APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIX B 1-1

BODY WEIGHT CHANGES (THIRTEEN−WEEK STUDY:SUMMARY)

RAT : MALE

STUDY NO. : 0220
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 0	1	2	3	4	5	6
Control	124± 4	149± 5	182± 6	209± 5	229± 7	245± 8	259± 8
80 ppm	124± 4	149± 5	185± 5	212± 6	229± 8	247± 10	261± 13
400 ppm	124± 4	149± 6	185± 9	210± 14	227± 16	244± 20	256± 24
2000 ppm	124± 4	146± 6	180± 6	204± 7	221± 11	237± 13	252± 15
10000 ppm	124± 4	142± 6*	175± 9	198± 13	217± 16	234± 17	248± 20
50000 ppm	124± 4	141± 4*	172± 5**	196± 7*	214± 9*	232± 10	245± 10

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

STUDY NO. : 0220
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 7	8	9	10	11	12	13
Control	275± 8	290± 10	298± 10	310± 11	321± 11	328± 11	337± 11
80 ppm	276± 14	294± 14	304± 14	316± 14	326± 15	337± 16	345± 16
400 ppm	270± 26	286± 29	296± 28	307± 28	317± 29	328± 29	335± 28
2000 ppm	265± 15	280± 16	291± 17	301± 18	313± 17	322± 18	329± 18
10000 ppm	260± 22	275± 23	286± 24	295± 25	307± 25	314± 25	322± 24
50000 ppm	260± 11	274± 10	285± 11	295± 10	307± 10	315± 11	323± 10

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

APPENDIX B 1-2

BODY WEIGHT CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

RAT : FEMALE

STUDY NO. : 0220
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 0	1	2	3	4	5	6
Control	103± 3	116± 2	132± 4	143± 4	148± 4	157± 6	162± 6
80 ppm	103± 3	118± 4	135± 5	144± 5	152± 5	160± 5	166± 6
400 ppm	103± 3	116± 3	130± 4	138± 7	144± 9	151± 11	156± 12
2000 ppm	103± 3	114± 3	130± 5	139± 5	144± 4	150± 6	155± 7
10000 ppm	103± 3	113± 4	130± 4	138± 5	144± 6	151± 6	154± 7
50000 ppm	103± 3	107± 3**	121± 4**	130± 4**	136± 5**	140± 6**	145± 7**

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

STUDY NO. : 0220
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 7	8	9	10	11	12	13
Control	167± 8	173± 8	178± 9	175± 9	185± 9	186± 9	191± 10
80 ppm	170± 6	175± 5	180± 7	174± 9	186± 7	190± 6	193± 6
400 ppm	159± 13	161± 12**	167± 12*	170± 15	173± 14	177± 15	181± 15
2000 ppm	161± 8	162± 7*	167± 7*	172± 7	175± 7	178± 8	182± 7
10000 ppm	158± 7	161± 7**	164± 7**	167± 7	170± 6**	173± 5*	176± 5**
50000 ppm	151± 7**	156± 6**	156± 6**	159± 7**	162± 5**	164± 7**	166± 6**

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

APPENDIX B 1-3

BODY WEIGHT CHANGES (THIRTEEN−WEEK STUDY:SUMMARY)

MOSUE : MALE

STUDY NO. : 0221
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 0	1	2	3	4	5	6
Control	23.0± 0.7	24.1± 0.7	25.2± 0.8	26.0± 0.8	26.8± 0.9	27.6± 1.2	28.5± 1.1
80 ppm	23.0± 0.7	23.5± 1.3	24.5± 1.1	25.5± 1.0	26.3± 1.2	27.0± 1.2	28.1± 1.7
400 ppm	23.0± 0.7	23.4± 1.0	24.4± 0.8	24.9± 0.7	25.8± 0.9	26.6± 0.9	27.5± 1.1
2000 ppm	23.0± 0.7	23.3± 1.5	23.8± 1.5*	24.4± 1.2**	25.5± 1.1*	25.9± 1.1**	26.7± 1.6*
10000 ppm	23.0± 0.7	23.1± 0.9	23.3± 1.0**	23.9± 1.1**	24.5± 1.2**	24.9± 1.4**	25.5± 1.6**
50000 ppm	23.0± 0.7	22.4± 1.6	22.9± 0.9**	23.4± 0.8**	23.9± 0.6**	24.4± 0.5**	24.5± 0.6**

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

STUDY NO. : 0221
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 7	8	9	10	11	12	13
Control	28.8± 1.3	30.4± 1.6	31.2± 1.7	32.2± 1.8	32.7± 1.8	32.6± 2.0	33.6± 2.0
80 ppm	28.0± 1.7	29.7± 2.1	30.3± 2.4	31.3± 2.6	32.1± 2.7	31.6± 2.8	32.7± 3.2
400 ppm	27.6± 1.1	28.9± 1.1	29.5± 1.3	30.6± 1.3	31.2± 1.8	31.4± 1.7	32.5± 1.7
2000 ppm	26.9± 1.4	27.9± 1.7	28.7± 1.5	29.6± 1.9	30.1± 2.2	29.9± 2.4	31.0± 2.0
10000 ppm	25.9± 1.6**	26.4± 1.8**	26.8± 1.8**	27.3± 1.9**	27.8± 1.9**	27.8± 2.1**	28.4± 2.2**
50000 ppm	24.7± 0.4**	25.0± 0.6**	25.1± 0.5**	25.7± 0.7**	25.8± 0.7**	25.9± 0.8**	26.2± 0.9**

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

APPENDIX B 1-4

BODY WEIGHT CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE: FEMALE

STUDY NO. : 0221
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 0	1	2	3	4	5	6
Control	19.1± 0.7	19.7± 0.9	20.3± 0.7	20.7± 1.1	21.2± 0.9	21.7± 1.1	22.4± 1.0
80 ppm	19.1± 0.7	19.3± 0.8	20.0± 0.5	20.5± 0.6	21.5± 0.8	21.2± 0.8	22.4± 0.7
400 ppm	19.1± 0.7	19.5± 0.7	19.9± 0.8	20.9± 0.8	21.4± 0.8	21.5± 0.8	22.6± 0.8
2000 ppm	19.1± 0.6	19.4± 0.7	19.8± 0.8	20.2± 0.8	20.8± 0.9	21.3± 1.0	22.4± 0.9
10000 ppm	19.1± 0.7	18.8± 0.9	19.2± 0.9**	19.5± 0.9**	19.9± 1.1**	20.1± 1.2**	21.1± 1.2**
50000 ppm	19.1± 0.6	17.8± 1.5**	19.1± 0.4**	19.5± 0.4**	19.7± 0.6**	19.9± 0.5**	20.4± 0.6**

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

STUDY NO. : 0221
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 7	8	9	10	11	12	13
Control	22.2± 1.1	22.6± 1.4	22.6± 1.8	23.7± 1.2	23.9± 1.5	23.8± 1.5	24.0± 2.0
80 ppm	22.2± 0.6	22.6± 1.1	22.6± 0.9	23.3± 1.0	23.7± 0.9	23.9± 0.9	23.4± 1.0
400 ppm	22.5± 1.4	22.8± 1.2	22.6± 1.0	23.4± 1.0	23.7± 1.7	24.0± 1.5	23.7± 1.2
2000 ppm	21.9± 1.1	22.4± 1.2	22.5± 1.4	22.9± 1.1	23.6± 1.8	23.5± 1.4	23.3± 1.4
10000 ppm	20.9± 1.3*	21.4± 1.4	21.5± 1.9	22.2± 1.2*	22.4± 1.4	22.7± 1.7	22.3± 1.7*
50000 ppm	20.9± 0.7*	21.1± 0.8*	21.6± 1.1	22.0± 1.0**	22.0± 0.7*	22.0± 1.0*	22.0± 1.0*

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

APPENDIX B 2-1

FOOD CONSUMPTION CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

RAT : MALE

STUDY NO. : 0220
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	12.3± 0.5	13.5± 0.6	14.7± 0.7	14.9± 0.6	15.0± 0.5	14.8± 0.7	15.3± 0.8
80 ppm	12.5± 0.5	13.9± 0.5	15.1± 0.7	15.2± 0.8	16.1± 1.7	16.1± 2.1	16.3± 2.1
400 ppm	12.4± 0.5	14.0± 0.9	14.9± 1.3	14.8± 1.4	15.6± 1.4	15.3± 2.1	15.3± 2.0
2000 ppm	11.9± 0.4	13.7± 0.6	14.3± 0.8	14.6± 1.1	15.3± 1.3	15.4± 1.3	15.1± 1.0
10000 ppm	11.1± 0.7**	13.3± 0.9	14.2± 1.3	14.6± 1.1	15.0± 1.3	15.0± 1.7	15.0± 1.7
50000 ppm	10.8± 0.4**	13.6± 0.7	14.6± 0.6	15.0± 1.0	15.7± 1.0	15.7± 0.7	16.0± 0.8

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

STUDY NO. : 0220
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	15.9± 0.9	16.0± 1.3	15.9± 1.3	16.5± 1.3	16.5± 1.6	16.4± 1.8
80 ppm	16.8± 2.3	17.0± 1.8	16.6± 2.1	17.1± 1.9	17.1± 1.5	16.7± 1.2
400 ppm	15.7± 2.2	15.9± 2.1	15.5± 1.7	16.2± 1.9	16.4± 1.7	15.9± 1.5
2000 ppm	15.5± 1.1	15.6± 1.2	15.6± 1.1	16.0± 1.0	16.1± 1.1	15.8± 0.9
10000 ppm	15.3± 1.8	15.6± 1.4	15.4± 1.5	15.6± 1.7	15.8± 1.5	15.9± 1.4
50000 ppm	16.3± 0.7	16.6± 1.0	16.4± 0.7	16.6± 0.7	17.1± 1.1	17.0± 1.0

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

APPENDIX B 2-2

FOOD CONSUMPTION CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

RAT : FEMALE

STUDY NO. : 0220
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± 0.4	11.0± 0.5	11.4± 0.6	11.3± 0.6	12.0± 0.7	11.4± 0.8	11.6± 1.2
80 ppm	10.9± 0.5	11.3± 0.5	11.6± 0.5	11.5± 0.6	12.2± 0.6	11.6± 1.4	11.7± 0.9
400 ppm	10.4± 0.4	10.7± 0.4	11.0± 0.8	10.6± 1.0	11.4± 1.3	10.6± 1.7	10.5± 1.6
2000 ppm	9.8± 0.2*	10.6± 0.4	11.1± 0.8	10.8± 0.6	11.3± 0.5	10.6± 1.0	11.4± 1.9
10000 ppm	9.3± 0.3**	10.6± 0.3	10.8± 0.4	10.8± 0.3	11.0± 0.5*	10.6± 0.6	10.5± 0.4
50000 ppm	8.1± 0.9**	9.9± 0.4**	10.0± 0.4**	10.0± 0.4**	10.1± 0.4**	9.7± 0.5**	9.8± 0.5**

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

STUDY NO. : 0220
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	11.8± 1.0	11.9± 0.9	11.5± 1.1	12.5± 1.6	11.6± 0.9	12.3± 1.3
80 ppm	11.4± 1.0	11.9± 1.1	11.0± 0.9	12.3± 1.8	12.3± 1.5	12.0± 1.4
400 ppm	9.7± 1.2**	11.1± 1.4	10.8± 1.4	11.0± 1.4	11.2± 1.3	11.1± 1.3
2000 ppm	10.1± 1.5*	11.1± 1.1	11.0± 1.1	11.5± 1.3	11.0± 1.1	11.4± 0.9
10000 ppm	10.4± 0.5	10.7± 0.6*	10.3± 0.6*	10.5± 0.4*	10.5± 0.5	10.7± 0.6*
50000 ppm	9.9± 0.4**	9.7± 0.6**	9.6± 0.5**	9.9± 0.5**	9.8± 0.7**	9.9± 0.4**

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

APPENDIX B 2-3

FOOD CONSUMPTION CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : MALE

STUDY NO. : 0221
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	5.2± 0.5	4.9± 0.5	4.8± 0.3	4.9± 0.4	5.3± 0.5	5.2± 0.5	5.0± 0.5
80 ppm	5.1± 0.4	5.0± 0.6	4.9± 0.4	4.9± 0.6	5.2± 0.5	5.3± 0.5	5.2± 0.5
400 ppm	4.9± 0.4	4.8± 0.4	4.7± 0.4	4.9± 0.5	5.3± 0.6	5.3± 0.7	5.0± 0.4
2000 ppm	4.8± 0.8	4.7± 0.7	4.4± 0.4	4.6± 0.4	4.8± 0.3	4.9± 0.5	4.8± 0.4
10000 ppm	4.7± 0.4	4.3± 0.4*	4.1± 0.4**	4.4± 0.4*	4.7± 0.4*	4.6± 0.5	4.5± 0.4
50000 ppm	4.6± 0.4	4.3± 0.3*	4.0± 0.4**	4.2± 0.3**	4.4± 0.4**	4.1± 0.3**	4.2± 0.3**

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

STUDY NO. : 0221
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	5.7± 0.6	5.7± 0.3	5.0± 0.5	4.7± 0.5	5.2± 0.6	5.1± 0.5
80 ppm	5.9± 0.8	5.8± 0.5	5.3± 0.6	4.8± 0.4	5.1± 0.6	5.5± 0.5
400 ppm	5.7± 0.6	5.9± 0.4	5.2± 0.4	5.0± 0.4	5.1± 0.5	5.5± 0.5
2000 ppm	5.2± 0.5	5.4± 0.6	4.9± 0.3	4.6± 0.2	4.8± 0.4	5.2± 0.4
10000 ppm	5.2± 0.6	5.0± 0.6*	4.6± 0.4	4.6± 0.5	4.6± 0.3*	4.7± 0.3
50000 ppm	4.4± 0.6**	4.5± 0.4**	4.2± 0.3**	4.2± 0.4	4.2± 0.4**	4.3± 0.4**

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

APPENDIX B 2-4

FOOD CONSUMPTION CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : FEMALE

STUDY NO. : 0221
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	4.9± 0.3	4.5± 0.4	4.8± 0.4	4.8± 0.4	5.3± 0.3	5.1± 0.5	5.0± 0.4
80 ppm	5.2± 0.7	4.8± 0.3	5.1± 0.7	4.7± 0.3	5.6± 0.7	5.4± 0.8	5.6± 0.7*
400 ppm	5.3± 0.5	4.8± 0.3	5.0± 0.4	5.1± 0.4	5.6± 0.4	5.3± 0.5	5.4± 0.5
2000 ppm	4.9± 0.7	4.6± 0.4	4.7± 0.5	4.9± 0.6	5.5± 0.5	5.5± 0.4	5.3± 0.4
10000 ppm	4.5± 0.5	3.9± 0.4**	4.0± 0.5**	4.5± 0.4	4.7± 0.5*	4.8± 0.5	4.6± 0.3
50000 ppm	4.4± 0.7	4.1± 0.4*	3.8± 0.3**	4.0± 0.3**	4.5± 0.4**	4.5± 0.4	4.5± 0.4

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

STUDY NO. : 0221
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	5.6± 0.6	5.8± 0.5	5.0± 0.4	5.3± 0.5	5.2± 0.3	5.5± 0.3
80 ppm	6.1± 0.6	6.3± 0.6	5.7± 0.6*	5.5± 0.6	5.7± 0.7	6.0± 0.7
400 ppm	6.0± 0.7	6.2± 0.5	5.3± 0.4	5.3± 0.5	5.6± 0.3	5.6± 0.4
2000 ppm	5.9± 0.7	6.2± 0.7	5.5± 0.4	5.6± 0.5	5.8± 0.4*	5.9± 0.5
10000 ppm	5.4± 0.6	5.3± 0.5	4.8± 0.4	4.9± 0.5	4.9± 0.4	5.1± 0.3
50000 ppm	4.8± 0.5*	5.2± 0.5	4.6± 0.5	4.7± 0.6	4.9± 0.5	5.0± 0.4

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

APPENDIX B 3-1

CHEMICAL INTAKE CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

RAT : MALE

STUDY NO. : 0220
ANIMAL : RAT F344
UNIT : mg／kg／d a y
REPORT TYPE : A1 13
SEX : FEMALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 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
80 ppm	7.369± 0.174	6.711± 0.168	6.448± 0.224	6.053± 0.299	6.101± 0.309	5.624± 0.644	5.497± 0.379
400 ppm	35.914± 1.019	32.988± 0.691	31.730± 1.225	29.346± 1.329	29.970± 1.909	27.015± 2.448	26.390± 2.358
2000 ppm	171.924± 4.751	162.890± 5.558	159.725± 7.802	149.319± 6.634	150.835± 5.553	137.091± 10.017	142.279± 20.042
10000 ppm	821.486± 32.956	821.155± 24.610	785.231± 11.605	751.443± 17.617	731.835± 42.265	685.012± 31.909	666.523± 30.101
50000 ppm	3794.435±434.728	4078.684±150.780	3851.401±110.297	3678.666±149.281	3593.608±143.518	3350.914±125.476	3238.854±143.744

STUDY NO. : 0220
ANIMAL : RAT F344
UNIT : mg／kg／d a y
REPORT TYPE : A1 13
SEX : FEMALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 8	9	10	11	12	13
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
80 ppm	5.212± 0.401	5.258± 0.356	5.041± 0.322	5.283± 0.718	5.195± 0.585	4.967± 0.503
400 ppm	24.184± 1.833	26.503± 1.846	25.459± 1.534	25.358± 1.490	25.131± 1.462	24.524± 1.658
2000 ppm	124.776± 17.429	133.616± 12.231	127.534± 10.346	130.901± 12.990	123.405± 10.638	125.073± 9.610
10000 ppm	644.570± 29.676	653.828± 48.565	620.236± 40.380	619.376± 35.359	608.919± 37.308	608.133± 43.629
50000 ppm	3186.619±167.225	3129.161±175.771	3007.063±122.073	3068.219±168.998	2972.625±145.457	2982.145± 72.396

APPENDIX B 3-2

CHEMICAL INTAKE CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

RAT : FEMALE

STUDY NO. : 0220
ANIMAL : RAT F344
UNIT : mg／kg／d a y
REPORT TYPE : A1 13
SEX : MALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2	3	4	5	6	7
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
80 ppm	6.699± 0.246	5.996± 0.116	5.724± 0.188	5.311± 0.139	5.207± 0.404	4.917± 0.495	4.706± 0.476
400 ppm	33.437± 1.145	30.268± 1.184	28.439± 0.945	26.072± 1.048	25.638± 0.945	23.857± 1.246	22.594± 1.203
2000 ppm	162.212± 5.225	152.836± 4.640	140.118± 5.190	131.930± 4.997	129.063± 5.314	122.024± 4.088	113.783± 4.265
10000 ppm	776.510± 27.210	758.614± 23.535	714.509± 24.246	673.700± 18.092	642.993± 18.240	605.404± 29.105	576.097± 29.998
50000 ppm	3819.398±134.287	3949.602±186.325	3707.822±130.781	3498.271±180.360	3373.688±157.593	3209.896± 81.628	3082.101±100.507

STUDY NO. : 0220
ANIMAL : RAT F344
UNIT : mg／kg／d a y
REPORT TYPE : A1 13
SEX : MALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 8	9	10	11	12	13
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
80 ppm	4.581± 0.493	4.481± 0.406	4.198± 0.425	4.191± 0.347	4.054± 0.269	3.881± 0.169
400 ppm	21.900± 1.258	21.449± 1.327	20.253± 1.033	20.433± 1.210	20.037± 1.167	18.993± 1.000
2000 ppm	110.763± 3.234	107.470± 3.262	103.220± 3.619	102.025± 1.986	99.751± 2.218	96.280± 2.935
10000 ppm	554.594± 28.961	546.096± 27.926	521.193± 20.296	506.268± 23.504	503.935± 21.296	492.131± 23.495
50000 ppm	2971.365±107.786	2908.485±135.178	2785.560± 93.276	2707.184±101.142	2717.195±139.863	2633.802±128.922

APPENDIX B 3-3

CHEMICAL INTAKE CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : MALE

STUDY NO. : 0221
ANIMAL : MOUSE BDF1
UNIT : mg／kg／d a y
REPORT TYPE : A1 13
SEX : MALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2	3	4	5	6	7
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
80 ppm	17.304± 1.881	16.309± 1.726	15.244± 1.080	15.013± 1.463	15.457± 1.328	15.198± 1.263	14.768± 1.243
400 ppm	84.361± 6.845	78.114± 5.509	75.540± 5.729	75.227± 6.954	78.737± 7.084	77.530± 8.287	71.714± 5.506
2000 ppm	408.212± 52.231	399.938± 83.840	361.046± 40.516	365.129± 34.637	367.676± 28.811	368.714± 35.483	358.029± 29.826
10000 ppm	2034.693±121.993	1821.421±155.725	1713.126±134.984	1783.122±147.806	1875.077±149.567	1817.624±168.547	1736.161±150.808
50000 ppm	*267.765±*73.437	9405.179±740.400	8534.910±685.689	8708.264±506.385	9070.668±763.064	8324.477±538.489	8584.237±654.596

STUDY NO. : 0221
ANIMAL : MOUSE BDF1
UNIT : mg／kg／d a y
REPORT TYPE : A1 13
SEX : MALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 8	9	10	11	12	13
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
80 ppm	15.874± 1.755	15.450± 1.477	13.672± 1.422	12.025± 1.014	12.957± 1.447	13.531± 1.421
400 ppm	79.392± 8.160	79.453± 5.296	68.162± 5.632	64.621± 4.818	65.458± 6.665	67.240± 6.179
2000 ppm	372.396± 37.674	378.287± 45.903	333.195± 29.492	309.565± 16.992	320.411± 36.612	334.554± 39.476
10000 ppm	1961.336±214.833	1874.267±210.439	1683.198±164.898	1671.217±164.031	1642.983±139.241	1659.736±130.241
50000 ppm	8823.417±*26.416	9007.323±781.583	8160.849±531.633	8148.607±798.494	8145.578±666.421	8153.404±638.041

APPENDIX B 3-4

CHEMICAL INTAKE CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

MOUSE: FEMALE

STUDY NO. : 0221
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
80 ppm	21.693± 2.675	19.013± 0.917	19.794± 2.436	17.642± 1.154	21.053± 2.423	19.350± 3.029	20.065± 2.488
400 ppm	109.215± 10.903	95.689± 8.127	95.699± 7.219	95.275± 6.498	104.663± 6.103	94.010± 8.225	96.323± 8.640
2000 ppm	501.094± 73.264	459.544± 37.355	467.093± 45.042	474.987± 46.619	513.994± 44.435	490.263± 27.182	479.702± 28.942
10000 ppm	2414.325±270.390	2043.118±204.547	2057.446±286.116	2242.306±212.042	2343.675±250.702	2286.227±242.709	2209.745±142.630
50000 ppm	*565.124±*00.942	*594.923±*52.332	9725.681±658.670	*217.705±662.563	*211.009±*82.229	*099.360±*37.610	*796.601±*06.309

STUDY NO. : 0221
ANIMAL : MOUSE BDF1
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
80 ppm	21.490± 1.954	22.307± 2.500	19.458± 2.086	18.416± 1.827	19.048± 2.360	20.432± 2.680
400 ppm	104.843± 10.993	109.804± 10.691	90.104± 6.395	88.866± 5.532	93.056± 8.609	95.412± 9.175
2000 ppm	528.605± 45.690	548.770± 56.090	480.861± 20.899	477.944± 47.794	493.677± 48.599	506.879± 43.562
10000 ppm	2508.519±274.389	2490.555±297.964	2183.871±225.678	2186.191±191.321	2159.759±180.795	2300.698±140.614
50000 ppm	*425.927±*92.846	*147.738±*00.920	*543.254±*75.698	*743.175±*50.160	*263.036±*82.358	*376.418±954.392

APPENDIX B 4-1

HEMATOLOGY (THIRTEEN−WEEK STUDY: SUMMARY)

RAT : MALE

STUDY NO. : 0220
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 fℓ		MCH pg		MCHC g/dℓ		PLATELET $10^3/\mu\ell$	
Control	10	9.49±	0.30	16.6±	0.3	45.3±	1.1	47.7±	0.6	17.5±	0.6	36.6±	1.1	789±	42
80 ppm	10	9.40±	0.43	16.2±	0.4	45.2±	2.2	48.1±	0.4	17.3±	0.6	36.0±	1.3	829±	48
400 ppm	10	8.95±	0.26*	15.6±	0.5**	44.0±	1.4	49.1±	0.6**	17.4±	0.2	35.4±	0.3*	900±	44**
2000 ppm	10	8.87±	0.23*	15.4±	0.3**	44.1±	1.2	49.7±	0.6**	17.4±	0.2	34.9±	0.5**	924±	33**
10000 ppm	9	8.70±	0.12**	15.2±	0.3**	43.1±	0.5*	49.5±	0.6**	17.5±	0.3	35.3±	0.4*	974±	35**
50000 ppm	10	8.49±	0.29**	15.0±	0.3**	41.7±	1.5**	49.1±	0.4**	17.7±	0.8	36.0±	1.7	1004±	60**

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

STUDY NO. : 0220
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	33±	7	16.2±	1.1	25.6±	2.9
80 ppm	10	35±	8	16.5±	1.4	25.7±	3.7
400 ppm	10	49±	7**	17.6±	1.9	25.4±	2.7
2000 ppm	10	59±	11**	19.3±	2.2*	27.6±	2.3
10000 ppm	9	59±	7**	23.8±	3.6**	29.0±	1.9
50000 ppm	10	55±	8**	26.2±	4.2**	33.0±	4.1**

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

STUDY NO. : 0220
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	OTHER
Control	10	5.88± 1.81	0± 0	24± 4	2± 1	0± 0	4± 1	70± 4	0± 0
80 ppm	10	5.50± 1.83	0± 0	25± 5	2± 1	0± 0	4± 2	69± 6	0± 0
400 ppm	10	5.87± 1.98	0± 0	26± 4	1± 1	0± 0	3± 1	69± 4	0± 0
2000 ppm	10	6.73± 2.02	0± 0	23± 6	1± 1	0± 0	4± 1	72± 6	0± 0
10000 ppm	9	7.00± 1.21	0± 0	25± 6	1± 1	0± 0	4± 2	70± 6	0± 0
50000 ppm	10	6.84± 1.23	0± 0	29± 5	1± 1	0± 0	4± 2	66± 5	0± 0

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

APPENDIX B 4-2

HEMATOLOGY (THIRTEEN−WEEK STUDY: SUMMARY)

RAT: FEMALE

STUDY NO. : 0220
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 fℓ		MCH pg		MCHC g/dℓ		PLATELET $10^3/\mu\ell$	
Control	10	8.62±	0.42	16.2±	0.6	43.8±	2.4	50.8±	0.4	18.9±	0.9	37.1±	2.0	841±	50
80 ppm	10	8.31±	0.15	15.5±	0.3**	42.9±	0.8	51.7±	0.4**	18.6±	0.1	36.1±	0.4	893±	42
400 ppm	10	7.89±	0.34**	15.0±	0.5**	42.0±	1.9	53.2±	0.6**	19.0±	0.5	35.8±	1.0*	931±	40**
2000 ppm	9	7.60±	0.27**	14.6±	0.5**	40.9±	1.7**	53.8±	0.6**	19.1±	0.4**	35.6±	1.1**	955±	40**
10000 ppm	10	7.62±	0.27**	14.6±	0.4**	40.7±	1.4**	53.5±	0.4**	19.2±	0.7*	35.9±	1.1*	1007±	77**
50000 ppm	9	7.63±	0.26**	14.4±	0.4**	40.4±	1.5**	52.9±	0.6**	18.8±	0.5	35.6±	1.2**	1055±	74**

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

STUDY NO. : 0220
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

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

Group Name	NO. of Animals	RETICULOCYTE ‰		PROTHROMBIN TIME sec		APTT sec	
Control	10	31±	5	12.3±	0.5	18.9±	2.0
80 ppm	10	43±	7*	12.1±	0.6	18.9±	2.0
400 ppm	10	61±	7**	12.0±	0.5	19.5±	2.8
2000 ppm	9	78±	7**	11.9±	0.4	22.1±	3.8*
10000 ppm	10	70±	12**	13.0±	1.0	25.5±	1.3**
50000 ppm	9	73±	12**	13.3±	1.8	25.9±	3.1**

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

STUDY NO. : 0220
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		OTHER	
Control	10	3.61±	1.28	0±	1	25±	7	2±	1	0±	0	4±	2	69±	7	0±	0
80 ppm	10	3.27±	1.01	0±	0	24±	6	1±	1	0±	0	4±	1	70±	6	0±	0
400 ppm	10	3.79±	0.88	0±	0	23±	7	1±	1	0±	0	3±	2	72±	6	0±	0
2000 ppm	9	3.04±	1.14	0±	1	23±	6	1±	1	0±	0	4±	2	72±	7	0±	0
10000 ppm	10	3.78±	1.88	0±	0	18±	3	1±	1	0±	0	4±	1	77±	3	0±	0
50000 ppm	9	3.70±	1.06	0±	1	25±	8	1±	1	0±	0	4±	1	70±	8	0±	0

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

APPENDIX B 4-3

HEMATOLOGY (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : MALE

STUDY NO. : 0221
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$		HEMOGLOBIN g/dℓ		HEMATOCRIT %		MCV f ℓ		MCH p g		MCHC g/dℓ		PLATELET $10^3/\mu\ell$	
Control	10	10.54±	0.34	15.6±	0.4	46.4±	1.5	44.0±	0.4	14.8±	0.2	33.7±	0.6	1475±	119
80 ppm	9	10.31±	0.45	15.3±	0.2	45.3±	2.1	44.0±	0.5	14.8±	0.6	33.8±	1.5	1462±	92
400 ppm	9	10.44±	0.16	15.4±	0.3	46.1±	1.0	44.2±	0.3	14.7±	0.2	33.4±	0.6	1571±	64
2000 ppm	10	10.01±	0.83	14.9±	0.9	44.4±	3.7	44.3±	0.7	14.9±	0.6	33.7±	1.2	1584±	220
10000 ppm	9	9.67±	0.25**	14.5±	0.4**	43.9±	1.3**	45.4±	0.6**	15.0±	0.2	33.0±	0.5	1753±	86**
50000 ppm	9	9.21±	0.11**	14.0±	0.3**	42.8±	0.6**	46.5±	0.6**	15.2±	0.3*	32.8±	0.4*	2336±	186**

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

STUDY NO. : 0221
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		OTHER	
Control	10	1.73±	0.80	0±	0	16±	5	1±	1	0±	0	4±	2	79±	5	0±	0
80 ppm	9	1.66±	0.80	0±	0	15±	2	1±	1	0±	0	4±	2	80±	2	0±	0
400 ppm	9	1.47±	0.59	0±	0	18±	6	2±	1	0±	0	3±	1	77±	6	0±	0
2000 ppm	10	1.24±	0.44	0±	1	18±	5	1±	1	0±	0	3±	1	78±	5	0±	0
10000 ppm	9	0.90±	0.46*	0±	1	21±	4	1±	1	0±	0	2±	1*	75±	4	0±	0
50000 ppm	9	1.05±	0.49	0±	1	33±	12**	0±	0*	0±	0	2±	1*	64±	13**	0±	0

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

APPENDIX B 4-4

HEMATOLOGY (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : FEMALE

STUDY NO. : 0221
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	10.24± 0.34	15.5± 0.4	45.3± 1.7	44.2± 0.6	15.2± 0.5	34.3± 1.3	1199± 101
80 ppm	10	10.42± 0.39	15.7± 0.4	46.1± 1.6	44.2± 0.5	15.1± 0.4	34.1± 0.7	1245± 104
400 ppm	7	10.41± 0.20	15.5± 0.4	46.3± 1.0	44.5± 0.7	14.9± 0.2	33.5± 0.8	1244± 148
2000 ppm	10	9.92± 0.55	15.1± 0.4	44.1± 2.5	44.5± 0.7	15.3± 0.7	34.3± 1.5	1275± 124
10000 ppm	10	9.84± 0.54	15.2± 0.4	44.6± 2.5	45.3± 0.8**	15.5± 1.0	34.2± 2.3	1475± 123**
50000 ppm	10	9.38± 0.29**	14.6± 0.4**	43.6± 1.6	46.5± 0.7**	15.6± 0.3*	33.6± 0.7	1585± 57**

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

STUDY NO. : 0221
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		OTHER	
Control	10	1.78±	0.74	0±	1	15±	3	2±	1	0±	0	3±	1	80±	4	0±	0
80 ppm	10	1.16±	0.46	0±	0	17±	4	1±	1	0±	0	3±	1	79±	4	0±	0
400 ppm	7	1.38±	0.83	0±	0	17±	4	1±	1	0±	0	3±	1	79±	3	0±	0
2000 ppm	10	1.00±	0.46	0±	0	19±	5	1±	2	0±	0	3±	2	77±	4	0±	0
10000 ppm	10	0.91±	0.50*	1±	1	18±	6	1±	1	0±	0	2±	1	79±	7	0±	0
50000 ppm	10	0.56±	0.24**	1±	1	23±	8**	0±	1	0±	0	2±	1	74±	7	0±	0

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

APPENDIX B 5-1

BIOCHEMISTRY (THIRTEEN−WEEK STUDY: SUMMARY)

RAT : MALE

STUDY NO. : 0220
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	6.7± 0.1	3.9± 0.1	1.4± 0.0	0.23± 0.04	191± 14	58± 4	89± 27
80 ppm	10	6.7± 0.2	3.9± 0.1	1.4± 0.1	0.22± 0.06	186± 15	58± 3	98± 40
400 ppm	10	6.6± 0.1	3.8± 0.1	1.4± 0.1	0.21± 0.05	183± 10	58± 2	81± 22
2000 ppm	10	6.5± 0.2	3.8± 0.1	1.4± 0.1	0.23± 0.04	183± 14	65± 4**	89± 10
10000 ppm	9	6.7± 0.2	3.9± 0.1	1.4± 0.1	0.22± 0.04	184± 10	73± 5**	83± 10
50000 ppm	10	7.1± 0.2**	4.1± 0.1**	1.4± 0.0	0.22± 0.03	188± 9	80± 6**	71± 29

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

STUDY NO. : 0220
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	116± 9	88± 22	29± 8	160± 44	310± 24	1± 0	83± 9
80 ppm	10	116± 11	74± 15	23± 3	148± 74	308± 17	1± 1	92± 18
400 ppm	10	117± 9	61± 6	18± 1*	118± 25	305± 23	1± 1	86± 10
2000 ppm	10	131± 7	60± 6*	18± 2**	133± 29	302± 22	1± 0	94± 14
10000 ppm	9	143± 8**	52± 3**	16± 1**	118± 32	281± 23*	1± 0	83± 12
50000 ppm	10	159± 18**	51± 3**	17± 2**	141± 26	267± 23**	1± 1	88± 9

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

STUDY NO. : 0220
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	17.5± 1.2	0.5± 0.1	142± 1	3.4± 0.2	106± 1	10.4± 0.1	5.4± 0.5
80 ppm	10	16.2± 1.0	0.5± 0.0	143± 2	3.4± 0.3	105± 2	10.4± 0.3	5.5± 0.9
400 ppm	10	16.2± 1.3	0.5± 0.1	143± 1	3.5± 0.3	105± 1	10.4± 0.1	5.7± 0.7
2000 ppm	10	16.1± 1.3*	0.5± 0.1	143± 2	3.5± 0.3	105± 2	10.4± 0.2	5.8± 0.8
10000 ppm	9	16.4± 0.5	0.5± 0.1	143± 1	3.5± 0.1	105± 2	10.6± 0.2	5.5± 0.5
50000 ppm	10	17.5± 1.4	0.5± 0.1	143± 2	3.8± 0.2*	103± 1**	10.9± 0.2**	5.6± 0.4

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

APPENDIX B 5-2

BIOCHEMISTRY(THIRTEEN−WEEK STUDY: SUMMARY)

RAT : FEMALE

STUDY NO. : 0220
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (14)

Group Name	NO. of Animals	TOTAL PROTEIN g/dℓ	ALBUMIN g/dℓ	A/G RATIO	T-BILIRUBIN mg/dℓ	GLUCOSE mg/dℓ	T-CHOLESTEROL mg/dℓ	TRIGLYCERIDE mg/dℓ
Control	10	6.4± 0.2	3.7± 0.1	1.4± 0.1	0.35± 0.16	138± 15	76± 6	38± 4
80 ppm	10	6.5± 0.2	3.8± 0.1	1.4± 0.1	0.33± 0.08	141± 13	79± 4	39± 5
400 ppm	10	6.4± 0.3	3.7± 0.2	1.4± 0.1	0.31± 0.08	138± 15	78± 9	35± 4
2000 ppm	9	6.6± 0.3	3.8± 0.2	1.4± 0.1	0.32± 0.05	139± 18	91± 6	33± 4*
10000 ppm	10	6.9± 0.3**	3.9± 0.1	1.3± 0.1	0.31± 0.11	140± 16	107± 6**	33± 3*
50000 ppm	9	7.2± 0.3**	4.1± 0.2**	1.3± 0.1**	0.27± 0.04	132± 11	121± 12**	30± 3**

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

STUDY NO. : 0220
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (14)

Group Name	NO. of Animals	PHOSPHOLIPID mg/dℓ	GOT IU/ℓ	GPT IU/ℓ	LDH IU/ℓ	ALP IU/ℓ	G-GTP IU/ℓ	CPK IU/ℓ
Control	10	143± 11	74± 9	23± 4	256± 121	234± 23	1± 1	121± 31
80 ppm	10	150± 8	75± 25	25± 15	236± 92	226± 20	1± 1	112± 32
400 ppm	10	148± 18	69± 13	20± 8	243± 94	210± 30	1± 1	117± 24
2000 ppm	9	165± 11**	75± 23	20± 7	315± 139	187± 19**	1± 1	136± 26
10000 ppm	10	187± 14**	57± 3**	15± 1**	216± 86	162± 16**	1± 1	108± 26
50000 ppm	9	210± 20**	49± 3**	13± 1**	197± 45	163± 15**	3± 1**	101± 17

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

STUDY NO. : 0220
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (14)

Group Name	NO. of Animals	UREA NITROGEN mg/dl	CREATININE mg/dl	SODIUM mEq/l	POTASSIUM mEq/l	CHLORIDE mEq/l	CALCIUM mg/dl	INORGANIC PHOSPHORUS mg/dl
Control	10	16.4± 1.8	0.5± 0.1	143± 1	3.3± 0.3	108± 1	10.0± 0.2	5.1± 1.2
80 ppm	10	16.9± 2.2	0.5± 0.1	143± 2	3.3± 0.3	108± 1	10.1± 0.2	5.2± 1.4
400 ppm	10	17.1± 1.6	0.4± 0.1	143± 1	3.5± 0.3	108± 2	10.0± 0.2	5.1± 1.0
2000 ppm	9	16.8± 2.1	0.5± 0.1	143± 2	3.5± 0.4	107± 2	10.2± 0.3	5.5± 1.1
10000 ppm	10	16.3± 1.6	0.5± 0.1	143± 1	3.5± 0.3	107± 2	10.3± 0.4*	5.1± 1.1
50000 ppm	9	18.0± 2.6	0.5± 0.1	143± 1	3.8± 0.4**	106± 1*	10.6± 0.3**	5.4± 0.7

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

APPENDIX B 5-3

BIOCHEMISTRY (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : MALE

STUDY NO. : 0221
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± 0.1	2.9± 0.1	1.2± 0.0	0.33± 0.11	263± 33	85± 7	53± 14
80 ppm	9	5.2± 0.2	2.8± 0.1	1.2± 0.1	0.35± 0.10	239± 52	83± 12	55± 18
400 ppm	9	5.3± 0.2	2.9± 0.1	1.2± 0.1	0.30± 0.09	211± 56	89± 7	57± 16
2000 ppm	10	5.4± 0.2	3.0± 0.1*	1.2± 0.0	0.34± 0.14	213± 42	97± 11*	61± 14
10000 ppm	9	5.4± 0.1	3.0± 0.1**	1.3± 0.1	0.38± 0.07	183± 43**	86± 8	56± 19
50000 ppm	9	5.0± 0.2**	2.7± 0.1**	1.2± 0.1	0.32± 0.11	148± 31**	86± 9	61± 8

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

STUDY NO. : 0221
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	38±	6	10±	3	207±	76	188±	9	49±	28	26.4±	4.7	153±	2
80 ppm	9	40±	6	12±	3	200±	32	199±	23	42±	11	27.4±	5.5	153±	2
400 ppm	9	36±	2	11±	2	184±	27	179±	9	42±	12	29.0±	5.2	153±	2
2000 ppm	10	41±	9	12±	2	236±	71	175±	19	64±	64	26.6±	2.7	153±	2
10000 ppm	9	36±	5	11±	2	191±	32	164±	10**	32±	7	25.6±	3.6	154±	2
50000 ppm	9	41±	7	12±	2	197±	36	142±	16**	40±	16	24.4±	3.2	155±	2**

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

STUDY NO. : 0221
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	4.2± 0.2	120± 2	8.8± 0.2	6.7± 1.1
80 ppm	9	4.3± 0.2	120± 2	8.8± 0.3	6.9± 1.1
400 ppm	9	4.3± 0.4	121± 3	8.8± 0.2	6.6± 0.7
2000 ppm	10	4.2± 0.6	120± 2	9.0± 0.4	5.9± 0.7
10000 ppm	9	4.0± 0.3	121± 2	9.1± 0.1**	5.8± 0.7
50000 ppm	9	4.0± 0.3	121± 2	9.0± 0.4	6.3± 0.9

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

APPENDIX B 5-4

BIOCHEMISTRY (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : FEMALE

STUDY NO. : 0221
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	5.2± 0.1	3.0± 0.0	1.4± 0.1	0.38± 0.15	184± 38	71± 6	40± 8
80 ppm	10	5.2± 0.3	3.1± 0.2	1.5± 0.1	0.42± 0.19	157± 28	66± 7	37± 4
400 ppm	7	5.2± 0.2	3.1± 0.2	1.5± 0.1	0.41± 0.11	159± 35	64± 8	38± 6
2000 ppm	10	5.2± 0.2	3.1± 0.1	1.5± 0.1	0.33± 0.09	157± 41	66± 9	44± 7
10000 ppm	10	5.3± 0.2	3.3± 0.1**	1.6± 0.2**	0.42± 0.09	145± 24*	64± 7	46± 7
50000 ppm	10	5.3± 0.1	3.2± 0.1**	1.6± 0.1**	0.44± 0.10	133± 26**	52± 5**	38± 6

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

STUDY NO. : 0221
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	47± 6	13± 2	271± 66	278± 31	80± 61	19.3± 1.7	153± 2
80 ppm	10	50± 6	13± 2	291± 95	301± 35	54± 14	19.9± 2.5	154± 3
400 ppm	7	49± 9	13± 3	270± 76	277± 24	52± 20	20.5± 1.8	153± 2
2000 ppm	10	53± 15	13± 4	276± 106	268± 33	68± 52	20.2± 2.3	156± 2
10000 ppm	10	57± 14	14± 3	293± 83	266± 23	56± 44	20.9± 2.0	154± 3
50000 ppm	10	56± 10	14± 2	276± 36	267± 20	50± 26	22.9± 1.9**	155± 1

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

Group Name	NO. of Animals	POTASSIUM mEq／ℓ		CHLORIDE mEq／ℓ		CALCIUM mg／dℓ		INORGANIC PHOSPHORUS mg／dℓ	
Control	10	4.5±	0.3	118±	3	8.7±	0.4	5.9±	0.8
80 ppm	10	4.5±	0.5	119±	5	8.7±	0.4	5.9±	1.0
400 ppm	7	4.5±	0.5	121±	3	8.8±	0.3	6.0±	1.1
2000 ppm	10	4.2±	0.3	121±	1	8.8±	0.4	6.0±	1.2
10000 ppm	10	4.2±	0.3	119±	4	8.9±	0.5	5.9±	0.8
50000 ppm	10	3.9±	0.4**	120±	3	9.0±	0.2	6.6±	0.6

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

APPENDIX B 6-1

URINALYSIS (THIRTEEN−WEEK STUDY: SUMMARY)

RAT : MALE

STUDY NO. : 0220
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	3	7	0		0	0	3	7	0	0		10	0	0	0	0	0		0	9	1	0	0	0		10	0	0	0	
80 ppm	10	0	0	0	0	3	6	1		0	0	4	6	0	0		10	0	0	0	0	0		1	9	0	0	0	0		10	0	0	0	
400 ppm	10	0	0	0	0	6	4	0		0	0	3	7	0	0		10	0	0	0	0	0		0	9	1	0	0	0		10	0	0	0	
2000 ppm	10	0	0	0	0	5	5	0		0	0	1	9	0	0		10	0	0	0	0	0		0	9	1	0	0	0		10	0	0	0	
10000 ppm	10	0	0	0	0	6	4	0		0	0	2	8	0	0		10	0	0	0	0	0		0	9	1	0	0	0		10	0	0	0	
50000 ppm	10	0	0	0	2	5	3	0		0	0	1	9	0	0		10	0	0	0	0	0		0	10	0	0	0	0		10	0	0	0	

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

STUDY NO. : 0220
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	9	0	0	1	0		10	0	0	0	0	
80 ppm	10	10	0	0	0	0		10	0	0	0	0	
400 ppm	10	10	0	0	0	0		10	0	0	0	0	
2000 ppm	10	10	0	0	0	0		10	0	0	0	0	
10000 ppm	10	10	0	0	0	0		10	0	0	0	0	
50000 ppm	10	10	0	0	0	0		10	0	0	0	0	

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

APPENDIX B 6-2

URINALYSIS (THIRTEEN−WEEK STUDY: SUMMARY)

RAT : FEMALE

STUDY NO. : 0220
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	4	6	0		0	2	6	2	0	0		10	0	0	0	0	0		7	3	0	0	0	0		10	0	0	0	
80 ppm	10	0	0	1	1	2	6	0		1	1	6	2	0	0		10	0	0	0	0	0		7	2	1	0	0	0		10	0	0	0	
400 ppm	10	0	0	1	0	2	7	0		0	3	5	2	0	0		10	0	0	0	0	0		8	2	0	0	0	0		10	0	0	0	
2000 ppm	10	0	0	0	2	3	4	1		1	3	5	1	0	0		10	0	0	0	0	0		5	5	0	0	0	0		10	0	0	0	
10000 ppm	10	0	0	1	1	4	3	1		0	2	6	2	0	0		10	0	0	0	0	0		8	2	0	0	0	0		10	0	0	0	
50000 ppm	10	0	1	1	2	2	4	0		0	4	5	1	0	0		10	0	0	0	0	0		7	3	0	0	0	0		10	0	0	0	

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

STUDY NO. : 0220 URINALYSIS
ANIMAL : RAT F344
SAMPLING DATE : 013-6
SEX : FEMALE REPORT TYPE : A1

Group Name	NO. of Animals	Occult blood −	±	+	2+	3+	CHI	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0		10	0	0	0	0	
80 ppm	10	10	0	0	0	0		10	0	0	0	0	
400 ppm	10	10	0	0	0	0		10	0	0	0	0	
2000 ppm	10	10	0	0	0	0		10	0	0	0	0	
10000 ppm	10	10	0	0	0	0		10	0	0	0	0	
50000 ppm	10	10	0	0	0	0		10	0	0	0	0	

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

APPENDIX B 6-3

URINALYSIS (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : MALE

STUDY NO. : 0221
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	4	4	2	0	0		0	0	5	5	0	0		10	0	0	0	0	0		3	7	0	0	0	0		10	0	0	0	0	
80 ppm	10	0	0	2	5	3	0	0		0	0	8	2	0	0		10	0	0	0	0	0		6	4	0	0	0	0		10	0	0	0	0	
400 ppm	10	0	0	4	5	1	0	0		0	1	8	0	1	0		10	0	0	0	0	0		8	2	0	0	0	0	*	10	0	0	0	0	
2000 ppm	10	0	0	2	7	1	0	0		0	1	7	2	0	0		10	0	0	0	0	0		6	4	0	0	0	0		10	0	0	0	0	
10000 ppm	10	0	0	2	5	3	0	0		0	0	6	4	0	0		10	0	0	0	0	0		6	4	0	0	0	0		10	0	0	0	0	
50000 ppm	10	0	0	1	5	4	0	0		0	0	7	3	0	0		10	0	0	0	0	0		4	6	0	0	0	0		10	0	0	0	0	

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

STUDY NO. : 0221 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	
80 ppm	10	10	0	0	0	0	
400 ppm	10	10	0	0	0	0	
2000 ppm	10	10	0	0	0	0	
10000 ppm	10	10	0	0	0	0	
50000 ppm	10	10	0	0	0	0	

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

APPENDIX B 6-4

URINALYSIS (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : FEMALE

STUDY NO. : 0221
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	1	5	3	1	0	0		0	1	8	1	0	0		10	0	0	0	0	0		4	6	0	0	0	0		10	0	0	0	0	
80 ppm	10	0	1	1	6	2	0	0		0	4	6	0	0	0		10	0	0	0	0	0		4	6	0	0	0	0		10	0	0	0	0	
400 ppm	9	0	0	5	4	0	0	0		0	1	7	1	0	0		9	0	0	0	0	0		4	5	0	0	0	0		9	0	0	0	0	
2000 ppm	10	0	0	7	3	0	0	0		0	1	8	1	0	0		10	0	0	0	0	0		3	5	2	0	0	0		10	0	0	0	0	
10000 ppm	10	0	1	3	4	2	0	0		0	0	10	0	0	0		10	0	0	0	0	0		2	6	2	0	0	0		10	0	0	0	0	
50000 ppm	10	0	1	5	1	3	0	0		0	1	8	1	0	0		10	0	0	0	0	0		2	7	1	0	0	0		10	0	0	0	0	

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

STUDY NO. : 0221
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	
80 ppm	10	10	0	0	0	0	
400 ppm	9	9	0	0	0	0	
2000 ppm	10	10	0	0	0	0	
10000 ppm	10	10	0	0	0	0	
50000 ppm	10	10	0	0	0	0	

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

APPENDIX B 7-1

GROSS FINDINGS (THIRTEEN−WEEK STUDY: SUMMARY)

RAT : MALE :SACRIFICED ANIMALS

STUDY NO. : 0220
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	80 ppm 10 (%)	400 ppm 10 (%)	2000 ppm 10 (%)
spleen	dark		0 (0)	0 (0)	5 (50)	10 (100)

STUDY NO. : 0220
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name NO. of Animals	10000 ppm 10 (%)	50000 ppm 10 (%)
spleen	dark		10 (100)	10 (100)

APPENDIX B 7-2

GROSS FINDINGS (THIRTEEN−WEEK STUDY: SUMMARY)

RAT : FEMALE :SACRIFICED ANIMALS

STUDY NO. : 0220
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	80 ppm 10 (%)	400 ppm 10 (%)	2000 ppm 10 (%)
spleen	dark		0 (0)	0 (0)	10 (100)	10 (100)
liver	herniation		1 (10)	0 (0)	0 (0)	0 (0)
kidney	white zone		0 (0)	0 (0)	0 (0)	1 (10)
ovary	cyst		0 (0)	1 (10)	0 (0)	1 (10)

STUDY NO. : 0220
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name NO. of Animals	10000 ppm 10 (%)	50000 ppm 10 (%)
spleen	dark		10 (100)	10 (100)
liver	herniation		0 (0)	0 (0)
kidney	white zone		0 (0)	0 (0)
ovary	cyst		0 (0)	1 (10)

APPENDIX B 7-3

GROSS FINDINGS (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : FEMALE DEAD AND MORIBUND ANIMALS

STUDY NO. : 0221
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name NO. of Animals	Control 0 (%)	80 ppm 0 (%)	400 ppm 1 (%)	2000 ppm 0 (%)
thymus	atrophic		- (-)	- (-)	1 (100)	- (-)

STUDY NO. : 0221
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name NO. of Animals	10000 ppm 0 (%)	50000 ppm 0 (%)
thymus	atrophic		- (-)	- (-)

APPENDIX B 7-4

GROSS FINDINGS (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : MALE :SACRIFICED ANIMALS

STUDY NO. : 0221
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	80 ppm 10 (%)	400 ppm 10 (%)	2000 ppm 10 (%)
spleen	dark		0 (0)	0 (0)	0 (0)	0 (0)
	black zone		1 (10)	0 (0)	0 (0)	0 (0)
kidney	hydronephrosis		0 (0)	1 (10)	0 (0)	1 (10)

Organ	Findings	Group Name NO. of Animals	10000 ppm 10 (%)	50000 ppm 10 (%)
spleen	dark		0 (0)	10 (100)
	black zone		0 (0)	0 (0)
kidney	hydronephrosis		0 (0)	0 (0)

APPENDIX B 7-5

GROSS FINDINGS (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : FEMALE :SACRIFICED ANIMALS

STUDY NO. : 0221
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	80 ppm 10 (%)	400 ppm 9 (%)	2000 ppm 10 (%)
spleen	dark		0 (0)	0 (0)	0 (0)	0 (0)
	black zone		0 (0)	0 (0)	0 (0)	1 (10)
ovary	cyst		1 (10)	0 (0)	0 (0)	0 (0)

STUDY NO. : 0221
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name NO. of Animals	10000 ppm 10 (%)	50000 ppm 10 (%)
spleen	dark		0 (0)	10 (100)
	black zone		2 (20)	0 (0)
ovary	cyst		0 (0)	0 (0)

APPENDIX B 8-1

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

RAT : MALE

STUDY NO. : 0220
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	314± 11	0.218± 0.015	0.053± 0.006	2.857± 0.174	0.945± 0.044	1.032± 0.064
80 ppm	10	322± 16	0.239± 0.027	0.052± 0.004	2.938± 0.088	0.957± 0.069	1.029± 0.040
400 ppm	10	311± 28	0.213± 0.049	0.056± 0.006	2.980± 0.098	0.920± 0.079	1.027± 0.066
2000 ppm	10	306± 18	0.195± 0.016	0.056± 0.005	2.980± 0.066	0.905± 0.077	1.033± 0.045
10000 ppm	10	300± 23	0.202± 0.024	0.057± 0.006	3.050± 0.096**	0.901± 0.055	1.031± 0.091
50000 ppm	10	299± 9*	0.184± 0.017**	0.058± 0.005	3.114± 0.089**	0.893± 0.032	1.017± 0.044

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

STUDY NO. : 0220
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	1.920± 0.085	0.537± 0.023	8.008± 0.386	1.896± 0.025
80 ppm	10	1.980± 0.104	0.581± 0.040	8.266± 0.441	1.899± 0.053
400 ppm	10	2.064± 0.169	0.615± 0.067*	8.272± 0.785	1.880± 0.056
2000 ppm	10	2.084± 0.133*	0.641± 0.045**	8.856± 0.478**	1.892± 0.070
10000 ppm	10	2.109± 0.185*	0.648± 0.049**	9.992± 0.730**	1.916± 0.051
50000 ppm	10	2.136± 0.105**	0.644± 0.031**	11.909± 0.510**	1.920± 0.038

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

APPENDIX B 8-2

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

RAT : FEMALE

STUDY NO. : 0220
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	181± 10	0.194± 0.016	0.059± 0.007	0.111± 0.020	0.643± 0.072	0.766± 0.037
80 ppm	10	182± 6	0.197± 0.016	0.058± 0.004	0.116± 0.016	0.635± 0.056	0.776± 0.055
400 ppm	10	170± 14	0.170± 0.021*	0.055± 0.007	0.106± 0.013	0.608± 0.041	0.769± 0.043
2000 ppm	10	170± 6	0.178± 0.027	0.057± 0.004	0.106± 0.012	0.619± 0.055	0.785± 0.046
10000 ppm	10	164± 4**	0.160± 0.017**	0.054± 0.005	0.111± 0.006	0.605± 0.026	0.780± 0.030
50000 ppm	10	154± 7**	0.161± 0.024**	0.055± 0.004	0.103± 0.025	0.559± 0.036**	0.713± 0.022*

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

STUDY NO. : 0220
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	1.233± 0.069	0.365± 0.023	4.276± 0.304	1.759± 0.033
80 ppm	10	1.258± 0.064	0.397± 0.028	4.375± 0.149	1.747± 0.063
400 ppm	10	1.267± 0.094	0.446± 0.046**	4.318± 0.331	1.767± 0.042
2000 ppm	10	1.289± 0.078	0.492± 0.028**	4.923± 0.275**	1.764± 0.060
10000 ppm	10	1.229± 0.039	0.473± 0.030**	5.235± 0.204**	1.779± 0.032
50000 ppm	10	1.189± 0.054	0.433± 0.028**	6.127± 0.317**	1.764± 0.025

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

APPENDIX B 8-3

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

MOUSE: MALE

STUDY NO. : 0221
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	30.9± 1.8	0.043± 0.009	0.010± 0.004	0.200± 0.033	0.139± 0.007	0.160± 0.011
80 ppm	10	30.2± 3.3	0.035± 0.006*	0.009± 0.005	0.207± 0.030	0.139± 0.011	0.156± 0.011
400 ppm	10	30.0± 1.9	0.035± 0.006*	0.009± 0.004	0.200± 0.036	0.143± 0.009	0.155± 0.014
2000 ppm	10	28.3± 2.2	0.037± 0.005	0.009± 0.004	0.195± 0.020	0.144± 0.014	0.147± 0.009*
10000 ppm	10	25.7± 2.2**	0.033± 0.005**	0.009± 0.003	0.187± 0.023	0.136± 0.019	0.151± 0.010
50000 ppm	10	23.4± 0.9**	0.030± 0.005**	0.010± 0.003	0.187± 0.032	0.127± 0.012	0.143± 0.006**

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

STUDY NO. : 0221
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	0.416± 0.017	0.046± 0.005	1.046± 0.074	0.455± 0.015
80 ppm	10	0.610± 0.601	0.047± 0.006	1.045± 0.072	0.456± 0.013
400 ppm	10	0.403± 0.016	0.045± 0.003	1.102± 0.054	0.458± 0.013
2000 ppm	10	0.425± 0.110	0.048± 0.010	1.094± 0.086	0.454± 0.015
10000 ppm	10	0.383± 0.022*	0.043± 0.007	1.085± 0.102	0.450± 0.016
50000 ppm	10	0.363± 0.016**	0.068± 0.006**	1.100± 0.051	0.457± 0.009

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

APPENDIX B 8-4

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

MOUSE: FEMALE

STUDY NO. : 0221
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	21.7± 1.8	0.044± 0.006	0.012± 0.003	0.016± 0.007	0.116± 0.006	0.153± 0.015
80 ppm	10	20.7± 1.2	0.039± 0.006	0.011± 0.004	0.021± 0.005	0.116± 0.007	0.146± 0.013
400 ppm	9	20.9± 1.1	0.042± 0.006	0.013± 0.002	0.022± 0.006	0.123± 0.010	0.152± 0.010
2000 ppm	10	20.7± 1.2	0.040± 0.007	0.011± 0.002	0.019± 0.003	0.119± 0.013	0.140± 0.010*
10000 ppm	10	19.4± 1.2**	0.037± 0.005	0.011± 0.002	0.019± 0.005	0.113± 0.008	0.144± 0.008
50000 ppm	10	19.2± 0.7**	0.040± 0.004	0.012± 0.002	0.017± 0.006	0.110± 0.006	0.134± 0.007**

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

STUDY NO. : 0221
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	0.295± 0.014	0.050± 0.006	0.858± 0.086	0.465± 0.017
80 ppm	10	0.280± 0.018	0.047± 0.007	0.813± 0.062	0.465± 0.015
400 ppm	9	0.307± 0.014	0.049± 0.009	0.850± 0.056	0.464± 0.014
2000 ppm	10	0.292± 0.018	0.050± 0.008	0.850± 0.067	0.475± 0.010
10000 ppm	10	0.280± 0.014	0.045± 0.007	0.830± 0.054	0.469± 0.016
50000 ppm	10	0.274± 0.012*	0.055± 0.005	0.901± 0.043	0.465± 0.015

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

APPENDIX B 9-1

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

RAT : MALE

STUDY NO. : 0220
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	314± 11	0.070± 0.005	0.017± 0.002	0.910± 0.053	0.301± 0.014	0.328± 0.015
80 ppm	10	322± 16	0.074± 0.008	0.016± 0.002	0.913± 0.042	0.297± 0.018	0.320± 0.014
400 ppm	10	311± 28	0.068± 0.013	0.018± 0.003	0.963± 0.065	0.296± 0.014	0.331± 0.022
2000 ppm	10	306± 18	0.064± 0.003	0.019± 0.002	0.977± 0.047*	0.296± 0.012	0.339± 0.020
10000 ppm	10	300± 23	0.067± 0.005	0.019± 0.002*	1.023± 0.064**	0.302± 0.013	0.344± 0.014
50000 ppm	10	299± 9*	0.061± 0.005**	0.020± 0.002**	1.044± 0.037**	0.298± 0.010	0.341± 0.010

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

STUDY NO. : 0220
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	0.611± 0.021	0.171± 0.006	2.549± 0.087	0.604± 0.022
80 ppm	10	0.615± 0.021	0.180± 0.007*	2.566± 0.068	0.590± 0.026
400 ppm	10	0.664± 0.030**	0.197± 0.007**	2.658± 0.069*	0.608± 0.044
2000 ppm	10	0.682± 0.020**	0.210± 0.006**	2.897± 0.070**	0.621± 0.047
10000 ppm	10	0.704± 0.029**	0.216± 0.007**	3.338± 0.057**	0.642± 0.039
50000 ppm	10	0.715± 0.027**	0.215± 0.008**	3.988± 0.123**	0.643± 0.021

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

APPENDIX B 9-2

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

RAT : FEMALE

STUDY NO. : 0220
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	181± 10	0.108± 0.009	0.032± 0.003	0.061± 0.009	0.356± 0.026	0.425± 0.023
80 ppm	10	182± 6	0.108± 0.007	0.032± 0.002	0.064± 0.009	0.348± 0.023	0.426± 0.022
400 ppm	10	170± 14	0.100± 0.007	0.033± 0.005	0.063± 0.009	0.361± 0.042	0.455± 0.028*
2000 ppm	10	170± 6	0.104± 0.013	0.034± 0.003	0.062± 0.007	0.364± 0.032	0.462± 0.023**
10000 ppm	10	164± 4**	0.098± 0.010	0.033± 0.003	0.067± 0.004	0.369± 0.014	0.477± 0.019**
50000 ppm	10	154± 7**	0.104± 0.017	0.036± 0.002	0.067± 0.017	0.363± 0.033	0.462± 0.015**

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

STUDY NO. : 0220
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	0.683± 0.028	0.203± 0.010	2.366± 0.067	0.976± 0.054
80 ppm	10	0.690± 0.021	0.218± 0.011*	2.402± 0.081	0.959± 0.033
400 ppm	10	0.749± 0.053*	0.263± 0.014**	2.548± 0.060	1.048± 0.084
2000 ppm	10	0.759± 0.052**	0.289± 0.013**	2.896± 0.142**	1.038± 0.037
10000 ppm	10	0.750± 0.014**	0.289± 0.017**	3.199± 0.124**	1.087± 0.028**
50000 ppm	10	0.771± 0.023**	0.281± 0.015**	3.973± 0.165**	1.145± 0.051**

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

APPENDIX B 9-3

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

MOUSE: MALE

STUDY NO. : 0221
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	30.9± 1.8	0.139± 0.031	0.033± 0.014	0.651± 0.112	0.451± 0.037	0.517± 0.028
80 ppm	10	30.2± 3.3	0.119± 0.014	0.031± 0.014	0.698± 0.158	0.465± 0.059	0.521± 0.047
400 ppm	10	30.0± 1.9	0.115± 0.016	0.030± 0.014	0.672± 0.132	0.477± 0.034	0.519± 0.049
2000 ppm	10	28.3± 2.2	0.132± 0.013	0.033± 0.014	0.690± 0.067	0.511± 0.039*	0.523± 0.038
10000 ppm	10	25.7± 2.2**	0.127± 0.018	0.036± 0.011	0.728± 0.084	0.526± 0.043**	0.590± 0.064**
50000 ppm	10	23.4± 0.9**	0.128± 0.023	0.042± 0.012	0.805± 0.153	0.546± 0.059**	0.613± 0.032**

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

STUDY NO. : 0221
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	1.350± 0.070	0.150± 0.020	3.388± 0.193	1.476± 0.096
80 ppm	10	2.085± 2.201	0.157± 0.023	3.481± 0.212	1.528± 0.181
400 ppm	10	1.350± 0.095	0.150± 0.009	3.683± 0.120**	1.534± 0.111
2000 ppm	10	1.520± 0.478	0.170± 0.035	3.873± 0.192**	1.612± 0.127
10000 ppm	10	1.495± 0.108	0.166± 0.018	4.222± 0.148**	1.764± 0.177**
50000 ppm	10	1.554± 0.044**	0.291± 0.026**	4.708± 0.137**	1.959± 0.079**

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

APPENDIX B 9-4

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

MOUSE: FEMALE

STUDY NO. : 0221
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	21.7± 1.8	0.201± 0.021	0.054± 0.015	0.075± 0.035	0.538± 0.054	0.707± 0.060
80 ppm	10	20.7± 1.2	0.189± 0.020	0.054± 0.018	0.102± 0.023	0.561± 0.037	0.705± 0.050
400 ppm	9	20.9± 1.1	0.203± 0.031	0.063± 0.011	0.105± 0.027	0.586± 0.035	0.729± 0.047
2000 ppm	10	20.7± 1.2	0.193± 0.026	0.055± 0.009	0.092± 0.013	0.575± 0.071	0.678± 0.041
10000 ppm	10	19.4± 1.2**	0.191± 0.031	0.054± 0.011	0.098± 0.028	0.584± 0.039	0.745± 0.049
50000 ppm	10	19.2± 0.7**	0.207± 0.020	0.061± 0.011	0.090± 0.030	0.574± 0.043	0.698± 0.037

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

STUDY NO. : 0221
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	1.368± 0.062	0.231± 0.020	3.959± 0.120	2.161± 0.201
80 ppm	10	1.353± 0.051	0.227± 0.030	3.927± 0.199	2.250± 0.109
400 ppm	9	1.460± 0.048*	0.233± 0.045	4.065± 0.174	2.224± 0.124
2000 ppm	10	1.413± 0.059	0.240± 0.030	4.110± 0.199	2.304± 0.127
10000 ppm	10	1.447± 0.073*	0.231± 0.030	4.286± 0.164**	2.427± 0.126**
50000 ppm	10	1.428± 0.068	0.286± 0.027**	4.694± 0.146**	2.425± 0.128**

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

APPENDIX B 10-1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN−WEEK STUDY: SUMMARY)

RAT : MALE : SACRIFICED ANIMALS

STUDY NO. : 0220
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control				80 ppm				400 ppm				2000 ppm			
		No. of Animals	10				10				10				10			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Respiratory system]																		
nasal cavit	inflammation:transitional epithelium		1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Hematopoietic system]																		
bone marrow	increased hematopoiesis		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	3 (30)	0 (0)	0 (0)	0 (0)	5 (50)	0 (0)	0 (0)	0 * (0)
spleen	engorgement of erythrocyte		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 ** (0)	9 (90)	1 (10)	0 (0)	0 ** (0)
[Digestive system]																		
tongue	foreign body granuloma		0 (0)	0 (0)	0 (0)	0 (0)	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	granulation		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	swelling:central		0 (0)	0 (0)	0 (0)	0 (0)	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	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		8 (80)	2 (20)	0 (0)	0 (0)	2 (20)	8 (80)	0 (0)	0 * (0)	4 (40)	6 (60)	0 (0)	0 (0)	2 (20)	6 (60)	2 (20)	0 * (0)
[Endocrine system]																		
pituitary	Rathke pouch		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

Organ	Findings	Group Name	10000 ppm				50000 ppm			
		No. of Animals	10				10			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Respiratory system]										
nasal cavit	inflammation:transitional epithelium		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Hematopoietic system]										
bone marrow	increased hematopoiesis		7 (70)	0 (0)	0 (0)	0 ** (0)	6 (60)	1 (10)	0 (0)	0 ** (0)
spleen	engorgement of erythrocyte		6 (60)	4 (40)	0 (0)	0 ** (0)	9 (90)	1 (10)	0 (0)	0 ** (0)
[Digestive system]										
tongue	foreign body granuloma		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
liver	granulation		1 (10)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)
	swelling:central		0 (0)	0 (0)	0 (0)	0 (0)	6 (60)	0 (0)	0 (0)	0 * (0)
[Urinary system]										
kidney	basophilic change		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
	eosinophilic body		0 (0)	6 (60)	4 (40)	0 ** (0)	5 (50)	5 (50)	0 (0)	0 (0)
[Endocrine system]										
pituitary	Rathke pouch		1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Organ	Findings	Group Name	Control				80 ppm				400 ppm				2000 ppm			
		No. of Animals	10				10				10				10			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Special sense organs/appandage]																		
Harder gl	lymphocytic infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

Organ	Findings	Group Name	10000 ppm				50000 ppm			
		No. of Animals	10				10			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Special sense organs/appandage]										
Harder gl	lymphocytic infiltration		1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

APPENDIX B 10-2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN−WEEK STUDY: SUMMARY)

RAT : FEMALE : SACRIFICED ANIMALS

Organ	Findings	Group Name / No. of Animals	Control 10				80 ppm 10				400 ppm 10				2000 ppm 10			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Respiratory system]																		
nasal cavit	inflammation:transitional epithelium		7 (70)	0 (0)	0 (0)	0 (0)	8 (80)	0 (0)	0 (0)	0 (0)	7 (70)	0 (0)	0 (0)	0 (0)	4 (40)	0 (0)	0 (0)	0 (0)
lung	foamy cell		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Hematopoietic system]																		
bone marrow	granulation		1 (10)	0 (0)	0 (0)	0 (0)	2 (20)	1 (10)	0 (0)	0 (0)	4 (40)	4 (40)	0 (0)	0 ** (0)	1 (10)	6 (60)	0 (0)	0 * (0)
	increased hematopoiesis		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	7 (70)	0 (0)	0 (0)	0 ** (0)	4 (40)	5 (50)	0 (0)	0 ** (0)
spleen	deposit of hemosiderin		5 (50)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 * (0)	10 (100)	0 (0)	0 (0)	0 * (0)	5 (50)	5 (50)	0 (0)	0 ** (0)
	engorgement of erythrocyte		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 ** (0)	9 (90)	1 (10)	0 (0)	0 ** (0)
[Digestive system]																		
liver	herniation		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)
	granulation		1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	3 (30)	0 (0)	0 (0)	0 (0)
[Urinary system]																		
kidney	mineralization:cortico-medullary junction		1 (10)	9 (90)	0 (0)	0 (0)	1 (10)	9 (90)	0 (0)	0 (0)	5 (50)	5 (50)	0 (0)	0 (0)	6 (60)	4 (40)	0 (0)	0 (0)

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

Organ	Findings	Group Name	10000 ppm				50000 ppm			
		No. of Animals	10				10			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Respiratory system]										
nasal cavit	inflammation:transitional epithelium		3 (30)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 ** (0)
lung	foamy cell		1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Hematopoietic system]										
bone marrow	granulation		0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	increased hematopoiesis		5 (50)	5 (50)	0 (0)	0 ** (0)	6 (60)	3 (30)	0 (0)	0 ** (0)
spleen	deposit of hemosiderin		2 (20)	8 (80)	0 (0)	0 ** (0)	1 (10)	9 (90)	0 (0)	0 ** (0)
	engorgement of erythrocyte		3 (30)	7 (70)	0 (0)	0 ** (0)	3 (30)	7 (70)	0 (0)	0 ** (0)
[Digestive system]										
liver	herniation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	granulation		2 (20)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)
[Urinary system]										
kidney	mineralization:cortico-medullary junction		9 (90)	0 (0)	0 (0)	0 ** (0)	6 (60)	2 (20)	0 (0)	0 ** (0)

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

Organ	Findings	Group Name	Control				80 ppm				400 ppm				2000 ppm			
		No. of Animals	10				10				10				10			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Endocrine system]																		
pituitary	Rathke pouch		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
thyroid	ultimibranchial body remanet		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Reproductive system]																		
ovary	cyst		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
[Special sense organs/appandage]																		
Harder gl	lymphocytic infiltration		1 (10)	0 (0)	0 (0)	0 (0)	2 (20)	2 (20)	0 (0)	0 (0)	3 (30)	0 (0)	0 (0)	0 (0)	1 (10)	1 (10)	0 (0)	0 (0)

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

Organ	Findings	Group Name	10000 ppm				50000 ppm			
		No. of Animals	10				10			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Endocrine system]										
pituitary	Rathke pouch		1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
thyroid	ultimibranchial body remanet		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
[Reproductive system]										
ovary	cyst		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
[Special sense organs/appandage]										
Harder gl	lymphocytic infiltration		1 (10)	1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

APPENDIX B 10-3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN−WEEK STUDY: SUMMARY)

MOUSE: FEMALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0221
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name / No. of Animals	Control 0				80 ppm 0				400 ppm 1				2000 ppm 0			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Respiratory system]																		
nasal cavit	degeneration:olfactory epithelium		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	1 (100)	0 (0)	0 (0)	0 (0)	- (-)	- (-)	- (-)	- (-)
[Hematopoietic system]																		
thymus	atrophy		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	0 (0)	0 (0)	1 (100)	0 (0)	- (-)	- (-)	- (-)	- (-)
spleen	atrophy		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	0 (0)	0 (0)	1 (100)	0 (0)	- (-)	- (-)	- (-)	- (-)

<1>:Slight <2>:Moderate <3>:Marked <4>:Severe

Organ	Findings	Group Name	10000 ppm				50000 ppm			
		No. of Animals	0				0			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Respiratory system]										
nasal cavit	degeneration:olfactory epithelium		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
[Hematopoietic system]										
thymus	atrophy		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
spleen	atrophy		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)

<1>:Slight <2>:Moderate <3>:Marked <4>:Severe

APPENDIX B 10-4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN−WEEK STUDY: SUMMARY)

MOUSE: MALE : SACRIFICED ANIMALS

STUDY NO. : 0221
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name / No. of Animals	Control 10				80 ppm 10				400 ppm 10				2000 ppm 10			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Respiratory system]																		
nasal cavit	eosinophilic change:olfactory epithelium		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)
	eosinophilic change:respiratory epithelium		1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
lung	cytologic alteration:NOS		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Hematopoietic system]																		
spleen	deposit of hemosiderin		0 (0)	0 (0)	0 (0)	0 (0)	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 melanin		2 (20)	1 (10)	0 (0)	0 (0)	3 (30)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
	extramedullary hematopoiesis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	7 (70)	0 (0)	0 (0)	0 ** (0)	5 (50)	5 (50)	0 (0)	0 ** (0)
[Digestive system]																		
liver	granulation		3 (30)	0 (0)	0 (0)	0 (0)	2 (20)	1 (10)	0 (0)	0 (0)	3 (30)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
[Urinary system]																		
kidney	vacuolization of proximal tubule		6 (60)	1 (10)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	2 (20)	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)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

Organ	Findings	Group Name	10000 ppm				50000 ppm			
		No. of Animals	10				10			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Respiratory system]										
nasal cavit	eosinophilic change:olfactory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	eosinophilic change:respiratory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
lung	cytologic alteration:NOS		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Hematopoietic system]										
spleen	deposit of hemosiderin		9 (90)	0 (0)	0 (0)	0 ** (0)	10 (100)	0 (0)	0 (0)	0 ** (0)
	deposit of melanin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)
	extramedullary hematopoiesis		3 (30)	7 (70)	0 (0)	0 ** (0)	0 (0)	2 (20)	8 (80)	0 ** (0)
[Digestive system]										
liver	granulation		1 (10)	0 (0)	0 (0)	0 (0)	4 (40)	0 (0)	0 (0)	0 (0)
[Urinary system]										
kidney	vacuolization of proximal tubule		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)

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

Organ	Findings	Group Name	Control				80 ppm				400 ppm				2000 ppm			
		No. of Animals	10				10				10				10			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Urinary system]																		
urin bladd	hyaline droplet degeneration:superficial cell of transit		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	6 (60)	4 (40)	0 (0)	0 ** (0)
[Endocrine system]																		
thyroid	cyst		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)
adrenal	deposit of melanin		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)
	accesory cortical nodule		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)

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

Organ	Findings	Group Name	10000 ppm				50000 ppm			
		No. of Animals	10				10			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Urinary system]										
urin bladd	hyaline droplet degeneration:superficial cell of transit		0 (0)	10 (100)	0 (0)	0 ** (0)	0 (0)	10 (100)	0 (0)	0 ** (0)
[Endocrine system]										
thyroid	cyst		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
adrenal	deposit of melanin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	accesory cortical nodule		1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

APPENDIX B 10-5

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN−WEEK STUDY: SUMMARY)

MOUSE: FEMALE : SACRIFICED ANIMALS

Organ	Findings	Group Name / No. of Animals	Control 10				80 ppm 10				400 ppm 9				2000 ppm 10			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Respiratory system]																		
nasal cavit	eosinophilic change:olfactory epithelium		3 (30)	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 change:respiratory epithelium		2 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (22)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)
[Hematopoietic system]																		
spleen	deposit of hemosiderin		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	8 (89)	0 (0)	0 (0)	0 ** (0)	8 (80)	0 (0)	0 (0)	0 ** (0)
	deposit of melanin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)
	extramedullary hematopoiesis		5 (50)	2 (20)	0 (0)	0 (0)	9 (90)	1 (10)	0 (0)	0 (0)	7 (78)	1 (11)	0 (0)	0 (0)	8 (80)	2 (20)	0 (0)	0 (0)
[Digestive system]																		
liver	granulation		2 (20)	0 (0)	0 (0)	0 (0)	3 (30)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)
[Urinary system]																		
urin bladd	hyaline droplet degeneration:superficial cell of transit		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Endocrine system]																		
adrenal	accesory cortical nodule		1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (22)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

Organ	Findings	Group Name	10000 ppm				50000 ppm			
		No. of Animals	10				10			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Respiratory system]										
nasal cavit	eosinophilic change:olfactory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	eosinophilic change:respiratory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
[Hematopoietic system]										
spleen	deposit of hemosiderin		8 (80)	0 (0)	0 (0)	0 ** (0)	10 (100)	0 (0)	0 (0)	0 ** (0)
	deposit of melanin		0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	extramedullary hematopoiesis		3 (30)	7 (70)	0 (0)	0 * (0)	2 (20)	7 (70)	1 (10)	0 * (0)
[Digestive system]										
liver	granulation		1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
[Urinary system]										
urin bladd	hyaline droplet degeneration:superficial cell of transit		10 (100)	0 (0)	0 (0)	0 ** (0)	0 (0)	10 (100)	0 (0)	0 ** (0)
[Endocrine system]										
adrenal	accesory cortical nodule		1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

APPENDIX B 11-1

IDENTITY AND PURITY OF BIPHENYL

PERFORMED AT THE JAPAN BIOASSAY LABORATORY

(THIRTEEN−WEEK STUDY)

STABILITY OF ANTHRACENE AT THE JAPAN BIOASSAY LABORATORY(THIRTEEN-WEEK STUDIES)

Lot no.304P4138

1.Sample storage: Anthracene were stored for about 16 weeks at 5°C.

2. Gas Chromatography

Instrument: Hewlett Packard 5890A

Column: Methyl Silicone(0.2mmϕ × 30m)

Column Temperature: 170°C

Flow Rate: 1 ml/min

Detector: FID(Hydrogen Flame Ionization)

Injection Volume: 1 μl

Results: Major peak and six impurities

Date	Peak No.	Retention Time(min)	AREA (measurement)	AREA (percent of total peak)
10/21/92	1	5.1	78	0.0155
	2	10.683	674	0.134
	3	13.995	6611	1.31
	4	19.47	2602	0.516
	5	20.308	485500	96.3
	6	20.905	1512	0.300
	7	22.065	7091	1.41
02/09/93	1	5.1	85	0.0166
	2	10.692	656	0.129
	3	14.008	6399	1.25
	4	19.497	2617	0.513
	5	20.342	492352	96.4
	6	20.953	1544	0.302
	7	22.1	6946	1.36

3. Conclusions: Gas chromtography indicated six impurities with concentration totaling <3.7% of the major peak.
Consequently,Anthracene was stable as the chemical when stored for about 16 weeks at 5°C.

APPENDIX B 11-2

STABILITY OF ANTHRACENEAT THE JAPAN BIOASSAY LABORATORY

(THIRTEEN−WEEK STUDY)

IDENTITY AND PURITY OF ANTHRACENE PERFORMED AT THE JAPAN BIOASSAY LABORATORY
(THIRTEEN-WEEK STUDIES)

Lot no. 304P4138

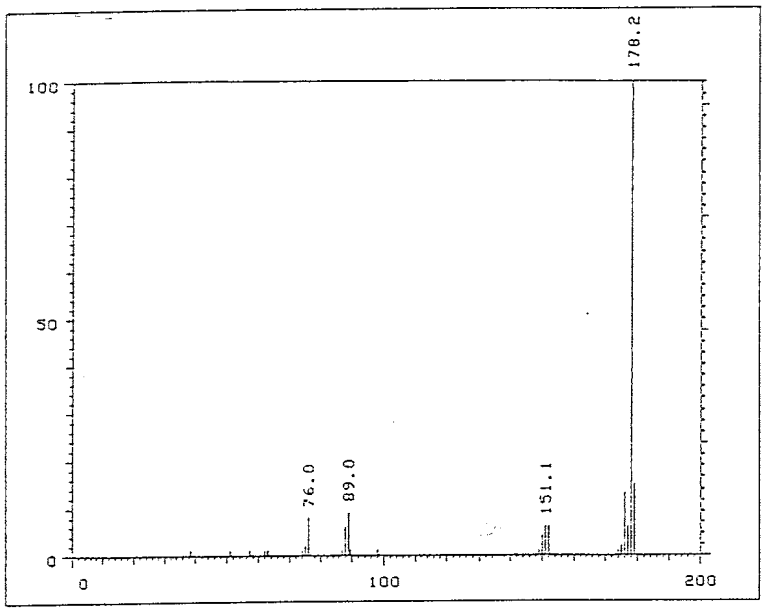
1. Spectral data

(1) Mass Spectrometry

Instrument: Hitachi M-80B

Ionization: EI(Electron Ionization)

Ionization Voltage: 70eV



Mass Spectrum of ANTHRACENE

Result:

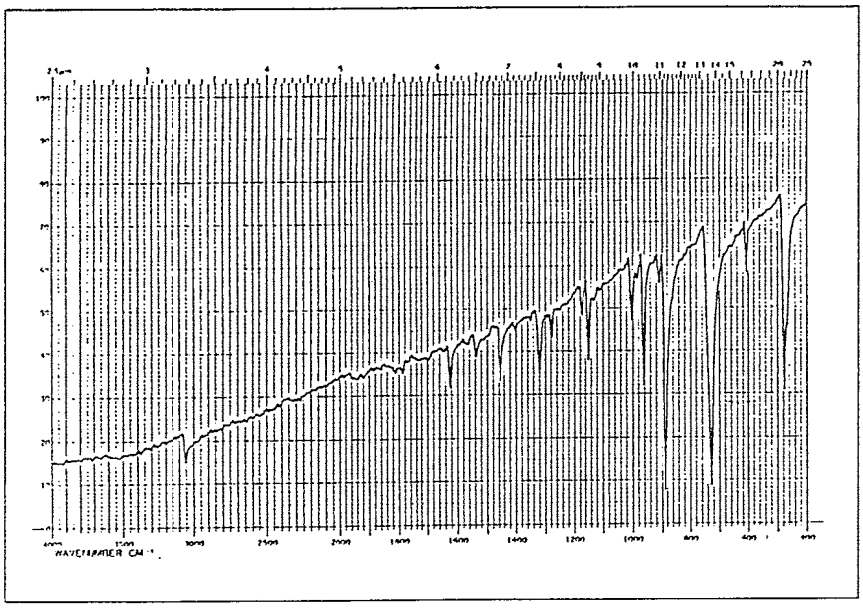
	Molecular Weight
Theoretical Value	178.1(Calculated)
Literature Values	178(Sadtler Handbook by Sadtler Research Laboratories, Inc.)
Determined	178.2

(2) Infrared Spectrometry

Instrument : Hitachi 270-30

Cell : KBr(Wafer)

Slit : Medium



Infrared Spectrum of ANTHRACENE

Results:

	Wave Number	
	Determines	Literature Values
	(CM^{-1})	
	460～ 490	460～ 490
	700～ 750	700～ 750
	860～ 900	860～ 900
	940～ 970	940～ 970
	990～1010	990～1010
	1130～1160	1130～1160
	1300～1330	1300～1330
	1440～1470	1440～1470
		1530～1550
	1610～1640	1610～1640
	3030～3080	3010～3050
		(Sadtler Handbook by Sadtler Research Laboratories, Inc.)

2. Conclusions: The result of the Mass spectrum agreed with the theoretical value and the Infrared spectrum agreed with the literature values.

APPENDIX B 11-3

ANALYSYS OF ANTHRACENE CONCENTRATION IN FORMULATED DIETS OF THE THIRTEEN –WEEK STUDIES

ANALYSIS OF ANTHRACENE CONCENTRATION AND HOMOGENEITY IN FORMULATED DIETS OF THE THIRTEEN-WEEK STUDIES

(Rat)(MOUSE)

	Concentration of Anthracene in feed for Target Concentration(ppm)				
Date	80 (a) (b)	400 (a) (b)	2000 (a) (b)	10000 (a) (b)	50000 (a) (b)
10/15/92	71.7(89.6) (6.6)	373 (93.3) (3.6)	2020 (101) (0.9)	10400 (104) (2.6)	55000 (110) (1.7)

(a) Percent of target concentration
(b) Homogeneity(C.V.(%) n=7)

Analytical method: The sample were analyzed by the Gas Chromatography.

Instrument :Hewlett Packard 5890A
Column :Methylsilicon (0.2mmϕ × 30m)
Column Temperature :260℃
Flow Rate :1ml/min
Detector :FID
Injection Volume :1μl

APPENDIX B 11-4

STABILITY OF ANTHRACENE IN FORMULATED DIETS OF THE THIRTEEN - WEEK STUDIES

STABILITY OF ANTHRACENE IN FORMULATED DIETS OF THE THIRTEEN-WEEK STUDIES

(Rat)(Mouse)

	Concentration of Anthracene in feed for Target Concentration(ppm)	
Date	80 (a)	50000 (a)
08/18/92(b)	70.8(100)	50300 (100)
10/15/92(c)	73.2(103)	53100 (106)

(a) Percent of concentration on preparation day
(b) Date of preparation
(c) Formulated diets were stored for about 2 months at 8°C.

Analytical method: The sample were analyzed by the Gas Chromatography.

Instrument :Hewlett Packard 5890A
Column :Methylsilicon (0.2mmϕ × 30m)
Column Temperature :260℃
Flow Rate :1ml/min
Detector :FID
Injection Volume :1μl

APPENDIX C 1

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALSYS

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS

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

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

APPENDIX C 2

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

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