グリオキサルのラット及びマウスを用いた
経口投与によるがん原性予備試験(混水試験)報告書

試験番号

13 週間試験：ラット/0234；マウス/0235

APPENDIX

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIX B 1-1

CLINICAL OBSERVATION (THIRTEEN-WEEK STUDY: SUMMARY)

RAT : MALE

STUDY NO. : 0234
ANIMAL : RAT F344
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
		1	1	1	1	1	1	1	1	1	1	1	1	1
LACRYMATION	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	1	1	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0

APPENDIX B 1-2

CLINICAL OBSERVATION (THIRTEEN-WEEK STUDY: SUMMARY)

RAT : FEMALE

STUDY NO. : 0234
ANIMAL : RAT F344
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
		1	1	1	1	1	1	1	1	1	1	1	1	1
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	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	1
EXTERNAL MASS	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	1	1	0	0
	1000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
M.PERI MOUTH	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	1	1	0	0
	1000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0

APPENDIX B 1-3

CLINICAL OBSERVATION (THIRTEEN-WEEK STUDY: SUMMARY)

MOSUE : MALE

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7
		1	1	1	1	1	1	1	1	1	1	1	1	1
DEATH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	1	1	1	1
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	8000 ppm	0	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
	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	1	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	8000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
INTERNAL MASS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	1	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	8000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
OLIGO-STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	1	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	8000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0

APPENDIX B 1-4

CLINICAL OBSERVATION (THIRTEEN-WEEK STUDY: SUMMARY)

MOSUE: FEMALE

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
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
		1	1	1	1	1	1	1	1	1	1	1	1	1
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	8000 ppm	0	1	1	1	1	1	1	1	1	4	6	5	6

APPENDIX B 2-1

BODY WEIGHT CHANGES (THIRTEEN-WEEK STUDY: SUMMARY)

RAT : MALE

STUDY NO. : 0234
ANIMAL : RAT F344
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	122± 4	145± 6	174± 8	195± 11	207± 9	222± 16	240± 17
250 ppm	122± 4	143± 5	169± 7	187± 12	201± 16	211± 20	226± 24
500 ppm	122± 4	144± 5	173± 7	194± 9	211± 11	222± 13	239± 14
1000 ppm	122± 4	143± 6	168± 7	186± 11	202± 14	214± 16	230± 18
2000 ppm	122± 4	141± 6	165± 7*	185± 9	201± 12	214± 13	228± 13
4000 ppm	122± 4	126± 6**	144± 8**	159± 9**	172± 10**	183± 12**	195± 12**

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

STUDY NO. : 0234
ANIMAL : RAT F344
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	251± 20	260± 23	272± 25	281± 25	284± 25	285± 24	293± 23
250 ppm	237± 28	244± 31	257± 34	264± 35	266± 35	265± 33	273± 33
500 ppm	252± 16	260± 18	273± 20	279± 21	281± 22	281± 21	289± 22
1000 ppm	240± 20	248± 23	259± 25	266± 26	269± 25	269± 24	277± 26
2000 ppm	239± 12	246± 11	260± 11	268± 12	272± 13	271± 12	278± 14
4000 ppm	204± 12**	211± 12**	221± 12**	230± 12**	234± 12**	236± 11**	241± 11**

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

APPENDIX B 2-2

BODY WEIGHT CHANGES (THIRTEEN-WEEK STUDY: SUMMARY)

RAT : FEMALE

STUDY NO. : 0234
ANIMAL : RAT F344
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	104± 3	116± 4	129± 5	140± 6	150± 8	156± 10	163± 10
250 ppm	104± 3	117± 4	130± 5	142± 6	151± 7	157± 9	163± 9
500 ppm	104± 3	116± 3	131± 4	141± 5	149± 6	155± 7	162± 8
1000 ppm	104± 3	115± 4	129± 3	139± 5	147± 5	153± 7	159± 5
2000 ppm	104± 3	112± 4	125± 5	134± 6*	141± 7	145± 8**	152± 7**
4000 ppm	104± 3	103± 3**	115± 2**	125± 3**	133± 2**	137± 3**	143± 3**

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

STUDY NO. : 0234
ANIMAL : RAT F344
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	168± 10	171± 11	177± 10	181± 10	183± 11	181± 9	187± 11
250 ppm	168± 9	172± 11	176± 10	182± 11	183± 12	182± 10	188± 13
500 ppm	167± 8	168± 9	174± 8	177± 8	178± 10	176± 9	180± 10
1000 ppm	165± 8	167± 8	172± 8	176± 9	178± 10	177± 9	181± 11
2000 ppm	157± 8*	158± 8*	163± 9**	167± 8**	169± 8**	169± 9*	172± 9**
4000 ppm	147± 5**	150± 5**	154± 5**	158± 5**	159± 5**	158± 4**	160± 5**

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

APPENDIX B 2-3

BODY WEIGHT CHANGES (THIRTEEN-WEEK STUDY: SUMMARY)

MOSUE : MALE

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
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	22.5± 0.6	22.9± 0.5	23.8± 0.5	24.7± 0.7	25.6± 0.9	26.4± 0.7	27.8± 0.8
500 ppm	22.5± 0.7	22.9± 0.9	23.8± 1.0	24.5± 1.6	25.6± 1.5	26.0± 1.5	27.5± 1.7
1000 ppm	22.5± 0.6	23.1± 0.7	24.2± 0.7	24.9± 0.9	25.8± 0.8	26.7± 0.8	27.6± 1.0
2000 ppm	22.5± 0.6	23.3± 0.8	24.0± 1.0	25.1± 1.1	25.5± 1.2	26.3± 1.4	27.3± 1.7
4000 ppm	22.5± 0.6	22.2± 0.7	22.6± 1.4*	23.6± 0.9	24.2± 0.8*	24.7± 0.8**	25.4± 0.8**
8000 ppm	22.5± 0.6	20.9± 0.7**	21.7± 0.8**	22.5± 1.0**	23.2± 0.9**	23.4± 1.1**	24.2± 0.9**

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

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
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	28.4± 1.0	29.3± 1.1	29.8± 1.5	31.0± 1.5	31.4± 1.6	32.7± 1.6	33.5± 1.4
500 ppm	28.1± 1.9	29.1± 2.3	29.3± 2.6	30.1± 2.4	30.5± 2.6	31.5± 2.8	32.1± 2.8
1000 ppm	28.4± 1.0	29.2± 1.1	29.5± 1.4	30.8± 1.6	31.7± 1.7	32.2± 1.7	33.1± 1.7
2000 ppm	27.6± 2.0	28.2± 2.2	27.9± 3.3	29.9± 1.8	30.4± 1.9	31.1± 2.0	31.4± 2.5
4000 ppm	25.7± 0.9**	26.4± 0.9**	26.3± 0.9**	27.0± 1.2**	27.0± 1.1**	27.3± 1.2**	27.8± 1.3**
8000 ppm	24.8± 1.1**	25.1± 1.1**	24.8± 1.0**	25.3± 1.1**	25.3± 0.9**	25.6± 1.0**	25.6± 0.9**

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

APPENDIX B 2-4

BODY WEIGHT CHANGES (THIRTEEN-WEEK STUDY: SUMMARY)

MOSUE: FEMALE

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
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	18.1± 0.7	18.4± 1.0	19.1± 1.0	19.9± 0.8	20.1± 1.4	20.6± 1.4	21.5± 1.0
500 ppm	18.2± 0.7	18.2± 0.7	19.0± 0.7	19.5± 0.7	20.2± 0.6	20.9± 1.2	21.6± 0.9
1000 ppm	18.2± 0.6	18.4± 0.6	19.2± 0.8	19.8± 0.6	20.4± 0.8	20.9± 0.9	21.8± 1.0
2000 ppm	18.2± 0.6	18.3± 0.4	19.0± 0.7	19.6± 0.5	20.2± 0.5	20.7± 0.6	21.5± 0.7
4000 ppm	18.1± 0.7	18.3± 0.6	19.0± 0.8	19.3± 0.8	19.7± 0.6	20.6± 0.9	20.9± 0.7
8000 ppm	18.2± 0.6	16.6± 0.7**	17.5± 1.1**	17.9± 1.5**	18.4± 1.4*	19.2± 1.1*	19.8± 1.4**

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

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
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	22.7± 1.0	22.2± 1.4	22.0± 1.2	23.3± 1.2	23.5± 1.2	23.4± 1.2	23.3± 1.5
500 ppm	22.3± 0.8	21.8± 0.6	22.2± 1.0	22.7± 0.9	23.6± 1.1	23.1± 0.9	23.5± 1.0
1000 ppm	22.6± 0.8	22.1± 0.7	22.6± 1.1	23.0± 0.9	23.4± 0.8	23.4± 1.2	23.5± 0.8
2000 ppm	22.2± 0.9	21.8± 0.7	21.9± 0.8	22.5± 1.3	23.4± 1.2	22.9± 0.9	23.3± 0.7
4000 ppm	21.2± 0.8**	21.3± 0.9	21.6± 0.9	21.9± 0.8**	22.8± 1.7	22.4± 0.7	22.2± 0.8
8000 ppm	20.3± 1.1**	20.6± 1.0**	20.5± 1.2**	21.2± 1.0**	21.1± 0.9**	21.5± 1.0**	21.8± 1.4*

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

APPENDIX B 3-1

WATER CONSUMPTION CHANGES : SUMMARY, RAT: MALE

(THIRTEEN-WEEK STUDY)

STUDY NO. : 0234
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(4)	2-7(4)	3-7(4)	4-7(4)	5-7(4)	6-7(4)	7-7(4)
Control	17.3± 0.8	18.5± 1.0	18.9± 1.8	19.0± 4.6	16.2± 2.4	17.6± 4.6	18.5± 4.1
250 ppm	16.7± 0.9	17.8± 1.0	17.6± 1.6	17.2± 2.1	14.5± 2.5	15.3± 2.5	16.4± 4.1
500 ppm	17.2± 0.8	18.5± 1.0	18.1± 1.0	18.1± 1.7	15.7± 1.7	16.3± 1.6	17.3± 2.4
1000 ppm	14.9± 0.8**	15.3± 0.7*	15.0± 1.4**	14.6± 1.1*	13.2± 1.3**	14.0± 1.4	14.1± 1.9*
2000 ppm	13.3± 0.7**	14.1± 1.0**	13.7± 1.2**	13.2± 1.0**	12.6± 1.1**	13.1± 1.0**	13.4± 1.2**
4000 ppm	11.0± 0.8**	13.3± 5.2**	11.4± 1.4**	10.6± 0.9**	9.7± 1.2**	10.2± 1.0**	10.5± 1.1**

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

STUDY NO. : 0234
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(4)	9-7(4)	10-7(4)	11-7(4)	12-7(4)	13-7(4)
Control	16.0± 1.7	17.5± 1.7	17.8± 1.8	16.4± 1.5	15.3± 1.5	15.1± 1.4
250 ppm	15.0± 3.2	16.7± 3.5	16.3± 3.1	15.2± 2.9	14.2± 2.8	14.5± 2.2
500 ppm	16.4± 3.5	19.7± 8.3	19.0± 8.8	16.1± 2.9	15.4± 4.4	15.8± 3.4
1000 ppm	13.3± 1.8	14.8± 1.8	14.4± 2.0	13.5± 1.8*	12.6± 1.7	13.2± 1.9
2000 ppm	12.6± 0.9*	14.0± 1.2*	13.4± 1.1**	13.3± 1.1*	12.1± 1.0*	12.7± 1.2*
4000 ppm	9.5± 0.9**	10.8± 0.9**	10.4± 1.0**	10.4± 0.7**	9.5± 0.6**	10.1± 0.7**

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

APPENDIX B 3-2

WATER CONSUMPTION CHANGES : SUMMARY, RAT: FEMALE

(THIRTEEN-WEEK STUDY)

STUDY NO. : 0234
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(4)	2-7(4)	3-7(4)	4-7(4)	5-7(4)	6-7(4)	7-7(4)
Control	17.6± 4.0	17.3± 3.5	16.6± 1.7	17.1± 2.5	15.0± 1.6	15.0± 2.3	14.8± 1.9
250 ppm	15.8± 1.1	15.6± 0.9	15.8± 0.9	15.4± 1.2	13.9± 1.0	14.2± 1.2	14.8± 1.2
500 ppm	16.6± 3.0	16.8± 3.0	15.8± 1.3	15.9± 1.6	15.4± 4.2	17.5± 8.3	14.8± 2.7
1000 ppm	13.1± 1.1**	13.9± 2.9	12.7± 1.2**	13.0± 1.6*	13.1± 3.3	12.1± 3.1	13.4± 4.7
2000 ppm	11.3± 0.8**	11.5± 0.7**	11.4± 0.7**	10.9± 0.8**	9.8± 0.8**	9.9± 0.9**	10.1± 0.8**
4000 ppm	10.0± 0.9**	9.8± 0.7**	9.5± 0.7**	9.1± 0.6**	8.3± 0.6**	8.7± 1.2**	8.7± 0.9**

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

STUDY NO. : 0234
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(4)	9-7(4)	10-7(4)	11-7(4)	12-7(4)	13-7(4)
Control	15.0± 3.9	14.5± 2.2	17.3± 6.4	16.8± 6.8	13.6± 2.4	14.1± 2.0
250 ppm	13.8± 1.0	14.3± 1.0	15.1± 1.7	15.1± 2.4	13.4± 3.6	14.0± 1.2
500 ppm	12.8± 1.2	17.0± 7.8	18.5± 8.2	15.4± 3.6	12.3± 1.6	14.1± 3.2
1000 ppm	11.8± 2.9	13.0± 4.8	11.6± 1.7*	14.9± 5.9	12.9± 5.2	13.3± 4.9
2000 ppm	9.2± 0.7**	9.9± 1.0**	10.0± 1.2**	9.9± 1.3**	8.9± 1.0**	9.5± 0.9**
4000 ppm	7.9± 0.6**	8.6± 0.8**	8.5± 0.8**	8.2± 0.5**	7.5± 0.6**	7.9± 0.6**

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

APPENDIX B 3-3

WATER CONSUMPTION CHANGES : SUMMARY, MOUSE: MALE

(THIRTEEN-WEEK STUDY)

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(4)	2-7(4)	3-7(4)	4-7(4)	5-7(4)	6-7(4)	7-7(4)
Control	4.1± 0.3	4.3± 0.5	4.0± 0.3	3.9± 0.3	4.0± 0.4	3.8± 0.4	3.8± 0.4
500 ppm	4.2± 0.6	4.3± 0.8	4.0± 0.8	3.7± 0.3	3.7± 0.8	3.7± 0.9	3.6± 1.0
1000 ppm	4.0± 0.5	4.1± 0.5	3.8± 0.6	3.7± 0.5	3.8± 0.8	3.4± 0.6	3.5± 0.8
2000 ppm	3.3± 0.4	2.9± 0.2*	2.9± 0.3*	3.0± 0.5*	2.9± 0.3*	2.7± 0.3*	2.6± 0.3*
4000 ppm	2.5± 0.2**	2.2± 0.5**	2.3± 0.5**	2.2± 0.5**	2.3± 0.5**	2.0± 0.5**	2.0± 0.2**
8000 ppm	1.9± 0.1**	1.6± 0.2**	1.6± 0.2**	1.6± 0.2**	1.6± 0.2**	1.5± 0.2**	1.6± 0.2**

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

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(4)	9-7(4)	10-7(4)	11-7(4)	12-7(4)	13-7(4)
Control	3.8± 0.5	3.8± 0.3	3.8± 0.5	3.5± 0.3	3.5± 0.4	3.4± 0.3
500 ppm	3.5± 0.4	3.3± 0.4	3.7± 1.1	3.5± 0.6	3.6± 0.6	3.6± 0.6
1000 ppm	3.4± 0.5	3.5± 0.8	3.6± 0.9	3.5± 1.0	3.1± 0.3	3.2± 0.4
2000 ppm	2.8± 0.6*	2.6± 0.3*	2.5± 0.2*	2.5± 0.3*	2.6± 0.3*	2.6± 0.3
4000 ppm	2.0± 0.2**	1.9± 0.4**	1.8± 0.1**	1.8± 0.1**	1.8± 0.2**	2.1± 0.3**
8000 ppm	1.6± 0.2**	1.4± 0.3**	1.4± 0.2**	1.4± 0.2**	1.5± 0.1**	1.5± 0.1**

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

APPENDIX 3-4

WATER CONSUMPTION CHANGES : SUMMARY, MOUSE: FEMALE

(THIRTEEN-WEEK STUDY)

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(4)	2-7(4)	3-7(4)	4-7(4)	5-7(4)	6-7(4)	7-7(4)
Control	4.0± 0.4	4.1± 0.5	4.1± 0.5	4.5± 0.8	4.4± 0.6	4.4± 0.8	4.7± 1.1
500 ppm	3.7± 0.5	4.4± 1.1	4.2± 1.0	4.4± 1.1	4.7± 1.3	3.9± 0.6	4.3± 1.0
1000 ppm	3.4± 0.3	3.5± 0.4	3.6± 0.4	3.9± 0.7	3.7± 0.3	3.5± 0.4	3.9± 0.6
2000 ppm	3.0± 0.4*	3.0± 0.5*	2.7± 0.3**	2.9± 0.5*	3.0± 0.4*	2.8± 0.3**	2.9± 0.4*
4000 ppm	2.5± 0.2**	2.4± 0.3**	2.1± 0.3**	2.1± 0.2**	2.3± 0.4**	2.3± 0.3**	2.6± 0.7**
8000 ppm	1.8± 0.1**	1.7± 0.3**	1.4± 0.2**	1.4± 0.2**	1.7± 0.5**	1.6± 0.4**	1.6± 0.3**

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

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(4)	9-7(4)	10-7(4)	11-7(4)	12-7(4)	13-7(4)
Control	4.3± 0.6	4.2± 0.7	4.7± 1.2	4.4± 0.6	4.1± 0.7	4.1± 0.9
500 ppm	3.9± 0.6	4.3± 0.7	4.0± 0.6	4.2± 0.6	4.3± 0.8	3.9± 0.4
1000 ppm	3.9± 0.6	3.7± 0.3	3.8± 0.4	3.6± 0.4*	3.6± 0.4	3.6± 0.3
2000 ppm	2.7± 0.4**	2.7± 0.3*	2.9± 0.3**	3.0± 0.6**	2.9± 0.8	2.8± 0.3*
4000 ppm	2.4± 0.5**	2.4± 0.5**	2.5± 0.8**	2.8± 0.7**	2.5± 0.7**	2.5± 0.4**
8000 ppm	1.6± 0.3**	1.7± 0.7**	1.8± 0.8**	1.8± 0.4**	1.7± 0.3**	1.7± 0.2**

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

APPENDIX B 4-1

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : MALE

(THIRTEEN-WEEK STUDY)

STUDY NO. : 0234
ANIMAL : RAT F344
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	13.1± 0.7	14.4± 1.1	15.3± 1.1	14.6± 1.0	13.7± 2.3	14.5± 1.2	14.7± 1.9
250 ppm	12.7± 0.6	14.0± 0.7	14.6± 1.1	14.1± 1.2	12.3± 1.7	13.3± 2.2	13.8± 2.6
500 ppm	13.1± 0.7	14.6± 0.5	15.4± 0.9	15.3± 1.0	13.8± 1.3	14.8± 1.1	14.9± 1.4
1000 ppm	12.5± 0.6	14.2± 0.8	14.6± 1.1	14.6± 1.1	13.1± 1.4	13.8± 1.4	13.8± 1.7
2000 ppm	11.8± 0.6**	13.8± 0.7	14.7± 0.8	14.7± 1.0	13.5± 1.2	14.2± 0.9	14.3± 1.0
4000 ppm	9.5± 0.6**	12.4± 0.8**	13.0± 0.6**	12.7± 0.9**	11.4± 1.2**	12.1± 0.7**	12.4± 0.6**

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

STUDY NO. : 0234
ANIMAL : RAT F344
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	13.8± 1.7	13.6± 1.6	14.9± 1.9	13.7± 1.5	13.8± 1.5	13.9± 1.5
250 ppm	12.7± 2.2	12.7± 2.2	13.5± 2.1	12.5± 1.8	12.6± 1.9	13.3± 1.8
500 ppm	13.8± 1.2	14.3± 1.3	14.6± 1.4	13.5± 1.3	13.5± 1.3	14.0± 1.6
1000 ppm	13.1± 1.8	13.1± 1.7	14.0± 1.8	13.1± 1.6	13.0± 1.5	13.2± 1.7
2000 ppm	13.8± 0.8	13.9± 1.1	14.6± 0.9	14.0± 0.9	13.7± 1.0	13.8± 1.0
4000 ppm	12.0± 0.5*	12.1± 0.7*	12.9± 0.8**	12.4± 0.7	12.5± 0.5	12.6± 0.6

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

APPENDIX B 4-2

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

(THIRTEEN-WEEK STUDY)

STUDY NO. : 0234
ANIMAL : RAT F344
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	11.5± 0.5	11.8± 0.7	12.0± 0.8	12.3± 0.9	11.0± 0.7	11.3± 1.3	11.2± 0.9
250 ppm	11.2± 0.5	11.7± 0.6	11.9± 0.7	12.2± 0.9	11.0± 1.1	11.1± 1.2	11.2± 0.9
500 ppm	11.1± 0.6	11.7± 0.7	11.8± 0.8	11.9± 1.1	10.8± 0.8	10.9± 1.0	10.8± 1.0
1000 ppm	11.0± 0.5	11.7± 0.6	12.0± 0.7	12.0± 0.9	10.8± 0.8	10.8± 0.9	10.9± 0.8
2000 ppm	9.8± 0.3**	10.9± 0.5**	11.3± 0.7	11.3± 0.8	9.9± 0.8*	10.2± 0.8	10.3± 0.6
4000 ppm	7.6± 0.5**	10.3± 0.6**	10.8± 0.7**	10.5± 0.7**	9.4± 0.6**	9.7± 0.5**	9.9± 0.8**

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

STUDY NO. : 0234
ANIMAL : RAT F344
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	10.3± 1.1	10.5± 0.9	11.0± 0.9	10.6± 0.9	10.5± 0.4	10.8± 1.0
250 ppm	10.4± 1.2	10.7± 0.9	11.2± 0.9	10.6± 1.2	10.6± 0.9	10.7± 1.3
500 ppm	10.0± 1.2	10.3± 0.7	10.6± 0.7	10.0± 1.2	10.4± 0.6	10.1± 0.9
1000 ppm	10.3± 1.0	10.4± 1.0	10.7± 0.9	10.4± 1.1	11.1± 1.7	10.4± 1.3
2000 ppm	9.7± 0.7	9.6± 0.8	10.1± 0.7*	9.9± 0.9	10.1± 0.9	9.7± 0.8
4000 ppm	9.4± 0.6	9.0± 0.7**	9.8± 0.7**	9.3± 0.6*	9.7± 0.6	9.2± 0.5**

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

APPENDIX B 4-3

FOOD CONSUMPTION CHANGES : SUMMARY, MOSUE : MALE

(THIRTEEN-WEEK STUDY)

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
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	3.5± 0.2	3.6± 0.2	3.6± 0.2	3.7± 0.2	3.6± 0.2	3.9± 0.2	3.8± 0.4
500 ppm	3.4± 0.3	3.7± 0.3	3.6± 0.3	3.8± 0.2	3.6± 0.2	3.9± 0.3	3.8± 0.3
1000 ppm	3.5± 0.2	3.7± 0.2	3.8± 0.2	3.9± 0.3	3.7± 0.1	3.9± 0.2	3.8± 0.2
2000 ppm	3.4± 0.1	3.5± 0.2	3.6± 0.2	3.6± 0.2	3.6± 0.2	3.6± 0.4	3.6± 0.3
4000 ppm	3.1± 0.2**	3.2± 0.4**	3.3± 0.2*	3.4± 0.2*	3.4± 0.2	3.3± 0.2**	3.5± 0.9
8000 ppm	2.8± 0.2**	3.3± 0.2*	3.3± 0.3*	3.5± 0.2	3.3± 0.2*	3.4± 0.2**	3.5± 0.2

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

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
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	3.9± 0.2	3.6± 0.3	4.0± 0.2	4.0± 0.3	4.0± 0.3	4.0± 0.2
500 ppm	3.8± 0.3	3.4± 0.4	3.9± 0.2	3.8± 0.3	3.9± 0.2	3.9± 0.2
1000 ppm	3.9± 0.2	3.6± 0.2	3.9± 0.2	4.1± 0.2	4.0± 0.2	4.0± 0.2
2000 ppm	3.7± 0.3	3.2± 0.4	3.8± 0.3	3.7± 0.2	3.8± 0.2	3.8± 0.4
4000 ppm	3.4± 0.2**	3.1± 0.2*	3.4± 0.2**	3.4± 0.2**	3.3± 0.2**	3.4± 0.2**
8000 ppm	3.5± 0.2**	3.2± 0.2	3.5± 0.2**	3.5± 0.2**	3.4± 0.2**	3.4± 0.2**

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

APPENDIX B 4-4

FOOD CONSUMPTION CHANGES : SUMMARY, MOSUE : FEMALE

(THIRTEEN-WEEK STUDY)

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
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	3.1± 0.3	3.2± 0.2	3.2± 0.2	3.3± 0.3	3.4± 0.2	3.5± 0.2	3.6± 0.3
500 ppm	2.9± 0.2	3.1± 0.2	3.1± 0.2	3.3± 0.2	3.3± 0.2	3.4± 0.2	3.5± 0.2
1000 ppm	2.9± 0.2	3.2± 0.2	3.2± 0.2	3.3± 0.1	3.3± 0.2	3.4± 0.2	3.5± 0.2
2000 ppm	2.9± 0.1	3.1± 0.2	3.2± 0.2	3.3± 0.2	3.3± 0.2	3.4± 0.2	3.4± 0.2
4000 ppm	2.8± 0.2**	3.0± 0.2*	3.0± 0.2*	3.1± 0.1	3.1± 0.2*	3.2± 0.1**	3.2± 0.3**
8000 ppm	2.3± 0.1**	2.9± 0.2**	2.9± 0.2**	3.0± 0.2*	3.1± 0.2*	3.1± 0.2**	3.2± 0.3**

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

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
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	3.6± 0.2	3.3± 0.3	3.8± 0.3	3.8± 0.2	3.6± 0.2	3.7± 0.2
500 ppm	3.6± 0.2	3.4± 0.2	3.7± 0.2	3.7± 0.2	3.4± 0.2	3.6± 0.1
1000 ppm	3.6± 0.2	3.4± 0.2	3.6± 0.1	3.7± 0.2	3.6± 0.2	3.7± 0.2
2000 ppm	3.5± 0.2	3.2± 0.2	3.5± 0.3*	3.6± 0.3	3.4± 0.3	3.6± 0.1
4000 ppm	3.3± 0.2*	3.2± 0.2	3.4± 0.1**	3.6± 0.3	3.3± 0.2	3.5± 0.2*
8000 ppm	3.3± 0.2**	3.0± 0.2**	3.3± 0.2**	3.3± 0.2**	3.2± 0.3*	3.4± 0.2**

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

APPENDIX B 5-1

CHEMICAL INTAKE CHANGES: SUMMARY, RAT : MALE

(THIRTEEN-WEEK STUDY)

STUDY NO. : 0234
ANIMAL : RAT F344
UNIT : mg／kg／d a y
REPORT TYPE : A1 13
SEX : MALE

CHEMICAL INTAKE CHENGES (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	29.150± 1.119	26.419± 1.054	23.535± 1.117	21.306± 1.374	17.151± 1.439	16.769± 1.216	17.096± 2.554
500 ppm	59.701± 2.732	53.441± 2.694	46.844± 2.626	43.021± 4.715	35.201± 3.314	34.131± 2.486	34.422± 4.540
1000 ppm	104.536± 5.227	91.088± 3.574	80.389± 6.155	72.537± 3.483	61.283± 3.282	60.898± 2.749	58.542± 4.182
2000 ppm	188.522± 7.098	170.895± 9.109	148.199± 8.019	131.313± 5.542	118.372± 6.930	114.708± 6.265	111.988± 6.903
4000 ppm	349.262± 20.815	370.395±152.712	286.273± 29.222	245.082± 13.472	212.302± 16.198	207.931± 9.651	205.923± 11.676

STUDY NO. : 0234
ANIMAL : RAT F344
UNIT : mg/kg/d a y
REPORT TYPE : A1 13
SEX : MALE

CHEMICAL INTAKE CHENGES (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	15.209± 1.546	16.057± 1.472	15.311± 1.082	14.189± 1.192	13.334± 1.091	13.254± 0.659
500 ppm	31.626± 6.901	36.023± 15.497	34.155± 15.913	28.616± 4.476	27.322± 7.528	27.171± 5.189
1000 ppm	53.484± 3.450	57.051± 4.390	53.981± 3.943	50.199± 3.292	46.625± 3.243	47.508± 3.705
2000 ppm	102.558± 6.080	108.111± 7.191	99.697± 6.722	98.107± 5.771	89.604± 6.084	91.489± 6.114
4000 ppm	181.158± 13.909	196.324± 16.817	180.914± 13.177	176.661± 9.198	161.639± 7.834	167.627± 10.604

APPENDIX B 5-2

CHEMICAL INTAKE CHANGES: SUMMARY, RAT : FEMALE

(THIRTEEN-WEEK STUDY)

STUDY NO. : 0234
ANIMAL : RAT F344
UNIT : mg/kg/day
REPORT TYPE : A1 13
SEX : FEMALE

CHEMICAL INTAKE CHENGES (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	33.849± 2.630	29.962± 1.996	27.867± 1.660	25.514± 1.449	22.183± 1.195	21.772± 1.210	22.022± 1.661
500 ppm	71.281± 13.414	64.260± 11.746	56.283± 3.943	53.239± 4.246	49.421± 12.225	53.556± 24.202	44.931± 8.521
1000 ppm	113.391± 7.593	108.354± 22.845	91.802± 7.543	87.956± 10.082	85.449± 20.706	75.432± 18.317	81.000± 27.290
2000 ppm	202.299± 9.107	183.884± 6.842	170.090± 8.064	154.101± 6.628	135.269± 5.934	129.874± 8.913	128.729± 7.107
4000 ppm	388.958± 29.544	339.921± 22.107	302.356± 20.673	273.600± 17.003	243.136± 17.724	243.693± 30.198	235.129± 18.117

STUDY NO. : 0234
ANIMAL : RAT F344
UNIT : mg／kg／d a y
REPORT TYPE : A1 13
SEX : FEMALE

CHEMICAL INTAKE CHENGES (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	20.044± 1.502	20.252± 0.830	20.845± 2.759	20.725± 3.627	18.377± 5.161	18.607± 1.109
500 ppm	38.546± 3.955	48.824± 21.803	52.149± 22.770	43.163± 8.181	35.122± 4.283	38.919± 7.808
1000 ppm	70.894± 16.282	75.521± 26.160	66.151± 7.396	83.143± 32.249	72.580± 28.200	72.861± 26.007
2000 ppm	116.207± 6.874	121.183± 9.677	120.057± 12.353	117.091± 11.925	105.955± 8.445	110.731± 7.714
4000 ppm	211.471± 14.729	222.493± 18.908	213.913± 15.465	207.716± 9.877	189.438± 12.760	198.163± 14.484

APPENDIX B 5-3

CHEMICAL INTAKE CHANGES: SUMMARY, MOUSE: MALE

(THIRTEEN-WEEK STUDY)

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
UNIT : mg/kg/d a y
REPORT TYPE : A1 13
SEX : MALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2	3	4	5	6	7
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
500 ppm	92.325± 12.654	90.609± 15.145	80.705± 16.126	73.291± 7.135	71.412± 15.979	67.629± 17.164	63.958± 19.866
1000 ppm	170.961± 20.442	167.086± 17.843	153.255± 21.500	144.250± 17.457	143.931± 30.322	123.990± 21.473	124.526± 30.894
2000 ppm	280.421± 42.743	244.263± 24.376	234.547± 27.620	233.937± 48.061	219.452± 27.938	195.855± 23.723	192.889± 31.080
4000 ppm	444.173± 31.674	380.851± 84.336	388.993± 89.016	368.951± 86.788	364.027± 70.186	320.876± 73.056	314.149± 33.194
8000 ppm	732.041± 42.736	582.895± 64.994	572.889± 62.073	559.070± 82.671	540.218± 51.531	489.381± 62.058	523.428± 58.042

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
UNIT : mg／kg／d a y
REPORT TYPE : A1 13
SEX : MALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 8	9	10	11	12	13
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
500 ppm	60.576± 9.562	55.371± 7.471	62.817± 21.108	57.612± 14.256	57.762± 14.181	57.095± 12.569
1000 ppm	115.064± 17.693	116.101± 28.450	116.763± 33.702	109.736± 34.390	96.111± 10.660	96.291± 13.402
2000 ppm	200.290± 56.514	193.381± 46.156	170.625± 15.494	166.044± 23.430	164.722± 16.104	168.870± 18.039
4000 ppm	297.353± 34.774	288.787± 58.112	269.856± 16.105	259.351± 17.372	260.449± 22.901	307.618± 42.145
8000 ppm	511.139± 57.105	454.184± 83.730	455.650± 51.711	439.215± 54.282	456.658± 34.558	480.891± 44.009

APPENDIX B 5-4

CHEMICAL INTAKE CHANGES: SUMMARY, MOUSE: FEMALE

(THIRTEEN-WEEK STUDY)

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
UNIT : mg／kg／d a y
REPORT TYPE : A1 13
SEX : FEMALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2	3	4	5	6	7
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
500 ppm	100.173± 12.554	115.911± 30.422	108.418± 28.021	109.232± 28.665	113.935± 32.682	90.402± 13.216	95.508± 20.235
1000 ppm	184.743± 18.933	183.883± 18.880	183.144± 20.286	190.168± 31.161	177.275± 17.229	161.426± 20.750	170.080± 22.739
2000 ppm	324.127± 47.386	318.969± 47.299	277.116± 29.254	289.293± 47.128	289.803± 40.759	265.189± 28.102	260.936± 34.532
4000 ppm	539.071± 50.712	497.131± 61.884	439.728± 62.536	434.870± 49.324	451.120± 79.761	442.135± 68.809	484.549±130.351
8000 ppm	844.813± 71.827	761.623±109.704	608.361± 69.416	591.269± 62.778	701.599±171.090	631.258±130.738	638.413±107.647

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
UNIT : mg／kg／d a y
REPORT TYPE : A1 13
SEX : FEMALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 8	9	10	11	12	13
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
500 ppm	89.753± 13.224	97.779± 18.295	87.949± 14.892	88.463± 13.189	93.952± 19.651	82.103± 9.121
1000 ppm	178.250± 22.904	162.148± 15.043	165.595± 17.689	154.026± 18.978	152.991± 18.842	151.687± 13.032
2000 ppm	250.229± 32.493	248.039± 26.209	255.616± 24.813	252.853± 54.988	256.820± 65.840	240.078± 25.625
4000 ppm	457.712± 95.511	444.109± 93.416	448.740±150.003	489.565±119.915	449.157±130.555	445.006± 77.176
8000 ppm	634.401±105.151	664.368±257.193	672.196±289.526	679.814±123.889	646.586± 85.192	629.202± 42.825

APPENDIX B 6-1

HEMATOLOGY (THIRTEEN-WEEK STUDY : SUMMARY)

RAT : MALE

STUDY NO. : 0234
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HEMATOLOGY(1) (SUMMARY)
SURVIVAL ANIMALS (14)

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	9	9.23± 0.26	16.1± 0.5	43.3± 1.0	46.9± 0.7	17.4± 0.3	37.1± 0.3	696± 50
250 ppm	10	9.25± 0.28	16.2± 0.4	43.7± 0.9	47.2± 0.8	17.5± 0.3	37.2± 0.5	708± 41
500 ppm	10	9.23± 0.30	15.9± 0.2	42.9± 1.6	46.4± 0.5	17.3± 0.6	37.2± 1.6	694± 32
1000 ppm	9	9.23± 0.26	16.1± 0.3	43.2± 1.2	46.8± 1.1	17.5± 0.4	37.3± 0.6	685± 32
2000 ppm	10	9.35± 0.23	16.0± 0.4	43.6± 1.0	46.7± 0.4	17.1± 0.3	36.6± 0.7	720± 26
4000 ppm	10	9.43± 0.20	16.4± 0.5	44.4± 0.7	47.1± 0.7	17.4± 0.5	36.8± 0.9	695± 43

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

STUDY NO. : 0234
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HEMATOLOGY(1) (SUMMARY)
SURVIVAL ANIMALS (14)

Group Name	NO. of Animals	RETICULOCYTE ‰	PROTHROMBIN TIME sec	APTT sec
Control	9	24± 5	14.3± 0.9	24.3± 1.1
250 ppm	10	24± 4	13.9± 1.1	23.4± 2.4
500 ppm	10	26± 5	13.8± 1.5	23.5± 2.6
1000 ppm	9	25± 5	13.3± 1.6	22.4± 1.4
2000 ppm	10	25± 5	14.0± 1.8	24.0± 2.0
4000 ppm	10	25± 7	13.6± 1.2	23.4± 1.7

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

STUDY NO. : 0234
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HEMATOLOGY(2) (SUMMARY)
SURVIVAL ANIMALS (14)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHERS
Control	9	5.80± 1.12	0± 0	25± 3	2± 1	0± 0	4± 2	69± 2	0± 0
250 ppm	10	6.27± 1.25	0± 0	26± 4	2± 1	0± 0	3± 2	69± 3	0± 0
500 ppm	10	6.13± 1.36	0± 0	23± 6	2± 1	0± 0	3± 1	72± 6	0± 0
1000 ppm	9	5.97± 0.57	0± 0	22± 3	1± 1	0± 0	2± 1	74± 3	0± 0
2000 ppm	10	6.24± 1.59	0± 0	23± 4	1± 1	0± 0	3± 1	73± 5	0± 0
4000 ppm	10	7.17± 1.81	0± 0	24± 3	1± 1	0± 0	3± 1	72± 4	0± 0

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

(HCL071)

APPENDIX B 6-2

HEMATOLOGY (THIRTEEN-WEEK STUDY : SUMMARY)

RAT : FEMALE

STUDY NO. : 0234
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HEMATOLOGY(1) (SUMMARY)
SURVIVAL ANIMALS (14)

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	8.77± 0.24	16.4± 0.5	43.7± 1.5	49.8± 0.6	18.7± 0.4	37.5± 1.0	804± 32
250 ppm	10	8.60± 0.39	16.1± 0.4	42.5± 1.9	49.5± 0.5	18.8± 0.9	38.0± 1.7	804± 65
500 ppm	10	8.74± 0.28	16.2± 0.6	43.2± 1.1	49.4± 0.5	18.5± 0.3	37.4± 0.6	847± 31
1000 ppm	9	8.60± 0.35	15.9± 0.6	42.5± 1.7	49.5± 0.4	18.6± 0.5	37.5± 1.2	799± 42
2000 ppm	10	8.49± 0.54	16.1± 0.5	41.9± 2.6	49.4± 0.5	19.0± 1.4	38.5± 2.7	792± 70
4000 ppm	10	8.75± 0.26	15.9± 0.5	42.8± 1.3	49.0± 0.4**	18.2± 0.3	37.1± 0.7	760± 27

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

(HCL070)

STUDY NO. : 0234
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HEMATOLOGY(1) (SUMMARY)
SURVIVAL ANIMALS (14)

Group Name	NO. of Animals	RETICULOCYTE ‰		PROTHROMBIN TIME sec		APTT sec	
Control	10	28±	6	12.4±	0.4	17.4±	1.3
250 ppm	10	25±	5	12.4±	0.5	16.4±	1.2
500 ppm	10	25±	5	12.3±	0.2	17.5±	2.0
1000 ppm	9	31±	7	12.2±	0.2	17.4±	1.8
2000 ppm	10	24±	5	12.1±	0.2	18.3±	2.0
4000 ppm	10	23±	3	12.0±	0.2*	19.4±	1.8*

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

STUDY NO. : 0234
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HEMATOLOGY(2) (SUMMARY)
SURVIVAL ANIMALS (14)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHERS
Control	10	3.36± 1.25	0± 0	24± 5	2± 1	0± 0	3± 1	70± 4	0± 0
250 ppm	10	3.00± 1.26	0± 0	26± 5	1± 1	0± 0	4± 2	69± 5	0± 0
500 ppm	10	3.79± 1.44	0± 1	23± 6	1± 1	0± 0	4± 2	71± 6	0± 0
1000 ppm	9	3.16± 1.31	0± 0	25± 9	1± 1	0± 0	3± 2	71± 10	0± 0
2000 ppm	10	4.02± 2.25	0± 0	23± 6	1± 1	0± 0	4± 2	72± 7	0± 0
4000 ppm	10	4.55± 1.77	0± 1	19± 6	1± 1	0± 0	3± 2	77± 7	0± 0

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

APPENDIX B 6-3

HEMATOLOGY (THIRTEEN-WEEK STUDY : SUMMARY)

MOUSE: MALE

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HEMATOLOGY(1) (SUMMARY)
SURVIVAL ANIMALS (14)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV f ℓ	MCH p g	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	10	10.77± 0.21	15.7± 0.5	48.9± 1.0	45.5± 0.5	14.6± 0.3	32.2± 0.7	1554± 77
500 ppm	9	10.48± 0.33	15.4± 0.4	47.8± 1.4	45.6± 0.5	14.7± 0.4	32.3± 0.8	1504± 85
1000 ppm	10	10.49± 0.30	15.4± 0.3	47.9± 1.3	45.7± 0.6	14.7± 0.2	32.1± 0.5	1506± 96
2000 ppm	9	10.63± 0.25	15.6± 0.4	48.2± 1.4	45.3± 0.9	14.7± 0.1	32.4± 0.7	1563± 43
4000 ppm	10	10.52± 0.35	15.4± 0.5	47.6± 1.9	45.3± 0.6	14.6± 0.1	32.3± 0.3	1514± 85
8000 ppm	10	10.15± 0.58**	15.2± 0.7	45.7± 2.6**	45.1± 0.7	15.0± 0.7	33.2± 1.3	1354± 105**

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

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HEMATOLOGY(2) (SUMMARY)
SURVIVAL ANIMALS (14)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHERS
Control	10	1.49± 0.75	0± 0	16± 3	2± 1	0± 0	4± 1	79± 3	0± 0
500 ppm	9	1.16± 0.73	0± 0	14± 3	1± 1	0± 0	4± 2	81± 4	0± 0
1000 ppm	10	1.12± 0.51	0± 0	16± 4	1± 1	0± 0	3± 2	79± 4	0± 0
2000 ppm	9	1.08± 0.69	0± 0	16± 5	1± 1	0± 0	3± 2	79± 5	0± 0
4000 ppm	10	1.01± 0.51	0± 0	17± 6	1± 1	0± 0	3± 1	79± 7	0± 0
8000 ppm	10	0.98± 0.84	0± 0	19± 6	0± 1	0± 0	3± 1	78± 7	0± 0

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

(HCL071)

APPENDIX B 6-4

HEMATOLOGY (THIRTEEN-WEEK STUDY : SUMMARY)

MOUSE: FEMALE

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

HEMATOLOGY(1) (SUMMARY)
SURVIVAL ANIMALS (14)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV f ℓ	MCH p g	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	10	10.59± 0.20	16.0± 0.5	48.3± 1.3	45.6± 0.5	15.1± 0.3	33.0± 0.4	1293± 84
500 ppm	9	10.44± 0.31	15.7± 0.4	47.1± 1.4	45.1± 0.4	15.1± 0.2	33.4± 0.5	1331± 51
1000 ppm	10	10.46± 0.36	15.7± 0.4	47.4± 1.9	45.3± 0.7	15.0± 0.4	33.1± 1.0	1302± 93
2000 ppm	10	10.37± 0.24	15.4± 0.4	46.9± 1.2	45.2± 0.4	14.9± 0.1	32.9± 0.4	1282± 52
4000 ppm	10	10.23± 0.34	15.2± 0.5**	46.6± 1.8	45.5± 0.3	14.9± 0.1	32.7± 0.3	1267± 64
8000 ppm	10	10.32± 0.48	15.4± 0.7*	46.8± 2.1	45.4± 0.8	14.9± 0.3	32.8± 0.4	1212± 129

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

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

HEMATOLOGY(2) (SUMMARY)
SURVIVAL ANIMALS (14)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHERS
Control	10	1.17± 1.10	0± 0	19± 7	1± 1	0± 0	3± 1	77± 6	0± 0
500 ppm	9	1.09± 0.71	0± 0	17± 6	0± 1	0± 0	2± 1	80± 6	0± 0
1000 ppm	10	1.45± 1.32	0± 0	15± 5	1± 1	0± 0	3± 1	81± 5	0± 0
2000 ppm	10	1.04± 0.85	0± 0	20± 6	1± 1	0± 0	3± 1	76± 6	0± 0
4000 ppm	10	1.05± 0.60	0± 0	20± 5	1± 1	0± 0	3± 2	77± 4	0± 0
8000 ppm	10	1.11± 1.05	0± 0	20± 5	1± 1	0± 0	3± 1	77± 5	0± 0

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

APPENDIX B 7-1

BIOCHEMISTRY (THIRTEEN-WEEK STUDY : SUMMARY)

RAT : MALE

STUDY NO. : 0234
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (14)

Group Name	NO. of Animals	TOTAL PROTEIN g/dℓ	ALBUMIN g/dℓ	A/G RATIO	T-BILIRUBIN mg/dℓ	GLUCOSE mg/dℓ	T-CHOLESTEROL mg/dℓ	TRIGLYCERIDE mg/dℓ
Control	9	6.7± 0.3	3.9± 0.1	1.4± 0.1	0.22± 0.05	186± 12	62± 6	88± 22
250 ppm	10	6.7± 0.3	3.9± 0.1	1.4± 0.1	0.23± 0.07	190± 21	61± 8	94± 32
500 ppm	10	6.6± 0.3	3.9± 0.1	1.4± 0.1	0.24± 0.13	186± 14	61± 7	100± 20
1000 ppm	9	6.5± 0.3	3.8± 0.1	1.4± 0.1	0.21± 0.07	185± 19	63± 11	87± 19
2000 ppm	10	6.2± 0.2**	3.7± 0.1*	1.5± 0.1*	0.22± 0.05	184± 13	54± 6	98± 15
4000 ppm	10	6.0± 0.3**	3.6± 0.1**	1.5± 0.1*	0.25± 0.09	176± 15	50± 7**	83± 22

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

STUDY NO. : 0234
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (14)

Group Name	NO. of Animals	PHOSPHOLIPID mg/dℓ	GOT IU/ℓ	GPT IU/ℓ	LDH IU/ℓ	ALP IU/ℓ	G-GTP IU/ℓ	CPK IU/ℓ
Control	9	119± 11	79± 12	27± 4	172± 42	287± 27	1± 1	87± 11
250 ppm	10	122± 15	71± 9	20± 2	177± 48	286± 25	1± 1	88± 14
500 ppm	10	119± 11	68± 9	18± 3	175± 55	256± 20*	1± 0	84± 21
1000 ppm	9	120± 17	66± 8	16± 3**	194± 40	249± 17**	2± 1	88± 9
2000 ppm	10	106± 7	61± 4**	14± 2**	165± 35	246± 28**	1± 0	83± 8
4000 ppm	10	97± 12**	58± 4**	12± 1**	182± 67	238± 22**	1± 1	90± 11

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

STUDY NO. : 0234
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (14)

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	9	17.2± 1.0	0.5± 0.0	144± 1	3.7± 0.2	107± 1	10.2± 0.2	5.0± 0.9
250 ppm	10	16.9± 1.5	0.5± 0.0	143± 2	3.7± 0.2	108± 1	10.1± 0.2	5.2± 0.9
500 ppm	10	17.3± 0.8	0.5± 0.0	143± 1	3.7± 0.2	107± 1	10.2± 0.1	5.5± 1.0
1000 ppm	9	17.7± 1.4	0.5± 0.1	143± 2	3.5± 0.3	106± 1	10.2± 0.2	5.6± 0.7
2000 ppm	10	19.4± 1.3**	0.5± 0.0	143± 1	3.7± 0.2	106± 2	10.2± 0.3	6.2± 0.9*
4000 ppm	10	21.9± 2.0**	0.5± 0.1	143± 1	3.8± 0.4	106± 1	10.0± 0.2	6.6± 0.6**

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

APPENDIX B 7-2

BIOCHEMISTRY (THIRTEEN-WEEK STUDY : SUMMARY)

RAT : FEMALE

STUDY NO. : 0234
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (14)

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	6.9±	0.3	4.0±	0.1	1.4±	0.1	0.28±	0.10	153±	14	82±	7	42±	6
250 ppm	10	6.6±	0.3	3.8±	0.1*	1.4±	0.1	0.31±	0.12	145±	17	74±	5	38±	6
500 ppm	10	6.6±	0.4	3.9±	0.2*	1.4±	0.1	0.28±	0.09	145±	12	73±	9*	38±	4
1000 ppm	9	6.3±	0.4**	3.7±	0.1**	1.5±	0.1	0.37±	0.14	154±	18	69±	8**	39±	5
2000 ppm	10	6.0±	0.4**	3.6±	0.1**	1.5±	0.1*	0.45±	0.21	143±	20	60±	4**	37±	3
4000 ppm	10	5.6±	0.2**	3.5±	0.1**	1.6±	0.1**	0.34±	0.06	143±	17	41±	6**	36±	8

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

STUDY NO. : 0234
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (14)

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	155± 12	72± 11	21± 3	253± 81	217± 27	2± 1	116± 21
250 ppm	10	141± 14	73± 10	19± 4	311± 136	188± 31	1± 1	121± 35
500 ppm	10	137± 19	76± 18	18± 8	254± 83	186± 35*	1± 1	100± 19
1000 ppm	9	131± 11	70± 16	15± 6	287± 112	172± 15**	1± 0*	102± 22
2000 ppm	10	117± 7**	66± 10	11± 2**	320± 169	168± 17**	1± 0*	112± 30
4000 ppm	10	86± 8**	68± 9	11± 1**	308± 199	179± 20**	1± 0	115± 50

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

STUDY NO. : 0234
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (14)

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	19.5±	1.9	0.5±	0.0	145±	1	3.4±	0.2	109±	1	10.1±	0.3	4.9±	1.0
250 ppm	10	18.4±	2.2	0.5±	0.1	145±	1	3.5±	0.3	109±	1	10.0±	0.2	4.7±	1.1
500 ppm	10	19.2±	2.0	0.5±	0.1	145±	2	3.4±	0.2	110±	2	10.1±	0.2	4.7±	1.0
1000 ppm	9	19.9±	1.9	0.5±	0.1	143±	1	3.6±	0.2	109±	1	9.8±	0.3	5.0±	1.3
2000 ppm	10	20.5±	1.5	0.5±	0.1	143±	2*	3.7±	0.3*	108±	1	9.7±	0.3*	5.1±	0.7
4000 ppm	10	24.7±	2.8**	0.4±	0.1	143±	2*	3.9±	0.3**	109±	1	9.8±	0.6*	5.8±	1.1

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

APPENDIX B 7-3

BIOCHEMISTRY (THIRTEEN-WEEK STUDY : SUMMARY)

MOUSE: MALE

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (14)

Group Name	NO. of Animals	TOTAL PROTEIN g/dl	ALBUMIN g/dl	A/G RATIO	T-BILIRUBIN mg/dl	GLUCOSE mg/dl	T-CHOLESTEROL mg/dl	TRIGLYCERIDE mg/dl
Control	10	5.5± 0.2	3.0± 0.1	1.2± 0.1	0.33± 0.08	204± 25	93± 7	74± 12
500 ppm	9	5.6± 0.3	3.0± 0.1	1.2± 0.1	0.30± 0.08	186± 38	86± 13	63± 14
1000 ppm	10	5.4± 0.3	2.9± 0.1	1.2± 0.0	0.29± 0.07	171± 31	79± 9	68± 16
2000 ppm	9	5.4± 0.3	3.0± 0.2	1.2± 0.1	0.32± 0.09	185± 37	78± 11	56± 14
4000 ppm	10	5.2± 0.2**	2.9± 0.1	1.3± 0.0	0.32± 0.09	168± 25*	74± 7**	54± 10*
8000 ppm	10	4.7± 0.2**	2.7± 0.1**	1.3± 0.0**	0.28± 0.05	139± 20**	58± 4**	41± 4**

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

(HCL074)

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (14)

Group Name	NO. of Animals	GOT IU/ℓ		GPT IU/ℓ		LDH IU/ℓ		ALP IU/ℓ		CPK IU/ℓ		UREA NITROGEN mg/dℓ		SODIUM mEq/ℓ	
Control	10	49±	5	16±	2	231±	36	185±	12	44±	15	27.5±	2.8	154±	2
500 ppm	9	50±	9	15±	6	220±	34	184±	9	36±	10	27.9±	5.0	154±	1
1000 ppm	10	52±	10	14±	2	229±	37	183±	12	47±	11	26.0±	2.7	154±	1
2000 ppm	9	50±	8	15±	4	249±	48	187±	15	62±	33	26.0±	8.8	154±	2
4000 ppm	10	50±	9	13±	3	266±	65	196±	9	58±	28	24.4±	4.0	154±	2
8000 ppm	10	50±	12	12±	3**	241±	57	190±	16	57±	24	25.3±	2.5	154±	1

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

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (14)

Group Name	NO. of Animals	POTASSIUM mEq／ℓ		CHLORIDE mEq／ℓ		CALCIUM mg／dℓ		INORGANIC PHOSPHORUS mg／dℓ	
Control	10	4.4±	0.3	122±	3	9.1±	0.3	6.8±	1.3
500 ppm	9	4.4±	0.4	123±	2	9.0±	0.3	6.7±	0.8
1000 ppm	10	4.5±	0.4	122±	3	8.9±	0.3	6.9±	1.1
2000 ppm	9	4.7±	0.4	121±	4	8.9±	0.3	6.8±	1.7
4000 ppm	10	4.6±	0.5	122±	2	8.8±	0.2	7.6±	1.9
8000 ppm	10	4.4±	0.3	123±	1	8.4±	0.3**	6.7±	0.8

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

APPENDIX B 7-4

BIOCHEMISTRY (THIRTEEN-WEEK STUDY : SUMMARY)

MOUSE: FEMALE

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (14)

Group Name	NO. of Animals	TOTAL PROTEIN g／dℓ	ALBUMIN g／dℓ	A/G RATIO	T-BILIRUBIN mg／dℓ	GLUCOSE mg／dℓ	T-CHOLESTEROL mg／dℓ	TRIGLYCERIDE mg／dℓ
Control	10	5.6± 0.3	3.3± 0.1	1.5± 0.1	0.34± 0.10	148± 25	76± 10	44± 11
500 ppm	9	5.5± 0.3	3.2± 0.2	1.5± 0.1	0.30± 0.09	136± 20	72± 7	42± 7
1000 ppm	10	5.4± 0.2	3.2± 0.2	1.4± 0.1	0.33± 0.06	144± 22	68± 11	42± 11
2000 ppm	10	5.3± 0.3	3.2± 0.2	1.5± 0.1	0.30± 0.08	140± 21	68± 9	44± 11
4000 ppm	10	5.1± 0.3**	3.0± 0.2**	1.5± 0.1	0.33± 0.09	136± 16	66± 10	45± 8
8000 ppm	10	5.0± 0.2**	3.0± 0.1**	1.5± 0.1	0.30± 0.13	133± 16	64± 9	45± 7

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

(HCL074)

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (14)

Group Name	NO. of Animals	GOT IU/ℓ		GPT IU/ℓ		LDH IU/ℓ		ALP IU/ℓ		CPK IU/ℓ		UREA NITROGEN mg/dl		SODIUM mEq/ℓ	
Control	10	64±	22	21±	5	299±	103	325±	40	71±	43	21.8±	3.7	155±	2
500 ppm	9	57±	10	17±	4	244±	48	298±	25	55±	18	20.9±	2.7	154±	2
1000 ppm	10	55±	9	17±	4	258±	38	302±	29	77±	37	21.0±	1.5	154±	1
2000 ppm	10	59±	16	15±	4*	279±	97	301±	31	76±	41	21.2±	2.8	154±	2
4000 ppm	10	54±	7	13±	2**	246±	46	291±	23	69±	45	21.9±	2.4	154±	1
8000 ppm	10	56±	14	13±	3**	272±	95	288±	35	89±	53	24.8±	5.0	154±	2

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

(HCL074)

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (14)

Group Name	NO. of Animals	POTASSIUM mEq／ℓ		CHLORIDE mEq／ℓ		CALCIUM mg／dℓ		INORGANIC PHOSPHORUS mg／dℓ	
Control	10	4.9±	0.3	122±	2	9.0±	0.4	6.2±	1.0
500 ppm	9	4.6±	0.2	122±	1	9.0±	0.3	5.8±	1.0
1000 ppm	10	4.8±	0.4	122±	1	8.9±	0.4	5.8±	0.9
2000 ppm	10	4.7±	0.3	123±	2	8.9±	0.4	6.4±	0.5
4000 ppm	10	4.6±	0.5	123±	1	8.8±	0.3	7.2±	1.1
8000 ppm	10	4.3±	0.3**	121±	2	8.7±	0.3	7.6±	0.7**

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

APPENDIX B 8-1

URINALYSIS (THIRTEEN-WEEK STUDY : SUMMARY)

RAT : MALE

STUDY NO. : 0234
ANIMAL : RAT F344
SAMPLING DATE : 013-6
SEX : MALE REPORT TYPE : A1

URINALYSIS

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	2	6	2		0	0	2	8	0	0		10	0	0	0	0	0		0	10	0	0	0	0		10	0	0	0	
250 ppm	10	0	0	0	0	1	5	4		0	0	0	10	0	0		10	0	0	0	0	0		1	9	0	0	0	0		10	0	0	0	
500 ppm	10	0	0	0	0	0	8	2		0	0	0	10	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	2	6	2		0	0	2	8	0	0		10	0	0	0	0	0		0	9	1	0	0	0		10	0	0	0	
2000 ppm	10	0	0	0	0	1	5	4		0	0	0	10	0	0		10	0	0	0	0	0		0	10	0	0	0	0		10	0	0	0	
4000 ppm	10	0	0	0	0	0	5	5		0	0	0	9	1	0		10	0	0	0	0	0		0	10	0	0	0	0		10	0	0	0	

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

(JCL101)

STUDY NO. : 0234
ANIMAL : RAT F344
SAMPLING DATE : 013-6
SEX : MALE REPORT TYPE : A1

URINALYSIS

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	
4000 ppm	10	10	0	0	0	0		10	0	0	0	0	

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

APPENDIX B 8-2

URINALYSIS (THIRTEEN-WEEK STUDY : SUMMARY)

RAT : FEMALE

STUDY NO. : 0234
ANIMAL : RAT F344
SAMPLING DATE : 013-6
SEX : FEMALE REPORT TYPE : A1

URINALYSIS

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	9	1		0	0	9	1	0	0		10	0	0	0	0	0		5	5	0	0	0	0		10	0	0	0	
250 ppm	10	0	0	0	0	0	7	3		0	0	10	0	0	0		10	0	0	0	0	0		4	6	0	0	0	0		10	0	0	0	
500 ppm	10	0	0	0	0	0	8	2		0	0	8	2	0	0		10	0	0	0	0	0		3	7	0	0	0	0		10	0	0	0	
1000 ppm	10	0	0	0	0	1	9	0		0	0	6	4	0	0		10	0	0	0	0	0		2	8	0	0	0	0		10	0	0	0	
2000 ppm	10	0	0	0	1	0	7	2		0	0	3	7	0	0	**	10	0	0	0	0	0		1	9	0	0	0	0		10	0	0	0	
4000 ppm	10	0	0	0	0	0	6	4		0	0	3	7	0	0	**	10	0	0	0	0	0		0	10	0	0	0	0	**	10	0	0	0	

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

(JCL101)

STUDY NO. : 0234
ANIMAL : RAT F344
SAMPLING DATE : 013-6
SEX : FEMALE REPORT TYPE : A1

URINALYSIS

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	
4000 ppm	10	10	0	0	0	0		10	0	0	0	0	

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

(JCL101)

APPENDIX B 8-3

URINALYSIS (THIRTEEN-WEEK STUDY : SUMMARY)

MOUSE: MALE

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
SAMPLING DATE : 013-6
SEX : MALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	±	+	2+	3+	4+	CHI	Occult blood −	±	+	2+	3+	CHI
Control	10	0	0	0	0	2	8	0		0	0	6	4	0	0		10	0	0	0	0	0		0	10	0	0	0	0		10	0	0	0	0	
500 ppm	10	0	0	0	0	4	6	0		0	0	3	7	0	0		10	0	0	0	0	0		0	10	0	0	0	0		10	0	0	0	0	
1000 ppm	10	0	0	0	0	6	4	0		0	0	2	8	0	0		10	0	0	0	0	0		0	9	1	0	0	0		10	0	0	0	0	
2000 ppm	9	0	0	0	1	6	2	0	*	0	0	0	9	0	0	**	9	0	0	0	0	0		0	9	0	0	0	0		9	0	0	0	0	
4000 ppm	10	0	0	2	6	2	0	0	**	0	0	0	9	1	0	*	10	0	0	0	0	0		0	9	1	0	0	0		10	0	0	0	0	
8000 ppm	10	0	2	5	2	1	0	0	**	0	0	0	8	2	0	**	10	0	0	0	0	0		0	10	0	0	0	0		10	0	0	0	0	

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

(JCL101)

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
SAMPLING DATE : 013-6
SEX : MALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0	
500 ppm	10	10	0	0	0	0	
1000 ppm	10	10	0	0	0	0	
2000 ppm	9	9	0	0	0	0	
4000 ppm	10	10	0	0	0	0	
8000 ppm	10	10	0	0	0	0	

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

APPENDIX B 8-4

URINALYSIS (THIRTEEN-WEEK STUDY : SUMMARY)

MOUSE: FEMALE

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
SAMPLING DATE : 013-6
SEX : FEMALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	±	+	2+	3+	4+	CHI	Occult blood −	±	+	2+	3+	CHI
Control	10	0	0	1	1	5	3	0		0	1	9	0	0	0		10	0	0	0	0	0		1	9	0	0	0	0		10	0	0	0	0	
500 ppm	10	0	1	2	4	2	1	0		0	0	10	0	0	0		10	0	0	0	0	0		0	10	0	0	0	0		10	0	0	0	0	
1000 ppm	10	0	0	3	4	1	2	0		0	1	8	1	0	0		10	0	0	0	0	0		0	10	0	0	0	0		10	0	0	0	0	
2000 ppm	10	0	0	2	2	5	1	0		0	0	2	8	0	0	**	10	0	0	0	0	0		0	10	0	0	0	0		10	0	0	0	0	
4000 ppm	10	0	3	1	2	4	0	0		0	0	3	7	0	0	**	10	0	0	0	0	0		0	9	1	0	0	0		10	0	0	0	0	
8000 ppm	10	0	4	2	1	3	0	0		0	0	2	6	2	0	**	10	0	0	0	0	0		0	6	4	0	0	0		10	0	0	0	0	

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

(JCL101)

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
SAMPLING DATE : 013-6
SEX : FEMALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0	
500 ppm	10	10	0	0	0	0	
1000 ppm	10	10	0	0	0	0	
2000 ppm	10	10	0	0	0	0	
4000 ppm	10	10	0	0	0	0	
8000 ppm	10	10	0	0	0	0	

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

APPENDIX B 9-1

GROSS FINDINGS (THIRTEEN-WEEK STUDY : SUMMARY)

RAT : MALE : SACRIFICED ANIMALS

STUDY NO. : 0234
ANIMAL : RAT F344
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 (%)
thymus	red zone		1 (10)	1 (10)	0 (0)	2 (20)
liver	nodule		0 (0)	0 (0)	0 (0)	1 (10)
	herniation		0 (0)	0 (0)	1 (10)	1 (10)

STUDY NO. : 0234
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name NO. of Animals	2000 ppm 10 (%)	4000 ppm 10 (%)
thymus	red zone		1 (10)	0 (0)
liver	nodule		0 (0)	0 (0)
	herniation		0 (0)	0 (0)

APPENDIX B 9-2

GROSS FINDINGS (THIRTEEN-WEEK STUDY : SUMMARY)

RAT : FEMALE : SACRIFICED ANIMALS

STUDY NO. : 0234
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

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 (%)
subcutis	mass		0 (0)	0 (0)	1 (10)	0 (0)
liver	nodule		0 (0)	0 (0)	0 (0)	1 (10)
	herniation		3 (30)	0 (0)	0 (0)	0 (0)

STUDY NO. : 0234
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name NO. of Animals	2000 ppm 10 (%)	4000 ppm 10 (%)
subcutis	mass		0 (0)	0 (0)
liver	nodule		1 (10)	0 (0)
	herniation		0 (0)	0 (0)

APPENDIX B 9-3

GROSS FINDINGS (THIRTEEN-WEEK STUDY : SUMMARY)

MOUSE : MALE : DWAD AND MORIBUND ANIMALS

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name NO. of Animals	Control 0 (%)	500 ppm 0 (%)	1000 ppm 0 (%)	2000 ppm 1 (%)
kidney	atrophic		- (-)	- (-)	- (-)	1 (100)
	hydronephrosis		- (-)	- (-)	- (-)	1 (100)
ureter	dilated		- (-)	- (-)	- (-)	1 (100)

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name NO. of Animals	4000 ppm 0 (%)	8000 ppm 0 (%)
kidney	atrophic		- (-)	- (-)
	hydronephrosis		- (-)	- (-)
ureter	dilated		- (-)	- (-)

APPENDIX B 9-4

GROSS FINDINGS (THIRTEEN-WEEK STUDY : SUMMARY)

MOUSE : MALE : SACRIFICED ANIMALS

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	500 ppm 10 (%)	1000 ppm 10 (%)	2000 ppm 9 (%)
spleen	black zone		0 (0)	2 (20)	0 (0)	0 (0)
kidney	hydronephrosis		1 (10)	2 (20)	0 (0)	1 (11)
testis	absence		0 (0)	1 (10)	0 (0)	0 (0)

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name NO. of Animals	4000 ppm 10 (%)	8000 ppm 10 (%)
spleen	black zone		0 (0)	0 (0)
kidney	hydronephrosis		1 (10)	0 (0)
testis	absence		0 (0)	0 (0)

APPENDIX B 9-5

GROSS FINDINGS (THIRTEEN-WEEK STUDY : SUMMARY)

MOUSE : FEMALE : SACRIFICED ANIMALS

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

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

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name NO. of Animals	4000 ppm 10 (%)	8000 ppm 10 (%)
spleen	black zone		0 (0)	0 (0)
kidney	malposition		0 (0)	1 (10)
	hydronephrosis		0 (0)	1 (10)
uterus	deformed		0 (0)	1 (10)
	dilated lumen		0 (0)	1 (10)

APPENDIX B 10-1

ORGAN WEIGHT (THIRTEEN-WEEK STUDY : SUMMARY),ABSOLUTE

RAT : MALE

STUDY NO. : 0234
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	277± 22	0.240± 0.040	0.052± 0.011	2.725± 0.119	0.849± 0.064	1.012± 0.139
250 ppm	10	258± 31	0.222± 0.034	0.054± 0.010	2.679± 0.203	0.800± 0.075	0.928± 0.107
500 ppm	10	274± 21	0.239± 0.046	0.051± 0.009	2.751± 0.109	0.841± 0.066	0.955± 0.066
1000 ppm	10	262± 23	0.234± 0.021	0.053± 0.010	2.672± 0.112	0.791± 0.067	0.893± 0.074
2000 ppm	10	263± 11	0.234± 0.025	0.053± 0.010	2.732± 0.087	0.783± 0.034	0.901± 0.030
4000 ppm	10	228± 11**	0.189± 0.027**	0.053± 0.011	2.658± 0.075	0.707± 0.029**	0.824± 0.046**

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

(HCL040)

STUDY NO. : 0234
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.714± 0.081	0.469± 0.021	6.800± 0.549	1.879± 0.066
250 ppm	10	1.622± 0.160	0.450± 0.052	6.369± 0.882	1.875± 0.060
500 ppm	10	1.722± 0.154	0.485± 0.028	6.727± 0.518	1.882± 0.034
1000 ppm	10	1.654± 0.189	0.460± 0.047	6.396± 0.744	1.874± 0.064
2000 ppm	10	1.718± 0.065	0.479± 0.025	6.617± 0.393	1.874± 0.036
4000 ppm	10	1.547± 0.083**	0.419± 0.021**	5.815± 0.272**	1.831± 0.043

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

(HCL040)

APPENDIX B 10-2

ORGAN WEIGHT (THIRTEEN-WEEK STUDY : SUMMARY),ABSOLUTE

RAT : FEMALE

STUDY NO. : 0234
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	175± 11	0.213± 0.013	0.066± 0.014	0.110± 0.015	0.605± 0.029	0.738± 0.041
250 ppm	10	176± 12	0.197± 0.018	0.062± 0.012	0.109± 0.010	0.625± 0.053	0.765± 0.047
500 ppm	10	170± 8	0.201± 0.016	0.056± 0.012	0.107± 0.013	0.605± 0.052	0.753± 0.033
1000 ppm	10	172± 11	0.203± 0.028	0.057± 0.013	0.104± 0.013	0.595± 0.050	0.778± 0.153
2000 ppm	10	164± 8*	0.190± 0.018*	0.052± 0.007*	0.101± 0.014	0.562± 0.035	0.702± 0.030
4000 ppm	10	153± 4**	0.179± 0.016**	0.054± 0.005	0.106± 0.020	0.543± 0.037*	0.685± 0.029**

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

STUDY NO. : 0234
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.160± 0.063	0.353± 0.024	4.040± 0.334	1.770± 0.028
250 ppm	10	1.173± 0.071	0.364± 0.029	4.090± 0.408	1.776± 0.033
500 ppm	10	1.167± 0.054	0.367± 0.026	3.977± 0.274	1.771± 0.032
1000 ppm	10	1.219± 0.131	0.386± 0.054	4.141± 0.824	1.728± 0.062
2000 ppm	10	1.175± 0.061	0.366± 0.021	3.864± 0.192	1.741± 0.029
4000 ppm	10	1.215± 0.037	0.356± 0.027	3.798± 0.142	1.726± 0.043

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

APPENDIX B 10-3

ORGAN WEIGHT (THIRTEEN-WEEK STUDY : SUMMARY),ABSOLUTE

MOUSE: MALE

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	29.9± 1.4	0.043± 0.009	0.013± 0.003	0.200± 0.028	0.138± 0.008	0.155± 0.009
500 ppm	10	28.8± 2.6	0.038± 0.008	0.010± 0.003	0.210± 0.018	0.145± 0.007	0.160± 0.008
1000 ppm	10	29.5± 1.8	0.036± 0.006	0.012± 0.002	0.208± 0.018	0.149± 0.006	0.162± 0.009
2000 ppm	9	28.2± 2.2	0.035± 0.005	0.012± 0.003	0.220± 0.021	0.147± 0.013	0.164± 0.016
4000 ppm	10	25.6± 1.3**	0.033± 0.006**	0.011± 0.002	0.216± 0.020	0.139± 0.016	0.151± 0.011
8000 ppm	10	24.0± 0.9**	0.026± 0.006**	0.009± 0.002	0.221± 0.028	0.128± 0.007	0.153± 0.008

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

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.429± 0.035	0.047± 0.004	1.109± 0.056	0.445± 0.011
500 ppm	10	0.562± 0.326	0.047± 0.010	1.108± 0.074	0.440± 0.016
1000 ppm	10	0.425± 0.022	0.046± 0.007	1.128± 0.065	0.448± 0.015
2000 ppm	9	0.555± 0.377	0.045± 0.009	1.090± 0.085	0.442± 0.017
4000 ppm	10	0.410± 0.025	0.042± 0.006	0.996± 0.057**	0.447± 0.011
8000 ppm	10	0.412± 0.020	0.038± 0.006*	0.937± 0.057**	0.448± 0.012

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

APPENDIX B 10-4

ORGAN WEIGHT (THIRTEEN-WEEK STUDY : SUMMARY),ABSOLUTE

MOUSE: FEMALE

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	20.3± 1.4	0.036± 0.006	0.012± 0.003	0.031± 0.010	0.117± 0.012	0.150± 0.010
500 ppm	10	20.4± 0.8	0.038± 0.004	0.012± 0.003	0.035± 0.007	0.112± 0.009	0.155± 0.009
1000 ppm	10	20.4± 0.8	0.039± 0.004	0.011± 0.003	0.035± 0.005	0.117± 0.011	0.149± 0.010
2000 ppm	10	20.4± 0.9	0.037± 0.008	0.012± 0.003	0.031± 0.006	0.114± 0.011	0.150± 0.007
4000 ppm	10	20.3± 0.6	0.036± 0.003	0.010± 0.002	0.030± 0.004	0.112± 0.010	0.142± 0.012
8000 ppm	10	20.4± 1.1	0.035± 0.006	0.011± 0.003	0.027± 0.006	0.104± 0.011	0.138± 0.015

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

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.270± 0.027	0.047± 0.011	0.824± 0.075	0.457± 0.014
500 ppm	10	0.274± 0.019	0.052± 0.008	0.834± 0.052	0.457± 0.010
1000 ppm	10	0.283± 0.018	0.048± 0.005	0.845± 0.060	0.458± 0.017
2000 ppm	10	0.293± 0.021	0.042± 0.006	0.825± 0.034	0.455± 0.015
4000 ppm	10	0.316± 0.014**	0.046± 0.008	0.832± 0.034	0.452± 0.014
8000 ppm	10	0.364± 0.144**	0.047± 0.011	0.813± 0.072	0.441± 0.015

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

APPENDIX B 11-1

ORGAN WEIGHT (THIRTEEN-WEEK STUDY : SUMMARY),RELATIVE

RAT : MALE

STUDY NO. : 0234
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	277± 22	0.086± 0.012	0.019± 0.005	0.989± 0.080	0.308± 0.025	0.368± 0.066
250 ppm	10	258± 31	0.086± 0.009	0.021± 0.004	1.044± 0.071	0.311± 0.011	0.361± 0.028
500 ppm	10	274± 21	0.087± 0.012	0.019± 0.003	1.005± 0.050	0.307± 0.017	0.349± 0.017
1000 ppm	10	262± 23	0.090± 0.010	0.020± 0.003	1.026± 0.099	0.302± 0.013	0.341± 0.015
2000 ppm	10	263± 11	0.089± 0.009	0.020± 0.004	1.042± 0.055	0.298± 0.011	0.343± 0.015
4000 ppm	10	228± 11**	0.083± 0.010	0.024± 0.005	1.168± 0.050**	0.310± 0.010	0.362± 0.011

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

STUDY NO. : 0234
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.621± 0.037	0.170± 0.009	2.463± 0.196	0.682± 0.045
250 ppm	10	0.630± 0.015	0.175± 0.009	2.462± 0.095	0.735± 0.084
500 ppm	10	0.628± 0.028	0.177± 0.007	2.452± 0.060	0.689± 0.047
1000 ppm	10	0.630± 0.031	0.176± 0.009	2.434± 0.131	0.717± 0.044
2000 ppm	10	0.655± 0.030	0.182± 0.010**	2.518± 0.066	0.715± 0.037
4000 ppm	10	0.678± 0.015**	0.184± 0.005**	2.552± 0.073*	0.804± 0.032**

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

APPENDIX B 11-2

ORGAN WEIGHT (THIRTEEN-WEEK STUDY : SUMMARY),RELATIVE

RAT : FEMALE

STUDY NO. : 0234
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	175± 11	0.122± 0.008	0.038± 0.007	0.063± 0.007	0.347± 0.014	0.423± 0.022
250 ppm	10	176± 12	0.112± 0.009	0.036± 0.007	0.062± 0.003	0.355± 0.016	0.436± 0.022
500 ppm	10	170± 8	0.118± 0.011	0.033± 0.006	0.063± 0.008	0.355± 0.018	0.443± 0.019
1000 ppm	10	172± 11	0.118± 0.013	0.033± 0.007	0.060± 0.007	0.345± 0.012	0.450± 0.064
2000 ppm	10	164± 8*	0.116± 0.013	0.032± 0.005	0.062± 0.009	0.344± 0.014	0.430± 0.017
4000 ppm	10	153± 4**	0.118± 0.010	0.035± 0.003	0.069± 0.013	0.355± 0.020	0.449± 0.012

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

STUDY NO. : 0234
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.665± 0.031	0.202± 0.008	2.311± 0.092	1.016± 0.049
250 ppm	10	0.668± 0.015	0.207± 0.010	2.322± 0.089	1.014± 0.067
500 ppm	10	0.686± 0.030	0.216± 0.013	2.336± 0.099	1.042± 0.043
1000 ppm	10	0.707± 0.043	0.224± 0.019**	2.395± 0.344	1.006± 0.051
2000 ppm	10	0.719± 0.022*	0.224± 0.012**	2.364± 0.047	1.067± 0.048
4000 ppm	10	0.796± 0.017**	0.233± 0.013**	2.490± 0.099**	1.131± 0.032**

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

APPENDIX B 11-3

ORGAN WEIGHT (THIRTEEN-WEEK STUDY : SUMMARY),RELATIVE

MOUSE: MALE

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	29.9± 1.4	0.143± 0.026	0.042± 0.011	0.670± 0.093	0.462± 0.037	0.520± 0.041
500 ppm	10	28.8± 2.6	0.132± 0.025	0.037± 0.012	0.727± 0.098	0.505± 0.035	0.560± 0.062
1000 ppm	10	29.5± 1.8	0.123± 0.018	0.039± 0.008	0.708± 0.078	0.507± 0.034	0.551± 0.045
2000 ppm	9	28.2± 2.2	0.125± 0.012	0.043± 0.013	0.783± 0.077*	0.525± 0.048**	0.584± 0.069*
4000 ppm	10	25.6± 1.3**	0.129± 0.019	0.041± 0.009	0.844± 0.076**	0.542± 0.052**	0.593± 0.060*
8000 ppm	10	24.0± 0.9**	0.110± 0.023**	0.038± 0.010	0.922± 0.104**	0.532± 0.025**	0.636± 0.028**

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

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.439± 0.143	0.157± 0.014	3.709± 0.127	1.493± 0.098
500 ppm	10	1.964± 1.149	0.165± 0.033	3.861± 0.243	1.539± 0.146
1000 ppm	10	1.441± 0.065	0.154± 0.016	3.826± 0.172	1.522± 0.097
2000 ppm	9	2.040± 1.603	0.160± 0.040	3.873± 0.095	1.581± 0.164
4000 ppm	10	1.604± 0.086*	0.165± 0.022	3.895± 0.103	1.752± 0.085**
8000 ppm	10	1.720± 0.052**	0.156± 0.019	3.906± 0.189	1.868± 0.065**

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

APPENDIX B 11-4

ORGAN WEIGHT (THIRTEEN-WEEK STUDY : SUMMARY),RELATIVE

MOUSE: FEMALE

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	20.3± 1.4	0.178± 0.021	0.058± 0.011	0.152± 0.046	0.574± 0.037	0.741± 0.070
500 ppm	10	20.4± 0.8	0.186± 0.017	0.057± 0.015	0.169± 0.033	0.549± 0.041	0.759± 0.050
1000 ppm	10	20.4± 0.8	0.192± 0.016	0.055± 0.011	0.172± 0.024	0.575± 0.051	0.734± 0.057
2000 ppm	10	20.4± 0.9	0.179± 0.037	0.058± 0.017	0.151± 0.031	0.560± 0.046	0.737± 0.035
4000 ppm	10	20.3± 0.6	0.175± 0.015	0.047± 0.012	0.149± 0.016	0.551± 0.048	0.698± 0.051
8000 ppm	10	20.4± 1.1	0.170± 0.023	0.053± 0.017	0.131± 0.028	0.510± 0.039**	0.673± 0.051*

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

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.332± 0.067	0.229± 0.047	4.059± 0.172	2.263± 0.160
500 ppm	10	1.341± 0.074	0.252± 0.038	4.087± 0.170	2.241± 0.079
1000 ppm	10	1.392± 0.087	0.237± 0.024	4.147± 0.165	2.253± 0.088
2000 ppm	10	1.438± 0.081	0.205± 0.025	4.043± 0.180	2.233± 0.102
4000 ppm	10	1.552± 0.064**	0.226± 0.038	4.093± 0.132	2.222± 0.036
8000 ppm	10	1.799± 0.796**	0.227± 0.043	3.977± 0.217	2.160± 0.092

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

APPENDIX B 12-1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN-WEEK STUDY: SUMMARY)

RAT : MALE : SACRIFICED ANIMALS

STUDY NO. : 0234
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

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

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:squamous epithelium		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)
[Hematopoietic system]																		
thymus			<10>				<10>				<10>				<10>			
	congestion		1	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
[Circulatory system]																		
heart			<10>				<10>				<10>				<10>			
	granulation		4	0	0	0	2	0	0	0	3	0	0	0	2	0	0	0
			(40)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
[Digestive system]																		
liver			<10>				<10>				<10>				<10>			
	herniation		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)
pancreas			<10>				<10>				<10>				<10>			
	atrophy		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	2000 ppm				4000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
nasal cavit			<10>				<10>			
	inflammation:squamous epithelium		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Hematopoietic system]										
thymus			<10>				<10>			
	congestion		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Circulatory system]										
heart			<10>				<10>			
	granulation		2	0	0	0	2	0	0	0
			(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
[Digestive system]										
liver			<10>				<10>			
	herniation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
pancreas			<10>				<10>			
	atrophy		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : SLight 2 : Moderate 3 : Ma rked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : a / b * 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>			
	basophilic change		0	0	0	0	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)
	eosinophilic body		9	1	0	0	6	3	0	0	10	0	0	0	6	3	0	0
			(90)	(10)	(0)	(0)	(60)	(30)	(0)	(0)	(100)	(0)	(0)	(0)	(60)	(30)	(0)	(0)
	ossification		0	0	0	0	0	0	0	0	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>			
	ultimibranchial body remanet		3	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(30)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
[Reproductive system]																		
prostate			<10>				<10>				<10>				<10>			
	inflammation		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)
[Special sense organs/appandage]																		
Harder gl			<10>				<10>				<10>				<10>			
	lymphocytic infiltration		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	2000 ppm				4000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[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		10	0	0	0	10	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	ossification		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
[Endocrine system]										
thyroid			<10>				<10>			
	ultimibranchial body remanet		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Reproductive system]										
prostate			<10>				<10>			
	inflammation		0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)
[Special sense organs/appandage]										
Harder gl			<10>				<10>			
	lymphocytic infiltration		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

APPENDIX B 12-2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN-WEEK STUDY: SUMMARY)

RAT : FEMALE : SACRIFICED ANIMALS

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:squamous epithelium		4 (40)	1 (10)	0 (0)	0 (0)	5 (50)	1 (10)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	4 (40)	0 (0)	0 (0)	0 (0)
	inflammation:respiratory 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>			
	bronchiolar-alveolar cell hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
[Hematopoietic system]																		
bone marrow			<10>				<10>				<10>				<10>			
	granulation		2 (20)	1 (10)	0 (0)	0 (0)	3 (30)	0 (0)	0 (0)	0 (0)	1 (10)	1 (10)	0 (0)	0 (0)	3 (30)	3 (30)	0 (0)	0 (0)
[Circulatory system]																		
heart			<10>				<10>				<10>				<10>			
	granulation		2 (20)	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)
[Digestive system]																		
liver			<10>				<10>				<10>				<10>			
	herniation		2 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

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

Organ	Findings	Group Name	2000 ppm				4000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
nasal cavit			<10>				<10>			
	inflammation:squamous epithelium		0	0	0	0 *	4	0	0	0
			(0)	(0)	(0)	(0)	(40)	(0)	(0)	(0)
	inflammation:respiratory epithelium		2	1	0	0	0	0	0	0
			(20)	(10)	(0)	(0)	(0)	(0)	(0)	(0)
lung			<10>				<10>			
	bronchiolar-alveolar cell hyperplasia		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Hematopoietic system]										
bone marrow			<10>				<10>			
	granulation		1	2	0	0	1	1	0	0
			(10)	(20)	(0)	(0)	(10)	(10)	(0)	(0)
[Circulatory system]										
heart			<10>				<10>			
	granulation		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]										
liver			<10>				<10>			
	herniation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Ma rked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : a / b * 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		3	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(30)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
[Endocrine system]																		
thyroid			<10>				<10>				<10>				<10>			
	ultimibranchial body remanet		1	0	0	0	1	0	0	0	2	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
[Special sense organs/appandage]																		
Harder gl			<10>				<10>				<10>				<10>			
	lymphocytic infiltration		1	0	0	0	2	0	0	0	2	0	0	0	3	1	0	0
			(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(30)	(10)	(0)	(0)

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

Organ	Findings	Group Name	2000 ppm				4000 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	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
[Endocrine system]										
thyroid			<10>				<10>			
	ultimibranchial body remanet		0	0	0	0	1	1	0	0
			(0)	(0)	(0)	(0)	(10)	(10)	(0)	(0)
[Special sense organs/appandage]										
Harder gl			<10>				<10>			
	lymphocytic infiltration		2	1	0	0	1	0	0	0
			(20)	(10)	(0)	(0)	(10)	(0)	(0)	(0)

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

APPENDIX B 12-3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN-WEEK STUDY: SUMMARY)

MOUSE : MALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control				500 ppm				1000 ppm				2000 ppm			
		No. of Animals on Study	0				0				0				1			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
spleen			< 0>				< 0>				< 0>				< 1>			
	deposit of hemosiderin		-	-	-	-	-	-	-	-	-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
[Circulatory system]																		
heart			< 0>				< 0>				< 0>				< 1>			
	necrosis:focal		-	-	-	-	-	-	-	-	-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
[Urinary system]																		
kidney			< 0>				< 0>				< 0>				< 1>			
	inflammatory polyp		-	-	-	-	-	-	-	-	-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
	hydronephrosis		-	-	-	-	-	-	-	-	-	-	-	-	0	0	1	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(0)	(0)	(100)	(0)

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

Organ	Findings	Group Name	4000 ppm				8000 ppm			
		No. of Animals on Study	0				0			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]										
spleen			< 0>				< 0>			
	deposit of hemosiderin		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Circulatory system]										
heart			< 0>				< 0>			
	necrosis:focal		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Urinary system]										
kidney			< 0>				< 0>			
	inflammatory polyp		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	hydronephrosis		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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

APPENDIX B 12-4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN-WEEK STUDY: SUMMARY)

MOUSE : MALE : SACRIFICED ANIMALS

STUDY NO. : 0235
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control				500 ppm				1000 ppm				2000 ppm			
		No. of Animals on Study	10				10				10				9			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
spleen			<10>				<10>				<10>				< 9>			
	deposit of melanin		0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]																		
liver			<10>				<10>				<10>				< 9>			
	necrosis:focal		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	granulation		4	0	0	0	3	0	0	0	3	0	0	0	2	0	0	0
			(40)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(22)	(0)	(0)	(0)
pancreas			<10>				<10>				<10>				< 9>			
	granulation		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)
[Urinary system]																		
kidney			<10>				<10>				<10>				< 9>			
	inflammatory polyp		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	vacuolization of proximal tubule		10	0	0	0	8	0	0	0	7	0	0	0	7	0	0	0
			(100)	(0)	(0)	(0)	(80)	(0)	(0)	(0)	(70)	(0)	(0)	(0)	(78)	(0)	(0)	(0)

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

Organ	Findings	Group Name	4000 ppm				8000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]										
spleen			<10>				<10>			
	deposit of melanin		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
[Digestive system]										
liver			<10>				<10>			
	necrosis:focal		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	granulation		1	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
pancreas			<10>				<10>			
	granulation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Urinary system]										
kidney			<10>				<10>			
	inflammatory polyp		0	0	1	0	0	0	0	0
			(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)
	vacuolization of proximal tubule		2	0	0	0 **	0	0	0	0 **
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				500 ppm				1000 ppm				2000 ppm			
		No. of Animals on Study	10				10				10				9			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																		
kidney			<10>				<10>				<10>				< 9>			
	hydronephrosis		0	0	1	0	0	0	2	0	0	0	0	0	0	0	1	0
			(0)	(0)	(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(11)	(0)
urin bladd			<10>				< 8>				<10>				< 9>			
	inflammation		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(13)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Endocrine system]																		
pituitary			<10>				<10>				<10>				< 9>			
	Rathke pouch		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)	(11)	(0)	(0)	(0)
parathyroid			<10>				<10>				<10>				< 9>			
	cyst		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)
adrenal			<10>				<10>				<10>				< 9>			
	accesory cortical nodule		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Reproductive system]																		
testis			<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)

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

Organ	Findings	Group Name	4000 ppm				8000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]										
kidney			<10>				<10>			
	hydronephrosis		0	0	1	0	0	0	0	0
			(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)
urin bladd			<10>				<10>			
	inflammation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Endocrine system]										
pituitary			<10>				<10>			
	Rathke pouch		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
parathyroid			<10>				<10>			
	cyst		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
adrenal			<10>				<10>			
	accesory cortical nodule		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Reproductive system]										
testis			<10>				<10>			
	atrophy		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				500 ppm				1000 ppm				2000 ppm			
		No. of Animals on Study	10				10				10				9			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Body cavities]																		
adipose			<10>				<10>				<10>				< 9>			
	mineralization		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)	(11)	(0)	(0)	(0)

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

Organ	Findings	Group Name	4000 ppm				8000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Body cavities]										
adipose			<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 : Ma rked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : a / b * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

APPENDIX B 12-5

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN-WEEK STUDY: SUMMARY)

MOUSE: FEMALE : SACRIFICED ANIMALS

Organ	Findings	Group Name	Control				500 ppm				1000 ppm				2000 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
spleen			<10>				<10>				<10>				<10>			
	deposit of melanin		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)
	extramedullary hematopoiesis		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)
[Digestive system]																		
salivary gl			<10>				<10>				<10>				<10>			
	mineralization		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
liver			<10>				<10>				<10>				<10>			
	granulation		5	0	0	0	3	1	0	0	7	0	0	0	4	0	0	0
			(50)	(0)	(0)	(0)	(30)	(10)	(0)	(0)	(70)	(0)	(0)	(0)	(40)	(0)	(0)	(0)
pancreas			<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)
[Urinary system]																		
kidney			<10>				<10>				<10>				<10>			
	hydronephrosis		0	0	0	0	0	0	0	0	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 : Ma rked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : a / b * 100
Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	4000 ppm				8000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]										
spleen			<10>				<10>			
	deposit of melanin		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	extramedullary hematopoiesis		2	0	0	0	1	0	0	0
			(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
[Digestive system]										
salivary gl			<10>				<10>			
	mineralization		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
liver			<10>				<10>			
	granulation		2	0	0	0	4	0	0	0
			(20)	(0)	(0)	(0)	(40)	(0)	(0)	(0)
pancreas			<10>				<10>			
	atrophy		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
[Urinary system]										
kidney			<10>				<10>			
	hydronephrosis		0	0	0	0	0	0	1	0
			(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)

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

Organ	Findings	Group Name	Control				500 ppm				1000 ppm				2000 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																		
urin bladd			<10>				<10>				<10>				<10>			
	inflammation		0	0	0	0	0	0	0	0	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]																		
adrenal			<10>				<10>				<10>				<10>			
	spindle-cell hyperplasia		8	0	0	0	10	0	0	0	7	0	0	0	7	0	0	0
			(80)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(70)	(0)	(0)	(0)	(70)	(0)	(0)	(0)
	accesory cortical nodule		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)
[Nervous system]																		
spinal cord			<10>				<10>				<10>				<10>			
	epidermal cyst		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)
[Special sense organs/appandage]																		
eye			<10>				<10>				<10>				<10>			
	keratitis		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)	(0)	(0)	(0)

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

Organ	Findings	Group Name	4000 ppm				8000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]										
urin bladd			<10>				<10>			
	inflammation		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
[Endocrine system]										
adrenal			<10>				<10>			
	spindle-cell hyperplasia		10	0	0	0	5	0	0	0
			(100)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
	accesory cortical nodule		1	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
[Nervous system]										
spinal cord			< 9>				<10>			
	epidermal cyst		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Special sense organs/appandage]										
eye			<10>				<10>			
	keratitis		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

APPENDIX B 13-1

IDENTITY OF GLYOXAL

(THIRTEEN-WEEK STUDIES)

IDENTITY OF GLYOXAL(THIRTEEN-WEEK STUDIES)

Test Substance Lot No.: WDL5585

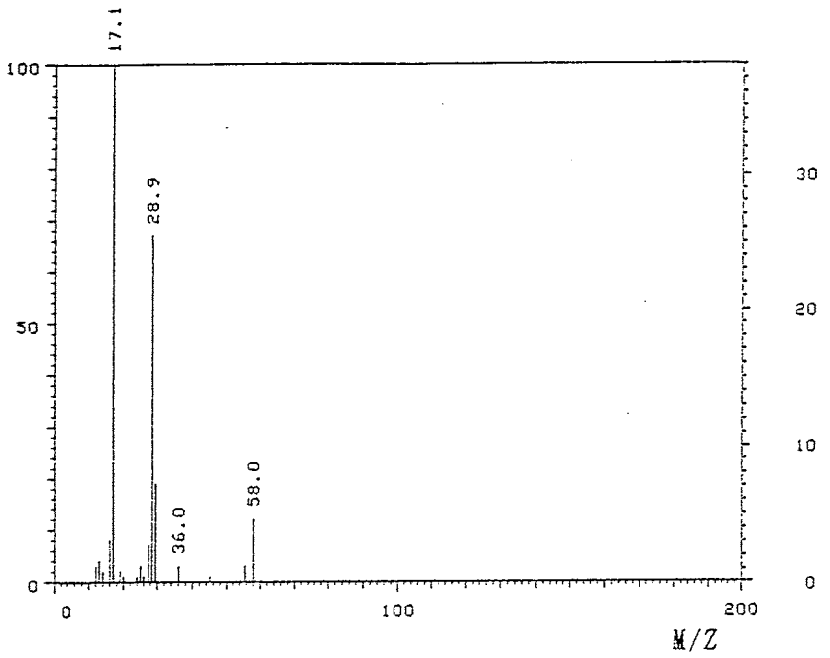
1. Spectral data

Mass Spectrometry

Instrument: Hitachi M-80B Mass Spectrometer

Ionization: EI(Electron Ionization)

Ionization Voltage: 70eV



Mass Spectrum of Test Substance

Results:	Determined Molecular and Fragment Peak(M/Z)	Literature Value* Molecular and Fragment Peak(M/Z)
	58.0 28.9 17.1	58.0 29.0 17.0 (*EPA/NIH Mass Spectral Data Base (1978) V. 1, p. 7.)

2. Conclusions: The result of the mass spectrum agreed with the literature value. Consequently, the test substance was identified as glyoxal.

APPENDIX B 13-2

STABILITY OF GLYOXAL

(THIRTEEN-WEEK STUDIES)

STABILITY OF GLYOXAL(THIRTEEN-WEEK STUDIES)

Test Substance Lot No.: WDL5585

1. Sample storage: This lot was used from 1993.3.9 to 1993.6.23. Test substance was stored at room temperature.

2. Gas Chromatography

Instrument: Hewlett Packard 5890A Gass Chromatograph

Column: Methyl Silicone(0.2mmϕ × 50m)

Column Temperature: 200°C

Flow Rate: 1 ml/min

Detector: FID(Flame Ionization Detector)

Injection Volume: 1 μl

Pre-Treatment: Glyoxal was allowed to react with quinoxaline, and analyzed. First, 50% hydroxylammonium chloride(0.02ml), 36% hydrochloric acid(0.1ml), 4% o-phenylene diamine dihydrochloride(0.05ml) were added to a glyoxal solution (1ml). This mixture was stirred at 75°C for 0.5 hr. Then, this solution was extracted with ethyl acetate(2ml) and analyzed.

Results: Chromatogram indicated one major peak(peak No.2) and solvent peak(peak No.1) analyzed at 1993.3.1 and one major peak(peak No.2) and solvent peak(peak No.1) analyzed at 1993.6.24. The new treace impurity peak in the test substance analyzed at 1993.6.24 was not detected.

Date	Peak No.	Retention Time(min)	Retention Time Relative to Major Peak	Area (percent of Major peak)
1993.3.1	1	2.822(Solvent peak)		
(date analyzed)	2	3.533	1.00	100
1993.6.24	1	2.82(Solvent peak)		
(date analyzed)	2	3.532	1.00	100

3. Conclusions: The results indicated that the test sabstance did not change when stored in the dark at 5°C during this period(for about 15 weeks).

APPENDIX B 13-3

CONCENTRATION GLYOXAL IN DRINKING WATER

(THIRTEEN-WEEK STUDIES)

CONCENTRATION OF GLYOXAL IN DRINKING WATER(THIRTEEN-WEEK STUDIES)

(Rat)

	Target Concentration(ppm)				
Date analyzed	250	500	1000	2000	4000
1993.3.23	257.0(102.8)*	518.4(103.7)	1064.9(106.5)	2134.0(106.7)	4286.0(107.2)

(Mouse)

	Target Concentration(ppm)				
Date analyzed	500	1000	2000	4000	8000
1993.3.9	496.8(99.4)*	996.3(99.6)	2034.2(101.7)	4020.1(100.5)	8007.6(100.1)

(*) % of target concentration

Analytical method : The sample were analyzed by the gas chromatography.

Instrument : Hewlett Packard 5890A
Column : METHYL SILICONE(0.2mmϕ × 50m)
Column Temperature: 200℃
Carrier : He
Flow Rate : 1ml/min
Detector : FID(Flame Ionization Detector)
Injection Volume : 1μl

Pre-Treatment : Glyoxal was allowed to react with quinoxaline, and analyzed. First, 50% hydroxylammonium chloride(0.02ml), 36% hydrochloric acid(0.1ml), 4% o-phenylene diamine dihydrochloride(0.05ml) were added to a glyoxal solution(1ml). This mixture was stirred at 75℃ for 0.5 hr. Then, this solution was extracted with ethyl acetate(2ml) and analyzed.

APPENDIX B 13-4

STABILITY OF GLYOXAL IN DRINKING WATER

(THIRTEEN-WEEK STUDIES)

STABILITY OF GLYOXAL IN DRINKING WATER(THIRTEEN-WEEK STUDIES)

(Rat)

	Target Concentration(ppm)	
Date analyzed	250	4000
1993.3.1(a)	252.1	4107.0
1993.3.8(b)	246.7	3986.6

(MOUSE)

	Target Concentration(ppm)	
Date analyzed	500	8000
1993.3.1(a)	505.9	8186.2
1993.3.8(b)	497.8	8086.0

(a) Date of preparation
(b) The stability of glyoxal in drinking water was established for 7 days when stored at 25℃.

Analytical method: The sample were analyzed by the gas chromatography.

Instrument : Hewlett Packard 5890A
Column : METHYL SILICONE(0.2mmϕ × 50m)
Column Temperature: 200℃
Carrier : He
Flow Rate : 1ml/min
Detector : FID(Flame Ionization Detector)
Injection Volume : 1μl

Pre-Treatment : Glyoxal was allowed to react with quinoxaline, and analyzed. First, 50% hydroxylammonium chloride(0.02ml), 36% hydrochloric acid(0.1ml), 4% o-phenylene diamine dihydrochloride(0.05ml) were added to a glyoxal solution(1ml). This mixture was stirred at 75℃ for 0.5 hr. Then, this solution was extracted with ethyl acetate(2ml) and analyzed.

APPENDIX C 1

METHODS FOR HEMATOLOGY,BIOCHEMISTRY,AND URINALYSIS

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS

Item	Method	Unit
Hematology		
Red blood cell (RBC)	Light scattering method [1]	$\times 10^6/\mu l$
Hemoglobin (Hgb)	Cyanmethemoglobin method [1]	g/dl
Hematocrit (Hct)	Calculated as RBC×MCV/10 [1]	%
Mean corpuscular volume (MCV)	Light scattering method [1]	fl
Mean corpuscular hemoglobin (MCH)	Calculated as Hgb/RBC×10 [1]	pg
Mean corpuscular hemoglobin concentration (MCHC)	Calculated as Hgb/Hct×100 [1]	g/dl
Platelet	Light scattering method [1]	$\times 10^3/\mu l$
White blood cell (WBC)	Light scattering method [1]	$\times 10^3/\mu l$
Differential WBC	Pattern recognition method [2] (May-Grunwald-Giemsa staining)	%
Reticulocyte	Pattern recognition method [2] (New methyleneblue staining)	‰
Prothrombin time	Quick one stage method [3]	sec
Activated partial thromboplastin time (APTT)	Ellagic acid activated method [3]	sec
Biochemistry		
Total protein (TP)	Biuret method [4]	g/dl
Albumin (Alb)	BCG method [4]	g/dl
A/G ratio	Calculated as Alb/(TP-Alb) [4]	
T-bilirubin	Michaelson method [4]	mg/dl
Glucose	Enzymatic method (HK・G-6-PDH) [4]	mg/dl
T-cholesterol	Enzymatic method (CEH・COD・POD) [4]	mg/dl
Triglyceride	Enzymatic method (GK・GPO・POD) [4]	mg/dl
Phospholipid	Enzymatic method (PLD・COD・POD) [4]	mg/dl
Glutamic oxaloacetic transaminase (GOT)	Karmen method [4]	IU/l
Glutamic pyruvic transaminase (GPT)	Karmen method [4]	IU/l
Lactate dehydrogenase (LDH)	Wroblewski-LaDue method [4]	IU/l
Alkaline phosphatase (ALP)	GSCC method [4]	IU/l
γ-Glutamyl transpeptidase (G-GTP)	L-γ-Glutamyl-p-nitroanilide substrate method [4]	IU/l
Creatine phosphokinase (CPK)	GSCC method [4]	IU/l
Urea nitrogen	Enzymatic method (Urease・GLDH) [4]	mg/dl
Creatinine	Jaffe metod [4]	mg/dl
Sodium	Flame photometry [5]	mEq/l
Potassium	Flame photometry [5]	mEq/l
Chloride	Coulometric titration [5]	mEq/l
Calcium	OCPC method [4]	mg/dl
Inorganic phosphorus	Enzymatic method (SPL・PGM・G-6-PDH) [4]	mg/dl
Urinalysis		
pH,Protein,Glucose,Ketone body,Bilirubin, Occult Blood,Urobilinogen	Urinalysis reagent paper metod [6]	

1) Automatic blood cell analyzer (Technicon H・1 : Technicon Instruments Corporation,USA)
2) Automatic blood cell differntial analyzer (Hitachi 8200 : Hitachi ,Ltd.,Japan)
3) Automatic coagulometer (Amelung KC-10 : Heinrich Amelung GmbH, Germany)
4) Automatic analyzer (Hitachi 705 : Hitachi ,Ltd.,Japan)
5) Flame photometer (Hitachi 750 : Hitachi ,Ltd.,Japan)
6) Ames reagent strips for urinalysis (Multistix,Uro-Labstix : Miles Sankyo Co.,Ltd.,Japan)

APPENDIX C 2

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

	TEST ITEM	DECIMAL PLACE	UNIT
HEMATOLOGY	Red blood cell	2	$\times 10^6 / \mu l$
	Hemoglobin	1	g/dl
	Hematocrit	1	%
	MCV	1	fl
	MCH	1	pg
	MCHC	1	g/dl
	Platelet	0	$\times 10^3 / \mu l$
	Prothorombin time	1	sec.
	APTT	1	sec.
	White blood cell	2	$\times 10^3 / \mu l$
	Differential WBC	0	%
	Reticulocyte	1	%
BIOCHEMISTRY	Total protein	1	g/dl
	Albumin	1	g/dl
	A/G ratio	1	
	T−bilirubin	2	mg/dl
	Glucose	0	mg/dl
	T−cholesterol	0	mg/dl
	Triglyceride	0	mg/dl
	Phospholipid	0	mg/dl
	GOT	0	IU/l
	GPT	0	IU/l
	LDH	0	IU/l
	ALP	0	IU/l
	γ −GTP	0	IU/l
	CPK	0	IU/l
	Urea nitrogen	1	mg/dl
	Creatinine	1	mg/dl
	Sodium	0	mEq/l
	Potassium	1	mEq/l
	Chloride	0	mEq/l
	Calcium	1	mg/dl
	Inorganic phosphorus	1	mg/dl