7± 0.6	9.9± 0.8	10.0± 0.7	9.8± 0.7	10.0± 0.7	10.0± 0.8
1250 ppm	9.8± 1.0	9.7± 0.8	9.7± 0.8	9.5± 0.8	9.5± 0.7	9.6± 0.8
2500 ppm	9.4± 0.5	9.6± 0.7	9.6± 0.6	9.5± 0.7	9.5± 0.7	9.7± 0.6
5000 ppm	9.4± 0.6	9.8± 0.7	9.6± 0.8	9.7± 0.5	9.4± 0.6	9.4± 0.5
10000 ppm	9.0± 0.8	8.9± 0.8*	8.8± 0.7**	9.0± 0.8*	9.0± 0.8*	9.0± 0.7*
20000 ppm	8.2± 0.9**	8.4± 0.8**	7.7± 0.6**	8.0± 0.8**	7.7± 0.9**	7.9± 0.8**

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. : 0459
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
1250 ppm	0.144± 0.007	0.128± 0.006	0.117± 0.004	0.112± 0.004	0.096± 0.005	0.090± 0.003	0.084± 0.004
2500 ppm	0.277± 0.015	0.250± 0.010	0.227± 0.012	0.214± 0.009	0.191± 0.017	0.176± 0.008	0.160± 0.007
5000 ppm	0.517± 0.025	0.474± 0.018	0.447± 0.052	0.421± 0.028	0.381± 0.020	0.360± 0.016	0.333± 0.011
10000 ppm	0.950± 0.082	0.855± 0.044	0.792± 0.048	0.778± 0.046	0.791± 0.296	0.666± 0.096	0.603± 0.045
20000 ppm	2.381± 0.275	1.734± 0.103	1.566± 0.181	1.561± 0.122	1.420± 0.179	1.381± 0.133	1.311± 0.136

STUDY NO. : 0459
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
1250 ppm	0.083± 0.004	0.081± 0.005	0.077± 0.006	0.079± 0.005	0.080± 0.014	0.074± 0.005
2500 ppm	0.163± 0.007	0.155± 0.008	0.150± 0.009	0.149± 0.010	0.151± 0.010	0.146± 0.008
5000 ppm	0.341± 0.022	0.317± 0.019	0.308± 0.018	0.302± 0.015	0.293± 0.016	0.298± 0.016
10000 ppm	0.621± 0.052	0.595± 0.060	0.562± 0.047	0.581± 0.095	0.568± 0.039	0.569± 0.059
20000 ppm	1.405± 0.218	1.255± 0.242	1.311± 0.265	1.437± 0.306	1.476± 0.331	1.451± 0.289

APPENDIX E 2

CHEMICAL INTAKE CHANGES : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0459
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
1250 ppm	0.168± 0.012	0.185± 0.068	0.183± 0.109	0.175± 0.056	0.181± 0.084	0.168± 0.080	0.171± 0.076
2500 ppm	0.314± 0.016	0.293± 0.022	0.327± 0.096	0.347± 0.150	0.293± 0.111	0.262± 0.045	0.389± 0.251
5000 ppm	0.717± 0.200	0.696± 0.265	0.601± 0.110	0.650± 0.197	0.671± 0.301	0.715± 0.268	0.693± 0.264
10000 ppm	1.205± 0.439	1.115± 0.290	0.958± 0.064	0.956± 0.088	0.970± 0.263	0.933± 0.168	0.911± 0.345
20000 ppm	2.412± 0.237	1.981± 0.103	1.739± 0.183	1.783± 0.220	1.587± 0.248	1.612± 0.125	1.387± 0.164

STUDY NO. : 0459
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
1250 ppm	0.167± 0.062	0.151± 0.077	0.153± 0.050	0.132± 0.040	0.137± 0.050	0.154± 0.047
2500 ppm	0.297± 0.112	0.377± 0.169	0.259± 0.079	0.273± 0.091	0.344± 0.187	0.300± 0.173
5000 ppm	0.691± 0.215	0.515± 0.092	0.565± 0.155	0.589± 0.174	0.734± 0.413	0.637± 0.203
10000 ppm	0.902± 0.223	0.965± 0.538	0.943± 0.575	1.028± 0.563	1.160± 0.554	0.953± 0.332
20000 ppm	1.550± 0.128	1.509± 0.195	1.544± 0.292	1.624± 0.263	1.604± 0.248	1.790± 0.287

APPENDIX F 1

HEMATOLOGY : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0459
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	9.27±	0.21	15.8±	0.2	44.7±	0.9	48.3±	0.7	17.1±	0.3	35.4±	0.6	802±	49
1250 ppm	10	9.22±	0.22	16.0±	0.3	44.6±	1.2	48.4±	0.4	17.3±	0.4	35.9±	0.8	777±	63
2500 ppm	10	9.22±	0.17	16.1±	0.3	44.8±	0.8	48.5±	0.4	17.5±	0.3	35.9±	0.6	790±	59
5000 ppm	10	9.12±	0.20	15.9±	0.2	44.5±	1.2	48.8±	0.5	17.4±	0.3	35.7±	0.7	727±	69*
10000 ppm	10	8.85±	0.15**	15.5±	0.3	43.7±	1.0	49.4±	0.7**	17.6±	0.4*	35.6±	0.9	666±	74**
20000 ppm	9	8.44±	0.23**	15.4±	0.4*	44.4±	1.4	52.6±	1.7**	18.2±	0.5**	34.6±	1.5	653±	58**

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

STUDY NO. : 0459
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	1.8± 0.2	16.6± 0.5	20.5± 1.8
1250 ppm	10	1.8± 0.2	16.5± 1.0	22.1± 1.5
2500 ppm	10	1.9± 0.2	17.2± 1.6	21.5± 2.1
5000 ppm	10	1.9± 0.2	16.6± 1.8	21.9± 2.1
10000 ppm	10	2.0± 0.3	16.2± 0.8	20.4± 1.7
20000 ppm	9	1.8± 0.6	16.6± 0.9	21.0± 1.3

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

STUDY NO. : 0459
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	OTHER
Control	10	5.63± 1.29	2± 1	20± 4	1± 1	0± 0	3± 1	75± 5	0± 0
1250 ppm	10	4.93± 1.03	2± 1	22± 5	1± 1	0± 0	3± 1	73± 5	0± 0
2500 ppm	10	5.11± 1.17	1± 1	21± 4	1± 1	0± 0	2± 1	74± 5	0± 0
5000 ppm	10	5.71± 1.61	1± 1	20± 2	1± 1	0± 0	3± 2	75± 3	0± 0
10000 ppm	10	5.22± 1.43	1± 1	19± 2	1± 1	0± 0	2± 1	77± 3	0± 0
20000 ppm	9	5.55± 1.50	1± 1	18± 4	1± 1	0± 0	4± 1	77± 4	0± 0

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. : 0459
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	8.58± 0.26	15.9± 0.4	43.4± 1.4	50.6± 0.4	18.5± 0.3	36.6± 0.6	828± 53
1250 ppm	10	8.51± 0.27	15.6± 0.4	43.1± 1.5	50.6± 0.6	18.4± 0.3	36.3± 0.8	820± 36
2500 ppm	10	8.47± 0.26	15.6± 0.4	42.9± 1.4	50.7± 0.8	18.5± 0.2	36.5± 0.5	778± 41
5000 ppm	10	8.40± 0.17	15.6± 0.5	42.8± 0.9	50.9± 0.8	18.6± 0.6	36.5± 0.8	791± 64
10000 ppm	10	8.19± 0.27**	15.2± 0.5*	42.1± 1.4	51.4± 0.7	18.6± 0.2	36.2± 0.5	760± 55*
20000 ppm	10	7.86± 0.31**	14.9± 0.5**	41.9± 1.5	53.3± 1.2**	19.0± 0.4*	35.7± 1.0	711± 54**

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

STUDY NO. : 0459
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	1.8± 0.1	16.8± 0.8	17.7± 0.8
1250 ppm	10	1.7± 0.3	16.7± 0.8	17.1± 1.2
2500 ppm	10	1.7± 0.3	17.1± 0.4	17.6± 1.6
5000 ppm	10	1.9± 0.4	17.1± 0.7	17.4± 0.9
10000 ppm	10	2.0± 0.2	17.1± 0.6	17.7± 0.8
20000 ppm	10	2.3± 0.6*	17.3± 0.4	17.3± 1.1

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

STUDY NO. : 0459
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		OTHER	
Control	10	3.09±	0.78	1±	1	20±	3	1±	1	0±	0	3±	1	75±	4	0±	0
1250 ppm	10	3.19±	0.92	1±	1	19±	5	1±	1	0±	0	2±	1	78±	6	0±	0
2500 ppm	10	2.50±	0.43	1±	1	19±	3	1±	1	0±	0	3±	1	76±	4	0±	0
5000 ppm	10	3.04±	0.67	1±	1	18±	2	2±	1	0±	0	3±	1	76±	3	0±	0
10000 ppm	10	2.76±	0.75	2±	1	17±	5	1±	0	0±	0	2±	1	78±	4	0±	0
20000 ppm	10	3.04±	0.85	1±	1	19±	4	2±	1	0±	0	2±	1	77±	5	0±	0

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

APPENDIX G 1

BIOCHEMISTRY : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0459
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±	0.1	3.5±	0.1	1.3±	0.1	0.10±	0.02	188±	6	58±	6	38±	12
1250 ppm	10	6.3±	0.1	3.5±	0.1	1.3±	0.0	0.10±	0.01	187±	11	60±	4	34±	13
2500 ppm	10	6.3±	0.2	3.5±	0.1	1.2±	0.1	0.10±	0.01	185±	10	59±	5	39±	18
5000 ppm	10	6.2±	0.1	3.4±	0.1	1.2±	0.1	0.11±	0.01	184±	9	58±	4	52±	20
10000 ppm	10	6.1±	0.1*	3.4±	0.1	1.3±	0.1	0.11±	0.01	190±	17	65±	5**	56±	22
20000 ppm	9	6.0±	0.2**	3.5±	0.1	1.4±	0.1**	0.11±	0.01	172±	10*	65±	6**	31±	13

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

STUDY NO. : 0459
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	110±	9	82±	31	54±	13	178±	59	270±	17	1±	0	113±	12
1250 ppm	10	113±	6	82±	17	51±	10	185±	42	269±	12	1±	0	116±	16
2500 ppm	10	111±	6	79±	27	50±	12	191±	67	266±	14	1±	0	113±	8
5000 ppm	10	112±	7	86±	39	52±	15	197±	78	274±	18	1±	0	114±	10
10000 ppm	10	122±	9**	97±	41	56±	17	225±	87	277±	25	1±	0	104±	8
20000 ppm	9	122±	8**	104±	33	72±	50	214±	44	278±	17	1±	1	112±	12

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

STUDY NO. : 0459
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	19.3± 1.6	0.5± 0.1	142± 1	3.5± 0.3	107± 1	10.2± 0.2	5.7± 0.9
1250 ppm	10	19.2± 1.1	0.5± 0.1	142± 1	3.4± 0.2	106± 2	10.2± 0.2	5.8± 1.0
2500 ppm	10	18.3± 1.2	0.5± 0.1	142± 1	3.5± 0.4	107± 1	10.2± 0.1	5.7± 1.0
5000 ppm	10	18.9± 1.2	0.5± 0.1	141± 1	3.6± 0.3	107± 1	10.1± 0.1	5.7± 1.1
10000 ppm	10	20.6± 1.9	0.5± 0.1	141± 1*	3.8± 0.4*	106± 1	10.1± 0.2	5.6± 0.8
20000 ppm	9	25.8± 4.2*	0.5± 0.1	140± 1**	3.9± 0.4*	106± 2	9.9± 0.3**	5.6± 0.9

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

APPENDIX G 2

BIOCHEMISTRY : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0459
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	3.4± 0.1	1.2± 0.1	0.12± 0.01	146± 13	66± 5	11± 3
1250 ppm	10	6.2± 0.2	3.4± 0.1	1.2± 0.0	0.12± 0.01	145± 15	64± 6	11± 3
2500 ppm	10	6.1± 0.2	3.3± 0.1	1.2± 0.1	0.13± 0.02	139± 11	63± 7	9± 2
5000 ppm	10	6.0± 0.1	3.3± 0.1	1.3± 0.1	0.12± 0.01	149± 10	64± 6	10± 3
10000 ppm	10	5.9± 0.2*	3.3± 0.1	1.3± 0.1	0.13± 0.01	148± 9	60± 5	10± 2
20000 ppm	10	5.9± 0.2	3.4± 0.1	1.4± 0.1**	0.13± 0.01	141± 18	67± 8	12± 4

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

STUDY NO. : 0459
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± 8	83± 23	42± 16	271± 129	189± 19	2± 1	138± 41
1250 ppm	10	128± 12	72± 9	35± 8	236± 105	196± 17	1± 1	130± 42
2500 ppm	10	126± 11	79± 14	41± 12	293± 105	206± 20	1± 1	142± 32
5000 ppm	10	127± 9	78± 14	38± 10	264± 91	210± 16	2± 1	133± 32
10000 ppm	10	120± 8	75± 7	36± 7	290± 96	207± 24	2± 1	136± 30
20000 ppm	10	129± 14	85± 16	40± 7	322± 77	250± 23**	2± 0	138± 25

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

STUDY NO. : 0459
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	18.7± 2.0	0.5± 0.1	140± 1	3.7± 0.3	108± 2	9.8± 0.1	5.1± 1.4
1250 ppm	10	19.5± 1.6	0.5± 0.1	140± 1	3.6± 0.3	108± 2	9.8± 0.2	5.1± 1.0
2500 ppm	10	19.6± 2.7	0.5± 0.1	139± 2	3.9± 0.3	108± 2	9.8± 0.2	5.5± 0.9
5000 ppm	10	20.0± 3.6	0.5± 0.1	140± 1	3.8± 0.3	108± 2	9.8± 0.2	5.4± 1.4
10000 ppm	10	22.8± 3.3**	0.5± 0.0	139± 1	3.9± 0.2	107± 1	9.6± 0.2	5.5± 0.7
20000 ppm	10	28.4± 2.6**	0.5± 0.1	139± 1	4.0± 0.2	107± 1	9.6± 0.3	5.7± 0.8

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

APPENDIX H 1

URINALYSIS : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0459 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	1	5	4		0	2	8	0	0	0		10	0	0	0	0	0		7	3	0	0	0	0		10	0	0	0	
1250 ppm	10	0	0	1	0	0	3	6		0	4	6	0	0	0		10	0	0	0	0	0		6	4	0	0	0	0		10	0	0	0	
2500 ppm	10	0	0	0	0	0	3	7		0	1	8	1	0	0		10	0	0	0	0	0		5	5	0	0	0	0		10	0	0	0	
5000 ppm	10	0	0	0	0	0	3	7		0	0	9	1	0	0		10	0	0	0	0	0		1	8	1	0	0	0	*	10	0	0	0	
10000 ppm	10	0	0	0	1	3	2	4		0	2	7	1	0	0		10	0	0	0	0	0		2	6	2	0	0	0		10	0	0	0	
20000 ppm	9	0	1	3	2	2	0	1	*	2	5	1	1	0	0	*	9	0	0	0	0	0		8	1	0	0	0	0		9	0	0	0	

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

STUDY NO. : 0459 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	
1250 ppm	10	10	0	0	0	0		10	0	0	0	0	
2500 ppm	10	10	0	0	0	0		10	0	0	0	0	
5000 ppm	10	10	0	0	0	0		10	0	0	0	0	
10000 ppm	10	10	0	0	0	0		10	0	0	0	0	
20000 ppm	9	7	1	0	0	1		9	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. : 0459 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	8	2		1	8	1	0	0	0		10	0	0	0	0	0		9	1	0	0	0	0		10	0	0	0	
1250 ppm	10	0	0	0	0	1	8	1		1	5	4	0	0	0		10	0	0	0	0	0		7	3	0	0	0	0		10	0	0	0	
2500 ppm	10	0	0	0	0	0	6	4		0	6	4	0	0	0		10	0	0	0	0	0		7	3	0	0	0	0		10	0	0	0	
5000 ppm	10	0	0	0	0	0	6	4		0	6	2	2	0	0		10	0	0	0	0	0		4	6	0	0	0	0	*	10	0	0	0	
10000 ppm	10	0	0	0	0	1	6	3		0	3	7	0	0	0	*	10	0	0	0	0	0		2	8	0	0	0	0	**	10	0	0	0	
20000 ppm	10	0	0	6	2	0	2	0	**	2	7	1	0	0	0		10	0	0	0	0	0		7	3	0	0	0	0		10	0	0	0	

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

STUDY NO. : 0459 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	
1250 ppm	10	10	0	0	0	0		10	0	0	0	0	
2500 ppm	10	10	0	0	0	0		10	0	0	0	0	
5000 ppm	10	10	0	0	0	0		10	0	0	0	0	
10000 ppm	10	10	0	0	0	0		10	0	0	0	0	
20000 ppm	10	10	0	0	0	0		10	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. : 0459
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 (%)	1250 ppm 10 (%)	2500 ppm 10 (%)	5000 ppm 10 (%)
subcutis	dry		0 (0)	0 (0)	0 (0)	0 (0)
liver	herniation		3 (30)	0 (0)	0 (0)	0 (0)

STUDY NO. : 0459
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	10000 ppm	20000 ppm
		NO. of Animals	10 (%)	10 (%)
subcutis	dry		0 (0)	1 (10)
liver	herniation		2 (20)	0 (0)

APPENDIX I 2

GROSS FINDINGS : SUMMARY, RAT : FEMALE : ALL ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0459
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	1250 ppm 10 (%)	2500 ppm 10 (%)	5000 ppm 10 (%)
gl stomach	nodule		0 (0)	0 (0)	0 (0)	0 (0)
liver	herniation		0 (0)	3 (30)	2 (20)	2 (20)

Organ	Findings	Group Name / NO. of Animals	10000 ppm 10 (%)	20000 ppm 10 (%)
gl stomach	nodule		0 (0)	1 (10)
liver	herniation		1 (10)	2 (20)

APPENDIX I 3

GROSS FINDINGS : SUMMARY, RAT : MALE : DEAD AND MORIBUND ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0459
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name NO. of Animals	Control 0 (%)	1250 ppm 0 (%)	2500 ppm 0 (%)	5000 ppm 0 (%)
subcutis	dry		- (-)	- (-)	- (-)	- (-)

STUDY NO. : 0459
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name NO. of Animals	10000 ppm 0 (%)	20000 ppm 1 (%)
subcutis	dry		- (-)	1 (100)

APPENDIX I 4

GROSS FINDINGS : SUMMARY, RAT : MALE : SACRIFICED ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0459
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	1250 ppm 10 (%)	2500 ppm 10 (%)	5000 ppm 10 (%)
liver	herniation		3 (30)	0 (0)	0 (0)	0 (0)

STUDY NO. : 0459
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name	10000 ppm	20000 ppm
		NO. of Animals	10 (%)	9 (%)
liver	herniation		2 (20)	0 (0)

APPENDIX J 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0459
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	292± 17	0.224± 0.031	0.055± 0.009	3.062± 0.135	0.932± 0.056	0.970± 0.054
1250 ppm	10	293± 19	0.228± 0.036	0.052± 0.006	3.032± 0.086	0.935± 0.053	0.975± 0.050
2500 ppm	10	284± 15	0.227± 0.035	0.048± 0.003	2.982± 0.124	0.885± 0.048	0.956± 0.050
5000 ppm	10	290± 18	0.234± 0.044	0.052± 0.003	3.006± 0.135	0.936± 0.061	0.964± 0.053
10000 ppm	10	288± 24	0.240± 0.061	0.052± 0.003	2.967± 0.194	0.929± 0.087	0.980± 0.076
20000 ppm	9	239± 29**	0.158± 0.047**	0.051± 0.010	2.810± 0.125**	0.790± 0.089**	0.888± 0.066*

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

STUDY NO. : 0459
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	THYROID
Control	10	1.788± 0.112	0.540± 0.037	7.046± 0.546	1.926± 0.061	0.027± 0.004
1250 ppm	10	1.785± 0.097	0.544± 0.037	7.080± 0.463	1.954± 0.053	0.028± 0.005
2500 ppm	10	1.773± 0.073	0.523± 0.027	6.901± 0.376	1.900± 0.056	0.029± 0.007
5000 ppm	10	1.836± 0.084	0.537± 0.030	7.159± 0.525	1.900± 0.058	0.026± 0.003
10000 ppm	10	1.838± 0.149	0.533± 0.037	7.382± 0.700	1.900± 0.079	0.027± 0.003
20000 ppm	9	1.849± 0.155	0.448± 0.063**	6.616± 0.904	1.871± 0.034	0.029± 0.007

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. : 0459
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	162± 7	0.174± 0.019	0.057± 0.005	0.095± 0.014	0.606± 0.047	0.732± 0.040
1250 ppm	10	157± 13	0.179± 0.026	0.054± 0.006	0.092± 0.012	0.572± 0.051	0.716± 0.033
2500 ppm	10	152± 8	0.178± 0.021	0.055± 0.005	0.090± 0.007	0.569± 0.036	0.722± 0.020
5000 ppm	10	154± 9	0.178± 0.020	0.054± 0.005	0.089± 0.013	0.580± 0.034	0.733± 0.053
10000 ppm	10	150± 11	0.182± 0.018	0.051± 0.005*	0.085± 0.010	0.576± 0.039	0.712± 0.026
20000 ppm	10	135± 13**	0.145± 0.017*	0.046± 0.004**	0.075± 0.013**	0.511± 0.055**	0.653± 0.041**

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

STUDY NO. : 0459
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	THYROID
Control	10	1.097± 0.069	0.368± 0.024	3.860± 0.211	1.759± 0.044	0.024± 0.004
1250 ppm	10	1.094± 0.065	0.359± 0.035	3.748± 0.315	1.775± 0.052	0.024± 0.006
2500 ppm	10	1.080± 0.040	0.356± 0.020	3.626± 0.195	1.753± 0.031	0.023± 0.004
5000 ppm	10	1.119± 0.047	0.355± 0.026	3.719± 0.133	1.758± 0.040	0.026± 0.006
10000 ppm	10	1.119± 0.053	0.353± 0.020	3.718± 0.274	1.768± 0.057	0.025± 0.006
20000 ppm	10	1.149± 0.093	0.317± 0.027**	3.704± 0.396	1.723± 0.062	0.024± 0.005

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. : 0459
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	292± 17	0.076± 0.008	0.019± 0.004	1.050± 0.029	0.320± 0.006	0.333± 0.015
1250 ppm	10	293± 19	0.078± 0.011	0.018± 0.002	1.038± 0.045	0.320± 0.013	0.334± 0.015
2500 ppm	10	284± 15	0.080± 0.011	0.017± 0.001	1.052± 0.042	0.312± 0.012	0.337± 0.019
5000 ppm	10	290± 18	0.080± 0.012	0.018± 0.001	1.039± 0.049	0.323± 0.010	0.333± 0.014
10000 ppm	10	288± 24	0.083± 0.016	0.018± 0.002	1.035± 0.070	0.323± 0.016	0.342± 0.029
20000 ppm	9	239± 29**	0.065± 0.016	0.022± 0.003	1.187± 0.119*	0.331± 0.017	0.374± 0.031*

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

STUDY NO. : 0459
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	THYROID
Control	10	0.613± 0.019	0.185± 0.009	2.412± 0.064	0.661± 0.036	0.009± 0.002
1250 ppm	10	0.611± 0.018	0.186± 0.006	2.419± 0.064	0.670± 0.043	0.009± 0.002
2500 ppm	10	0.626± 0.028	0.184± 0.007	2.432± 0.064	0.671± 0.035	0.010± 0.002
5000 ppm	10	0.634± 0.017	0.185± 0.008	2.468± 0.056	0.657± 0.038	0.009± 0.001
10000 ppm	10	0.640± 0.024	0.186± 0.009	2.564± 0.052**	0.663± 0.042	0.009± 0.001
20000 ppm	9	0.779± 0.077**	0.187± 0.008	2.763± 0.127**	0.794± 0.112**	0.012± 0.003*

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. : 0459
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	162± 7	0.107± 0.010	0.035± 0.003	0.058± 0.008	0.374± 0.020	0.453± 0.023
1250 ppm	10	157± 13	0.114± 0.015	0.035± 0.004	0.059± 0.006	0.365± 0.021	0.458± 0.031
2500 ppm	10	152± 8	0.118± 0.015	0.036± 0.004	0.059± 0.005	0.375± 0.022	0.476± 0.027
5000 ppm	10	154± 9	0.116± 0.013	0.035± 0.003	0.058± 0.009	0.377± 0.016	0.477± 0.039
10000 ppm	10	150± 11	0.122± 0.011	0.034± 0.003	0.057± 0.008	0.385± 0.013	0.476± 0.035
20000 ppm	10	135± 13**	0.107± 0.012	0.034± 0.002	0.055± 0.006	0.378± 0.022	0.485± 0.040

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

STUDY NO. : 0459
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	THYROID
Control	10	0.678± 0.027	0.227± 0.013	2.383± 0.053	1.089± 0.064	0.015± 0.002
1250 ppm	10	0.699± 0.044	0.229± 0.016	2.388± 0.051	1.137± 0.088	0.016± 0.005
2500 ppm	10	0.712± 0.042	0.234± 0.010	2.385± 0.058	1.156± 0.062	0.015± 0.003
5000 ppm	10	0.728± 0.030	0.231± 0.015	2.419± 0.070	1.145± 0.065	0.017± 0.004
10000 ppm	10	0.747± 0.024**	0.236± 0.011	2.479± 0.074*	1.183± 0.077*	0.017± 0.004
20000 ppm	10	0.853± 0.078**	0.235± 0.013	2.735± 0.119**	1.279± 0.088**	0.018± 0.005

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)

STUDY NO. : 0459
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
ALL ANIMALS (0- 14W)

Organ	Findings	Group Name	Control				1250 ppm				2500 ppm				5000 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>			
	mineralization		0	0	0	0	1	0	0	0	2	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
{Hematopoietic system}																		
thymus			<10>				<10>				<10>				<10>			
	atrophy		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen			<10>				<10>				<10>				<10>			
	atrophy		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	deposit of hemosiderin		10	0	0	0	10	0	0	0	10	0	0	0	10	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Circulatory system}																		
heart			<10>				<10>				<10>				<10>			
	myocardial fibrosis		1	0	0	0	1	0	0	0	2	1	0	0	3	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(20)	(10)	(0)	(0)	(30)	(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	10000 ppm				20000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			<10>				<10>			
	mineralization		2	0	0	0	1	0	0	0
			(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Hematopoietic system}										
thymus			<10>				<10>			
	atrophy		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
spleen			<10>				<10>			
	atrophy		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	deposit of hemosiderin		10	0	0	0	9	1	0	0
			(100)	(0)	(0)	(0)	(90)	(10)	(0)	(0)
{Circulatory system}										
heart			<10>				<10>			
	myocardial fibrosis		0	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(30)	(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				1250 ppm				2500 ppm				5000 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>			
	herniation		3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(30)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	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)
{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)
	eosinophilic body		10	0	0	0	10	0	0	0	10	0	0	0	10	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	hyaline cast		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(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
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	urothelial hyperplasia:pelvis		0	0	0	0	0	0	0	0	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	10000 ppm				20000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
liver			<10>				<10>			
	herniation		2	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	granulation		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)
	eosinophilic body		9	0	0	0	8	0	0	0
			(90)	(0)	(0)	(0)	(80)	(0)	(0)	(0)
	hyaline cast		2	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:papilla		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	urothelial hyperplasia:pelvis		2	0	0	0	4	2	0	0 *
			(20)	(0)	(0)	(0)	(40)	(20)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				1250 ppm				2500 ppm				5000 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)
{Endocrine system}																		
pituitary			<10>				<10>				<10>				<10>			
	Rathke pouch		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)
	aberrant craniopharyngeal tissue		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thyroid			<10>				<10>				<10>				<10>			
	ultimibranchial 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)
{Nervous system}																		
brain			<10>				<10>				<10>				<10>			
	mineralization		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)

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	10000 ppm				20000 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		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Endocrine system}										
pituitary			<10>				<10>			
	Rathke pouch		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	aberrant craniopharyngeal tissue		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
thyroid			<10>				< 9>			
	ultimibranchial body remanet		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Nervous system}										
brain			<10>				<10>			
	mineralization		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				1250 ppm				2500 ppm				5000 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>			
	lymphocytic infiltration		1	0	0	0	2	0	0	0	2	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(20)	(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	10000 ppm				20000 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>			
	lymphocytic infiltration		2	0	0	0	1	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

APPENDIX L 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : ALL ANIMALS

(13-WEEK STUDY)

Organ	Findings	Group Name	Control				1250 ppm				2500 ppm				5000 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>			
	osseous metaplasia		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)
{Hematopoietic system}																		
bone marrow			<10>				<10>				<10>				<10>			
	granulation		2	0	0	0	0	0	0	0	0	1	0	0	2	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(20)	(0)	(0)	(0)
lymph node			<10>				<10>				<10>				<10>			
	granulation		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 hemosiderin		10	0	0	0	10	0	0	0	10	0	0	0	10	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Digestive system}																		
stomach			<10>				<10>				<10>				<10>			
	ectopia:glandular stomach		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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	10000 ppm				20000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
lung			<10>				<10>			
	osseous metaplasia		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}										
bone marrow			<10>				<10>			
	granulation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lymph node			<10>				<10>			
	granulation		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
spleen			<10>				<10>			
	deposit of hemosiderin		10	0	0	0	10	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Digestive system}										
stomach			<10>				<10>			
	ectopia:glandular stomach		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				1250 ppm				2500 ppm				5000 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>			
	herniation		0	0	0	0	3	0	0	0	2	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	granulation		1	0	0	0	1	0	0	0	1	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	hyaline cast		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:cortico-medullary junction		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)
	mineralization:papilla		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)
	urothelial hyperplasia:pelvis		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
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)

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	10000 ppm				20000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
liver			<10>				<10>			
	herniation		1	0	0	0	2	0	0	0
			(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	granulation		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Urinary system}										
kidney			<10>				<10>			
	hyaline cast		2	0	0	0	1	0	0	0
			(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	mineralization:cortico-medullary junction		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:papilla		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	urothelial hyperplasia:pelvis		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
urin bladd			<10>				<10>			
	simple hyperplasia:transitional epithelium		1	1	0	0	2	3	0	0 *
			(10)	(10)	(0)	(0)	(20)	(30)	(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				1250 ppm				2500 ppm				5000 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:transitionnal epithelium with papillary-like pattern		0 (0)	0 (0)	0 (0)	0 (0)	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}																		
pituitary			<10>				<10>				<10>				<10>			
	Rathke pouch		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
thyroid			<10>				<10>				<10>				<10>			
	ultimibranchial body remanet		1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
{Special sense organs/appendage}																		
Harder gl			<10>				<10>				<10>				<10>			
	lymphocytic infiltration		2 (20)	0 (0)	0 (0)	0 (0)	3 (30)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	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	10000 ppm				20000 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:transitionnal epithelium with papillary-like pattern		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)
{Endocrine system}										
pituitary			<10>				<10>			
	Rathke pouch		1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
thyroid			<10>				< 9>			
	ultimibranchial body remanet		1 (10)	0 (0)	0 (0)	0 (0)	1 (11)	0 (0)	0 (0)	0 (0)
{Special sense organs/appendage}										
Harder gl			<10>				<10>			
	lymphocytic infiltration		1 (10)	0 (0)	0 (0)	0 (0)	3 (30)	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 3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : DEAD AND MORIBUND ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0459
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control				1250 ppm				2500 ppm				5000 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}																		
thymus			< 0>				< 0>				< 0>				< 0>			
	atrophy		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
spleen			< 0>				< 0>				< 0>				< 0>			
	atrophy		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	deposit of hemosiderin		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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	10000 ppm				20000 ppm			
		No. of Animals on Study	0				1			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Hematopoietic system}										
thymus			< 0>				< 1>			
	atrophy		- (-)	- (-)	- (-)	- (-)	1 (100)	0 (0)	0 (0)	0 (0)
spleen			< 0>				< 1>			
	atrophy		- (-)	- (-)	- (-)	- (-)	1 (100)	0 (0)	0 (0)	0 (0)
	deposit of hemosiderin		- (-)	- (-)	- (-)	- (-)	0 (0)	1 (100)	0 (0)	0 (0)

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

APPENDIX L 4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : SACRIFICED ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0459
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name	Control				1250 ppm				2500 ppm				5000 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>			
	mineralization		0	0	0	0	1	0	0	0	2	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
{Hematopoietic system}																		
spleen			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		10	0	0	0	10	0	0	0	10	0	0	0	10	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Circulatory system}																		
heart			<10>				<10>				<10>				<10>			
	myocardial fibrosis		1	0	0	0	1	0	0	0	2	1	0	0	3	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(20)	(10)	(0)	(0)	(30)	(0)	(0)	(0)
{Digestive system}																		
liver			<10>				<10>				<10>				<10>			
	herniation		3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(30)	(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	10000 ppm				20000 ppm			
		No. of Animals on Study	10				9			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			<10>				< 9>			
	mineralization		2	0	0	0	1	0	0	0
			(20)	(0)	(0)	(0)	(11)	(0)	(0)	(0)
{Hematopoietic system}										
spleen			<10>				< 9>			
	deposit of hemosiderin		10	0	0	0	9	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Circulatory system}										
heart			<10>				< 9>			
	myocardial fibrosis		0	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(33)	(0)	(0)	(0)
{Digestive system}										
liver			<10>				< 9>			
	herniation		2	0	0	0	0	0	0	0
			(20)	(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				1250 ppm				2500 ppm				5000 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	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)
{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)
	eosinophilic body		10	0	0	0	10	0	0	0	10	0	0	0	10	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	hyaline cast		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(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
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	urothelial hyperplasia:pelvis		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
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)

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	10000 ppm				20000 ppm			
		No. of Animals on Study	10				9			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
liver			<10>				< 9>			
	granulation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Urinary system}										
kidney			<10>				< 9>			
	basophilic change		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	eosinophilic body		9	0	0	0	8	0	0	0
			(90)	(0)	(0)	(0)	(89)	(0)	(0)	(0)
	hyaline cast		2	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:papilla		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(22)	(0)	(0)	(0)
	urothelial hyperplasia:pelvis		2	0	0	0	4	2	0	0 **
			(20)	(0)	(0)	(0)	(44)	(22)	(0)	(0)
urin bladd			<10>				< 9>			
	simple hyperplasia:transitional epithelium		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(11)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
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(c) c : b / a * 100
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Organ	Findings	Group Name	Control				1250 ppm				2500 ppm				5000 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Endocrine system}																		
pituitary			<10>				<10>				<10>				<10>			
	Rathke pouch		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)
	aberrant craniopharyngeal tissue		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thyroid			<10>				<10>				<10>				<10>			
	ultimibranchial 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)
{Nervous system}																		
brain			<10>				<10>				<10>				<10>			
	mineralization		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)
{Special sense organs/appendage}																		
Harder gl			<10>				<10>				<10>				<10>			
	lymphocytic infiltration		1	0	0	0	2	0	0	0	2	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(20)	(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	10000 ppm				20000 ppm			
		No. of Animals on Study	10				9			
		Grade	1	2	3	4	1	2	.3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Endocrine system}										
pituitary			<10>				< 9>			
	Rathke pouch		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	aberrant craniopharyngeal tissue		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(11)	(0)	(0)	(0)
thyroid			<10>				< 9>			
	ultimibranchial body remanet		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Nervous system}										
brain			<10>				< 9>			
	mineralization		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Special sense organs/appendage}										
Harder gl			<10>				< 9>			
	lymphocytic infiltration		2	0	0	0	1	0	0	0
			(20)	(0)	(0)	(0)	(11)	(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 2-PHENOXYETHANOL

IN THE 13-WEEK DRINKING WATER STUDY

IDENTITY OF 2-PHENOXYETHANOL IN THE 13-WEEK DRINKING WATER STUDY

Test Substance : 2-Phenoxyethanol (Wako Pure Chemical Industries, Ltd.)

Lot No. : WAL4150

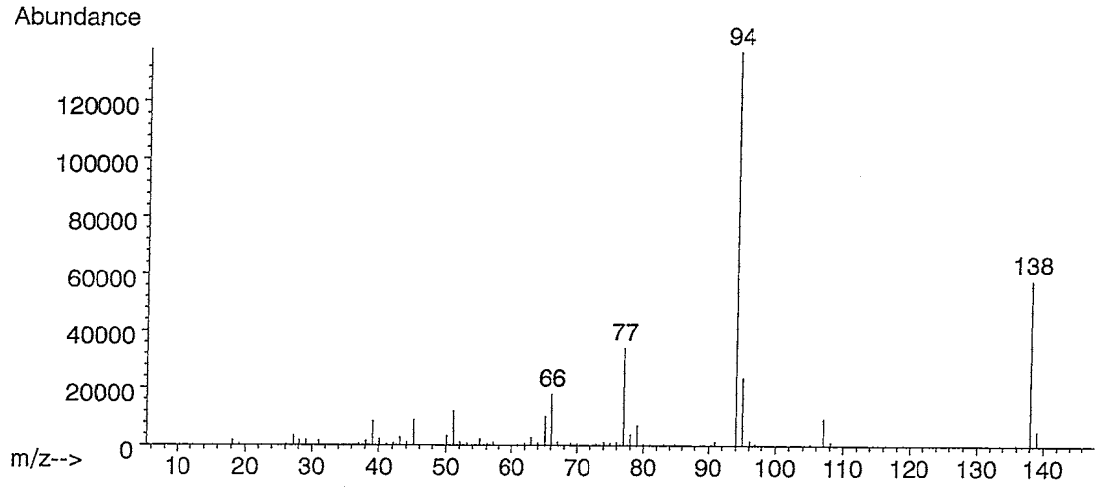
1. Spectral Data

Mass Spectrometry

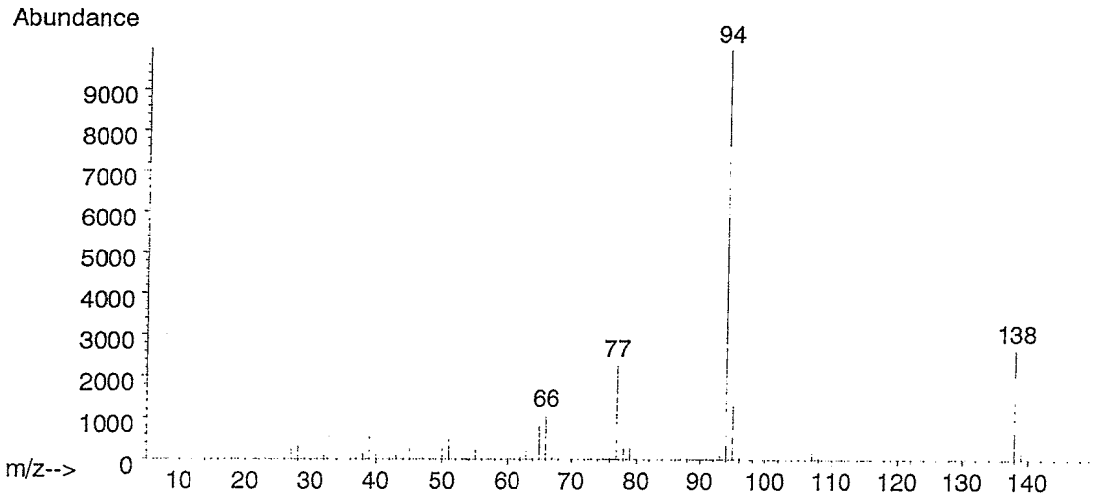
Instrument : Hewlett Packard 5989B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance



Mass Spectrum of Literature Data*

Result: The mass spectrum was consistent with literature spectrum.

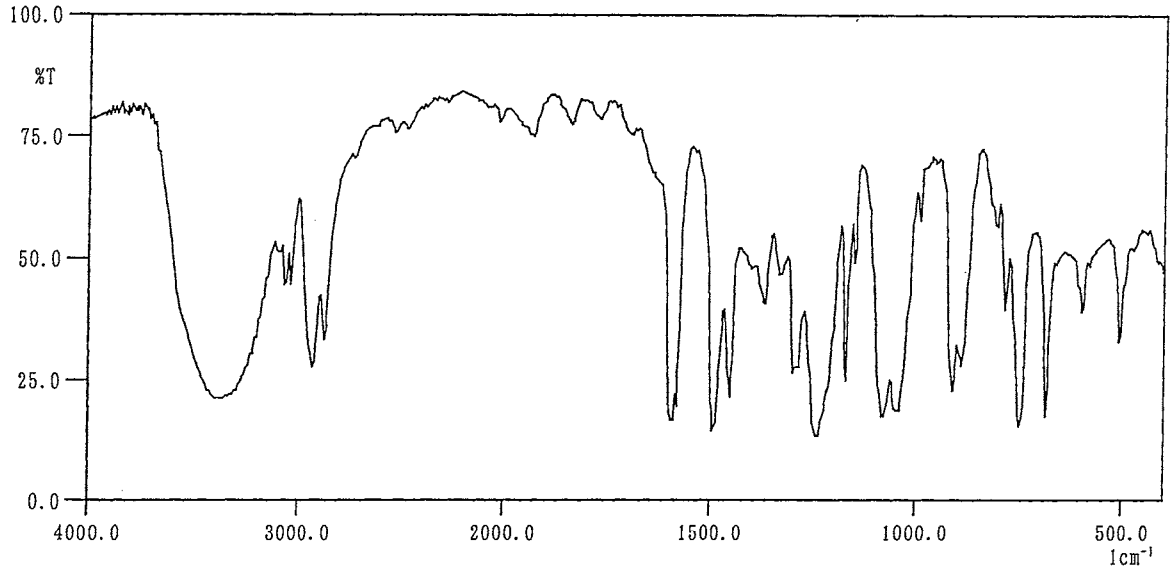
(*McLafferty, F.W. (1994)
Wiley Registry of Mass Spectral Data, (6th edition), Entry Number 25888
John Wiley and Sons, New York, NY)

Infrared Spectrometry

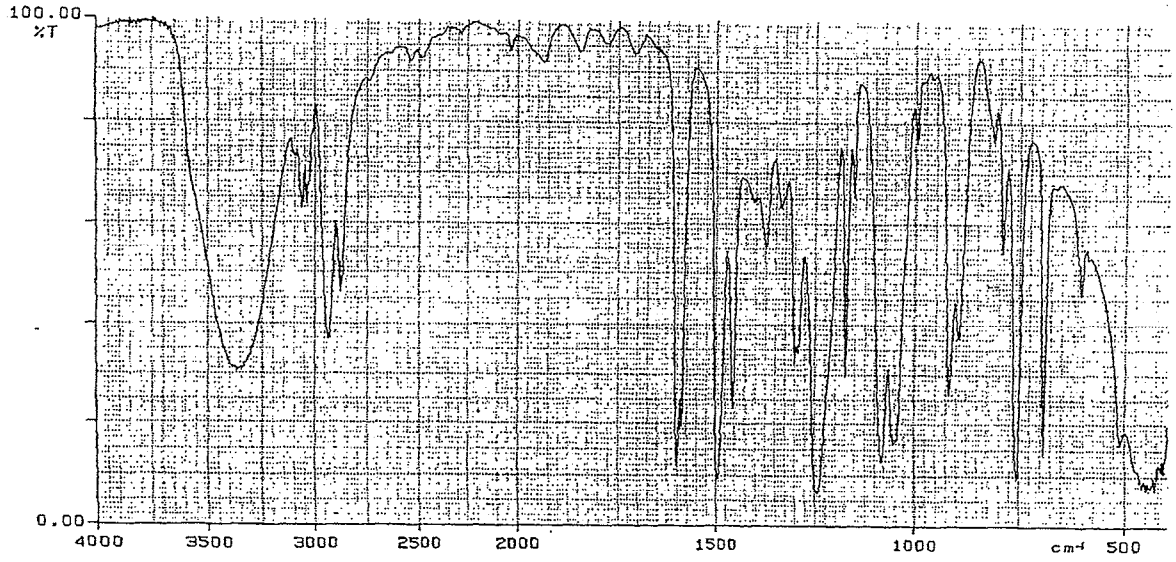
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 2 cm^{-1}



Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data*

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

2. Conclusion: The test substance was identified as 2-phenoxyethanol by mass spectrum and infrared spectrum.

APPENDIX M 2

STABILITY OF 2-PHENOXYETHANOL

IN THE 13-WEEK DRINKING WATER STUDY

STABILITY OF 2-PHENOXYETHANOL IN THE 13-WEEK DRINKING WATER STUDY

Test Substance : 2-Phenoxyethanol (Wako Pure Chemical Industries, Ltd.)

Lot No. : WAL4150

1. Sample : This lot was used from 2002.9.6 to 2002.12.10. Test substance was stored in a dark place at room temperature.

2. High Performance Liquid Chromatography

Instrument : Shimadzu LC-10 High Performance Liquid Chromatograph

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

Column Temperature : 40 °C

Flow Rate : 1 mL/min

Mobile Phase : Acetonitrile : Distilled Water = 4 : 6

Detector : UV (271 nm)

Injection Volume : 10 μL

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
2002.09.02	1	3.657	100
2002.12.16	1	3.480	100

Result: High performance liquid chromatography indicated one major peak (peak No.1) analyzed on 2002.9.2 and one major peak (peak No.1) analyzed on 2002.12.16. No new trace impurity peak in the test substance analyzed on 2002.12.16 was detected.

3. Conclusion: The test substance was stable for about 15 weeks in a dark place at room temperature.

APPENDIX M 3

CONCENTRATION OF 2-PHENOXYETHANOL IN FORMULATED WATER IN THE 13-WEEK DRINKING WATER STUDY

CONCENTRATION OF 2-PHENOXYETHANOL IN FORMULATED WATER IN THE 13-WEEK DRINKING WATER STUDY

	Target Concentration				
Date Analyzed	1250[a]	2500	5000	10000	20000
2002.09.06	1280 (102)[b]	2560 (102)	5070 (101)	10200 (102)	20200 (101)

[a] ppm
[b] %

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

Instrument : Shimadzu LC-10 High Performance Liquid Chromatograph
Column : TSK GEL ODS-80TM (4.6 mmϕ × 15 cm)
Column Temperature : 40 °C
Flow Rate : 1 mL/min
Mobile Phase : Acetonitrile : Distilled Water = 4 : 6
Detector : UV (271 nm)
Injection Volume : 10 μL

APPENDIX M 4

STABILITY OF 2-PHENOXYETHANOL IN FORMULATED WATER

STABILITY OF 2-PHENOXYETHANOL IN FORMULATED WATER

Date Prepared	Date Analyzed	Target Concentration	
		100[a]	25000
2002.05.15	2002.05.15	97.3 (100)[b]	24600 (100)
	2002.05.20[c]	98.7 (101)	25700 (104)

[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 : Shimadzu LC-10 High Performance Liquid Chromatograph
Column : TSK GEL ODS-80TM (4.6 mmϕ × 15 cm)
Column Temperature : 40 °C
Flow Rate : 1 mL/min
Mobile Phase : Acetonitrile : Distilled Water = 4 : 6
Detector : UV (271 nm)
Injection Volume : 10 μL

APPENDIX N 1

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS IN THE 13-WEEK DRINKING WATER STUDY OF 2-PHENOXYETHANOL

METHODS FOR HEMATOLOGY,BIOCHEMISTRY AND URINALYSIS IN THE 13-WEEK DRINKING WATER STUDY OF 2-PHENOXYETHANOL

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	Light scattering method [1]
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] (Wright 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	GlcK・G-6-PDH method [4]
T-cholesterol	CE・COD・POD method [4]
Triglyceride	LPL・GK・GPO・POD method [4]
Phospholipid	PLD・ChOD・POD method [4]
Glutamic oxaloacetic transaminase (GOT)	JSCC method [4]
Glutamic pyruvic transaminase (GPT)	JSCC method [4]
Lactate dehydrogenase (LDH)	SFBC method [4]
Alkaline phosphatase (ALP)	GSCC method [4]
γ-Glutamyl transpeptidase (γ-GTP)	L-γ-Glutamyl-p-nitroanilide method [4]
Creatine phosphokinase (CPK)	JSCC method [4]
Urea nitrogen	Urease・GLDH method [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	PNP・XOD・POD method [4]
Urinalysis	
pH,Protein,Glucose,Ketone body,Bilirubin,Occult Blood, Urobilinogen	Urinalysis reagent paper method [5]

1) Automatic blood cell analyzer (ADVIA120 : Bayer Corporation)

2) Automatic coagulometer (Sysmex CA-5000 : Sysmex Corporation)

3) Automatic blood cell differential analyzer (MICROX HEG-120NA : OMRON Corporation)

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

5) Ames reagent strips for urinalysis (Multistix : Bayer Corporation)

APPENDIX O 1

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK DRINKING WATER STUDY OF 2-PHENOXYETHANOL

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK DRINKING WATER STUDY OF 2-PHENOXYETHANOL

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	%	1
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