ヒドラジン一水加物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

APPENDIX

(B1-1～C3)
13 週間試験：ラット/0265；マウス/0266

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIX B 1-1

CLINICAL OBSERVATION (THIRTEEN−WEEK STUDY: SUMMARY)

RAT: MALE

STUDY NO. : 0265
ANIMAL : RAT F344
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 1-7 1	2-7 1	3-7 1	4-7 1	5-7 1	6-7 1	7-7 1	8-7 1	9-7 1	10-7 1	11-7 1	12-7 1	13-7 1
DEATH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	25 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	50 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	100 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	150 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	200 ppm	0	0	0	0	0	0	0	0	0	1	1	1	1
HUNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	25 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	50 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	100 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	150 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	200 ppm	0	0	0	0	0	0	0	1	1	0	0	0	0
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	25 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	50 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	100 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	150 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	200 ppm	0	2	0	0	0	0	0	0	1	0	0	0	0
IRREGULAR BREATHING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	25 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	50 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	100 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	150 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	200 ppm	0	0	0	0	0	0	0	0	1	0	0	0	0
ABNORMAL RESPIRATION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	25 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	50 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	100 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	150 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	200 ppm	0	0	0	0	0	0	0	0	1	0	0	0	0

STUDY NO. : 0265
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
SMALL STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	25 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	50 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	100 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	150 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	200 ppm	0	0	0	0	0	0	1	2	1	0	0	0	0

APPENDIX B 1-2

CLINICAL OBSERVATION (THIRTEEN−WEEK STUDY: SUMMARY)

RAT: 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
HUNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	25 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	50 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	100 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	150 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	200 ppm	0	0	0	0	0	0	0	0	0	0	0	0	1
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	25 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	50 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	100 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	150 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	200 ppm	0	1	0	0	0	0	0	0	0	0	0	0	0

APPENDIX B 1-3

CLINICAL OBSERVATION (THIRTEEN−WEEK STUDY: SUMMARY)

MOUSE: MALE

STUDY NO. : 0266
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
	25 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	50 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	100 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	150 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	200 ppm	0	0	0	0	0	0	0	0	0	0	0	1	1
HUNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	25 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	50 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	100 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	150 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	200 ppm	0	1	1	2	2	2	2	2	2	2	2	1	1
WASTING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	25 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	50 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	100 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	150 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	200 ppm	0	0	0	0	0	1	1	1	1	1	1	0	0
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	25 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	50 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	100 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	150 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	200 ppm	1	2	3	3	3	3	3	3	3	3	3	2	2

APPENDIX B 1-4

CLINICAL OBSERVATION (THIRTEEN−WEEK STUDY: SUMMARY)

MOUSE: FEMALE

STUDY NO. : 0266
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
WASTING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	25 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	50 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	100 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	150 ppm	0	1	1	1	0	0	0	0	0	0	0	0	0
	200 ppm	0	1	1	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
	25 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	50 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	100 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	150 ppm	1	1	1	1	1	1	1	1	1	2	2	1	1
	200 ppm	4	5	5	1	1	0	0	0	0	0	1	2	2

APPENDIX B 2-1

BODY WEIGHT CHANGES (THIRTEEN−WEEK STUDY:SUMMARY)

RAT : MALE

STUDY NO. : 0265
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± 5	148± 8	177± 10	200± 11	221± 10	236± 11	251± 10
25 ppm	122± 5	146± 8	172± 11	195± 13	214± 13	229± 13	241± 12
50 ppm	122± 5	142± 6	165± 9	184± 10*	202± 11	215± 10	227± 12
100 ppm	122± 5	137± 6**	158± 7*	175± 8**	191± 8*	200± 8**	207± 8**
150 ppm	122± 5	132± 6**	149± 8**	163± 8**	171± 8**	176± 11**	179± 12**
200 ppm	122± 5	114± 12**	123± 22**	138± 20**	147± 20**	145± 24**	143± 31**

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

STUDY NO. : 0265
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	261± 12	275± 10	284± 11	291± 13	298± 11	304± 10	307± 12
25 ppm	249± 14	263± 14	271± 14	277± 13	283± 13	288± 12	292± 12
50 ppm	233± 13	245± 15	253± 14	260± 15	266± 15	273± 14	278± 14
100 ppm	211± 8**	217± 8**	221± 9**	227± 10**	232± 10**	236± 10**	237± 11**
150 ppm	180± 10**	186± 13**	187± 14**	190± 15**	192± 15**	197± 19**	197± 21**
200 ppm	139± 34**	138± 37**	133± 40**	139± 36**	139± 35**	139± 32**	142± 33**

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. : 0265
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	101± 3	115± 4	127± 5	135± 6	143± 7	151± 9	155± 10
25 ppm	102± 3	113± 3	124± 4	132± 5	138± 5	145± 8	148± 8
50 ppm	102± 3	109± 4*	120± 5	129± 7	137± 9	143± 9	145± 8
100 ppm	101± 3	101± 4**	110± 5**	118± 6**	122± 6**	127± 7**	128± 8**
150 ppm	102± 3	91± 5**	102± 7**	111± 8**	115± 8**	120± 9**	119± 10**
200 ppm	102± 3	81± 7**	87± 12**	99± 9**	104± 8**	106± 9**	104± 10**

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

STUDY NO. : 0265
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	159± 11	162± 12	166± 13	168± 12	171± 13	172± 13	174± 12
25 ppm	150± 10	155± 8	157± 8	159± 9	164± 8	165± 10	169± 9
50 ppm	146± 9*	151± 9	152± 10*	155± 9*	158± 9	162± 11	166± 10
100 ppm	129± 9**	132± 9**	134± 8**	135± 10**	137± 10**	138± 10**	141± 10**
150 ppm	119± 10**	121± 11**	121± 11**	122± 12**	122± 12**	124± 12**	126± 13**
200 ppm	98± 11**	98± 14**	97± 13**	94± 14**	92± 16**	92± 18**	90± 19**

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. : 0266
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	24.3± 0.9	24.7± 0.9	26.0± 1.0	26.9± 1.1	28.1± 1.1	29.4± 1.2	30.2± 1.3
25 ppm	24.4± 0.8	24.3± 0.8	25.5± 0.9	26.0± 1.1	26.9± 1.2	27.4± 1.6	28.0± 1.5
50 ppm	24.3± 0.9	23.3± 0.8*	24.5± 0.7	25.4± 0.8	25.6± 1.5	26.1± 1.1*	26.7± 1.0*
100 ppm	24.3± 0.9	23.0± 0.9**	23.8± 0.8*	24.9± 1.0*	25.6± 1.0*	25.9± 0.8**	26.1± 1.1**
150 ppm	24.4± 0.8	21.9± 0.7**	22.5± 0.8**	23.8± 0.9**	24.3± 0.6**	24.6± 1.1**	24.9± 1.4**
200 ppm	24.4± 0.9	20.5± 1.7**	20.3± 3.5**	20.6± 4.1**	20.8± 4.5**	21.0± 4.6**	21.6± 5.1**

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

STUDY NO. : 0266
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	30.8± 1.3	32.1± 1.6	32.6± 1.7	33.3± 1.7	34.0± 1.6	34.5± 1.9	35.2± 1.6
25 ppm	27.6± 1.6	28.5± 1.5	28.7± 1.8	28.9± 1.4	30.1± 1.7	30.3± 1.6	30.7± 1.8**
50 ppm	26.3± 1.3*	27.1± 0.9*	27.2± 1.2*	27.7± 1.2*	28.8± 1.0	28.8± 1.3*	29.1± 1.0**
100 ppm	25.9± 1.0**	26.4± 1.0**	26.3± 0.9**	26.5± 1.0**	27.6± 1.0**	27.6± 0.8**	27.3± 1.1**
150 ppm	24.7± 1.1**	24.8± 1.5**	24.7± 1.2**	25.1± 0.9**	26.2± 1.4**	26.1± 1.1**	25.2± 1.1**
200 ppm	21.2± 4.5**	21.5± 4.5**	21.6± 4.4**	21.8± 4.2**	22.8± 4.5**	23.9± 2.4**	23.4± 1.9**

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. : 0266
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	19.3± 0.6	18.9± 1.1	20.5± 1.2	20.7± 1.1	20.7± 1.2	21.7± 1.4	21.7± 1.3
25 ppm	19.4± 0.6	19.2± 0.6	20.3± 0.9	20.6± 0.8	21.1± 1.0	21.8± 1.0	22.2± 0.8
50 ppm	19.3± 0.6	18.9± 0.6	19.7± 0.5	20.3± 0.8	20.7± 0.6	21.1± 1.0	21.9± 1.3
100 ppm	19.3± 0.6	18.8± 0.9	19.6± 0.5	19.9± 0.7	20.6± 0.8	21.3± 0.9	21.8± 0.7
150 ppm	19.3± 0.6	16.8± 1.5*	17.6± 2.5**	18.8± 2.2*	19.4± 2.4	20.3± 2.0	20.3± 2.0
200 ppm	19.3± 0.6	15.3± 0.9**	14.6± 1.7**	17.0± 2.0**	19.0± 1.2	18.9± 1.1**	19.3± 1.0**

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

STUDY NO. : 0266
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	22.3± 1.5	22.8± 1.8	22.4± 1.4	22.6± 1.3	23.6± 1.4	23.7± 1.4	23.8± 1.6
25 ppm	21.9± 1.0	22.3± 0.7	22.7± 1.1	22.6± 1.1	23.6± 1.3	23.4± 1.1	24.2± 1.0
50 ppm	21.8± 1.0	21.8± 0.7	22.2± 1.3	22.3± 0.9	23.2± 0.8	23.2± 1.1	23.1± 1.1
100 ppm	21.4± 1.2	21.5± 0.7	21.8± 0.7	21.8± 0.7	22.7± 0.8	22.7± 0.9	22.5± 1.3
150 ppm	20.4± 1.3**	21.0± 1.2*	21.2± 1.1	21.3± 1.1*	22.3± 0.8*	22.3± 0.9*	22.1± 0.8*
200 ppm	19.6± 0.9**	20.4± 1.3**	20.0± 1.0**	20.0± 0.7**	21.1± 1.4**	20.9± 1.5**	20.7± 1.7**

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

APPENDIX B 3-1

WATER CONSUMPTION CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

RAT : MALE

STUDY NO. : 0265
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 1	2	3	4	5	6	7
Control	17.5± 0.9	18.6± 1.4	21.8± 2.9	20.9± 1.5	18.6± 1.2	20.5± 1.4	18.5± 1.5
25 ppm	14.0± 1.3	15.9± 3.2	14.4± 1.3	14.8± 1.2	13.6± 0.9**	14.9± 0.9	13.4± 1.1
50 ppm	12.7± 0.8**	13.5± 1.1*	13.3± 1.0	14.8± 3.1	12.3± 1.1**	12.9± 1.2*	11.5± 1.1*
100 ppm	12.4± 1.0**	13.0± 1.1**	11.9± 1.0**	12.1± 0.7**	10.7± 1.0**	10.8± 1.3**	9.6± 0.9**
150 ppm	12.3± 2.1**	11.7± 1.1**	11.0± 1.0**	10.6± 1.6**	8.8± 1.6**	8.7± 1.9**	7.7± 0.8**
200 ppm	7.9± 2.7**	8.4± 2.6**	9.1± 1.5**	8.8± 1.3**	7.2± 1.8**	6.3± 2.6**	5.5± 2.3**

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

STUDY NO. : 0265
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 8	9	10	11	12	13
Control	19.6± 1.2	19.6± 1.4	18.1± 1.6	18.4± 1.3	18.8± 1.2	18.2± 1.2
25 ppm	14.7± 0.8**	14.6± 1.3	13.4± 0.6	14.0± 1.0	14.2± 1.1**	14.7± 0.8**
50 ppm	13.1± 1.2**	13.1± 1.1	12.0± 1.4*	12.9± 1.2*	13.6± 1.2**	13.2± 1.0**
100 ppm	10.2± 0.9**	10.5± 1.1**	10.1± 1.1**	12.0± 3.6**	10.8± 1.1**	10.9± 1.2**
150 ppm	8.8± 1.6**	8.8± 1.3**	8.4± 1.2**	8.4± 1.5**	8.8± 1.7**	9.1± 1.8**
200 ppm	5.8± 2.1**	5.9± 2.9**	6.0± 2.0**	6.0± 2.0**	5.9± 2.0**	7.0± 1.6**

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

APPENDIX B 3-2

WATER CONSUMPTION CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

RAT : FEMALE

STUDY NO. : 0265
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 1	2	3	4	5	6	7
Control	15.3± 1.5	15.7± 1.6	15.1± 2.1	15.3± 3.2	14.6± 2.3	15.5± 3.3	15.4± 4.7
25 ppm	11.6± 0.6	11.1± 0.6	10.5± 0.7	9.9± 0.7	9.5± 0.8	9.7± 0.9	9.0± 1.0
50 ppm	10.3± 0.7*	10.4± 0.5**	9.5± 0.7*	9.2± 0.9	8.6± 0.7*	8.6± 0.8*	8.7± 2.0
100 ppm	8.6± 0.7**	9.7± 1.1**	9.0± 0.6**	8.2± 0.6**	7.6± 0.6**	7.5± 0.7**	7.0± 0.9**
150 ppm	8.8± 1.9**	11.0± 3.8**	8.2± 0.9**	7.6± 0.8**	7.3± 1.5**	6.7± 0.9**	6.8± 1.3**
200 ppm	4.6± 1.3**	7.7± 1.5**	7.2± 0.6**	6.4± 0.9**	5.3± 0.7**	5.1± 1.0**	4.1± 0.6**

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

STUDY NO. : 0265
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 8	9	10	11	12	13
Control	15.8± 5.6	16.3± 6.1	13.4± 2.7	17.2± 11.8	16.9± 9.5	18.1± 8.0
25 ppm	9.7± 1.2	9.1± 0.8	8.4± 1.0	9.5± 0.7	9.4± 1.1	10.4± 0.9
50 ppm	9.9± 3.6	8.4± 0.7	7.8± 0.9	10.1± 3.9	12.3± 8.1	9.4± 0.9
100 ppm	6.7± 0.9**	6.8± 0.8**	6.6± 0.8**	6.7± 0.9**	6.7± 0.8**	7.9± 0.8**
150 ppm	6.8± 1.2**	6.2± 0.9**	5.8± 0.7**	5.9± 0.8**	6.1± 0.9**	6.9± 0.9**
200 ppm	4.4± 0.7**	4.5± 1.1**	4.0± 1.1**	4.2± 1.1**	4.4± 1.1**	4.8± 1.2**

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

APPENDIX B 3-3

WATER CONSUMPTION CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : MALE

STUDY NO. : 0266
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 1	2	3	4	5	6	7
Control	4.5± 0.7	4.5± 0.9	4.3± 0.7	4.1± 0.6	4.1± 0.5	4.1± 0.4	4.2± 0.7
25 ppm	2.7± 0.5	2.4± 0.3	2.2± 0.2	2.3± 0.2	2.3± 0.2	2.2± 0.3**	2.1± 0.3
50 ppm	2.2± 0.2*	1.8± 0.1*	2.0± 0.2*	1.9± 0.3**	1.9± 0.3*	1.8± 0.4**	1.8± 0.2*
100 ppm	2.0± 0.2**	1.6± 0.2**	1.8± 0.2**	1.8± 0.3**	1.7± 0.3**	1.7± 0.3**	1.7± 0.2**
150 ppm	1.5± 0.2**	1.4± 0.1**	1.6± 0.2**	1.5± 0.2**	1.4± 0.2**	1.4± 0.3**	1.5± 0.2**
200 ppm	1.2± 0.3**	1.2± 0.4**	1.3± 0.3**	1.2± 0.2**	1.3± 0.4**	1.2± 0.4**	1.2± 0.1**

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

STUDY NO. : 0266
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 8	9	10	11	12	13
Control	4.3± 0.5	4.0± 0.5	3.9± 0.4	3.9± 0.4	3.8± 0.4	3.7± 0.3
25 ppm	2.2± 0.3	1.8± 0.2	1.9± 0.2	2.1± 0.2	2.1± 0.1	2.3± 0.4**
50 ppm	1.9± 0.2*	1.6± 0.2	1.7± 0.3*	2.0± 0.2*	1.9± 0.2*	2.0± 0.3**
100 ppm	1.7± 0.2**	1.4± 0.2**	1.5± 0.2**	1.7± 0.2**	1.6± 0.1**	1.6± 0.2**
150 ppm	1.4± 0.3**	1.1± 0.2**	1.4± 0.2**	1.6± 0.2**	1.5± 0.3**	1.4± 0.2**
200 ppm	1.2± 0.2**	1.0± 0.3**	1.1± 0.2**	1.3± 0.2**	1.1± 0.2**	1.3± 0.2**

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

APPENDIX B 3-4

WATER CONSUMPTION CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : FEMALE

STUDY NO. : 0266
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 1	2	3	4	5	6	7
Control	4.3± 0.4	4.4± 0.5	4.4± 0.3	4.3± 0.5	4.2± 0.4	4.3± 0.3	4.5± 0.5
25 ppm	2.8± 0.5	2.9± 0.7	2.8± 0.3**	2.7± 0.3**	2.7± 0.6	2.8± 0.5	2.5± 0.2
50 ppm	2.2± 0.1	2.1± 0.2*	2.3± 0.2**	2.3± 0.2**	2.1± 0.2*	2.3± 0.2*	2.1± 0.2*
100 ppm	1.9± 0.2**	1.7± 0.2**	1.8± 0.2**	2.0± 0.3**	1.8± 0.2**	1.8± 0.3**	2.0± 0.6**
150 ppm	1.3± 0.3**	1.2± 0.3**	1.5± 0.2**	1.5± 0.3**	1.6± 0.4**	1.6± 0.4**	1.5± 0.2**
200 ppm	0.9± 0.1**	0.9± 0.2**	1.4± 0.3**	1.3± 0.2**	1.1± 0.1**	1.2± 0.1**	1.4± 0.2**

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

STUDY NO. : 0266
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 8	9	10	11	12	13
Control	4.5± 0.3	4.4± 0.6	4.6± 0.4	4.7± 0.4	4.7± 0.5	4.5± 0.4
25 ppm	2.6± 0.5**	2.7± 1.0	2.9± 0.9	2.8± 0.9	2.9± 0.3**	2.9± 0.3**
50 ppm	2.2± 0.3**	2.1± 0.3*	2.1± 0.2*	2.5± 0.2	2.5± 0.2**	2.5± 0.3**
100 ppm	1.9± 0.4**	1.7± 0.2**	1.7± 0.2**	2.2± 0.6**	2.2± 0.2**	2.0± 0.3**
150 ppm	1.4± 0.5**	1.5± 0.4**	1.4± 0.3**	1.7± 0.2**	1.7± 0.4**	1.7± 0.3**
200 ppm	1.3± 0.3**	1.2± 0.2**	1.2± 0.1**	1.5± 0.3**	1.5± 0.4**	1.4± 0.2**

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

APPENDIX B 4-1

FOOD CONSUMPTION CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

RAT : MALE

STUDY NO. : 0265
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 1	2	3	4	5	6	7
Control	13.4± 0.8	14.7± 1.1	15.6± 1.3	15.5± 1.0	15.3± 1.0	15.9± 0.9	15.4± 1.0
25 ppm	12.7± 0.7	14.0± 1.1	14.4± 1.3	14.1± 1.0**	14.2± 0.7	14.6± 0.7	14.3± 0.7
50 ppm	12.2± 0.6**	13.3± 0.9	14.0± 1.0*	13.5± 0.9**	13.6± 0.8**	14.0± 1.1	13.3± 1.2
100 ppm	11.2± 0.7**	12.5± 1.1**	13.1± 0.9**	12.5± 0.8**	12.6± 0.7**	12.7± 0.7**	12.0± 0.9**
150 ppm	10.7± 0.7**	12.0± 0.9**	12.2± 0.7**	11.4± 0.7**	11.0± 0.9**	11.0± 0.7**	10.7± 0.6**
200 ppm	8.8± 1.2**	10.2± 2.1**	11.1± 1.3**	10.2± 1.2**	9.1± 1.6**	8.5± 2.6**	7.9± 2.2**

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

STUDY NO. : 0265
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 8	9	10	11	12	13
Control	15.7± 1.0	15.3± 0.9	14.7± 1.1	15.1± 0.9	14.5± 0.7	14.8± 0.7
25 ppm	14.5± 1.0	14.1± 0.8	13.7± 0.7	13.8± 0.8	13.7± 0.5	14.1± 0.5
50 ppm	13.6± 1.2	13.3± 1.2	12.9± 1.2*	13.6± 1.2*	13.6± 0.9	13.8± 0.9
100 ppm	11.9± 0.8**	11.6± 1.3**	11.5± 1.2**	12.0± 1.3**	12.1± 1.2**	12.2± 1.2**
150 ppm	10.3± 0.7**	10.3± 1.0**	10.2± 1.1**	10.4± 1.0**	10.6± 1.2**	11.0± 1.3**
200 ppm	7.9± 2.3**	7.1± 2.1**	7.5± 2.1**	7.7± 1.8**	7.9± 1.8**	8.3± 2.0**

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

APPENDIX B 4-2

FOOD CONSUMPTION CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

RAT : FEMALE

STUDY NO. : 0265
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 1	2	3	4	5	6	7
Control	10.8± 0.7	11.3± 0.9	11.0± 1.1	10.2± 1.0	10.4± 1.0	10.2± 1.2	9.8± 1.2
25 ppm	10.5± 0.7	10.5± 0.8	10.2± 0.7	9.3± 0.8	9.6± 0.9	9.3± 1.0	8.7± 1.1*
50 ppm	9.8± 0.5**	10.5± 0.6	10.3± 0.7	9.6± 1.0	9.3± 0.8*	9.2± 1.0	8.9± 0.8
100 ppm	8.3± 0.6**	9.5± 0.4**	9.5± 0.5**	8.8± 0.3	8.3± 0.6**	8.1± 0.6**	7.9± 0.7**
150 ppm	6.8± 0.8**	9.0± 0.9**	8.8± 0.7**	8.2± 0.7**	8.1± 0.6**	7.7± 0.6**	7.3± 0.7**
200 ppm	5.5± 0.6**	7.0± 1.3**	8.1± 0.7**	7.5± 0.5**	7.1± 0.6**	6.6± 0.6**	5.8± 1.0**

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

STUDY NO. : 0265
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 8	9	10	11	12	13
Control	9.6± 1.4	9.7± 1.1	9.1± 0.9	9.6± 1.4	9.5± 1.3	9.8± 1.1
25 ppm	8.8± 0.8	8.7± 0.6*	8.0± 0.8*	8.8± 0.8	8.9± 1.1	9.5± 1.0
50 ppm	9.0± 0.9	8.7± 0.8*	8.5± 0.7	8.9± 0.9	9.0± 1.0	9.4± 0.8
100 ppm	7.9± 0.6**	7.4± 0.5**	7.4± 0.7**	7.5± 0.6**	7.5± 0.8**	8.1± 0.8**
150 ppm	7.2± 0.6**	7.1± 0.7**	6.9± 0.6**	7.1± 0.6**	7.2± 0.6**	7.5± 0.8**
200 ppm	5.8± 1.0**	5.9± 0.9**	5.5± 1.2**	5.3± 1.2**	5.7± 1.3**	5.7± 1.2**

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

APPENDIX B 4-3

FOOD CONSUMPTION CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : MALE

STUDY NO. : 0266
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 1	2	3	4	5	6	7
Control	3.9± 0.1	3.9± 0.4	3.8± 0.3	4.0± 0.2	4.0± 0.2	3.8± 0.2	3.9± 0.2
25 ppm	3.8± 0.3	3.8± 0.3	3.7± 0.2	3.7± 0.2	3.5± 0.3**	3.4± 0.3*	3.4± 0.3**
50 ppm	3.6± 0.2	3.7± 0.2	3.7± 0.2	3.6± 0.3*	3.5± 0.4*	3.5± 0.3	3.4± 0.2**
100 ppm	3.5± 0.4	3.6± 0.2	3.7± 0.2	3.5± 0.2**	3.6± 0.2*	3.4± 0.2*	3.4± 0.2**
150 ppm	3.1± 0.2**	3.5± 0.2*	3.5± 0.2*	3.5± 0.2**	3.4± 0.2**	3.3± 0.2**	3.4± 0.2**
200 ppm	3.0± 0.4**	3.2± 0.6**	3.4± 0.4**	3.4± 0.6**	3.3± 0.5**	3.1± 0.5**	3.1± 0.5**

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

STUDY NO. : 0266
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 8	9	10	11	12	13
Control	4.1± 0.3	4.1± 0.2	3.9± 0.2	4.0± 0.2	4.0± 0.2	4.0± 0.1
25 ppm	3.5± 0.2*	3.5± 0.2*	3.3± 0.2**	3.6± 0.3*	3.5± 0.1*	3.6± 0.2**
50 ppm	3.4± 0.2*	3.5± 0.3**	3.4± 0.3*	3.6± 0.1**	3.6± 0.3*	3.5± 0.2**
100 ppm	3.4± 0.2**	3.5± 0.2**	3.3± 0.2**	3.5± 0.2**	3.4± 0.1**	3.4± 0.2**
150 ppm	3.4± 0.2**	3.4± 0.2**	3.3± 0.2**	3.7± 0.2*	3.5± 0.2**	3.3± 0.2**
200 ppm	3.1± 0.6**	3.2± 0.6**	3.0± 0.7**	3.3± 0.7**	3.3± 0.1**	3.3± 0.1**

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

APPENDIX B 4-4

FOOD CONSUMPTION CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : FEMALE

STUDY NO. : 0266
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 1	2	3	4	5	6	7
Control	3.3± 0.3	3.6± 0.2	3.5± 0.2	3.4± 0.3	3.6± 0.3	3.5± 0.3	3.7± 0.5
25 ppm	3.3± 0.3	3.5± 0.3	3.5± 0.2	3.4± 0.3	3.6± 0.3	3.5± 0.3	3.4± 0.2
50 ppm	3.2± 0.2	3.2± 0.3**	3.3± 0.2	3.3± 0.2	3.5± 0.3	3.4± 0.2	3.3± 0.2
100 ppm	3.0± 0.2*	3.3± 0.2*	3.2± 0.3*	3.2± 0.3	3.2± 0.2**	3.2± 0.3	3.2± 0.3*
150 ppm	2.7± 0.2**	3.1± 0.3**	3.2± 0.3*	3.2± 0.4	3.2± 0.3**	3.2± 0.3	3.2± 0.3*
200 ppm	2.3± 0.3**	2.5± 0.3**	3.1± 0.3**	3.2± 0.3	2.8± 0.2**	2.9± 0.2**	2.9± 0.3**

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

STUDY NO. : 0266
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 8	9	10	11	12	13
Control	3.8± 0.4	3.9± 0.8	3.7± 0.6	3.9± 0.6	3.8± 0.5	3.7± 0.7
25 ppm	3.4± 0.2	3.5± 0.2	3.5± 0.3	3.6± 0.3	3.5± 0.3	3.6± 0.4
50 ppm	3.3± 0.2**	3.4± 0.2	3.4± 0.2	3.5± 0.2	3.4± 0.2*	3.4± 0.2
100 ppm	3.2± 0.2**	3.3± 0.2*	3.2± 0.2	3.4± 0.2**	3.3± 0.3**	3.4± 0.3
150 ppm	3.3± 0.3**	3.3± 0.2*	3.2± 0.3	3.3± 0.3**	3.3± 0.3**	3.4± 0.2
200 ppm	3.0± 0.3**	3.0± 0.2**	3.0± 0.4**	3.1± 0.4**	3.0± 0.3**	3.1± 0.3**

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

APPENDIX B 5-1

CHEMICAL INTAKE CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

RAT : MALE

STUDY NO. : 0265
ANIMAL : RAT F344
UNIT : mg/kg/day
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
25 ppm	2.397± 0.118	2.316± 0.425	1.846± 0.092	1.728± 0.071	1.485± 0.055	1.549± 0.077	1.348± 0.056
50 ppm	4.467± 0.187	4.084± 0.200	3.613± 0.138	3.689± 0.845	2.859± 0.228	2.845± 0.155	2.476± 0.160
100 ppm	9.114± 0.859	8.242± 0.447	6.776± 0.485	6.328± 0.274	5.326± 0.328	5.225± 0.565	4.578± 0.370
150 ppm	14.014± 2.527	11.842± 0.825	10.079± 0.752	9.318± 1.503	7.451± 1.012	7.297± 1.309	6.455± 0.508
200 ppm	13.762± 4.175	13.333± 2.309	13.203± 1.719	12.070± 1.151	9.922± 2.193	8.272± 2.362	7.557± 2.039

STUDY NO. : 0265
ANIMAL : RAT F344
UNIT : mg/kg/day
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
25 ppm	1.405± 0.077	1.348± 0.084	1.211± 0.040	1.238± 0.071	1.235± 0.079	1.254± 0.040
50 ppm	2.667± 0.126	2.587± 0.181	2.310± 0.191	2.425± 0.143	2.494± 0.190	2.372± 0.153
100 ppm	4.705± 0.375	4.751± 0.385	4.449± 0.341	5.182± 1.465	4.573± 0.330	4.596± 0.330
150 ppm	7.067± 0.971	7.033± 0.609	6.600± 0.587	6.553± 0.854	6.667± 0.784	6.882± 0.829
200 ppm	8.246± 1.188	8.698± 3.627	8.675± 2.211	8.734± 1.961	8.485± 2.207	10.009± 1.270

APPENDIX B 5-2

CHEMICAL INTAKE CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

RAT : FEMALE

STUDY NO. : 0265
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
25 ppm	2.581± 0.144	2.238± 0.090	1.987± 0.140	1.803± 0.122	1.635± 0.105	1.636± 0.147	1.507± 0.118
50 ppm	4.710± 0.330	4.326± 0.240	3.677± 0.206	3.348± 0.154	2.994± 0.162	2.950± 0.241	2.976± 0.675
100 ppm	8.517± 0.755	8.903± 1.314	7.672± 0.460	6.740± 0.359	5.977± 0.465	5.846± 0.437	5.433± 0.392
150 ppm	14.451± 2.895	16.025± 4.711	11.140± 0.946	9.887± 0.850	9.110± 1.806	8.388± 0.894	8.570± 1.422
200 ppm	11.197± 2.364	17.695± 3.004	14.646± 1.766	12.267± 1.234	10.041± 0.877	9.723± 1.133	8.373± 1.075

STUDY NO. : 0265
ANIMAL : RAT F344
UNIT : mg/kg/day
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
25 ppm	1.567± 0.178	1.448± 0.084	1.324± 0.113	1.457± 0.102	1.424± 0.118	1.533± 0.113
50 ppm	3.287± 1.213	2.771± 0.246	2.510± 0.262	3.155± 1.060	3.725± 2.233	2.837± 0.274
100 ppm	5.040± 0.437	5.089± 0.512	4.846± 0.425	4.847± 0.510	4.834± 0.334	5.588± 0.354
150 ppm	8.403± 1.079	7.670± 0.886	7.134± 0.556	7.299± 0.850	7.353± 1.005	8.217± 0.861
200 ppm	9.083± 1.317	9.211± 1.802	8.412± 1.492	9.011± 1.228	9.522± 1.067	10.704± 2.258

APPENDIX B 5-3

CHEMICAL INTAKE CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : MALE

STUDY NO. : 0266
ANIMAL : MOUSE BDF1
UNIT : mg/kg/day
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
25 ppm	2.723± 0.471	2.315± 0.274	2.143± 0.132	2.108± 0.177	2.079± 0.181	1.961± 0.269	1.934± 0.230
50 ppm	4.787± 0.483	3.650± 0.232	3.907± 0.388	3.706± 0.521	3.675± 0.600	3.454± 0.734	3.408± 0.370
100 ppm	8.803± 0.742	6.866± 1.138	7.097± 0.655	7.141± 1.102	6.445± 0.994	6.490± 0.787	6.510± 0.548
150 ppm	10.470± 0.958	9.115± 0.724	9.943± 0.965	9.435± 1.234	8.691± 1.000	8.477± 1.670	8.966± 1.133
200 ppm	11.783± 1.969	11.894± 2.894	12.482± 2.728	11.911± 2.742	12.652± 3.776	11.764± 3.297	11.894± 3.983

STUDY NO. : 0266
ANIMAL : MOUSE BDF1
UNIT : mg/kg/day
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
25 ppm	1.931± 0.217	1.572± 0.140	1.611± 0.147	1.739± 0.139	1.750± 0.090	1.853± 0.324
50 ppm	3.537± 0.391	2.999± 0.328	3.040± 0.472	3.412± 0.436	3.321± 0.337	3.477± 0.542
100 ppm	6.276± 0.426	5.276± 0.806	5.518± 0.674	6.186± 0.529	5.836± 0.387	5.714± 0.529
150 ppm	8.540± 1.433	6.788± 0.849	8.131± 1.374	9.291± 1.001	8.753± 1.587	8.386± 1.026
200 ppm	12.035± 4.347	10.063± 4.942	10.829± 4.210	12.217± 3.952	9.509± 1.585	10.825± 2.374

APPENDIX B 5-4

CHEMICAL INTAKE CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

MOUSE: FEMALE

STUDY NO. : 0266
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
25 ppm	3.613± 0.729	3.611± 0.826	3.359± 0.436	3.187± 0.299	3.099± 0.680	3.090± 0.579	2.905± 0.281
50 ppm	5.824± 0.324	5.266± 0.510	5.562± 0.452	5.494± 0.404	5.010± 0.549	5.215± 0.540	4.913± 0.418
100 ppm	9.964± 0.740	8.607± 0.748	9.273± 0.770	9.555± 1.263	8.612± 0.503	8.394± 1.070	9.076± 2.409
150 ppm	11.457± 1.816	10.485± 1.461	12.057± 2.359	11.373± 1.345	11.625± 2.499	11.616± 2.392	10.997± 1.130
200 ppm	11.708± 1.417	11.551± 1.647	15.839± 2.680	14.005± 2.510	11.604± 0.959	12.201± 1.206	14.187± 1.716

STUDY NO. : 0266
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
25 ppm	2.906± 0.586	2.909± 0.957	3.156± 0.949	2.979± 1.010	3.088± 0.370	2.973± 0.327
50 ppm	5.053± 0.634	4.636± 0.576	4.674± 0.344	5.412± 0.394	5.332± 0.422	5.300± 0.732
100 ppm	8.740± 1.818	7.642± 0.728	7.850± 0.961	9.486± 2.521	9.547± 0.835	8.762± 1.153
150 ppm	10.098± 2.821	10.784± 2.609	9.906± 2.009	11.105± 1.441	11.256± 2.232	11.623± 1.620
200 ppm	12.682± 2.305	11.540± 1.483	11.811± 1.237	13.889± 1.872	14.361± 2.724	13.180± 1.602

APPENDIX B 6-1

HEMATOLOGY (THIRTEEN−WEEK STUDY: SUMMARY)

RAT : MALE

STUDY NO. : 0265
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	10	9.25± 0.39	16.3± 0.4	46.2± 1.9	50.0± 0.7	17.7± 0.9	35.4± 1.7	734± 38
25 ppm	10	9.19± 0.14	16.1± 0.2	46.0± 0.9	50.1± 0.4	17.5± 0.3	34.8± 0.6	756± 42
50 ppm	9	9.17± 0.24	15.9± 0.5	45.9± 1.4	50.1± 0.6	17.3± 0.3	34.6± 0.6	722± 26
100 ppm	10	8.83± 0.30	15.2± 0.5**	44.5± 1.7	50.4± 0.7	17.2± 0.2	34.3± 0.5	722± 44
150 ppm	10	8.69± 0.29**	14.7± 0.4**	43.4± 1.4**	49.9± 0.7	16.9± 0.3**	33.9± 0.5**	738± 43
200 ppm	9	8.14± 0.59**	14.0± 0.6**	40.9± 3.0**	50.2± 1.6	17.2± 1.1	34.2± 2.1**	683± 95

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

STUDY NO. : 02G5
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	10	30±	5	16.6±	2.2	22.1±	2.0
25 ppm	10	31±	8	16.0±	2.4	21.4±	2.4
50 ppm	9	30±	5	13.9±	1.5	20.6±	2.5
100 ppm	10	37±	7	12.5±	0.7**	17.7±	3.0**
150 ppm	10	44±	8**	12.0±	0.4**	17.1±	1.9**
200 ppm	9	59±	22**	11.7±	0.3**	15.6±	1.6**

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

STUDY NO. : 0265
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	10	5.45± 1.34	0± 0	30± 5	1± 1	0± 0	5± 2	64± 6	0± 0
25 ppm	10	5.24± 0.95	0± 0	28± 6	2± 1	0± 0	4± 3	66± 7	0± 0
50 ppm	9	5.01± 1.58	0± 0	26± 4	1± 1	0± 0	5± 2	67± 5	0± 1
100 ppm	10	5.11± 1.32	0± 1	28± 5	2± 1	0± 0	4± 2	66± 5	0± 0
150 ppm	10	4.12± 1.28	0± 0	28± 7	1± 1	0± 0	5± 3	66± 8	0± 0
200 ppm	9	3.16± 1.28**	0± 1	30± 8	1± 1	0± 0	4± 1	64± 9	0± 1

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

APPENDIX B 6-2

HEMATOLOGY (THIRTEEN−WEEK STUDY: SUMMARY)

RAT: FEMALE

STUDY NO. : 0265
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	8	8.71±	0.28	16.2±	0.5	46.0±	1.7	52.8±	0.6	18.6±	0.2	35.2±	0.5	864±	42
25 ppm	10	8.52±	0.27	15.8±	0.5	45.0±	1.8	52.8±	0.8	18.6±	0.2	35.1±	0.6	811±	34
50 ppm	10	8.39±	0.41	15.6±	0.4*	43.8±	2.6	52.1±	0.8	18.6±	0.8	35.6±	1.9	776±	42*
100 ppm	10	8.32±	0.34*	15.0±	0.5**	42.8±	2.0**	51.5±	0.6**	18.0±	0.6	35.0±	1.0	791±	41
150 ppm	10	8.38±	0.31	14.6±	0.3**	42.0±	1.7**	50.1±	0.9**	17.4±	0.5**	34.7±	1.4	722±	60**
200 ppm	10	8.14±	0.18**	13.9±	0.6**	40.9±	1.3**	50.2±	0.8**	17.1±	0.5**	34.0±	1.1**	642±	97**

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

STUDY NO. : 0265
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	8	31± 6	11.6± 0.3	15.5± 1.1
25 ppm	10	32± 8	11.8± 0.4	16.4± 0.7
50 ppm	10	39± 7	11.8± 0.4	15.4± 1.7
100 ppm	10	45± 10**	11.8± 0.4	14.9± 1.3
150 ppm	10	44± 8*	11.6± 0.4	14.9± 1.5
200 ppm	10	58± 13**	11.7± 0.5	15.0± 1.1

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

STUDY NO. : 0265
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	8	3.02± 0.76	0± 1	23± 6	2± 1	0± 0	5± 2	69± 6	1± 1
25 ppm	10	3.71± 0.86	0± 1	26± 7	1± 1	0± 0	4± 1	68± 8	0± 1
50 ppm	10	4.14± 1.15	0± 0	26± 7	2± 1	0± 0	4± 2	69± 8	0± 0
100 ppm	10	4.09± 1.57	0± 1	23± 5	2± 1	0± 0	5± 2	70± 5	0± 1
150 ppm	10	3.49± 0.91	0± 1	24± 5	2± 1	0± 0	4± 3	70± 6	0± 0
200 ppm	10	2.50± 1.41	0± 0	34± 16	1± 1	0± 0	5± 2	59± 16	1± 1

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

APPENDIX B 6-3

HEMATOLOGY (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : MALE

STUDY NO. : 0266
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 fℓ	MCH pg	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	10	10.54± 0.30	15.5± 0.2	48.0± 2.2	45.5± 1.2	14.7± 0.2	32.4± 1.1	1429± 118
25 ppm	7	10.37± 0.26	15.2± 0.5	46.7± 1.4	45.1± 0.4	14.6± 0.2	32.4± 0.5	1421± 151
50 ppm	8	10.54± 0.32	15.2± 0.7	47.4± 2.3	44.9± 1.0	14.4± 0.3	32.1± 0.4	1427± 85
100 ppm	9	10.28± 0.36	15.0± 0.6	46.4± 2.1	45.1± 0.8	14.6± 0.1	32.4± 0.4	1335± 159
150 ppm	7	10.35± 0.54	15.0± 0.8	46.9± 2.7	45.3± 0.6	14.5± 0.2	32.1± 0.6	1346± 109
200 ppm	9	9.41± 2.42	15.2± 1.3	42.4± 10.8	45.1± 0.9	19.3± 14.3	32.4± 1.9	1132± 292**

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

STUDY NO. : 0266
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	0.80± 0.64	1± 1	20± 9	0± 1	0± 0	2± 1	77± 9	0± 0
25 ppm	9	0.70± 0.72	0± 1	17± 5	1± 2	0± 0	2± 1	79± 7	0± 0
50 ppm	10	0.48± 0.35	0± 1	14± 6	0± 0	0± 0	3± 2	82± 5	0± 1
100 ppm	8	0.40± 0.33	0± 0	19± 4	0± 0	0± 0	3± 2	79± 4	0± 0
150 ppm	9	0.47± 0.40	0± 0	13± 4	0± 1	0± 0	2± 1	84± 4	0± 1
200 ppm	9	0.66± 0.53	0± 0	14± 7	1± 1	0± 0	2± 1	83± 7	0± 0

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

APPENDIX B 6-4

HEMATOLOGY (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : FEMALE

STUDY NO. : 0266
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	10.20± 0.39	15.2± 0.5	46.9± 1.6	45.9± 0.5	14.9± 0.1	32.5± 0.3	1292± 142
25 ppm	9	10.06± 0.40	15.1± 0.8	46.4± 1.9	46.1± 0.6	15.0± 0.2	32.5± 0.5	1219± 61
50 ppm	10	9.79± 0.41	14.6± 0.6	45.1± 2.1	46.0± 0.8	14.9± 0.3	32.4± 0.4	1125± 161
100 ppm	8	9.69± 0.43	14.5± 0.6	45.4± 1.9	46.8± 0.8	15.0± 0.2	31.9± 0.4	1183± 105
150 ppm	9	9.41± 0.50**	13.8± 0.7**	43.7± 2.3**	46.5± 1.1	14.7± 0.3	31.6± 0.4**	1007± 324*
200 ppm	9	9.91± 0.36	14.5± 0.6	45.4± 1.4	45.8± 1.0	14.6± 0.3*	31.9± 0.5*	1149± 99*

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

STUDY NO. : 0266
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	1.39± 0.87	0± 0	14± 10	1± 1	0± 0	2± 1	82± 9	0± 0
25 ppm	7	1.03± 0.72	0± 1	14± 3	1± 1	0± 0	2± 1	82± 4	0± 0
50 ppm	8	1.69± 1.81	0± 0	13± 3	1± 1	0± 0	3± 1	83± 4	0± 0
100 ppm	9	0.69± 0.34	0± 0	12± 5	1± 1	0± 0	2± 1	85± 5	0± 0
150 ppm	7	0.78± 0.68	0± 0	15± 6	1± 1	0± 0	2± 2	81± 7	0± 0
200 ppm	9	0.44± 0.32**	1± 1	21± 13	1± 1	0± 0	3± 2	75± 14	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. : 0265
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	10	6.4± 0.1	3.6± 0.1	1.3± 0.0	0.17± 0.01	190± 9	60± 13	80± 29
25 ppm	10	6.3± 0.2	3.6± 0.1	1.3± 0.0	0.17± 0.01	197± 14	60± 4	89± 17
50 ppm	9	6.3± 0.1	3.6± 0.1	1.4± 0.1	0.17± 0.01	191± 8	62± 5	89± 16
100 ppm	10	6.3± 0.2	3.7± 0.1	1.4± 0.0*	0.17± 0.01	187± 11	75± 6*	49± 13
150 ppm	10	6.3± 0.2	3.7± 0.2	1.5± 0.1**	0.18± 0.02	171± 15*	84± 12**	31± 5**
200 ppm	9	6.3± 0.2	3.9± 0.1**	1.6± 0.1**	0.19± 0.02*	145± 24**	108± 13**	36± 11**

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

STUDY NO. : 0265
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	10	111± 23	73± 6	42± 3	146± 68	262± 35	1± 0	102± 25
25 ppm	10	111± 7	70± 6	40± 4	120± 20	249± 11	1± 0	94± 10
50 ppm	9	112± 9	77± 5	44± 4	139± 16	260± 14	0± 1	100± 15
100 ppm	10	125± 9	106± 23*	60± 15*	142± 28	250± 20	1± 1	91± 11
150 ppm	10	131± 20*	142± 31**	77± 21**	170± 49	255± 21	1± 0	98± 17
200 ppm	9	172± 25**	188± 51**	100± 32**	185± 61	287± 34	2± 1	91± 10

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

STUDY NO. : 0265
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	10	18.0± 1.8	0.5± 0.0	143± 1	3.4± 0.3	109± 1	10.3± 0.1	5.3± 0.7
25 ppm	10	19.8± 1.0	0.6± 0.1	141± 1*	3.5± 0.3	108± 1	10.3± 0.1	5.5± 0.5
50 ppm	9	19.9± 1.1	0.5± 0.1	141± 1*	3.6± 0.3	108± 2	10.4± 0.2	5.7± 0.6
100 ppm	10	22.6± 2.0**	0.5± 0.0	141± 1*	3.7± 0.2*	107± 1*	10.4± 0.2	5.6± 0.5
150 ppm	10	25.0± 2.8**	0.5± 0.0	142± 1	3.8± 0.2**	109± 2	10.4± 0.2	5.8± 0.6
200 ppm	9	31.2± 5.6**	0.5± 0.0	143± 1	3.9± 0.2**	111± 2	10.5± 0.2*	5.5± 0.8

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

APPENDIX B 7-2

BIOCHEMISTRY(THIRTEEN−WEEK STUDY: SUMMARY)

RAT : FEMALE

STUDY NO. : 0265
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	8	6.3±	0.3	3.6±	0.1	1.3±	0.1	0.17±	0.01	159±	12	75±	8	34±	29
25 ppm	10	6.0±	0.1*	3.4±	0.1	1.3±	0.1	0.17±	0.01	166±	8	69±	6	29±	7
50 ppm	10	6.0±	0.1*	3.5±	0.1	1.4±	0.1	0.17±	0.01	166±	6	71±	10	31±	10
100 ppm	10	5.9±	0.1**	3.5±	0.1	1.5±	0.1**	0.18±	0.01	166±	13	85±	10	28±	3
150 ppm	10	6.1±	0.1	3.7±	0.1	1.5±	0.1**	0.18±	0.01	143±	16	93±	14	26±	5
200 ppm	10	5.9±	0.3*	3.6±	0.2	1.5±	0.1**	0.22±	0.03**	105±	28*	112±	23*	42±	17**

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

STUDY NO. : 0265
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	8	134± 14	71± 5	37± 5	142± 37	198± 48	1± 1	98± 11
25 ppm	10	125± 12	74± 7	38± 7	169± 72	194± 39	1± 1	104± 22
50 ppm	10	128± 14	80± 5	41± 5	173± 77	202± 24	2± 1	104± 22
100 ppm	10	149± 16	119± 21**	57± 11**	238± 72	236± 22	2± 1	116± 25
150 ppm	10	156± 18	137± 32**	58± 16**	229± 91	268± 36**	4± 1**	108± 19
200 ppm	10	196± 38**	162± 41**	70± 20**	320± 229*	285± 37**	6± 2**	129± 59

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

STUDY NO. : 0265
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	8	18.7± 1.4	0.6± 0.1	142± 2	3.5± 0.2	110± 2	10.2± 0.2	4.7± 1.2
25 ppm	10	20.3± 2.2	0.5± 0.0*	140± 1	3.6± 0.2	110± 1	9.9± 0.2*	4.6± 0.9
50 ppm	10	22.6± 2.2	0.5± 0.0**	140± 1*	3.7± 0.1*	108± 1	10.1± 0.2	5.3± 0.8
100 ppm	10	27.3± 2.6**	0.5± 0.1*	141± 1	3.8± 0.2**	110± 2	10.2± 0.1	5.5± 0.7
150 ppm	10	30.3± 3.8**	0.5± 0.0*	142± 2	3.8± 0.2**	110± 2	10.3± 0.2	5.4± 0.6
200 ppm	10	41.1± 6.6**	0.5± 0.1	146± 4	3.9± 0.3**	114± 4	10.2± 0.3	5.4± 0.9

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

APPENDIX B 7-3

BIOCHEMISTRY (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : MALE

STUDY NO. : 0266
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	5.3± 0.2	3.1± 0.1	1.3± 0.1	0.24± 0.13	221± 40	90± 11	40± 12
25 ppm	7	5.2± 0.2	2.9± 0.1	1.3± 0.0	0.21± 0.03	211± 44	81± 5	33± 4
50 ppm	8	5.0± 0.2*	2.9± 0.2	1.4± 0.1	0.23± 0.05	203± 51	77± 7**	31± 7
100 ppm	8	4.9± 0.2**	2.8± 0.2*	1.4± 0.1	0.22± 0.02	188± 47	74± 6**	28± 5*
150 ppm	8	4.9± 0.2**	2.8± 0.1**	1.4± 0.1	0.25± 0.06	193± 22	75± 10**	27± 9*
200 ppm	8	4.7± 0.2**	2.8± 0.1**	1.5± 0.2*	0.25± 0.07	155± 15**	73± 5**	28± 4

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

STUDY NO. : 0266
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	47±	4	17±	3	240±	128	160±	8	94±	143	26.5±	5.3	156±	3
25 ppm	7	47±	6	17±	2	191±	35	164±	21	44±	18	28.0±	4.2	157±	3
50 ppm	8	49±	10	19±	3	241±	76	161±	16	73±	44	26.2±	5.0	155±	3
100 ppm	8	53±	10	19±	3	206±	33	162±	12	53±	18	24.7±	2.4	156±	3
150 ppm	8	60±	7*	22±	6*	257±	68	162±	19	80±	40	26.8±	4.2	156±	3
200 ppm	8	76±	14**	24±	4**	308±	152	200±	60	113±	135	30.5±	3.5	158±	3

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

STUDY NO. : 0266
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	4.5±	0.4	127±	4	9.1±	0.2	7.6±	0.7
25 ppm	7	4.3±	0.7	126±	2	8.8±	0.2	6.7±	1.2
50 ppm	8	4.2±	0.4	124±	4	8.9±	0.4	6.5±	1.4
100 ppm	8	4.3±	0.4	126±	3	8.8±	0.2	6.5±	0.7
150 ppm	8	4.0±	0.3	126±	4	8.6±	0.1**	6.6±	1.0
200 ppm	8	4.3±	0.7	126±	4	8.7±	0.2**	7.7±	1.5

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

APPENDIX B 7-4

BIOCHEMISTRY (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : FEMALE

STUDY NO. : 0266
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	5.3± 0.4	3.3± 0.2	1.7± 0.1	0.24± 0.13	151± 17	76± 8	25± 6
25 ppm	9	5.2± 0.3	3.2± 0.2	1.6± 0.1	0.22± 0.04	168± 22	76± 9	27± 4
50 ppm	10	5.0± 0.3	3.1± 0.2	1.6± 0.1	0.22± 0.06	167± 32	67± 8	23± 4
100 ppm	8	5.0± 0.3	3.1± 0.2	1.7± 0.1	0.32± 0.21	163± 12	69± 5	24± 4
150 ppm	10	4.7± 0.4**	3.0± 0.2**	1.7± 0.2	0.31± 0.14	155± 25	73± 8	30± 8
200 ppm	9	4.8± 0.2*	3.0± 0.1*	1.7± 0.1	0.20± 0.02	128± 25	70± 8	27± 6

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

STUDY NO. : 0266
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	62±	12	20±	5	256±	94	256±	32	73±	21	20.8±	3.4	156±	3
25 ppm	9	61±	11	22±	3	270±	85	262±	24	91±	65	21.2±	2.5	156±	3
50 ppm	10	66±	17	22±	3	295±	93	259±	34	118±	81	23.5±	2.9	158±	4
100 ppm	8	67±	17	21±	5	369±	226	248±	38	101±	68	25.7±	3.9	156±	2
150 ppm	10	63±	13	19±	4	397±	148	231±	46	119±	112	26.5±	4.8*	156±	3
200 ppm	9	76±	29	25±	5	330±	127	242±	29	123±	76	29.8±	6.4**	158±	4

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

STUDY NO. : 0266
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	4.7±	0.5	127±	4	9.0±	0.5	6.5±	1.2
25 ppm	9	4.6±	0.5	126±	3	9.1±	0.4	6.7±	1.6
50 ppm	10	4.3±	0.6	128±	4	8.9±	0.4	6.9±	1.1
100 ppm	8	4.3±	0.7	125±	4	8.7±	0.8	7.5±	1.6
150 ppm	10	4.4±	0.6	126±	3	8.8±	0.5	8.0±	1.2
200 ppm	9	4.2±	0.7	127±	5	9.2±	0.4	8.7±	2.2*

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

APPENDIX B 8-1

URINALYSIS (THIRTEEN−WEEK STUDY: SUMMARY)

RAT : MALE

STUDY NO. : 0265
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	0	9	1		0	0	6	4	0	0		10	0	0	0	0	0		0	2	8	0	0	0		10	0	0	0	
25 ppm	10	0	0	0	0	1	8	1		0	0	4	6	0	0		10	0	0	0	0	0		0	1	9	0	0	0		10	0	0	0	
50 ppm	10	0	0	0	0	0	6	4		0	0	2	8	0	0		10	0	0	0	0	0		0	1	9	0	0	0		10	0	0	0	
100 ppm	10	0	0	0	0	2	6	2		0	0	2	8	0	0		10	0	0	0	0	0		0	5	5	0	0	0		10	0	0	0	
150 ppm	10	0	0	0	3	3	3	1	*	0	0	1	9	0	0	*	10	0	0	0	0	0		0	4	6	0	0	0		10	0	0	0	
200 ppm	9	0	0	1	1	2	5	0		0	0	1	7	1	0		9	0	0	0	0	0		0	8	1	0	0	0	**	9	0	0	0	

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

STUDY NO. : 0265
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	
25 ppm	10	10	0	0	0	0		10	0	0	0	0	
50 ppm	10	10	0	0	0	0		10	0	0	0	0	
100 ppm	10	10	0	0	0	0		10	0	0	0	0	
150 ppm	10	10	0	0	0	0		10	0	0	0	0	
200 ppm	9	9	0	0	0	0		9	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. : 0265
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	2	8		0	0	7	3	0	0		10	0	0	0	0	0		9	1	0	0	0	0		10	0	0	0	
25 ppm	10	0	0	0	0	1	4	5		0	0	7	3	0	0		10	0	0	0	0	0		7	3	0	0	0	0		10	0	0	0	
50 ppm	10	0	0	0	1	1	6	2		0	0	2	8	0	0	*	10	0	0	0	0	0		5	5	0	0	0	0		10	0	0	0	
100 ppm	10	0	0	0	0	3	5	2	*	0	0	2	8	0	0	*	10	0	0	0	0	0		5	5	0	0	0	0		10	0	0	0	
150 ppm	10	0	0	2	0	4	3	1	**	0	0	0	8	2	0	**	10	0	0	0	0	0		3	6	1	0	0	0	*	10	0	0	0	
200 ppm	9	0	0	1	2	1	3	2		0	0	0	7	2	0	**	9	0	0	0	0	0		2	5	2	0	0	0	*	9	0	0	0	

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

STUDY NO. : 0265
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	
25 ppm	10	10	0	0	0	0		10	0	0	0	0	
50 ppm	10	10	0	0	0	0		10	0	0	0	0	
100 ppm	10	10	0	0	0	0		10	0	0	0	0	
150 ppm	10	10	0	0	0	0		10	0	0	0	0	
200 ppm	9	9	0	0	0	0		9	0	0	0	0	

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

APPENDIX B 8-3

URINALYSIS (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : MALE

STUDY NO. : 0266
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	1	1	8	0		0	0	5	3	2	0		10	0	0	0	0	0		0	7	3	0	0	0		10	0	0	0	0	
25 ppm	10	0	0	3	6	1	0	0	**	0	0	1	8	1	0		10	0	0	0	0	0		0	3	5	2	0	0		10	0	0	0	0	
50 ppm	10	0	0	1	5	4	0	0	**	0	0	0	8	2	0	*	10	0	0	0	0	0		0	0	9	1	0	0	**	10	0	0	0	0	
100 ppm	10	0	1	6	3	0	0	0	**	0	0	1	7	2	0		10	0	0	0	0	0		0	4	4	2	0	0		10	0	0	0	0	
150 ppm	10	0	4	5	1	0	0	0	**	0	0	0	7	3	0	*	10	0	0	0	0	0		1	4	4	1	0	0		10	0	0	0	0	
200 ppm	8	0	5	3	0	0	0	0	**	0	0	2	4	2	0		8	0	0	0	0	0		1	4	2	1	0	0		8	0	0	0	0	

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

STUDY NO. : 0266 URINALYSIS
ANIMAL : MOUSE BDF1
SAMPLING DATE : 013-6
SEX : MALE REPORT TYPE : A1

Group Name	NO. of Animals	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0	
25 ppm	10	10	0	0	0	0	
50 ppm	10	10	0	0	0	0	
100 ppm	10	10	0	0	0	0	
150 ppm	10	10	0	0	0	0	
200 ppm	8	8	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)

MOSUE : FEMALE

STUDY NO. : 0266
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	0	6	1	3	0		0	1	9	0	0	0		10	0	0	0	0	0		0	9	1	0	0	0		10	0	0	0	0	
25 ppm	10	0	4	4	1	1	0	0	**	0	0	7	3	0	0		10	0	0	0	0	0		0	3	7	0	0	0	**	10	0	0	0	0	
50 ppm	10	0	2	6	1	1	0	0	**	0	2	3	5	0	0	*	10	0	0	0	0	0		0	3	5	2	0	0	*	10	0	0	0	0	
100 ppm	8	0	6	2	0	0	0	0	**	0	1	4	3	0	0		8	0	0	0	0	0		0	4	2	2	0	0		8	0	0	0	0	
150 ppm	10	0	6	3	1	0	0	0	**	0	0	5	3	1	1		10	0	0	0	0	0		0	2	4	4	0	0	**	10	0	0	0	0	
200 ppm	7	0	5	1	1	0	0	0	**	0	0	1	5	1	0	**	7	0	0	0	0	0		1	0	4	2	0	0	**	7	0	0	0	0	

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

STUDY NO. : 0266
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	
25 ppm	10	10	0	0	0	0	
50 ppm	10	10	0	0	0	0	
100 ppm	8	8	0	0	0	0	
150 ppm	10	10	0	0	0	0	
200 ppm	7	7	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 : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0265
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name NO. of Animals	Control 0 (%)	25 ppm 0 (%)	50 ppm 0 (%)	100 ppm 0 (%)
subcutis	dry		- (-)	- (-)	- (-)	- (-)

STUDY NO. : 0265
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name NO. of Animals	150 ppm 0 (%)	200 ppm 1 (%)
subcutis	dry		- (-)	1 (100)

APPENDIX B 9-2

GROSS FINDINGS (THIRTEEN−WEEK STUDY: SUMMARY)

RAT : MALE :SACRIFICED ANIMALS

STUDY NO. : 0265
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	25 ppm 10 (%)	50 ppm 10 (%)	100 ppm 10 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)
	red		0 (0)	1 (10)	2 (20)	1 (10)
liver	herniation		0 (0)	0 (0)	0 (0)	1 (10)

STUDY NO. : 0265
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name NO. of Animals	150 ppm 10 (%)	200 ppm 9 (%)
thymus	atrophic		5 (50)	7 (78)
	red		1 (10)	0 (0)
liver	herniation		0 (0)	0 (0)

APPENDIX B 9-3

GROSS FINDINGS (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : FEMALE :SACRIFICED ANIMALS

STUDY NO. : 0265
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	25 ppm 10 (%)	50 ppm 10 (%)	100 ppm 10 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)
gl stomach	ulcer		0 (0)	0 (0)	0 (0)	0 (0)
liver	herniation		0 (0)	0 (0)	0 (0)	1 (10)

Organ	Findings	Group Name NO. of Animals	150 ppm 10 (%)	200 ppm 10 (%)
thymus	atrophic		2 (20)	9 (90)
gl stomach	ulcer		0 (0)	1 (10)
liver	herniation		0 (0)	0 (0)

APPENDIX B 9-4

GROSS FINDINGS (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : MALE DEAD AND MORIBUND ANIMALS

STUDY NO. : 0266
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 (%)	25 ppm 0 (%)	50 ppm 0 (%)	100 ppm 0 (%)
subcutis	dry		- (-)	- (-)	- (-)	- (-)
thymus	atrophic		- (-)	- (-)	- (-)	- (-)
spleen	atrophic		- (-)	- (-)	- (-)	- (-)
testis	atrophic		- (-)	- (-)	- (-)	- (-)

Organ	Findings	Group Name NO. of Animals	150 ppm 0 (%)	200 ppm 1 (%)
subcutis	dry		- (-)	1 (100)
thymus	atrophic		- (-)	1 (100)
spleen	atrophic		- (-)	1 (100)
testis	atrophic		- (-)	1 (100)

APPENDIX B 9-5

GROSS FINDINGS (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : MALE :SACRIFICED ANIMALS

STUDY NO. : 0266
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	25 ppm 10 (%)	50 ppm 10 (%)	100 ppm 10 (%)
spleen	black zone		2 (20)	1 (10)	0 (0)	0 (0)
liver	red zone		0 (0)	0 (0)	0 (0)	1 (10)
kidney	hydronephrosis		2 (20)	0 (0)	1 (10)	0 (0)
testis	atrophic		0 (0)	0 (0)	1 (10)	0 (0)

STUDY NO. : 0266
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name NO. of Animals	150 ppm 10 (%)	200 ppm 9 (%)
spleen	black zone		0 (0)	1 (11)
liver	red zone		0 (0)	0 (0)
kidney	hydronephrosis		0 (0)	1 (11)
testis	atrophic		1 (10)	0 (0)

APPENDIX B 9-6

GROSS FINDINGS (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : FEMALE :SACRIFICED ANIMALS

STUDY NO. : 0266
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	25 ppm 10 (%)	50 ppm 10 (%)	100 ppm 9 (%)
spleen	black zone		1 (10)	0 (0)	0 (0)	0 (0)
kidney	hydronephrosis		0 (0)	0 (0)	0 (0)	0 (0)

STUDY NO. : 0266
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name NO. of Animals	150 ppm 10 (%)	200 ppm 10 (%)
spleen	black zone		0 (0)	1 (10)
kidney	hydronephrosis		1 (10)	1 (10)

APPENDIX B 10-1

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

RAT : MALE

STUDY NO. : 0265
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	290± 11	0.222± 0.024	0.051± 0.005	2.710± 0.108	0.876± 0.054	1.007± 0.089
25 ppm	10	275± 11	0.226± 0.027	0.051± 0.004	2.703± 0.102	0.824± 0.051	0.957± 0.073
50 ppm	10	261± 13	0.184± 0.022*	0.049± 0.003	2.706± 0.135	0.797± 0.058*	1.022± 0.269
100 ppm	10	225± 8**	0.156± 0.023**	0.046± 0.003*	2.645± 0.108	0.706± 0.030**	0.871± 0.073
150 ppm	10	188± 19**	0.124± 0.032**	0.047± 0.005	2.484± 0.133**	0.608± 0.052**	0.799± 0.048**
200 ppm	9	136± 31**	0.086± 0.032**	0.038± 0.004**	2.048± 0.425**	0.500± 0.080**	0.679± 0.075**

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

STUDY NO. : 0265
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	1.753± 0.071	0.505± 0.024	7.133± 0.306	1.844± 0.048
25 ppm	10	1.754± 0.073	0.483± 0.028	6.964± 0.404	1.860± 0.032
50 ppm	10	1.772± 0.098	0.470± 0.025	6.880± 0.412	1.820± 0.060
100 ppm	10	1.712± 0.091	0.416± 0.026**	6.072± 0.346*	1.805± 0.041
150 ppm	10	1.607± 0.083**	0.373± 0.041**	5.240± 0.514**	1.738± 0.038**
200 ppm	9	1.394± 0.165**	0.283± 0.055**	4.214± 0.842**	1.695± 0.061**

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

APPENDIX B 10-2

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

RAT : FEMALE

STUDY NO. : 0265
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	164± 12	0.179± 0.020	0.056± 0.009	0.097± 0.021	0.581± 0.026	0.778± 0.110
25 ppm	10	159± 8	0.178± 0.015	0.050± 0.006	0.093± 0.027	0.537± 0.033	0.713± 0.050
50 ppm	10	155± 9	0.158± 0.013	0.053± 0.009	0.095± 0.015	0.525± 0.033	0.712± 0.058
100 ppm	10	134± 9**	0.118± 0.026**	0.047± 0.008	0.074± 0.016*	0.469± 0.018**	0.645± 0.056**
150 ppm	10	120± 13**	0.107± 0.014**	0.045± 0.008*	0.061± 0.014**	0.433± 0.045**	0.591± 0.052**
200 ppm	10	86± 18**	0.053± 0.028**	0.032± 0.006**	0.044± 0.012**	0.338± 0.055**	0.530± 0.056**

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

STUDY NO. : 0265
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	1.112± 0.069	0.331± 0.030	3.891± 0.260	1.734± 0.045
25 ppm	10	1.205± 0.076	0.324± 0.024	3.850± 0.311	1.733± 0.039
50 ppm	10	1.304± 0.085**	0.331± 0.022	3.945± 0.296	1.741± 0.071
100 ppm	10	1.238± 0.082**	0.297± 0.034	3.648± 0.199	1.662± 0.038*
150 ppm	10	1.193± 0.097	0.257± 0.038**	3.559± 0.332	1.650± 0.065**
200 ppm	10	1.075± 0.100	0.180± 0.041**	3.009± 0.493**	1.589± 0.045**

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. : 0266
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	32.0± 1.6	0.040± 0.005	0.010± 0.001	0.221± 0.025	0.158± 0.013	0.160± 0.008
25 ppm	10	27.9± 1.6**	0.034± 0.004*	0.011± 0.002	0.209± 0.031	0.146± 0.014	0.150± 0.007
50 ppm	10	26.3± 1.2**	0.029± 0.005**	0.010± 0.002	0.205± 0.035	0.143± 0.005	0.154± 0.013
100 ppm	10	25.1± 1.0**	0.027± 0.005**	0.010± 0.002	0.207± 0.036	0.136± 0.009*	0.150± 0.018
150 ppm	10	23.6± 1.2**	0.028± 0.004**	0.009± 0.002	0.198± 0.031	0.129± 0.006**	0.142± 0.010**
200 ppm	9	22.0± 1.8**	0.026± 0.005**	0.008± 0.002	0.206± 0.022	0.124± 0.014**	0.137± 0.006**

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

STUDY NO. : 0266
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	0.491± 0.108	0.053± 0.006	1.180± 0.045	0.449± 0.013
25 ppm	10	0.433± 0.023	0.043± 0.004**	1.088± 0.085	0.437± 0.017
50 ppm	10	0.489± 0.165	0.047± 0.007*	1.072± 0.035	0.437± 0.012
100 ppm	10	0.441± 0.025	0.041± 0.003**	1.045± 0.062**	0.443± 0.016
150 ppm	10	0.416± 0.020**	0.041± 0.006**	0.987± 0.098**	0.429± 0.023
200 ppm	9	0.442± 0.114**	0.032± 0.005**	0.935± 0.079**	0.429± 0.019

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. : 0266
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	20.8± 1.4	0.040± 0.007	0.013± 0.002	0.031± 0.007	0.119± 0.008	0.141± 0.011
25 ppm	10	21.3± 0.8	0.039± 0.007	0.011± 0.002	0.031± 0.009	0.126± 0.006	0.146± 0.015
50 ppm	10	20.5± 1.1	0.037± 0.006	0.011± 0.002	0.032± 0.009	0.116± 0.008	0.139± 0.009
100 ppm	9	20.4± 0.6	0.032± 0.004	0.010± 0.001	0.027± 0.008	0.118± 0.007	0.139± 0.007
150 ppm	10	20.3± 0.7	0.037± 0.007	0.011± 0.002	0.027± 0.008	0.113± 0.008	0.139± 0.010
200 ppm	10	19.5± 1.4*	0.040± 0.005	0.011± 0.002	0.023± 0.007	0.105± 0.013**	0.135± 0.009

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

STUDY NO. : 0266
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	0.282± 0.021	0.052± 0.009	0.879± 0.089	0.456± 0.012
25 ppm	10	0.309± 0.019	0.052± 0.005	0.887± 0.056	0.443± 0.012
50 ppm	10	0.312± 0.023	0.047± 0.006	0.850± 0.076	0.446± 0.016
100 ppm	9	0.325± 0.013**	0.043± 0.003*	0.860± 0.042	0.444± 0.021
150 ppm	10	0.325± 0.013**	0.055± 0.007	0.889± 0.045	0.438± 0.018
200 ppm	10	0.334± 0.035**	0.048± 0.009	0.876± 0.061	0.420± 0.016**

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. : 0265
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	290± 11	0.077± 0.008	0.017± 0.001	0.936± 0.041	0.302± 0.010	0.348± 0.030
25 ppm	10	275± 11	0.082± 0.009	0.019± 0.002	0.984± 0.040	0.300± 0.009	0.348± 0.025
50 ppm	10	261± 13	0.071± 0.009	0.019± 0.001	1.037± 0.052	0.305± 0.017	0.393± 0.113
100 ppm	10	225± 8**	0.069± 0.010	0.021± 0.001*	1.179± 0.039**	0.314± 0.008	0.388± 0.022
150 ppm	10	188± 19**	0.065± 0.012	0.025± 0.004**	1.332± 0.097**	0.325± 0.015*	0.428± 0.028**
200 ppm	9	136± 31**	0.063± 0.014*	0.029± 0.004**	1.513± 0.126**	0.372± 0.028**	0.512± 0.068**

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

STUDY NO. : 0265
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	0.605± 0.026	0.174± 0.006	2.462± 0.046	0.637± 0.032
25 ppm	10	0.638± 0.016	0.176± 0.010	2.531± 0.077	0.677± 0.028
50 ppm	10	0.678± 0.023	0.180± 0.007	2.637± 0.184	0.697± 0.023
100 ppm	10	0.763± 0.022**	0.185± 0.007	2.703± 0.072**	0.805± 0.035**
150 ppm	10	0.863± 0.072**	0.199± 0.007**	2.795± 0.075**	0.937± 0.113**
200 ppm	9	1.049± 0.131**	0.209± 0.017**	3.119± 0.179**	1.297± 0.261**

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. : 0265
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	164± 12	0.109± 0.007	0.034± 0.004	0.059± 0.011	0.356± 0.018	0.478± 0.087
25 ppm	10	159± 8	0.112± 0.009	0.031± 0.003	0.058± 0.014	0.338± 0.018	0.448± 0.021
50 ppm	10	155± 9	0.102± 0.006	0.034± 0.005	0.061± 0.008	0.338± 0.012	0.459± 0.024
100 ppm	10	134± 9**	0.088± 0.018*	0.035± 0.004	0.055± 0.010	0.351± 0.017	0.482± 0.026
150 ppm	10	120± 13**	0.090± 0.010**	0.037± 0.004	0.051± 0.009	0.361± 0.019	0.494± 0.031
200 ppm	10	86± 18**	0.059± 0.021**	0.038± 0.004	0.052± 0.008	0.398± 0.041	0.630± 0.069**

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

STUDY NO. : 0265
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	0.680± 0.025	0.202± 0.009	2.378± 0.093	1.064± 0.089
25 ppm	10	0.757± 0.026	0.204± 0.012	2.418± 0.116	1.091± 0.044
50 ppm	10	0.841± 0.037*	0.214± 0.015	2.542± 0.063	1.125± 0.062
100 ppm	10	0.925± 0.035**	0.222± 0.015**	2.729± 0.107**	1.246± 0.088*
150 ppm	10	0.996± 0.043**	0.213± 0.013	2.965± 0.071**	1.383± 0.115**
200 ppm	10	1.281± 0.162**	0.209± 0.009	3.534± 0.219**	1.917± 0.369**

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. : 0266
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	32.0± 1.6	0.124± 0.013	0.031± 0.006	0.692± 0.086	0.495± 0.041	0.500± 0.032
25 ppm	10	27.9± 1.6**	0.121± 0.018	0.039± 0.006	0.753± 0.127	0.523± 0.037	0.539± 0.039
50 ppm	10	26.3± 1.2**	0.110± 0.019	0.038± 0.008	0.780± 0.124	0.545± 0.021*	0.588± 0.061**
100 ppm	10	25.1± 1.0**	0.109± 0.019	0.040± 0.008	0.826± 0.154	0.544± 0.050	0.596± 0.060**
150 ppm	10	23.6± 1.2**	0.117± 0.017	0.037± 0.008	0.838± 0.125*	0.549± 0.018*	0.600± 0.033**
200 ppm	9	22.0± 1.8**	0.116± 0.017	0.036± 0.010	0.938± 0.097**	0.564± 0.045**	0.625± 0.037**

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

STUDY NO. : 0266
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	1.534± 0.335	0.167± 0.022	3.690± 0.183	1.404± 0.062
25 ppm	10	1.553± 0.074	0.156± 0.016	3.896± 0.147	1.569± 0.099
50 ppm	10	1.871± 0.686	0.176± 0.025	4.077± 0.170**	1.664± 0.100*
100 ppm	10	1.756± 0.083**	0.164± 0.011	4.160± 0.212**	1.762± 0.064**
150 ppm	10	1.766± 0.095**	0.172± 0.024	4.185± 0.340**	1.822± 0.141**
200 ppm	9	2.036± 0.651**	0.145± 0.019	4.255± 0.167**	1.963± 0.173**

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. : 0266
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	20.8± 1.4	0.191± 0.021	0.060± 0.011	0.148± 0.028	0.571± 0.020	0.677± 0.034
25 ppm	10	21.3± 0.8	0.183± 0.031	0.052± 0.006	0.148± 0.043	0.591± 0.028	0.682± 0.061
50 ppm	10	20.5± 1.1	0.178± 0.020	0.056± 0.009	0.154± 0.038	0.567± 0.044	0.680± 0.055
100 ppm	9	20.4± 0.6	0.158± 0.020*	0.051± 0.006	0.132± 0.039	0.577± 0.032	0.683± 0.046
150 ppm	10	20.3± 0.7	0.180± 0.033	0.052± 0.011	0.130± 0.038	0.556± 0.030	0.681± 0.043
200 ppm	10	19.5± 1.4*	0.204± 0.023	0.056± 0.012	0.117± 0.032	0.536± 0.047	0.694± 0.027

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

STUDY NO. : 0266
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	1.354± 0.061	0.247± 0.030	4.215± 0.240	2.196± 0.117
25 ppm	10	1.448± 0.063	0.244± 0.018	4.159± 0.229	2.079± 0.058
50 ppm	10	1.530± 0.131*	0.229± 0.019	4.145± 0.182	2.182± 0.131
100 ppm	9	1.592± 0.065**	0.208± 0.014*	4.213± 0.190	2.177± 0.109
150 ppm	10	1.597± 0.066**	0.271± 0.032	4.372± 0.174	2.156± 0.118
200 ppm	10	1.716± 0.164**	0.245± 0.036	4.495± 0.085**	2.159± 0.147

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 : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0265
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 0 1 (%)	Control 0 2 (%)	Control 0 3 (%)	Control 0 4 (%)	25 ppm 0 1 (%)	25 ppm 0 2 (%)	25 ppm 0 3 (%)	25 ppm 0 4 (%)	50 ppm 0 1 (%)	50 ppm 0 2 (%)	50 ppm 0 3 (%)	50 ppm 0 4 (%)	100 ppm 0 1 (%)	100 ppm 0 2 (%)	100 ppm 0 3 (%)	100 ppm 0 4 (%)
[Hematopoietic system]																		
bone marrow		< a >	< 0>				< 0>				< 0>				< 0>			
	congestion	b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
thymus		< a >	< 0>				< 0>				< 0>				< 0>			
	atrophy	b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
spleen		< a >	< 0>				< 0>				< 0>				< 0>			
	atrophy	b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	deposit of hemosiderin	b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Digestive system]																		
liver		< a >	< 0>				< 0>				< 0>				< 0>			
	micro vesicular fatty change	b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	cytoplasmic basophilic inclusion:decreased	b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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

Organ	Findings	Group Name	150 ppm				200 ppm			
		No. of Animals on Study	0				1			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]										
bone marrow			< 0>				< 1>			
	congestion		-	-	-	-	0	0	1	0
			(-)	(-)	(-)	(-)	(0)	(0)	(100)	(0)
thymus			< 0>				< 1>			
	atrophy		-	-	-	-	0	0	1	0
			(-)	(-)	(-)	(-)	(0)	(0)	(100)	(0)
spleen			< 0>				< 1>			
	atrophy		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
	deposit of hemosiderin		-	-	-	-	0	0	1	0
			(-)	(-)	(-)	(-)	(0)	(0)	(100)	(0)
[Digestive system]										
liver			< 0>				< 1>			
	micro vesicular fatty change		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
	cytoplasmic basophilic inclusion:decreased		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				25 ppm				50 ppm				100 ppm			
		No. of Animals on Study	0				0				0				0			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																		
kidney			< 0>				< 0>				< 0>				< 0>			
	mineralization:papilla		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Reproductive system]																		
testis			< 0>				< 0>				< 0>				< 0>			
	atrophy		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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

Organ	Findings	Group Name	150 ppm				200 ppm			
		No. of Animals on Study	0				1			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]										
kidney			< 0>				< 1>			
	mineralization:papilla		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
[Reproductive system]										
testis			< 0>				< 1>			
	atrophy		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)

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

APPENDIX B 12-2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN−WEEK STUDY: SUMMARY)

RAT : MALE : SACRIFICED ANIMALS

STUDY NO. : 0265
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 10 1 (%)	Control 10 2 (%)	Control 10 3 (%)	Control 10 4 (%)	25 ppm 10 1 (%)	25 ppm 10 2 (%)	25 ppm 10 3 (%)	25 ppm 10 4 (%)	50 ppm 10 1 (%)	50 ppm 10 2 (%)	50 ppm 10 3 (%)	50 ppm 10 4 (%)	100 ppm 10 1 (%)	100 ppm 10 2 (%)	100 ppm 10 3 (%)	100 ppm 10 4 (%)
[Respiratory system]																		
nasal cavit		<10>	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
	inflammation:squamous epithelium		(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(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)
	atrophy:olfactory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
lung		<10>	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
	hemorrhage		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)
[Hematopoietic system]																		
bone marrow		<10>	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	decreased hematopoiesis		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lymph node		<10>	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
	mastcell hyperplasia		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	150 ppm				200 ppm			
		No. of Animals on Study	10				9			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
nasal cavit			<10>				< 9>			
	inflammation:squamous epithelium		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	inflammation:respiratory epithelium		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(11)	(0)	(0)	(0)
	atrophy:olfactory epithelium		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lung			<10>				< 9>			
	hemorrhage		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Hematopoietic system]										
bone marrow			<10>				< 9>			
	decreased hematopoiesis		0	0	0	0	6	0	0	0
			(0)	(0)	(0)	(0)	(67)	(0)	(0)	(0)
lymph node			<10>				< 9>			
	mastcell hyperplasia		0	1	0	0	0	0	0	0
			(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				25 ppm				50 ppm				100 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]																		
thymus			<10>				<10>				<10>				<10>			
	atrophy		0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
spleen			<10>				<10>				<10>				<10>			
	atrophy		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	deposit of hemosiderin		10	0	0	0	10	0	0	0	10	0	0	0	1	7	2	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(10)	(70)	(20)	(0)
	engorgement of erythrocyte		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)	(100)	(0)	(0)	(0)
[Digestive system]																		
liver			<10>				<10>				<10>				<10>			
	herniation		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	micro vesicular fatty change		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	150 ppm				200 ppm			
		No. of Animals on Study	10				9			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]										
thymus			<10>				< 8>			
	atrophy		3	3	0	0	1	6	0	0
			(30)	(30)	(0)	(0)	(13)	(75)	(0)	(0)
spleen			<10>				< 9>			
	atrophy		0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(11)	(0)	(0)
	deposit of hemosiderin		0	7	3	0	0	1	8	0
			(0)	(70)	(30)	(0)	(0)	(11)	(89)	(0)
	engorgement of erythrocyte		9	1	0	0	0	8	0	0
			(90)	(10)	(0)	(0)	(0)	(89)	(0)	(0)
[Digestive system]										
liver			<10>				< 9>			
	herniation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	micro vesicular fatty change		2	0	0	0	6	3	0	0
			(20)	(0)	(0)	(0)	(67)	(33)	(0)	(0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 10 1 (%)	Control 10 2 (%)	Control 10 3 (%)	Control 10 4 (%)	25 ppm 10 1 (%)	25 ppm 10 2 (%)	25 ppm 10 3 (%)	25 ppm 10 4 (%)	50 ppm 10 1 (%)	50 ppm 10 2 (%)	50 ppm 10 3 (%)	50 ppm 10 4 (%)	100 ppm 10 1 (%)	100 ppm 10 2 (%)	100 ppm 10 3 (%)	100 ppm 10 4 (%)
[Digestive system]																		
liver		<10>																
	cytoplasmic basophilic inclusion:decreased		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
pancreas		<10>																
	atrophy		1 (10)	0 (0)	0 (0)	0 (0)	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>																
	basophilic change		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	eosinophilic body		10 (100)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0)
	mineralization:papilla		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Endocrine system]																		
pituitary		<10>																
	Rathke pouch		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)

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

Organ	Findings	Group Name	150 ppm				200 ppm			
		No. of Animals on Study	10				9			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]										
liver			<10>				< 9>			
	cytoplasmic basophilic inclusion:decreased		2	0	0	0	6	3	0	0
			(20)	(0)	(0)	(0)	(67)	(33)	(0)	(0)
pancreas			<10>				< 9>			
	atrophy		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Urinary system]										
kidney			<10>				< 9>			
	basophilic change		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	eosinophilic body		6	0	0	0	0	0	0	0
			(60)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:papilla		5	0	0	0	8	0	0	0
			(50)	(0)	(0)	(0)	(89)	(0)	(0)	(0)
[Endocrine system]										
pituitary			<10>				< 9>			
	Rathke pouch		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				25 ppm				50 ppm				100 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]																		
thyroid			<10>				<10>				<10>				<10>			
	ultimibranchial body remanet		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)	(0)	(0)	(0)	(0)
[Reproductive system]																		
prostate			<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)
	inflammation		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)
[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 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	150 ppm				200 ppm			
		No. of Animals on Study	10				9			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]										
thyroid			<10>				< 9>			
	ultimibranchial body remanet		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Reproductive system]										
prostate			<10>				< 9>			
	atrophy		0	0	0	0	5	0	0	0
			(0)	(0)	(0)	(0)	(56)	(0)	(0)	(0)
	inflammation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Special sense organs/appandage]										
Harder gl			<10>				< 9>			
	lymphocytic infiltration		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

APPENDIX B 12-3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN−WEEK STUDY: SUMMARY)

RAT : FEMALE : SACRIFICED ANIMALS

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 10				25 ppm 10				50 ppm 10				100 ppm 10			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
nasal cavit		<10>	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	inflammation:respiratory epithelium		(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lung		<10>	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	accumulation of foamy cells		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Hematopoietic system]																		
bone marrow		<10>	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	granulation		(10)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	decreased hematopoiesis		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thymus		<10>	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	atrophy		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen		<10>	0	10	0	0	0	10	0	0	0	9	1	0	0	6	4	0
	deposit of hemosiderin		(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(90)	(10)	(0)	(0)	(60)	(40)	(0)

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

Organ	Findings	Group Name	150 ppm				200 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
nasal cavit			<10>				<10>			
	inflammation:respiratory epithelium		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lung			<10>				<10>			
	accumulation of foamy cells		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
[Hematopoietic system]										
bone marrow			<10>				<10>			
	granulation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	decreased hematopoiesis		0	0	0	0	6	0	0	0
			(0)	(0)	(0)	(0)	(60)	(0)	(0)	(0)
thymus			<10>				<10>			
	atrophy		2	0	0	0	5	4	1	0
			(20)	(0)	(0)	(0)	(50)	(40)	(10)	(0)
spleen			<10>				<10>			
	deposit of hemosiderin		0	1	9	0	0	0	10	0
			(0)	(10)	(90)	(0)	(0)	(0)	(100)	(0)

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

Organ	Findings	Group Name	Control				25 ppm				50 ppm				100 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>			
	engorgement of erythrocyte		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)	(100)	(0)	(0)	(0)
[Digestive system]																		
stomach			<10>				<10>				<10>				<10>			
	erosion:glandular stomach		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
liver			<10>				<10>				<10>				<10>			
	herniation		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	micro vesicular fatty change		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	cytoplasmic basophilic inclusion:decreased		0	0	0	0	0	0	0	0	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>			
	hyaline cast		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	150 ppm				200 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]										
spleen			<10>				<10>			
	engorgement of erythrocyte		6	4	0	0	2	8	0	0
			(60)	(40)	(0)	(0)	(20)	(80)	(0)	(0)
[Digestive system]										
stomach			<10>				<10>			
	erosion:glandular stomach		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
liver			<10>				<10>			
	herniation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	micro vesicular fatty change		10	0	0	0	0	10	0	0
			(100)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
	cytoplasmic basophilic inclusion:decreased		10	0	0	0	0	10	0	0
			(100)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
[Urinary system]										
kidney			<10>				<10>			
	hyaline cast		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				25 ppm				50 ppm				100 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																		
kidney			<10>				<10>				<10>				<10>			
	mineralization:cortico-medullary junction		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)
	mineralization:papilla		0	0	0	0	0	0	0	0	0	0	0	0	4	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(40)	(0)	(0)	(0)
[Endocrine system]																		
pituitary			<10>				<10>				<10>				<10>			
	Rathke pouch		2	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)
[Special sense organs/appandage]																		
Harder gl			<10>				<10>				<10>				<10>			
	lymphocytic infiltration		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)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	150 ppm				200 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]										
kidney			<10>				<10>			
	mineralization:cortico-medullary junction		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:papilla		6	0	0	0	8	0	0	0
			(60)	(0)	(0)	(0)	(80)	(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)
[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 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

APPENDIX B 12-4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN−WEEK STUDY: SUMMARY)

MOUSE: MALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0266
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 0 1 (%)	Control 0 2 (%)	Control 0 3 (%)	Control 0 4 (%)	25 ppm 0 1 (%)	25 ppm 0 2 (%)	25 ppm 0 3 (%)	25 ppm 0 4 (%)	50 ppm 0 1 (%)	50 ppm 0 2 (%)	50 ppm 0 3 (%)	50 ppm 0 4 (%)	100 ppm 0 1 (%)	100 ppm 0 2 (%)	100 ppm 0 3 (%)	100 ppm 0 4 (%)
[Hematopoietic system]																		
thymus		< 0>		< 0>				< 0>				< 0>				< 0>		
	atrophy		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
spleen		< 0>		< 0>				< 0>				< 0>				< 0>		
	atrophy		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
[Circulatory system]																		
heart		< 0>		< 0>				< 0>				< 0>				< 0>		
	mineralization		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
[Reproductive system]																		
testis		< 0>		< 0>				< 0>				< 0>				< 0>		
	atrophy		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
[Musculoskeletal system]																		
muscle		< 0>		< 0>				< 0>				< 0>				< 0>		
	mineralization		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)

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

Organ	Findings	Group Name	150 ppm				200 ppm			
		No. of Animals on Study	0				1			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]										
thymus			< 0>				< 1>			
	atrophy		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
spleen			< 0>				< 1>			
	atrophy		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
[Circulatory system]										
heart			< 0>				< 1>			
	mineralization		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
[Reproductive system]										
testis			< 0>				< 1>			
	atrophy		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
[Musculoskeletal system]										
muscle			< 0>				< 1>			
	mineralization		-	-	-	-	0	0	1	0
			(-)	(-)	(-)	(-)	(0)	(0)	(100)	(0)

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

APPENDIX B 12-5

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN−WEEK STUDY: SUMMARY)

MOUSE: MALE : SACRIFICED ANIMALS

STUDY NO. : 0266
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control				25 ppm				50 ppm				100 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>			
	eosinophilic change:respiratory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
[Hematopoietic system]																		
spleen			<10>				<10>				<10>				<10>			
	deposit of melanin		2	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]																		
liver			<10>				<10>				<10>				<10>			
	granulation		3	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(30)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Urinary system]																		
kidney			<10>				<10>				<10>				<10>			
	infarct		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	150 ppm				200 ppm			
		No. of Animals on Study	10				9			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
nasal cavit			<10>				< 9>			
	eosinophilic change:respiratory epithelium		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(11)	(0)	(0)	(0)
[Hematopoietic system]										
spleen			<10>				< 9>			
	deposit of melanin		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(11)	(0)	(0)	(0)
[Digestive system]										
liver			<10>				< 9>			
	granulation		1	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(11)	(0)	(0)	(0)
[Urinary system]										
kidney			<10>				< 9>			
	infarct		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				25 ppm				50 ppm				100 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>			
	inflammatory polyp		0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)
	hydronephrosis		0	0	2	0	0	0	0	0	0	0	1	0	0	0	0	0
			(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)
	vacuolic change:proximal tubule		10	0	0	0	10	0	0	0	10	0	0	0	10	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
[Endocrine system]																		
pituitary			< 9>				<10>				<10>				<10>			
	Rathke pouch		0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
adrenal			<10>				<10>				<10>				<10>			
	accesory cortical nodule		2	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Reproductive system]																		
epididymis			<10>				<10>				<10>				<10>			
	mineralization		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	150 ppm				200 ppm			
		No. of Animals on Study	10				9			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]										
kidney			<10>				< 9>			
	inflammatory polyp		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(11)	(0)	(0)	(0)
	hydronephrosis		0	0	0	0	0	0	1	0
			(0)	(0)	(0)	(0)	(0)	(0)	(11)	(0)
	vacuolic change:proximal tubule		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Endocrine system]										
pituitary			<10>				< 9>			
	Rathke pouch		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
adrenal			<10>				< 9>			
	accesory cortical nodule		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Reproductive system]										
epididymis			<10>				< 9>			
	mineralization		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

APPENDIX B 12-6

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN−WEEK STUDY: SUMMARY)

MOUSE: FEMALE : SACRIFICED ANIMALS

Organ	Findings	Group Name	Control				25 ppm				50 ppm				100 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
[Respiratory system]																		
nasal cavit			<10>				<10>				<10>				< 9>			
	eosinophilic change:respiratory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(22)	(0)	(0)	(0)
lung			<10>				<10>				<10>				< 9>			
	accumulation of foamy cells		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Hematopoietic system]																		
spleen			<10>				<10>				<10>				< 9>			
	deposit of melanin		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]																		
stomach			<10>				<10>				<10>				< 9>			
	inflammatory infiltration		0	0	0	0	0	0	0	0	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>				< 9>			
	granulation		1	1	0	0	2	0	0	0	2	0	0	0	2	0	0	0
			(10)	(10)	(0)	(0)	(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(22)	(0)	(0)	(0)

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

Organ	Findings	Group Name	150 ppm				200 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
nasal cavit			<10>				<10>			
	eosinophilic change:respiratory epithelium		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
lung			<10>				<10>			
	accumulation of foamy cells		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[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]										
stomach			<10>				<10>			
	inflammatory infiltration		1	0	0	0	0	1	0	0
			(10)	(0)	(0)	(0)	(0)	(10)	(0)	(0)
liver			<10>				<10>			
	granulation		1	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				25 ppm				50 ppm				100 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>			
	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)
	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)
	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)
[Endocrine system]																		
pituitary			<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	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)

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

Organ	Findings	Group Name	150 ppm				200 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]										
kidney			<10>				<10>			
	inflammatory polyp		0	1	0	0	1	0	0	0
			(0)	(10)	(0)	(0)	(10)	(0)	(0)	(0)
	ossification		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	hydronephrosis		0	0	1	0	0	0	1	0
			(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)
[Endocrine system]										
pituitary			<10>				< 9>			
	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	1	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)

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

APPENDIX B 13-1

IDENTITY OF HYDRAZINE MONOHYDRATE

(THIRTEEN−WEEK STUDIES)

IDENTITY OF HYDRAZINE MONOHYDRATE(THIRTEEN-WEEK STUDIES)

Test Substance Lot No. KCP7905

1. Spectral data

(1)Mass Spectrometry

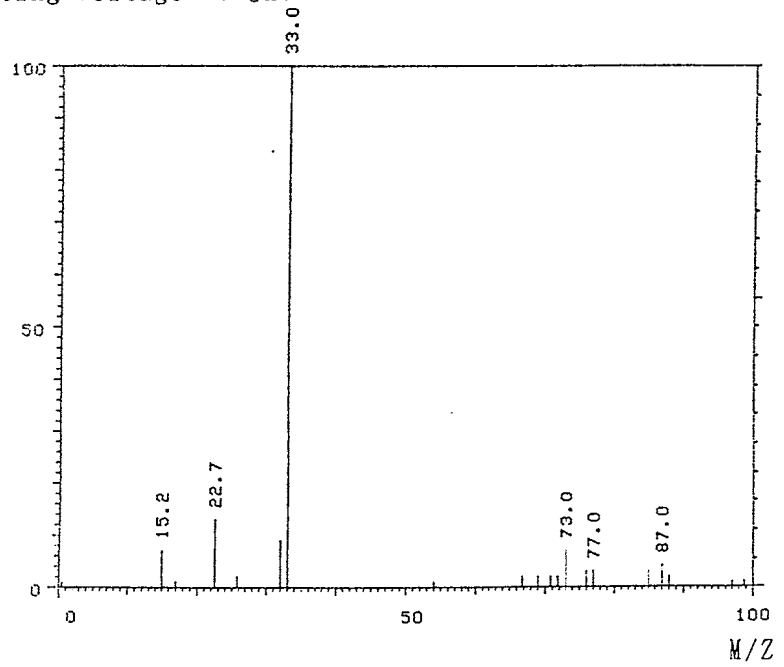
Instrument : Hitachi M-80B

Ionization : SIMS(Secondary Ionization Mass Spectrometry)

Matrix : Glycerol

Primary Ion : $Xenone^{+}$

Accelerating Voltage : 8kv



Mass Spectrum of Test Substance

Result: The mass spectrum was consistent with calculated spectrum.

Quasi Molecule Ion

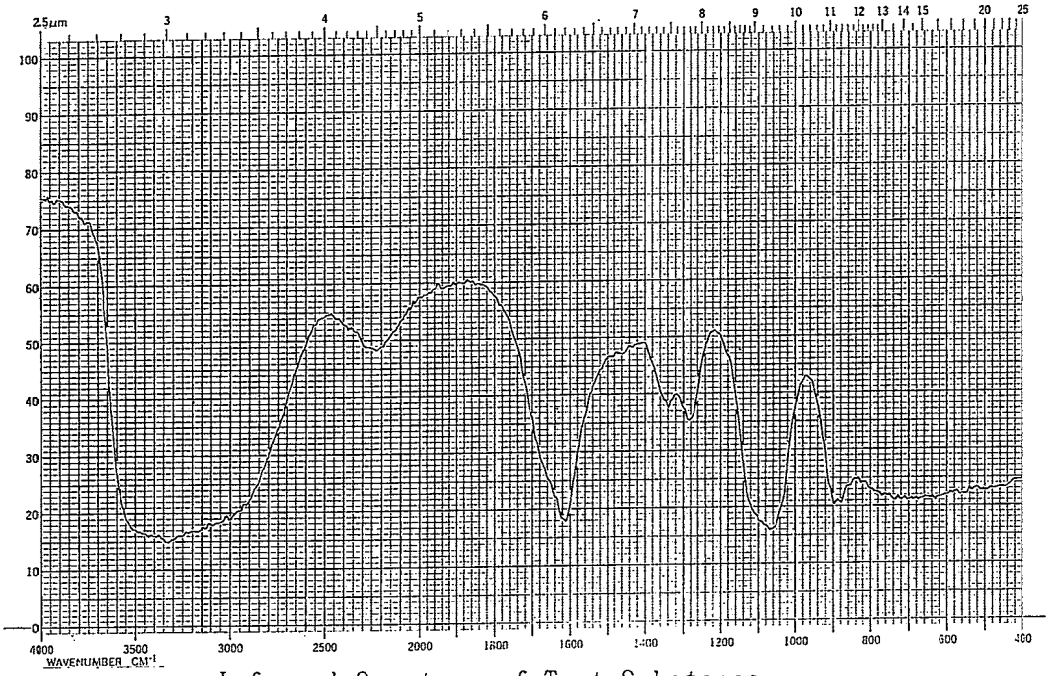
Calculated Value ($NH_2 \cdot NH_2 + H^+$)	33.0
Determined Value	33.0

(2)Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr Liquid Cell

Slit : Medium



Infrared Spectrum of Test Substance

Results: The infrared spectrum was consistent with literature spectrum.

Determined Values Wave Number(cm^{-1})	Literature Values* Wave Number(cm^{-1})
850～ 970	850～ 970
970～1220	970～1220
1220～1400	1220～1400
1500～1800	1500～1800
2000～2500	2000～2500
2500～3750	2500～3750

(*Performed by WAKO PURE CHEMICAL INSUSTRIES, LTD.)

2. Conclusions: The test substance was identified as Hydrazine monohydrate, by the mass spectrum and infrared spectrum.

APPENDIX B 13-2

STABILITY OF HYDRAZINE MONOHYDRATE

(THIRTEEN−WEEK STUDIES)

STABILITY OF HYDRAZINE MONOHYDRATE(THIRTEEN-WEEK STUDIES)

Test Substance Lot No. KCP7905

1. Sample: This lot was used form 1994. 5. 24 to 1994. 9. 1. The test substance was stored in the dark at room temperature.

2. Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr Liquid Cell

Slit : Medium

Results: Infrared spectrum of the test substance agreed with before use and after use.

1994. 04. 14(date analyzed) Wave Number(cm^{-1})	1994. 09. 06(date analyzed) Wave Number(cm^{-1})
850～ 970	850～ 970
970～1220	970～1220
1220～1400	1220～1400
1500～1800	1500～1800
2000～2500	2000～2500
2500～3750	2500～3750

3. High Performance Liquid Chromatography

Instrument : Shimadzu LC-10AD(Pump)
Esa Coulochem II (Detector)

Column : TSK GEL ODS-80TM(4. 6mm ϕ × 15cm)

Column Temperature : 50°C

Flow Rate : 1ml/min

Mobile Phase : Water (pH. 7. 0 Phosphate Buffer Powder + 0. 2mol/l Sodium Perchlorate Monohydrate)

Oxidation Voltage : 600mV(Analytical Cell)
650mV(Guard Cell)

Detector : ECD(Electrochemical Detector)

Injection Volume : 10 μ l

Results: Chromatogram indicated one major peak analyzed at 1994.4.14 and one major peak analyzed at 1994.9.6. The new trace impurity peak in the test substance analyzed at 1994.9.6 was not detected.

Date	Retention Time(min)	AREA
1994.04.14 (date analyzed)	2.358	353748
1994.09.06 (date analyzed)	2.360	352574

4. Conclusions: The test substance was stable for about 5 months in the dark at room temperature.

APPENDIX B 13-3

CONCENTRATION HYDRAZINE MONOHYDRATE IN DRINKING WATER

(THIRTEEN−WEEK STUDIES)

CONCENTRATION OF HYDRAZINE MONOHYDRATE IN DRINKING WATER(THIRTEEN-WEEK STUDIES)

(Rat)

	Target Concentration(ppm)				
Date analyzed	25	50	100	150	200
1994.05.31	26.4(105.6)*	49.5(99.0)	99.6(99.6)	152.4(101.6)	194.2(97.1)

(Mouse)

	Target Concentration(ppm)				
Date analyzed	25	50	100	150	200
1994.05.24	21.9(87.6)	43.5(87.0)	89.1(89.1)	138.9(92.6)	191.1(95.6)

(*) % of target concentration

Analytical method: The sample were analyzed by the HPLC.

Instrument : Shimadzu LC-10AD(Pump)
Esa Coulochem II (Detector)
Column : TSK GEL ODS-80TM(4.6mmϕ × 15cm)
Column Temperature: 50℃
Flow Rate : 1ml/min

Mobile Phase : Water(pH7.0 Phosphate Buffer Powder + 0.2mol/l Sodium Perchlorate Monohydrate)
Oxidation Voltage : 600mv(Analytical Cell)
650mv(Guard Cell)
Detector : ECD(Electrochemical Detector)
Injection Volume : 10μl

(Study No. 0265. 0266)

APPENDIX B 13-4

STABILITY OF HYDRAZINE MONOHYDRATE IN DRINKING WATER

(THIRTEEN−WEEK STUDIES)

STABILITY OF HYDRAZINE MONOHYDRATE IN DRINKING WATER(THIRTEEN-WEEK STUDIES)

(Rat)

	Target Concentration(ppm)	
Date analyzed	25	200
1994.05.23(a)	24.6(98.4)*	200.0(100.0)
1994.05.27(b)	21.9(87.6)	156.8(78.4)

(Mouse)

	Target Concentration(ppm)	
Date analyzed	25	200
1994.05.23(a)	24.6(98.4)	200.0(100.0)
1994.05.27(b)	21.3(85.2)	170.7(85.4)

(a) Date of preparation
(b) The stability of Hydrazine monohydrate in drinking water was established for 4 days when stored at room temperature.
(*) % of target concentration

Analytical method: The sample were analyzed by the HPLC.

Instrument : Shimadzu LC-10AD(Pump)
Esa Coulochem II (Detector)
Column : TSK GEL ODS-80TM(4.6mmϕ × 15cm)
Column Temperature: 50℃
Flow Rate : 1ml/min

Mobile Phase : Water(pH7.0 Phosphate Buffer Powder + 0.2mol/l Sodium Perchlorate Monohydrate)
Oxidation Voltage : 600mv(Analytical Cell)
650mv(Guard Cell)
Detector : ECD(Electrochemical Detector)
Injection Volume : 10μl

APPENDIX C 1

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALSYS

(TOW−WEEK STUDIES)

METHODS FOR HEMATOLOGY,BIOCHEMISTRY AND URINALYSIS

Item	Method
Hematology	
Red blood cell (RBC)	Light scattering method [1]
Hemoglobin (Hgb)	Cyanmethemoglobin method [1]
Hematocrit (Hct)	Calculated as RBC × MCV/10 [1]
Mean corpuscular volume (MCV)	Light scattering method [1]
Mean corpuscular hemoglobin (MCH)	Calculated as Hgb/RBC × 10 [1]
Mean corpuscular hemoglobin concentration (MCHC)	Calculated as Hgb/Hct × 100 [1]
Platelet	Light scattering method [1]
Reticulocyte	Pattern recognition method [3] (New methyleneblue staining)
Prothrombin time	Quick one stage method [2]
Activated partial thromboplastin time (APTT)	Ellagic acid activated method [2]
White blood cell (WBC)	Light scattering method [1]
Differential WBC	Pattern recognition method [3] (May-Grunwald-Giemsa staining)
Biochemistry	
Total protein (TP)	Biuret method [4]
Albumin (Alb)	BCG method [4]
A/G ratio	Calculated as Alb/(TP-Alb) [4]
T-bilirubin	Michaelson method [4]
Glucose	Enzymatic method (HK·G-6-PDH) [4]
T-cholesterol	Enzymatic method (CEH·COD·POD) [4]
Phospholipid	Enzymatic method (PLD·COD·POD) [4]
Glutamic oxaloacetic transaminase (GOT)	UV·Rate method [4]
Glutamic pyruvic transaminase (GPT)	UV·Rate method [4]
Lactate dehydrogenase (LDH)	UV·Rate method [4]
γ -Glutamyl transpeptidase (γ -GTP)	L- γ -Glutamyl-p-nitroanilide method [4]
Creatine phosphokinase (CPK)	UV·Rate method [4]
Urea nitrogen	Enzymatic method (Urease·GLDH) [4]
Creatinine	Jaffe method [4]
Sodium	Flame photometry [5]
Potassium	Flame photometry [5]
Chloride	Coulometric titration [5]
Calcium	OCPC method [4]
Inorganic phosphorus	Enzymatic method (SPL·PGM·G-6-PDH) [4]

1) Automatic blood cell analyzer (Technicon H·1 : Technicon Instruments Corporation,USA)
2) Automatic coagulometer (Amelung KC-10 : Heinrich Amelung GmbH,Germany)
3) Automatic blood cell differential analyzer (Hitachi 8200 : Hitachi,Ltd.,Japan)
4) Automatic analyzer (Hitachi 705 : Hitachi,Ltd.,Japan)
5) Flame photometer (Hitachi 750 : Hitachi,Ltd.,Japan)

APPENDIX C 2

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALSYS

(THIRTEEN−WEEK STUDIES)

METHODS FOR HEMATOLOGY,BIOCHEMISTRY AND URINALYSIS

Item	Method
Hematology	
Red blood cell (RBC)	Light scattering method [1]
Hemoglobin (Hgb)	Cyanmethemoglobin method [1]
Hematocrit (Hct)	Calculated as RBC × MCV/10 [1]
Mean corpuscular volume (MCV)	Light scattering method [1]
Mean corpuscular hemoglobin (MCH)	Calculated as Hgb/RBC × 10 [1]
Mean corpuscular hemoglobin concentration (MCHC)	Calculated as Hgb/Hct × 100 [1]
Platelet	Light scattering method [1]
Reticulocyte	Pattern recognition method [3] (New methyleneblue staining)
Prothrombin time	Quick one stage method [2]
Activated partial thromboplastin time (APTT)	Ellagic acid activated method [2]
White blood cell (WBC)	Light scattering method [1]
Differential WBC	Pattern recognition method [3] (May-Grunwald-Giemsa staining)
Biochemistry	
Total protein (TP)	Biuret method [4]
Albumin (Alb)	BCG method [4]
A/G ratio	Calculated as Alb/(TP-Alb) [4]
T-bilirubin	Alkaline azobilirubin method [4]
Glucose	Enzymatic method (GLK·G-6-PDH) [4]
T-cholesterol	Enzymatic method (CE·COD·POD) [4]
Triglyceride	Enzymatic method (LPL·GK·GPO·POD) [4]
Phospholipid	Enzymatic method (PLD·COD·POD) [4]
Glutamic oxaloacetic transaminase (GOT)	UV·Rate method [4]
Glutamic pyruvic transaminase (GPT)	UV·Rate method [4]
Lactate dehydrogenase (LDH)	UV·Rate method [4]
Alkaline phosphatase (ALP)	p-Nitrophenylphosphate method [4]
γ -Glutamyl transpeptidase (γ -GTP)	L- γ -Glutamyl-p-nitroanilide method [4]
Creatine phosphokinase (CPK)	UV·Rate method [4]
Urea nitrogen	Enzymatic method (Urease·GLDH) [4]
Creatinine	Jaffe method [4]
Sodium	Ion selective electrode method [4]
Potassium	Ion selective electrode method [4]
Chloride	Ion selective electrode method [4]
Calcium	OCPC method [4]
Inorganic phosphorus	Enzymatic method (PNP·XOD·POD) [4]
Urinalysis	
pH,Protein,Glucose,Ketone body,Bilirubin,Occult Blood, Urobilinogen	Urinalysis reagent paper method [5]

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

APPENDIX C 3

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

Item	Unit	Decimal place
Hematology		
Red blood cell (RBC)	$\times 10^6 / \mu L$	2
Hemoglobin	g/dL	1
Hematocrit	%	1
Mean corpuscular volume (MCV)	fL	1
Mean corpuscular hemoglobin (MCH)	pg	1
Mean corpuscular hemoglobin concentration (MCHC)	g/dL	1
Reticulocyte	‰	0
Prothrombin time	sec	1
Activated partial thromboplastin time (APTT)	sec	1
Platelet	$\times 10^3 / \mu L$	0
White blood cell (WBC)	$\times 10^3 / \mu L$	2
Differential WBC	%	0
Biochemistry		
Total protein	g/dL	1
Albumin	g/dL	1
A/G ratio	–	1
T-bilirubin	mg/dL	2
Glucose	mg/dL	0
T-cholesterol	mg/dL	0
Triglyceride	mg/dL	0
Phospholipid	mg/dL	0
Glutamic oxaloacetic transminase (GOT)	IU/L	0
Glutamic pyruvic transaminase (GPT)	IU/L	0
Lactate dehydrogenase (LDH)	IU/L	0
ALkaline phosphatase (ALP)	IU/L	0
γ -Glutamyl transpeptidase (γ -GTP)	IU/L	0
Creatine phosphokinase (CPK)	IU/L	0
Urea nitrogen	mg/dL	1
Creatinine	mg/dL	1
Sodium	mEq/L	0
Potassium	mEq/L	1
Chloride	mEq/L	0
Calcium	mg/dL	1
Inorganic phosphorus	mg/dL	1