N,N-ジメチルホルムアミドのラット及びマウスを用いた
吸 入 に よ る が ん 原 性 予 備 試 験 報 告 書

APPENDIX

（B1-1～C1）
2 週間試験：ラット/0263；マウス/0264

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIX B 1-1

BODY WEIGHT CHANGES :SUMMARY, RAT : MALE

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0275
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 0	1	1	2	3	4	5
Control	115± 4	119± 5	141± 9	169± 13	190± 14	215± 13	232± 14
50 ppm	115± 4	120± 4	143± 8	173± 12	193± 16	218± 15	237± 16
100 ppm	115± 4	119± 5	142± 7	170± 9	192± 15	213± 16	230± 18
200 ppm	115± 4	119± 4	141± 6	167± 10	189± 13	212± 14	231± 14
400 ppm	115± 4	119± 5	137± 7	160± 10	178± 13	198± 12*	215± 14
800 ppm	115± 4	119± 4	131± 5**	156± 9*	168± 11**	185± 13**	201± 14**

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

STUDY NO. : 0275
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 6	7	8	9	10	11	12
Control	247± 14	259± 15	271± 14	285± 17	293± 17	302± 17	311± 18
50 ppm	251± 17	263± 18	277± 18	287± 17	295± 17	303± 18	310± 18
100 ppm	246± 17	260± 17	273± 18	283± 20	292± 21	301± 21	309± 22
200 ppm	244± 14	258± 14	270± 16	280± 15	289± 18	296± 20	304± 19
400 ppm	227± 15*	238± 15*	250± 18*	257± 18**	263± 19**	271± 20**	275± 19**
800 ppm	208± 14**	219± 16**	229± 17**	235± 15**	241± 15**	249± 16**	252± 17**

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

STUDY NO. : 0275
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 13
Control	316± 17
50 ppm	315± 17
100 ppm	312± 22
200 ppm	310± 20
400 ppm	277± 18**
800 ppm	253± 18**

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

APPENDIX B 1-2

BODY WEIGHT CHANGES : SUMMARY, RAT : FEMALE

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0275
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 0	1	1	2	3	4	5
Control	96± 3	98± 3	109± 3	124± 4	132± 5	142± 6	148± 5
50 ppm	96± 3	98± 3	111± 4	126± 4	136± 5	146± 7	153± 7
100 ppm	96± 3	98± 3	110± 3	125± 4	136± 4	145± 5	152± 5
200 ppm	96± 2	97± 2	107± 3	122± 5	128± 4	137± 5	144± 5
400 ppm	96± 3	97± 3	106± 3	119± 5	124± 6**	132± 8**	140± 8*
800 ppm	96± 3	97± 2	101± 4**	113± 6**	115± 6**	120± 7**	129± 8**

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

STUDY NO. : 0275
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 6	7	8	9	10	11	12
Control	156± 6	162± 6	166± 7	172± 8	176± 8	181± 8	183± 8
50 ppm	159± 7	166± 8	172± 8	174± 8	180± 8	185± 8	188± 9
100 ppm	159± 6	164± 4	169± 5	172± 7	177± 6	181± 8	183± 7
200 ppm	151± 7	156± 6	161± 7	165± 8	168± 9	173± 9	176± 7
400 ppm	141± 8**	147± 9**	152± 10**	154± 9**	155± 10**	161± 10**	160± 11**
800 ppm	128± 9**	132± 10**	138± 11**	137± 9**	139± 10**	147± 12**	146± 14**

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

STUDY NO. : 0275
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 13
Control	185± 7
50 ppm	192± 10
100 ppm	187± 7
200 ppm	176± 9
400 ppm	161± 12*
800 ppm	142± 18**

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

APPENDIX B 1-3

BODY WEIGHT CHANGES :SUMMARY, MOSUE : MALE

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0276
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 0	1	1	2	3	4	5
Control	22.3± 0.8	22.5± 0.9	23.4± 1.1	24.8± 0.8	25.5± 1.0	26.1± 1.0	27.4± 1.0
50 ppm	22.3± 0.8	22.2± 0.8	22.8± 0.9	23.9± 0.9	24.5± 1.0	25.0± 0.7	26.1± 0.6*
100 ppm	22.3± 0.8	22.4± 0.7	23.1± 1.0	23.8± 0.9	24.7± 0.9	25.4± 1.2	25.9± 1.1*
200 ppm	22.3± 0.8	22.2± 1.0	22.8± 0.8	24.3± 0.9	25.3± 1.0	25.3± 1.0	25.5± 0.9**
400 ppm	22.4± 1.0	22.6± 0.9	23.6± 0.9	24.4± 1.2	25.2± 1.3	25.5± 1.4	26.2± 1.5
800 ppm	22.3± 1.1	22.4± 1.0	22.9± 1.0	23.3± 0.9**	23.6± 0.9**	24.0± 1.3**	25.4± 0.9**

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

STUDY NO. : 0276
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 6	7	8	9	10	11	12
Control	27.7± 1.2	28.2± 1.2	28.8± 1.2	29.6± 1.4	30.5± 1.5	31.1± 1.6	31.9± 1.7
50 ppm	26.4± 1.0*	26.5± 1.1**	27.0± 1.3**	27.7± 1.2**	28.1± 1.5**	28.7± 1.6**	29.2± 1.9**
100 ppm	26.1± 1.4*	27.1± 1.2	27.0± 1.2**	27.8± 1.2*	28.7± 1.3*	29.2± 1.5*	29.9± 1.8*
200 ppm	26.2± 0.6*	26.5± 0.8**	26.6± 0.8**	27.4± 0.9**	27.7± 0.8**	28.1± 0.9**	28.8± 1.3**
400 ppm	26.5± 1.4	26.8± 1.3*	26.9± 1.4**	27.4± 1.5**	28.0± 1.5**	28.7± 2.1**	28.7± 2.0**
800 ppm	24.8± 1.1**	24.7± 1.2**	25.1± 0.9**	25.4± 1.1**	25.7± 1.3**	25.7± 1.7**	26.5± 1.2**

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

STUDY NO. : 0276
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 13
Control	32.5± 1.8
50 ppm	29.6± 1.6**
100 ppm	30.3± 1.8*
200 ppm	29.5± 1.2**
400 ppm	29.5± 2.0**
800 ppm	26.2± 1.5**

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

APPENDIX B 1-4

BODY WEIGHT CHANGES : SUMMARY, MOSUE: FEMALE

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0276
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 0	1	1	2	3	4	5
Control	17.8± 0.8	18.0± 0.6	18.9± 0.7	20.0± 0.9	20.5± 0.9	20.9± 1.2	21.7± 1.1
50 ppm	17.8± 0.8	17.9± 0.7	18.5± 0.9	20.2± 1.0	20.8± 1.2	21.3± 1.2	22.3± 1.3
100 ppm	17.8± 0.8	17.9± 0.7	18.5± 0.7	20.0± 0.8	20.8± 0.7	21.8± 1.0	22.1± 0.6
200 ppm	17.8± 0.7	18.1± 0.7	18.8± 0.8	20.2± 1.0	21.2± 0.8	21.4± 1.1	21.8± 0.8
400 ppm	17.8± 0.9	17.6± 0.7	19.0± 0.6	20.1± 0.8	20.9± 0.7	21.9± 1.1	21.9± 0.8
800 ppm	17.9± 0.8	17.9± 0.6	18.7± 0.5	19.2± 0.6	19.7± 0.6	20.8± 0.6	22.1± 0.6

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

STUDY NO. : 0276
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 6	7	8	9	10	11	12
Control	22.2± 1.0	22.6± 1.1	23.0± 1.2	23.1± 1.5	23.6± 1.3	23.7± 1.2	23.6± 1.3
50 ppm	22.8± 1.1	23.1± 1.0	23.7± 2.0	23.4± 1.1	24.2± 1.7	24.4± 1.6	24.5± 1.3
100 ppm	22.8± 0.7	23.7± 1.0	24.2± 1.3	24.1± 1.3	23.9± 1.0	24.5± 1.0	24.7± 1.0
200 ppm	22.7± 1.3	23.5± 1.4	24.2± 0.9	24.1± 1.2	24.6± 1.7	24.4± 1.4	25.5± 1.4**
400 ppm	22.8± 0.7	23.7± 0.8	24.0± 0.7	23.9± 1.0	24.5± 1.0	24.6± 0.8	24.8± 0.9
800 ppm	21.5± 0.6	21.7± 0.6	22.5± 1.0	22.5± 1.0	23.0± 0.4	23.3± 0.7	23.1± 0.8

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

STUDY NO. : 0276
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 13
Control	24.3± 1.6
50 ppm	25.0± 1.1
100 ppm	24.4± 1.3
200 ppm	25.0± 1.4
400 ppm	25.1± 1.3
800 ppm	23.6± 0.7

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

APPENDIX B 2-1

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : MALE

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0275
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	14.1± 0.7	15.2± 1.4	15.7± 1.6	16.2± 0.9	16.9± 1.4	16.7± 0.9	16.8± 1.2
50 ppm	14.3± 0.7	15.5± 1.1	15.9± 1.5	16.4± 1.4	16.7± 1.2	16.7± 1.2	16.6± 1.3
100 ppm	13.9± 0.6	15.5± 0.7	15.7± 1.4	16.1± 1.6	16.4± 1.4	16.1± 1.4	16.4± 1.2
200 ppm	13.4± 0.7	14.4± 0.8	15.1± 0.9	15.9± 1.2	16.9± 1.3	16.0± 1.1	16.9± 1.0
400 ppm	12.8± 0.7**	14.0± 1.1	14.5± 1.3	15.1± 1.2	15.3± 0.9*	15.4± 1.5	15.6± 1.9
800 ppm	12.0± 0.8**	13.3± 1.3**	13.0± 1.1**	14.4± 1.3*	14.7± 1.7**	14.8± 1.8**	15.2± 1.7

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

STUDY NO. : 0275
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	16.4± 1.2	16.9± 1.2	16.5± 0.9	16.8± 1.0	16.4± 1.1	16.5± 0.8
50 ppm	16.7± 1.0	16.8± 0.9	16.4± 0.8	16.8± 0.9	16.1± 1.1	16.4± 0.7
100 ppm	16.7± 1.3	16.4± 1.4	16.3± 1.1	16.6± 0.9	16.4± 1.2	16.0± 1.1
200 ppm	16.2± 1.2	16.3± 1.4	16.1± 1.3	16.3± 1.3	15.7± 1.3	15.9± 1.2
400 ppm	15.3± 1.3	15.6± 1.4	15.6± 1.3	15.5± 1.6	15.3± 1.7	15.6± 1.5
800 ppm	15.1± 1.1	14.7± 0.9**	14.9± 1.7*	14.9± 1.8*	14.5± 1.8*	14.3± 1.6**

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

APPENDIX B 2-2

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0275
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	11.4± 0.6	11.9± 0.7	11.7± 0.7	11.5± 0.7	11.8± 0.7	11.7± 1.1	11.8± 1.1
50 ppm	11.4± 0.4	12.3± 0.7	12.4± 0.5	12.2± 0.7	12.1± 0.8	12.0± 0.8	12.5± 1.1
100 ppm	11.7± 0.5	12.1± 0.7	12.2± 0.6	12.1± 0.5	12.1± 0.6	11.5± 0.6	11.8± 0.5
200 ppm	10.3± 1.2	11.4± 1.0	10.9± 0.8	10.5± 0.6	11.6± 0.9	11.0± 0.9	11.3± 1.0
400 ppm	10.1± 0.5*	10.6± 0.7**	10.2± 1.0**	10.5± 1.6	11.2± 1.0	10.4± 1.4	10.6± 1.4
800 ppm	8.8± 0.6**	9.7± 0.9**	9.0± 0.8**	8.8± 1.0**	9.8± 1.1**	9.0± 1.7**	9.0± 1.5**

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

STUDY NO. : 0275
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	11.4± 0.8	11.7± 1.1	11.4± 0.9	11.8± 0.6	11.1± 0.8	11.0± 0.7
50 ppm	11.9± 1.1	12.1± 1.0	11.7± 0.8	12.5± 1.2	11.6± 1.3	11.6± 1.1
100 ppm	11.4± 0.6	11.5± 0.7	11.8± 1.1	11.6± 0.7	11.3± 0.6	11.1± 0.5
200 ppm	10.9± 0.9	10.8± 0.8	10.3± 1.2	11.3± 0.8	10.2± 0.7	10.0± 0.8
400 ppm	10.3± 1.2	9.7± 0.9**	9.4± 1.3**	10.4± 1.2	9.2± 1.4*	9.6± 1.7
800 ppm	9.2± 1.4**	8.1± 1.1**	8.6± 1.7**	9.9± 1.8*	9.0± 2.2*	8.5± 2.5*

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

APPENDIX B 2-3

FOOD CONSUMPTION CHANGES : SUMMARY, MOSUE : MALE

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0276
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	4.1± 0.2	4.1± 0.1	4.2± 0.2	4.2± 0.2	4.3± 0.1	4.2± 0.2	4.4± 0.2
50 ppm	3.8± 0.3	4.0± 0.2	4.0± 0.2	4.1± 0.2	4.2± 0.3	4.1± 0.2	4.2± 0.3
100 ppm	3.9± 0.3	4.0± 0.1	4.3± 0.2	4.3± 0.2	4.3± 0.2	4.3± 0.2	4.4± 0.1
200 ppm	3.8± 0.1	4.1± 0.2	4.1± 0.1	4.0± 0.2	4.0± 0.2*	4.1± 0.2	4.2± 0.1
400 ppm	3.6± 0.4**	4.3± 1.1	4.1± 0.4	4.1± 0.3	4.1± 0.3	4.2± 0.3	4.2± 0.3
800 ppm	3.2± 0.3**	4.3± 1.4	3.7± 0.4**	3.6± 0.4**	3.7± 0.3**	3.5± 0.3**	3.6± 0.2**

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

STUDY NO. : 0276
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	4.4± 0.2	4.5± 0.2	4.5± 0.2	4.4± 0.2	4.5± 0.2	4.4± 0.2
50 ppm	4.2± 0.3	4.4± 0.2	4.3± 0.3	4.4± 0.3	4.4± 0.3	4.3± 0.3
100 ppm	4.2± 0.2	4.5± 0.1	4.5± 0.2	4.4± 0.2	4.5± 0.2	4.4± 0.2
200 ppm	4.1± 0.2**	4.5± 0.2	4.2± 0.3	4.2± 0.2	4.3± 0.2	4.3± 0.2
400 ppm	4.2± 0.3	4.2± 0.2	4.3± 0.4	4.3± 0.3	4.2± 0.3*	4.3± 0.2
800 ppm	3.7± 0.2**	3.7± 0.3**	3.7± 0.4**	3.6± 0.3**	3.8± 0.2**	3.7± 0.3**

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

APPENDIX B 2-4

FOOD CONSUMPTION CHANGES : SUMMARY, MOSUE : FEMALE

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0276
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± 0.2	3.5± 0.2	3.7± 0.3	3.8± 0.3	4.0± 0.2	4.1± 0.3	4.2± 0.3
50 ppm	3.3± 0.3	3.7± 0.2	3.8± 0.3	4.0± 0.2	4.1± 0.2	4.1± 0.2	4.3± 0.2
100 ppm	3.3± 0.2	3.6± 0.3	3.8± 0.3	4.0± 0.4	4.1± 0.3	4.2± 0.3	4.3± 0.3
200 ppm	3.3± 0.3	3.7± 0.3	3.9± 0.3	3.8± 0.2	4.0± 0.2	4.1± 0.3	4.2± 0.3
400 ppm	3.0± 0.4	3.8± 0.9	3.6± 0.2	3.8± 0.3	3.8± 0.2	3.9± 0.2	4.2± 0.2
800 ppm	2.8± 0.4**	3.6± 0.8	3.6± 0.2	3.6± 0.3	3.6± 0.3*	3.4± 0.3**	3.7± 0.3**

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

STUDY NO. : 0276
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	4.2± 0.2	4.4± 0.2	4.3± 0.3	4.2± 0.2	4.2± 0.2	4.3± 0.3
50 ppm	4.4± 0.3	4.3± 0.3	4.4± 0.3	4.4± 0.3	4.4± 0.2	4.3± 0.4
100 ppm	4.3± 0.4	4.4± 0.3	4.2± 0.2	4.3± 0.4	4.4± 0.4	4.2± 0.3
200 ppm	4.3± 0.2	4.3± 0.2	4.3± 0.2	4.3± 0.2	4.4± 0.2	4.2± 0.4
400 ppm	4.3± 0.2	4.2± 0.3	4.3± 0.3	4.2± 0.3	4.3± 0.3	4.4± 0.3
800 ppm	3.8± 0.2**	3.8± 0.3**	3.9± 0.2**	3.8± 0.1*	3.8± 0.1	4.0± 0.3

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

APPENDIX B 3-1

HEMATOLOGY : SUMMARY, RAT : MALE

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0275
ANIMAL : RAT F344
SAMPLING DATE : 014-1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (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	9.40±	0.42	16.4±	0.4	46.2±	1.9	49.2±	0.5	17.5±	0.8	35.6±	1.4	708±	62
50 ppm	10	9.76±	0.15	16.2±	0.3	46.8±	1.0	48.0±	0.6**	16.7±	0.2	34.7±	0.6	795±	44**
100 ppm	10	9.86±	0.15*	16.2±	0.2	46.8±	0.8	47.5±	0.5**	16.5±	0.2	34.7±	0.6	822±	21**
200 ppm	10	9.91±	0.17**	15.9±	0.3**	46.1±	1.4	46.6±	0.8**	16.0±	0.2**	34.5±	0.8	842±	33**
400 ppm	10	9.70±	0.72*	15.4±	1.3**	44.6±	3.7	46.0±	0.8**	15.9±	0.2**	34.5±	0.4*	838±	51**
800 ppm	10	10.33±	0.29**	16.5±	0.4	47.8±	1.4	46.3±	0.5**	16.0±	0.3**	34.5±	0.6*	901±	35**

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

STUDY NO. : 0275
ANIMAL : RAT F344
SAMPLING DATE : 014-1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
SURVIVAL ANIMALS (14)

Group Name	NO. of Animals	RETICULOCYTE ‰	PROTHROMBIN TIME sec	APTT sec
Control	10	34± 9	17.4± 2.3	23.7± 0.9
50 ppm	10	32± 7	16.0± 1.9	24.0± 0.7
100 ppm	10	30± 6	16.4± 2.1	24.8± 1.6
200 ppm	10	33± 6	14.4± 1.2	24.2± 1.3
400 ppm	10	34± 10	11.9± 0.3**	20.1± 1.4**
800 ppm	10	30± 7	12.6± 1.3**	19.3± 2.3**

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

STUDY NO. : 0275
ANIMAL : RAT F344
SAMPLING DATE : 014-1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (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	4.85±	2.01	0±	1	30±	9	1±	1	0±	0	3±	1	65±	9	0±	0
50 ppm	10	5.37±	1.52	1±	1	27±	4	1±	1	0±	0	4±	2	67±	4	0±	0
100 ppm	10	5.34±	1.87	0±	0	27±	6	1±	1	0±	0	3±	1	69±	7	0±	0
200 ppm	10	5.52±	1.54	0±	1	30±	8	1±	1	0±	0	3±	1	66±	7	0±	0
400 ppm	10	4.29±	0.98	1±	1	30±	5	1±	1	0±	0	3±	1	65±	7	0±	0
800 ppm	10	4.91±	1.60	1±	1	29±	6	2±	2	0±	0	5±	2*	63±	7	0±	0

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

APPENDIX B 3-2

HEMATOLOGY : SUMMARY, RAT : FEMALE

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0275
ANIMAL : RAT F344
SAMPLING DATE : 014-1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
SURVIVAL ANIMALS (14)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$		HEMOGLOBIN g/dℓ		HEMATOCRIT %		MCV f ℓ		MCH p g		MCHC g/dℓ		PLATELET $10^3/\mu\ell$	
Control	10	8.69±	0.19	16.3±	0.4	45.9±	0.7	52.8±	0.6	18.8±	0.3	35.6±	0.7	763±	59
50 ppm	10	8.68±	0.52	16.2±	0.4	45.4±	2.5	52.3±	0.6	18.8±	1.2	35.9±	2.1	819±	29
100 ppm	10	8.87±	0.13	16.3±	0.3	46.2±	1.0	52.0±	0.7	18.4±	0.2	35.2±	0.7	884±	59**
200 ppm	10	9.12±	0.11*	16.2±	0.3	46.0±	0.5	50.5±	0.6**	17.8±	0.2**	35.3±	0.4	879±	35**
400 ppm	10	9.41±	0.22**	16.6±	0.3	46.9±	1.3	49.9±	0.6**	17.6±	0.1**	35.3±	0.5	810±	40
800 ppm	10	9.53±	0.46**	16.5±	1.1	46.5±	2.0	48.8±	0.9**	17.3±	0.8**	35.5±	1.6	920±	209**

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

STUDY NO. : 0275
ANIMAL : RAT F344
SAMPLING DATE : 014-1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
SURVIVAL ANIMALS (14)

Group Name	NO. of Animals	RETICULOCYTE ‰		PROTHROMBIN TIME sec		APTT sec	
Control	10	31±	9	11.7±	0.4	16.4±	1.0
50 ppm	10	31±	6	11.5±	0.3	16.8±	0.7
100 ppm	10	34±	8	11.8±	0.4	17.3±	0.9
200 ppm	10	34±	9	11.7±	0.6	17.5±	1.3
400 ppm	10	30±	5	12.3±	0.5	15.9±	1.1
800 ppm	10	34±	16	12.8±	1.2*	16.8±	1.2

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

STUDY NO. : 0275
ANIMAL : RAT F344
SAMPLING DATE : 014-1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
SURVIVAL ANIMALS (14)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHERS
Control	10	3.06± 0.81	0± 1	26± 4	2± 1	0± 0	5± 1	68± 5	0± 0
50 ppm	10	2.73± 0.64	0± 0	25± 4	1± 1	0± 0	4± 1	70± 3	0± 0
100 ppm	10	3.03± 0.98	0± 0	29± 9	1± 1	0± 0	4± 2	67± 9	0± 0
200 ppm	10	3.11± 0.51	1± 1	26± 3	1± 1	0± 0	3± 2	69± 3	0± 0
400 ppm	10	3.07± 1.39	1± 1	26± 6	1± 1	0± 0	3± 1	69± 8	0± 0
800 ppm	10	3.34± 1.04	0± 0	26± 7	1± 1	0± 0	4± 2	69± 9	0± 0

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

APPENDIX B 3-3

HEMATOLOGY : SUMMARY, MOSUE : MALE

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0276
ANIMAL : MOUSE BDF1
SAMPLING DATE : 014-1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (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	9	10.98± 0.28	16.2± 0.3	50.6± 1.3	46.1± 0.5	14.8± 0.1	32.1± 0.4	1397± 98
50 ppm	10	10.78± 0.33	15.9± 0.5	48.9± 1.6	45.3± 0.3*	14.8± 0.1	32.6± 0.2	1585± 98**
100 ppm	10	10.70± 0.22	15.7± 0.4	48.4± 1.5*	45.3± 0.8*	14.7± 0.1	32.5± 0.3	1612± 85**
200 ppm	10	10.81± 0.46	15.7± 0.5*	48.3± 1.8*	44.7± 0.8**	14.5± 0.4*	32.5± 0.6	1671± 142**
400 ppm	10	10.81± 0.28	15.6± 0.5*	47.8± 1.4**	44.2± 0.8**	14.4± 0.2*	32.6± 0.3	1668± 82**
800 ppm	10	10.83± 0.39	16.0± 0.6	49.3± 2.0	45.5± 0.5	14.8± 0.2	32.6± 0.4	1576± 176**

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

STUDY NO. : 0276
ANIMAL : MOUSE BDF1
SAMPLING DATE : 014-1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
SURVIVAL ANIMALS (14)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$		Differential WBC (%) N-BAND		N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHERS	
Control	9	1.55±	1.02	0±	1	15±	3	1±	1	0±	0	3±	1	80±	3	0±	0
50 ppm	10	1.30±	0.74	0±	0	17±	6	1±	1	0±	0	2±	1	79±	6	0±	0
100 ppm	10	1.16±	0.99	0±	1	13±	4	1±	1	0±	0	3±	2	83±	4	0±	0
200 ppm	10	1.23±	0.82	0±	0	16±	7	1±	1	0±	0	3±	1	80±	6	0±	0
400 ppm	10	1.01±	0.76	0±	1	14±	3	1±	1	0±	0	3±	2	82±	2	0±	0
800 ppm	10	0.39±	0.25**	0±	1	20±	12	1±	1	0±	0	2±	2	76±	12	0±	0

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

APPENDIX B 3-4

HEMATOLOGY : SUMMARY, MOSUE : FEMALE

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0276
ANIMAL : MOUSE BDF1
SAMPLING DATE : 014-1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
SURVIVAL ANIMALS (14)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV f ℓ	MCH p g	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	9	10.71± 0.24	16.2± 0.4	49.2± 1.2	46.0± 0.5	15.1± 0.2	32.9± 0.6	1167± 47
50 ppm	10	10.70± 0.26	16.2± 0.3	48.8± 1.3	45.6± 0.9	15.2± 0.3	33.2± 0.6	1382± 195
100 ppm	9	10.87± 0.30	16.1± 0.5	48.7± 1.3	44.8± 0.6**	14.8± 0.3	33.0± 0.3	1476± 62**
200 ppm	10	10.95± 0.36	16.0± 0.5	48.8± 1.7	44.6± 0.8**	14.6± 0.2**	32.7± 0.3	1511± 93**
400 ppm	9	10.86± 0.20	16.0± 0.4	48.8± 1.1	45.0± 0.6*	14.7± 0.3*	32.8± 0.5	1506± 95**
800 ppm	10	11.08± 0.55	16.7± 1.0	50.3± 2.9	45.4± 0.9	15.0± 0.2	33.1± 0.6	1529± 172**

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

STUDY NO. : 0276
ANIMAL : MOUSE BDF1
SAMPLING DATE : 014-1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
SURVIVAL ANIMALS (14)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHERS
Control	9	0.87± 0.66	0± 0	25± 8	0± 1	0± 0	2± 1	72± 9	0± 0
50 ppm	10	0.71± 0.58	0± 0	18± 8	1± 1	0± 0	3± 1	78± 7	0± 0
100 ppm	9	1.01± 1.26	0± 0	17± 7	0± 1	0± 0	2± 2	80± 7	0± 0
200 ppm	10	1.01± 0.92	0± 0	14± 4**	0± 0	0± 0	2± 1	83± 4**	0± 0
400 ppm	9	0.49± 0.20	0± 0	15± 7**	0± 0	0± 0	3± 2	82± 7*	0± 0
800 ppm	10	0.62± 0.57	0± 0	16± 5*	0± 0	0± 0	2± 1	82± 5*	0± 0

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

APPENDIX B 4-1

BIOCHEMISTRY : SUMMARY, RAT : MALE

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0275
ANIMAL : RAT F344
SAMPLING DATE : 014-2
SEX : MALE REPORT TYPE : A1

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	6.5±	0.1	3.8±	0.1	1.5±	0.1	0.16±	0.01	200±	19	56±	5	89±	37
50 ppm	10	6.7±	0.1*	3.9±	0.1	1.4±	0.1	0.16±	0.01	205±	13	89±	6**	96±	23
100 ppm	10	6.7±	0.1*	4.0±	0.1*	1.5±	0.1	0.17±	0.01	199±	14	97±	8**	82±	22
200 ppm	10	6.7±	0.2**	4.0±	0.1*	1.4±	0.1	0.17±	0.01	191±	14	111±	6**	84±	21
400 ppm	10	6.5±	0.2	3.9±	0.1	1.5±	0.1	0.18±	0.01	173±	12**	115±	12**	54±	12
800 ppm	10	6.8±	0.2**	4.1±	0.1**	1.5±	0.1	0.18±	0.01**	153±	16**	136±	9**	39±	12**

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

STUDY NO. : 0275
ANIMAL : RAT F344
SAMPLING DATE : 014-2
SEX : MALE REPORT TYPE : A1

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	107±	9	77±	7	45±	4	136±	30	281±	28	1±	1	99±	8
50 ppm	10	159±	11**	72±	7	44±	4	120±	16	249±	20	1±	1	90±	8
100 ppm	10	169±	13**	73±	10	44±	5	136±	24	251±	21	1±	1	94±	7
200 ppm	10	182±	13**	71±	8	46±	6	136±	21	236±	14**	1±	1	89±	8
400 ppm	10	168±	13**	64±	10	51±	19	128±	19	247±	25	0±	1	82±	10**
800 ppm	10	182±	16**	199±	143*	296±	264**	449±	592	256±	41	1±	0	103±	13

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

STUDY NO. : 0275
ANIMAL : RAT F344
SAMPLING DATE : 014-2
SEX : MALE REPORT TYPE : A1

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	18.6± 1.2	0.5± 0.0	144± 2	3.7± 0.2	107± 2	10.3± 0.3	5.7± 1.0
50 ppm	10	19.0± 1.0	0.5± 0.0	143± 2	3.7± 0.2	107± 2	10.5± 0.2	5.5± 1.1
100 ppm	10	18.7± 1.3	0.5± 0.0	143± 2	3.6± 0.3	107± 2	10.4± 0.2	5.4± 1.3
200 ppm	10	17.4± 1.0	0.5± 0.0	143± 2	3.7± 0.1	107± 3	10.5± 0.2	5.6± 1.1
400 ppm	10	17.3± 1.5	0.5± 0.0	141± 1**	3.9± 0.2	107± 2	10.3± 0.3	6.0± 0.8
800 ppm	10	18.3± 2.3	0.5± 0.0	142± 1	3.9± 0.3	107± 2	10.5± 0.2	5.9± 1.2

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

APPENDIX B 4-2

BIOCHEMISTRY : SUMMARY, RAT : FEMALE

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0275
ANIMAL : RAT F344
SAMPLING DATE : 014-2
SEX : FEMALE REPORT TYPE : A1

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	6.3±	0.2	3.7±	0.1	1.5±	0.1	0.17±	0.01	138±	14	81±	8	17±	4
50 ppm	10	6.3±	0.1	3.6±	0.1	1.4±	0.1	0.17±	0.01	142±	14	114±	11	22±	6
100 ppm	10	6.3±	0.1	3.7±	0.1	1.4±	0.1	0.17±	0.01	144±	15	118±	4	22±	5
200 ppm	10	6.2±	0.1	3.6±	0.1	1.4±	0.1	0.18±	0.01	142±	12	133±	14**	24±	4*
400 ppm	10	6.2±	0.2	3.7±	0.1	1.5±	0.0	0.19±	0.01**	134±	20	149±	9**	24±	5*
800 ppm	10	6.5±	0.4	3.9±	0.2	1.5±	0.1	0.21±	0.04**	131±	30	168±	41**	33±	11**

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

STUDY NO. : 0275
ANIMAL : RAT F344
SAMPLING DATE : 014-2
SEX : FEMALE REPORT TYPE : A1

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	138±	12	69±	5	37±	6	141±	32	201±	16	1±	1	100±	15
50 ppm	10	179±	15	67±	5	36±	3	161±	20	189±	17	1±	1	101±	8
100 ppm	10	186±	5*	68±	5	37±	4	158±	43	186±	24	1±	1	103±	14
200 ppm	10	190±	15**	69±	4	39±	4	153±	27	208±	18	2±	2	102±	12
400 ppm	10	211±	12**	71±	5	45±	8*	194±	76	245±	19**	4±	1**	104±	30
800 ppm	10	227±	50**	112±	52	136±	113**	333±	258**	242±	33**	16±	14**	114±	10

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

STUDY NO. : 0275
ANIMAL : RAT F344
SAMPLING DATE : 014-2
SEX : FEMALE REPORT TYPE : A1

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	16.7±	1.6	0.6±	0.1	143±	2	3.4±	0.2	108±	2	10.1±	0.2	4.8±	1.6
50 ppm	10	16.5±	1.7	0.5±	0.1	143±	1	3.5±	0.2	108±	1	10.1±	0.2	5.2±	1.5
100 ppm	10	16.1±	1.2	0.6±	0.1	143±	2	3.3±	0.2	108±	1	10.1±	0.1	4.7±	1.6
200 ppm	10	16.2±	1.3	0.5±	0.0	143±	2	3.3±	0.2	109±	1	10.1±	0.2	5.1±	1.4
400 ppm	10	16.7±	2.9	0.6±	0.1	144±	2	3.5±	0.2	109±	2	10.0±	0.2	4.7±	1.4
800 ppm	10	20.1±	2.7	0.6±	0.1	143±	1	3.7±	0.5	107±	1	10.2±	0.3	5.2±	1.6

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

APPENDIX B 4-3

BIOCHEMISTRY : SUMMARY, MOSUE : MALE

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0276
ANIMAL : MOUSE BDF1
SAMPLING DATE : 014-2
SEX : MALE REPORT TYPE : A1

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±	0.2	3.0±	0.1	1.4±	0.1	0.22±	0.06	234±	33	80±	7	30±	6
50 ppm	10	5.2±	0.2	3.0±	0.1	1.4±	0.1	0.19±	0.01	208±	24	82±	9	25±	9
100 ppm	10	5.1±	0.2	3.0±	0.1	1.4±	0.1	0.18±	0.02	225±	17	95±	11*	40±	12
200 ppm	10	5.1±	0.2	3.0±	0.1	1.4±	0.1	0.20±	0.06	219±	42	92±	9	34±	16
400 ppm	10	5.2±	0.2	3.1±	0.1	1.5±	0.0	0.18±	0.01*	208±	36	102±	16**	33±	20
800 ppm	10	5.1±	0.3	3.1±	0.2	1.6±	0.1**	0.20±	0.02	190±	51	96±	24	20±	15

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

STUDY NO. : 0276
ANIMAL : MOUSE BDF1
SAMPLING DATE : 014-2
SEX : MALE REPORT TYPE : A1

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	20±	6	261±	137	175±	9	131±	202	28.1±	2.6	155±	1
50 ppm	10	45±	8	22±	9	187±	34	160±	12	45±	20	28.9±	3.8	155±	1
100 ppm	10	42±	5	23±	7	175±	33	156±	11*	42±	15	29.1±	4.1	155±	1
200 ppm	10	52±	29	30±	15	248±	203	158±	17	73±	97	29.6±	2.7	154±	2
400 ppm	10	47±	14	38±	31	203±	62	166±	15	58±	42	29.7±	4.1	154±	2
800 ppm	10	151±	221	216±	491**	625±	1061	218±	21**	133±	144	33.1±	9.4	155±	2

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

STUDY NO. : 0276
ANIMAL : MOUSE BDF1
SAMPLING DATE : 014-2
SEX : MALE REPORT TYPE : A1

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± 0.7	126± 3	8.7± 0.4	8.2± 1.5
50 ppm	10	4.1± 0.4	126± 2	8.7± 0.2	7.2± 1.5
100 ppm	10	4.0± 0.4	126± 2	8.7± 0.2	7.1± 0.9
200 ppm	10	4.3± 0.8	125± 2	8.6± 0.2	7.5± 2.8
400 ppm	10	4.5± 0.4	126± 2	8.8± 0.3	7.5± 1.2
800 ppm	10	4.1± 0.5	126± 3	8.7± 0.4	7.3± 1.1

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

APPENDIX B 4-4

BIOCHEMISTRY : SUMMARY, MOSUE : FEMALE

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0276
ANIMAL : MOUSE BDF1
SAMPLING DATE : 014-2
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (14)

Group Name	NO. of Animals	TOTAL PROTEIN g/dℓ	ALBUMIN g/dℓ	A/G RATIO	T-BILIRUBIN mg/dℓ	GLUCOSE mg/dℓ	T-CHOLESTEROL mg/dℓ	TRIGLYCERIDE mg/dℓ
Control	9	5.4± 0.2	3.3± 0.1	1.6± 0.1	0.19± 0.02	176± 28	72± 6	15± 4
50 ppm	10	5.3± 0.1	3.2± 0.1	1.6± 0.1	0.19± 0.01	187± 32	91± 10*	16± 6
100 ppm	10	5.4± 0.2	3.3± 0.1	1.6± 0.1	0.18± 0.01	192± 26	96± 11**	16± 8
200 ppm	10	5.4± 0.1	3.3± 0.1	1.6± 0.1	0.18± 0.01	185± 27	100± 11**	20± 11
400 ppm	9	5.5± 0.2	3.4± 0.1	1.7± 0.1	0.20± 0.01	182± 30	100± 13**	15± 7
800 ppm	10	5.4± 0.4	3.5± 0.2	1.8± 0.1**	0.21± 0.02	170± 70	97± 24**	9± 4

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

STUDY NO. : 0276
ANIMAL : MOUSE BDF1
SAMPLING DATE : 014-2
SEX : FEMALE REPORT TYPE : A1

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	9	67±	14	24±	4	236±	40	310±	31	83±	31	23.9±	3.9	154±	2
50 ppm	10	77±	29	35±	11	263±	74	264±	57	99±	54	26.2±	4.6	154±	2
100 ppm	10	72±	25	41±	24	243±	81	254±	33*	83±	41	27.0±	5.2	154±	2
200 ppm	10	77±	20	59±	44**	266±	84	243±	30**	115±	80	25.2±	5.1	154±	1
400 ppm	9	82±	27	52±	9**	349±	159	248±	35**	182±	148	30.0±	6.3	155±	2
800 ppm	10	88±	36	89±	62**	381±	167*	277±	42	189±	151	39.4±	15.9**	153±	1

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

STUDY NO. : 0276
ANIMAL : MOUSE BDF1
SAMPLING DATE : 014-2
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (14)

Group Name	NO. of Animals	POTASSIUM mEq/ℓ		CHLORIDE mEq/ℓ		CALCIUM mg/dℓ		INORGANIC PHOSPHORUS mg/dℓ	
Control	9	4.1±	0.5	126±	2	8.8±	0.2	6.1±	0.9
50 ppm	10	3.7±	0.5	126±	2	8.8±	0.3	6.4±	0.8
100 ppm	10	3.6±	0.5*	126±	3	8.9±	0.3	6.5±	0.6
200 ppm	10	3.7±	0.2	126±	3	9.0±	0.2	6.3±	0.9
400 ppm	9	3.8±	0.4	127±	2	8.8±	0.4	6.7±	0.8
800 ppm	10	4.1±	0.6	125±	3	8.7±	0.4	7.0±	1.6

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

APPENDIX B 5-1

URINALYSIS : SUMMARY, RAT : MALE

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0275
ANIMAL : RAT F344
SAMPLING DATE : 015-7
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	1	0	0	3	6	0		0	3	7	0	0	0		10	0	0	0	0	0		2	7	1	0	0	0		10	0	0	0	
50 ppm	10	0	0	0	1	5	3	1		0	2	7	1	0	0		10	0	0	0	0	0		4	5	1	0	0	0		10	0	0	0	
100 ppm	10	0	0	0	3	4	3	0		0	6	4	0	0	0		10	0	0	0	0	0		5	5	0	0	0	0		10	0	0	0	
200 ppm	10	0	0	1	0	1	8	0		0	6	2	2	0	0		10	0	0	0	0	0		5	3	2	0	0	0		10	0	0	0	
400 ppm	10	0	0	0	1	1	8	0		0	0	6	4	0	0	*	10	0	0	0	0	0		0	5	5	0	0	0		10	0	0	0	
800 ppm	10	0	0	6	2	1	1	0	**	0	3	5	2	0	0		10	0	0	0	0	0		0	9	0	1	0	0		10	0	0	0	

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

STUDY NO. : 0275 URINALYSIS
ANIMAL : RAT F344
SAMPLING DATE : 015-7
SEX : MALE REPORT TYPE : A1

Group Name	NO. of Animals	Occult blood −	±	+	2+	3+	CHI	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0		10	0	0	0	0	
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	
200 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	
800 ppm	10	10	0	0	0	0		10	0	0	0	0	

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

APPENDIX B 5-2

URINALYSIS : SUMMARY, RAT : FEMALE

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0275
ANIMAL : RAT F344
SAMPLING DATE : 015-7
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	1	5	4	0		1	6	3	0	0	0		10	0	0	0	0	0		9	1	0	0	0	0		10	0	0	0	
50 ppm	10	0	0	1	0	3	6	0		1	5	4	0	0	0		10	0	0	0	0	0		9	1	0	0	0	0		10	0	0	0	
100 ppm	10	0	1	0	1	7	1	0		2	6	2	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
200 ppm	10	0	0	0	2	6	2	0		1	5	3	1	0	0		10	0	0	0	0	0		9	1	0	0	0	0		10	0	0	0	
400 ppm	10	0	0	2	0	4	4	0		3	4	3	0	0	0		10	0	0	0	0	0		7	3	0	0	0	0		10	0	0	0	
800 ppm	10	0	1	3	1	4	1	0		0	7	1	2	0	0		10	0	0	0	0	0		6	4	0	0	0	0		10	0	0	0	

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

STUDY NO. : 0275 URINALYSIS
ANIMAL : RAT F344
SAMPLING DATE : 015-7
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	
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	
200 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	
800 ppm	10	9	0	0	0	1		10	0	0	0	0	

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

APPENDIX B 5-3

URINALYSIS : SUMMARY, MOSUE : MALE

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0276 URINALYSIS
ANIMAL : MOUSE BDF1
SAMPLING DATE : 013-2
SEX : MALE REPORT TYPE : A1

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	±	+	2+	3+	4+	CHI	Occult blood −	±	+	2+	3+	CHI
Control	10	0	0	0	0	0	9	1		0	0	3	7	0	0		10	0	0	0	0	0		0	4	6	0	0	0		10	0	0	0	0	
50 ppm	10	0	0	1	3	2	4	0		0	0	7	3	0	0		10	0	0	0	0	0		0	4	6	0	0	0		10	0	0	0	0	
100 ppm	10	0	1	0	1	4	4	0		0	0	4	5	1	0		10	0	0	0	0	0		1	7	2	0	0	0		10	0	0	0	0	
200 ppm	9	0	0	0	4	3	1	1	**	0	0	6	1	1	1		9	0	0	0	0	0		0	5	4	0	0	0		9	0	0	0	0	
400 ppm	8	0	0	0	0	1	6	1		0	0	5	2	0	1		8	0	0	0	0	0		1	2	3	1	1	0		8	0	0	0	0	
800 ppm	10	0	1	1	3	4	1	0	**	0	0	7	3	0	0		10	0	0	0	0	0		2	6	2	0	0	0		10	0	0	0	0	

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

STUDY NO. : 0276 URINALYSIS
ANIMAL : MOUSE BDF1
SAMPLING DATE : 013-2
SEX : MALE REPORT TYPE : A1

Group Name	NO. of Animals	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0	
50 ppm	10	10	0	0	0	0	
100 ppm	10	10	0	0	0	0	
200 ppm	9	9	0	0	0	0	
400 ppm	8	8	0	0	0	0	
800 ppm	10	10	0	0	0	0	

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

APPENDIX B 5-4

URINALYSIS : SUMMARY, MOSUE : FEMALE

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0276
ANIMAL : MOUSE BDF1
SAMPLING DATE : 013-2
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	2	5	3	0		0	1	6	3	0	0		10	0	0	0	0	0		4	3	3	0	0	0		10	0	0	0	0	
50 ppm	10	0	0	1	1	3	5	0		0	1	5	4	0	0		10	0	0	0	0	0		1	4	5	0	0	0		10	0	0	0	0	
100 ppm	10	0	0	0	1	6	3	0		0	1	7	2	0	0		10	0	0	0	0	0		2	3	5	0	0	0		10	0	0	0	0	
200 ppm	10	0	0	0	3	6	1	0		0	1	8	1	0	0		10	0	0	0	0	0		4	5	0	1	0	0		10	0	0	0	0	
400 ppm	9	0	0	0	0	1	7	1		0	1	5	3	0	0		9	0	0	0	0	0		2	1	6	0	0	0		9	0	0	0	0	
800 ppm	10	0	0	2	1	3	4	0		0	0	4	4	2	0		10	0	0	0	0	0		4	1	3	2	0	0		10	0	0	0	0	

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

STUDY NO. : 0276
ANIMAL : MOUSE BDF1
SAMPLING DATE : 013-2
SEX : FEMALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0	
50 ppm	10	10	0	0	0	0	
100 ppm	10	10	0	0	0	0	
200 ppm	10	10	0	0	0	0	
400 ppm	9	9	0	0	0	0	
800 ppm	10	10	0	0	0	0	

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

APPENDIX B 6-1

GROSS FINDINGS : SUMMARY, RAT : MALE : SACRIFICED ANIMALS

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0275
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	50 ppm 10 (%)	100 ppm 10 (%)	200 ppm 10 (%)
liver	white zone		0 (0)	0 (0)	0 (0)	0 (0)
	red zone		0 (0)	0 (0)	0 (0)	0 (0)

STUDY NO. : 0275
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name / NO. of Animals	400 ppm 10	(%)	800 ppm 10	(%)
liver	white zone		0	(0)	1	(10)
	red zone		0	(0)	1	(10)

APPENDIX B 6-2

GROSS FINDINGS : SUMMARY, RAT : FEMALE : SACRIFICED ANIMALS

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0275
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	50 ppm 10 (%)	100 ppm 10 (%)	200 ppm 10 (%)
liver	white zone		0 (0)	0 (0)	0 (0)	0 (0)
	herniation		2 (20)	0 (0)	1 (10)	2 (20)
uterus	absence		0 (0)	0 (0)	0 (0)	0 (0)

STUDY NO. : 0275
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name	400 ppm	800 ppm
		NO. of Animals	10 (%)	10 (%)
liver	white zone		0 (0)	4 (40)
	herniation		0 (0)	0 (0)
uterus	absence		1 (10)	0 (0)

APPENDIX B 6-3

GROSS FINDINGS : SUMMARY, MOSUE : MALE : SACRIFICED ANIMALS

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0276
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	50 ppm 10 (%)	100 ppm 10 (%)	200 ppm 10 (%)
spleen	black zone		0 (0)	0 (0)	1 (10)	2 (20)
liver	white zone		0 (0)	0 (0)	0 (0)	0 (0)
	red zone		0 (0)	0 (0)	0 (0)	0 (0)
	brown zone		0 (0)	0 (0)	0 (0)	0 (0)
kidney	hydronephrosis		0 (0)	1 (10)	0 (0)	0 (0)
testis	atrophic		1 (10)	1 (10)	0 (0)	0 (0)

STUDY NO. : 0276
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name / NO. of Animals	400 ppm 10 (%)	800 ppm 10 (%)
spleen	black zone		0 (0)	0 (0)
liver	white zone		0 (0)	3 (30)
	red zone		0 (0)	1 (10)
	brown zone		0 (0)	1 (10)
kidney	hydronephrosis		0 (0)	0 (0)
testis	atrophic		0 (0)	0 (0)

APPENDIX B 6-4

GROSS FINDINGS : SUMMARY, MOSUE : FEMALE : SACRIFICED ANIMALS

(THIRTEEN - WEEK STUDY)

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	50 ppm 10 (%)	100 ppm 10 (%)	200 ppm 10 (%)
spleen	red zone		0 (0)	0 (0)	0 (0)	0 (0)
	black zone		0 (0)	0 (0)	0 (0)	0 (0)
ovary	cyst		0 (0)	0 (0)	1 (10)	0 (0)

Organ	Findings	Group Name NO. of Animals	400 ppm 9 (%)	800 ppm 10 (%)
spleen	red zone		1 (11)	0 (0)
	black zone		0 (0)	1 (10)
ovary	cyst		0 (0)	0 (0)

APPENDIX B 7-1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : MALE

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0275
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	293± 16	0.222± 0.019	0.050± 0.005	2.747± 0.052	0.883± 0.035	0.937± 0.043
50 ppm	10	293± 17	0.242± 0.035	0.052± 0.010	2.763± 0.108	0.895± 0.052	0.938± 0.039
100 ppm	10	290± 20	0.236± 0.032	0.051± 0.006	2.746± 0.106	0.901± 0.054	0.918± 0.037
200 ppm	10	287± 20	0.230± 0.030	0.050± 0.008	2.760± 0.101	0.891± 0.055	0.926± 0.047
400 ppm	10	259± 17**	0.183± 0.036*	0.046± 0.007	2.710± 0.144	0.814± 0.038*	0.848± 0.059**
800 ppm	10	236± 16**	0.181± 0.023*	0.045± 0.005	2.673± 0.095	0.746± 0.056**	0.837± 0.055**

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

STUDY NO. : 0275
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	1.756± 0.089	0.476± 0.025	7.578± 0.533	1.865± 0.031
50 ppm	10	1.788± 0.087	0.491± 0.034	8.503± 0.534**	1.884± 0.034
100 ppm	10	1.767± 0.100	0.491± 0.033	8.587± 0.623**	1.862± 0.038
200 ppm	10	1.815± 0.132	0.482± 0.037	8.678± 0.755**	1.868± 0.029
400 ppm	10	1.681± 0.090	0.438± 0.033*	7.905± 0.595	1.811± 0.048**
800 ppm	10	1.581± 0.135**	0.421± 0.031**	7.562± 0.642	1.755± 0.040**

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

APPENDIX B 7-2

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : FEMALE

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0275
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	171± 7	0.204± 0.030	0.057± 0.007	0.086± 0.007	0.597± 0.025	0.706± 0.030
50 ppm	10	177± 9	0.209± 0.022	0.056± 0.005	0.092± 0.011	0.644± 0.060	0.735± 0.041
100 ppm	10	173± 6	0.204± 0.023	0.052± 0.003	0.093± 0.011	0.624± 0.027	0.730± 0.019
200 ppm	10	161± 7	0.175± 0.015*	0.049± 0.004*	0.086± 0.013	0.599± 0.040	0.705± 0.039
400 ppm	10	151± 11**	0.156± 0.015**	0.045± 0.004**	0.060± 0.013**	0.542± 0.032	0.632± 0.032**
800 ppm	10	132± 15**	0.124± 0.034**	0.048± 0.011**	0.060± 0.017**	0.506± 0.059**	0.639± 0.031**

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

STUDY NO. : 0275
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	1.128± 0.042	0.344± 0.021	4.112± 0.220	1.706± 0.077
50 ppm	10	1.199± 0.051*	0.355± 0.030	4.532± 0.384*	1.763± 0.034*
100 ppm	10	1.188± 0.050	0.374± 0.014	4.536± 0.179*	1.730± 0.045
200 ppm	10	1.161± 0.045	0.331± 0.020	4.355± 0.286	1.739± 0.033
400 ppm	10	1.098± 0.071	0.309± 0.024	4.362± 0.407	1.680± 0.041
800 ppm	10	1.127± 0.077	0.297± 0.043*	4.834± 0.495**	1.621± 0.042**

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

APPENDIX B 7-3

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOSUE : MALE

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0276
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	28.8± 1.7	0.033± 0.007	0.011± 0.003	0.202± 0.039	0.154± 0.009	0.168± 0.010
50 ppm	10	25.7± 1.5**	0.032± 0.005	0.009± 0.003	0.212± 0.036	0.148± 0.011	0.156± 0.010
100 ppm	10	27.0± 1.8	0.033± 0.004	0.009± 0.003	0.203± 0.022	0.157± 0.013	0.160± 0.009
200 ppm	10	25.9± 1.4**	0.033± 0.004	0.010± 0.002	0.195± 0.032	0.157± 0.010	0.161± 0.014
400 ppm	10	25.8± 1.7**	0.033± 0.005	0.009± 0.002	0.220± 0.024	0.145± 0.010	0.161± 0.008
800 ppm	10	22.8± 1.9**	0.028± 0.008	0.009± 0.002	0.180± 0.029	0.130± 0.012**	0.158± 0.013

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

STUDY NO. : 0276
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	0.446± 0.023	0.042± 0.004	1.187± 0.053	0.445± 0.021
50 ppm	10	0.437± 0.028	0.042± 0.008	1.228± 0.080	0.437± 0.024
100 ppm	10	0.446± 0.030	0.046± 0.006	1.373± 0.113**	0.441± 0.012
200 ppm	10	0.435± 0.023	0.044± 0.006	1.333± 0.080*	0.445± 0.013
400 ppm	10	0.413± 0.021	0.046± 0.006	1.340± 0.118**	0.445± 0.012
800 ppm	10	0.389± 0.042**	0.037± 0.010	1.205± 0.148	0.422± 0.019*

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

APPENDIX B 7-4

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOSUE : FEMALE

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0276
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	20.1± 1.1	0.037± 0.005	0.012± 0.003	0.024± 0.005	0.119± 0.009	0.152± 0.010
50 ppm	10	20.6± 0.8	0.038± 0.005	0.013± 0.002	0.024± 0.004	0.126± 0.008	0.157± 0.011
100 ppm	10	20.4± 1.3	0.037± 0.009	0.012± 0.002	0.026± 0.010	0.123± 0.011	0.154± 0.016
200 ppm	10	21.1± 1.4	0.039± 0.006	0.013± 0.002	0.027± 0.005	0.128± 0.008	0.158± 0.013
400 ppm	9	20.7± 1.0	0.036± 0.006	0.011± 0.002	0.022± 0.004	0.122± 0.012	0.150± 0.011
800 ppm	10	19.6± 1.0	0.030± 0.008	0.011± 0.003	0.020± 0.003	0.110± 0.009	0.159± 0.009

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

STUDY NO. : 0276
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	0.289± 0.021	0.045± 0.006	0.909± 0.094	0.450± 0.014
50 ppm	10	0.303± 0.013	0.050± 0.005	0.987± 0.087	0.459± 0.012
100 ppm	10	0.301± 0.019	0.052± 0.009	0.999± 0.096	0.445± 0.011
200 ppm	10	0.313± 0.017	0.054± 0.010	1.060± 0.122	0.450± 0.017
400 ppm	9	0.299± 0.021	0.052± 0.010	1.040± 0.161	0.446± 0.023
800 ppm	10	0.291± 0.022	0.042± 0.008	1.016± 0.155	0.433± 0.013

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

APPENDIX B 8-1

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : MALE

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0275
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	293± 16	0.076± 0.005	0.017± 0.001	0.941± 0.052	0.302± 0.006	0.320± 0.007
50 ppm	10	293± 17	0.082± 0.013	0.018± 0.004	0.944± 0.048	0.306± 0.018	0.320± 0.012
100 ppm	10	290± 20	0.081± 0.008	0.018± 0.003	0.950± 0.063	0.311± 0.015	0.317± 0.012
200 ppm	10	287± 20	0.080± 0.009	0.017± 0.003	0.966± 0.042	0.311± 0.012	0.324± 0.012
400 ppm	10	259± 17**	0.071± 0.013	0.018± 0.003	1.049± 0.060**	0.315± 0.022	0.327± 0.010
800 ppm	10	236± 16**	0.077± 0.010	0.019± 0.002	1.136± 0.062**	0.316± 0.012	0.355± 0.012**

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

STUDY NO. : 0275
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	0.601± 0.023	0.163± 0.005	2.589± 0.082	0.639± 0.030
50 ppm	10	0.611± 0.022	0.167± 0.005	2.900± 0.036	0.645± 0.039
100 ppm	10	0.610± 0.021	0.169± 0.005	2.960± 0.065*	0.645± 0.046
200 ppm	10	0.634± 0.027*	0.168± 0.003	3.027± 0.099**	0.655± 0.042
400 ppm	10	0.651± 0.032**	0.169± 0.004	3.053± 0.082**	0.702± 0.036**
800 ppm	10	0.669± 0.025**	0.179± 0.009**	3.204± 0.166**	0.747± 0.052**

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

APPENDIX B 8-2

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : FEMALE

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0275
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	171± 7	0.119± 0.014	0.034± 0.004	0.050± 0.003	0.349± 0.012	0.413± 0.024
50 ppm	10	177± 9	0.118± 0.011	0.032± 0.003	0.052± 0.004	0.364± 0.027	0.416± 0.018
100 ppm	10	173± 6	0.118± 0.010	0.030± 0.003	0.054± 0.006	0.361± 0.019	0.422± 0.013
200 ppm	10	161± 7	0.108± 0.007	0.030± 0.003	0.053± 0.008	0.372± 0.018	0.438± 0.024
400 ppm	10	151± 11**	0.104± 0.006*	0.030± 0.004	0.040± 0.007	0.360± 0.015	0.420± 0.016
800 ppm	10	132± 15**	0.092± 0.019**	0.037± 0.008	0.045± 0.011	0.384± 0.027**	0.489± 0.058**

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

STUDY NO. : 0275
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	0.659± 0.018	0.201± 0.012	2.402± 0.098	0.998± 0.063
50 ppm	10	0.679± 0.013	0.201± 0.011	2.560± 0.118	0.999± 0.047
100 ppm	10	0.686± 0.015	0.217± 0.009*	2.623± 0.073	1.001± 0.037
200 ppm	10	0.721± 0.024**	0.205± 0.011	2.701± 0.097**	1.081± 0.054
400 ppm	10	0.729± 0.039**	0.205± 0.007	2.889± 0.102**	1.119± 0.087*
800 ppm	10	0.860± 0.083**	0.225± 0.022*	3.683± 0.388**	1.243± 0.154**

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

APPENDIX B 8-3

ORGAN WEIGHT, RELATIVE : SUMMARY, MOSUE : MALE

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0276
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	28.8± 1.7	0.115± 0.020	0.037± 0.012	0.703± 0.140	0.535± 0.036	0.583± 0.035
50 ppm	10	25.7± 1.5**	0.123± 0.017	0.037± 0.010	0.821± 0.120	0.573± 0.033	0.607± 0.043
100 ppm	10	27.0± 1.8	0.122± 0.015	0.035± 0.010	0.753± 0.094	0.583± 0.030*	0.594± 0.038
200 ppm	10	25.9± 1.4**	0.126± 0.012	0.039± 0.008	0.756± 0.123	0.610± 0.054**	0.623± 0.047
400 ppm	10	25.8± 1.7**	0.130± 0.019	0.036± 0.006	0.854± 0.089	0.563± 0.025	0.623± 0.028
800 ppm	10	22.8± 1.9**	0.122± 0.027	0.038± 0.010	0.795± 0.145	0.572± 0.038	0.693± 0.052**

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

STUDY NO. : 0276
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	1.549± 0.082	0.147± 0.012	4.125± 0.144	1.546± 0.097
50 ppm	10	1.703± 0.142**	0.162± 0.032	4.770± 0.170**	1.706± 0.154**
100 ppm	10	1.652± 0.056	0.169± 0.020	5.075± 0.151**	1.637± 0.100
200 ppm	10	1.681± 0.079*	0.170± 0.020	5.152± 0.211**	1.722± 0.062**
400 ppm	10	1.601± 0.087	0.178± 0.022*	5.186± 0.284**	1.729± 0.092**
800 ppm	10	1.702± 0.106**	0.160± 0.038	5.262± 0.318**	1.856± 0.117**

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

APPENDIX B 8-4

ORGAN WEIGHT, RELATIVE : SUMMARY, MOSUE : FEMALE

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0276
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	20.1± 1.1	0.184± 0.022	0.060± 0.015	0.119± 0.026	0.591± 0.037	0.756± 0.036
50 ppm	10	20.6± 0.8	0.184± 0.023	0.063± 0.012	0.117± 0.019	0.612± 0.038	0.763± 0.042
100 ppm	10	20.4± 1.3	0.179± 0.034	0.056± 0.008	0.129± 0.044	0.602± 0.050	0.751± 0.048
200 ppm	10	21.1± 1.4	0.184± 0.031	0.060± 0.008	0.130± 0.021	0.606± 0.050	0.745± 0.029
400 ppm	9	20.7± 1.0	0.175± 0.021	0.055± 0.010	0.105± 0.015	0.591± 0.050	0.724± 0.059
800 ppm	10	19.6± 1.0	0.152± 0.036	0.055± 0.012	0.103± 0.016	0.559± 0.041	0.810± 0.042*

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

STUDY NO. : 0276
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	1.439± 0.050	0.223± 0.028	4.525± 0.246	2.250± 0.147
50 ppm	10	1.473± 0.054	0.242± 0.017	4.792± 0.316	2.234± 0.125
100 ppm	10	1.473± 0.076	0.252± 0.030	4.888± 0.282	2.184± 0.134
200 ppm	10	1.480± 0.054	0.256± 0.042	5.006± 0.328	2.137± 0.140
400 ppm	9	1.443± 0.069	0.250± 0.041	4.998± 0.569	2.155± 0.121
800 ppm	10	1.485± 0.087	0.216± 0.038	5.170± 0.612	2.216± 0.125

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

APPENDIX B 9-1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : SACRIFICED ANIMALS

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0275
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control				50 ppm				100 ppm				200 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>			
	erosion: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)
[Digestive system]																		
liver			<10>				<10>				<10>				<10>			
	herniation		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)
	increase in mitosis		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:single cell		0	0	0	0	0	0	0	0	0	0	0	0	8	0	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(80)	(0)	(0)	(0)
	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)
	granulation		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(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	3	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(30)	(0)	(0)	(0)

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

Organ	Findings	Group Name	400 ppm				800 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
nasal cavit			<10>				<10>			
	erosion:respiratory epithelium		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]										
liver			<10>				<10>			
	herniation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	increase in mitosis		4	0	0	0	5	0	0	0 *
			(40)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
	necrosis:single cell		10	0	0	0 **	2	8	0	0 **
			(100)	(0)	(0)	(0)	(20)	(80)	(0)	(0)
	deposit of hemosiderin		5	0	0	0 *	10	0	0	0 **
			(50)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	granulation		1	0	0	0	0	1	0	0
			(10)	(0)	(0)	(0)	(0)	(10)	(0)	(0)
	swelling:central		8	0	0	0 **	9	0	0	0 **
			(80)	(0)	(0)	(0)	(90)	(0)	(0)	(0)

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

STUDY NO. : 0275
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control				50 ppm				100 ppm				200 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>			
	eosinophilic droplet: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)

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

Organ	Findings	Group Name	400 ppm				800 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]										
kidney			<10>				<10>			
	eosinophilic droplet:proximal tubule		9	0	0	0	8	0	0	0
			(90)	(0)	(0)	(0)	(80)	(0)	(0)	(0)

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

APPENDIX B 9-2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : SACRIFICED ANIMALS

(THIRTEEN - WEEK STUDY)

Organ	Findings	Group Name	Control				50 ppm				100 ppm				200 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Hematopoietic system]																		
bone marrow			<10>				<10>				<10>				<10>			
	granulation		2 (20)	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)
thymus			<10>				<10>				<10>				<10>			
	atrophy		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Digestive system]																		
liver			<10>				<10>				<10>				<10>			
	herniation		2 (20)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	3 (30)	0 (0)	0 (0)	0 (0)
	increase in mitosis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4 (40)	0 (0)	0 (0)	0 (0)
	necrosis:focal		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	necrosis:single cell		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	8 (80)	0 (0)	0 (0)	0 (0) **

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

Organ	Findings	Group Name	400 ppm				800 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]										
bone marrow			<10>				<10>			
	granulation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thymus			<10>				< 9>			
	atrophy		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(11)	(0)	(0)	(0)
[Digestive system]										
liver			<10>				<10>			
	herniation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	increase in mitosis		3	0	0	0	0	0	0	0
			(30)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:focal		0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)
	necrosis:single cell		9	0	0	0 **	5	5	0	0 **
			(90)	(0)	(0)	(0)	(50)	(50)	(0)	(0)

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

Organ	Findings	Group Name	Control				50 ppm				100 ppm				200 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]																		
liver			<10>				<10>				<10>				<10>			
	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)	10 (100)	0 (0)	0 (0)	0 ** (0)
	granulation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
	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			<10>				<10>				<10>				<10>			
	hyaline cast		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	mineralization:cortico-medullary junction		2 (20)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	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)	2 (20)	0 (0)	0 (0)	0 (0)
[Endocrine system]																		
thyroid			<10>				<10>				<10>				<10>			
	granulation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)

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

Organ	Findings	Group Name	400 ppm				800 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]										
liver			<10>				<10>			
	deposit of hemosiderin		10	0	0	0 **	10	0	0	0 **
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	granulation		0	0	0	0	1	2	0	0
			(0)	(0)	(0)	(0)	(10)	(20)	(0)	(0)
	swelling:central		8	0	0	0 **	10	0	0	0 **
			(80)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
[Urinary system]										
kidney			<10>				<10>			
	hyaline cast		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	mineralization:cortico-medullary junction		3	0	0	0	0	0	0	0
			(30)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:papilla		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
[Endocrine system]										
thyroid			<10>				<10>			
	granulation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				50 ppm				100 ppm				200 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Reproductive system]																		
uterus			<10>				<10>				<10>				<10>			
	aplasia		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Special sense organs/appandage]																		
Harder gl			<10>				<10>				<10>				<10>			
	granulation		3	0	0	0	0	0	0	0	1	0	0	0	3	0	0	0
			(30)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(30)	(0)	(0)	(0)

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

Organ	Findings	Group Name	400 ppm				800 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Reproductive system]										
uterus			<10>				<10>			
	aplasia		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Special sense organs/appandage]										
Harder gl			<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
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

APPENDIX B 9-3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : MALE : SACRIFICED ANIMALS

(THIRTEEN - WEEK STUDY)

STUDY NO. : 0276
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control				50 ppm				100 ppm				200 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
spleen			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		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)
[Circulatory system]																		
heart			<10>				<10>				<10>				<10>			
	necrosis		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)
[Digestive system]																		
stomach			<10>				<10>				<10>				<10>			
	erosion:forestomach		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)
	ulcer:forestomach		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyperplasia:forestomach		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	400 ppm				800 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]										
spleen			<10>				<10>			
	deposit of hemosiderin		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Circulatory system]										
heart			<10>				<10>			
	necrosis		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]										
stomach			<10>				<10>			
	erosion:forestomach		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	ulcer:forestomach		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyperplasia:forestomach		1	0	0	0	2	0	0	0
			(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				50 ppm				100 ppm				200 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
liver			<10>				<10>				<10>				<10>			
	necrosis: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)
	necrosis:focal		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:single cell		1	1	0	0	1	2	0	0	2	3	0	0	3	1	0	0
			(10)	(10)	(0)	(0)	(10)	(20)	(0)	(0)	(20)	(30)	(0)	(0)	(30)	(10)	(0)	(0)
	deposit of ceroid		0	0	0	0	0	0	0	0	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		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)
	mineralization		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	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			<10>				<10>				<10>				<10>			
	vacuolization of proximal tubule		10	0	0	0	10	0	0	0	10	0	0	0	9	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(90)	(0)	(0)	(0)

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

Organ	Findings	Group Name	400 ppm				800 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]										
liver			<10>				<10>			
	necrosis:central		0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)
	necrosis:focal		0	0	0	0	2	1	0	0
			(0)	(0)	(0)	(0)	(20)	(10)	(0)	(0)
	necrosis:single cell		2	0	1	0	0	9	1	0 **
			(20)	(0)	(10)	(0)	(0)	(90)	(10)	(0)
	deposit of ceroid		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	deposit of hemosiderin		0	0	0	0	4	0	0	0
			(0)	(0)	(0)	(0)	(40)	(0)	(0)	(0)
	mineralization		0	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(30)	(0)	(0)	(0)
	swelling:central		0	0	0	0	0	10	0	0 **
			(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
[Urinary system]										
kidney			<10>				<10>			
	vacuolization of proximal tubule		4	0	0	0 *	0	0	0	0 **
			(40)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				50 ppm				100 ppm				200 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>			
	hydronephrosis		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)
[Reproductive system]																		
testis			<10>				<10>				<10>				<10>			
	atrophy		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)
	spermatogenic granuloma		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
[Special sense organs/appandage]																		
eye			<10>				<10>				<10>				<10>			
	keratitis		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)

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

Organ	Findings	Group Name	400 ppm				800 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]										
kidney			<10>				<10>			
	hydronephrosis		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Reproductive system]										
testis			<10>				<10>			
	atrophy		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	spermatogenic granuloma		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Special sense organs/appandage]										
eye			<10>				<10>			
	keratitis		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

APPENDIX B 9-4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : FEMALE : SACRIFICED ANIMALS

(THIRTEEN - WEEK STUDY)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 10				50 ppm 10				100 ppm 10				200 ppm 10			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
nasal cavit			<10>				<10>				<10>				<10>			
	desquamation:olfactory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
[Hematopoietic system]																		
spleen			<10>				<10>				<10>				<10>			
	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)
[Digestive system]																		
stomach			<10>				<10>				<10>				<10>			
	ulcer:forestomach		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)
	hyperplasia:forestomach		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	erosion:glandular stomach		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

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

Organ	Findings	Group Name	400 ppm				800 ppm			
		No. of Animals on Study	9				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
nasal cavit			< 9>				<10>			
	desquamation:olfactory epithelium		1	0	0	0	0	0	0	0
			(11)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Hematopoietic system]										
spleen			< 9>				<10>			
	deposit of hemosiderin		1	0	0	0	1	0	0	0
			(11)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
[Digestive system]										
stomach			< 9>				<10>			
	ulcer:forestomach		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	hyperplasia:forestomach		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	erosion:glandular stomach		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				50 ppm				100 ppm				200 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
liver			<10>				<10>				<10>				<10>			
	increase in mitosis		0	0	0	0	1	0	0	0	0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	necrosis:focal		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)
	necrosis:single cell		0	0	0	0	3	2	0	0 *	3	4	0	0 **	3	3	2	0 **
			(0)	(0)	(0)	(0)	(30)	(20)	(0)	(0)	(30)	(40)	(0)	(0)	(30)	(30)	(20)	(0)
	deposit of hemosiderin		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)
	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)
[Nervous system]																		
brain			<10>				<10>				<10>				<10>			
	epidermal cyst		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)

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

Organ	Findings	Group Name	400 ppm				800 ppm			
		No. of Animals on Study	9				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]										
liver			< 9>				<10>			
	increase in mitosis		1	0	0	0	1	0	0	0
			(11)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	necrosis:focal		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:single cell		2	5	1	0 **	1	5	4	0 **
			(22)	(56)	(11)	(0)	(10)	(50)	(40)	(0)
	deposit of hemosiderin		1	0	0	0	2	0	0	0
			(11)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	swelling:central		0	0	0	0	6	0	0	0 *
			(0)	(0)	(0)	(0)	(60)	(0)	(0)	(0)
[Nervous system]										
brain			< 9>				<10>			
	epidermal cyst		1	0	0	0	0	0	0	0
			(11)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

APPENDIX B 10-1

IDENTITY OF *N,N*-DIMETHYLFORMAMIDE

(THIRTEEN - WEEK STUDY)

IDENTITY OF *N,N*-DIMETHYLFORMAMIDE(THIRTEEN-WEEK STUDIES)

Lot no. CAL4288

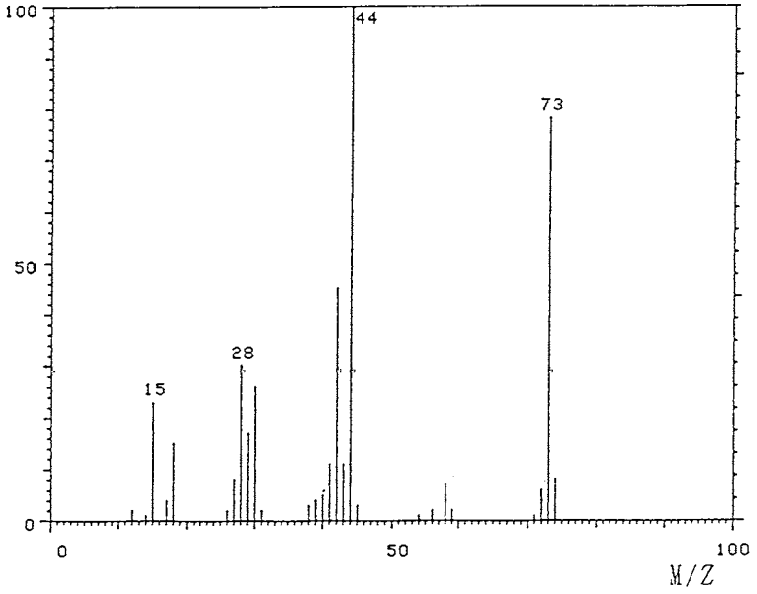
1. Spectral data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Results: The mass spectrum was consistent with literature spectrum.

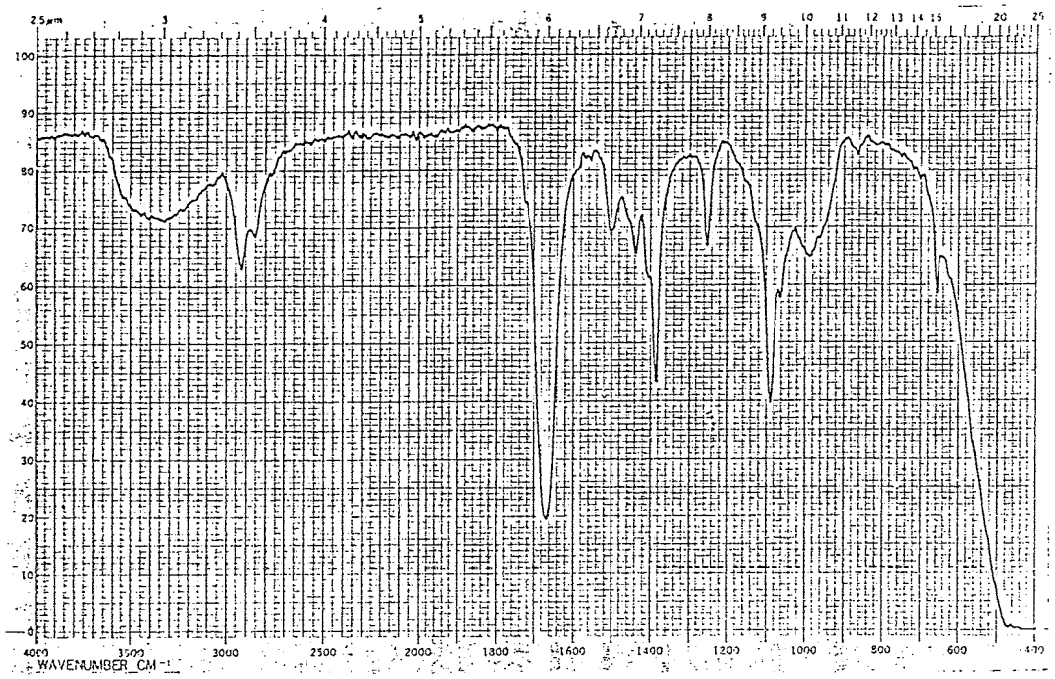
Determined Values Fragment Peak(M/Z)	Literature Values* Fragment Peak(M/Z)
15	15
28	28
44(Base Peak)	44(Base Peak)
73	73
	(*EPA/NIH Mass Spectral Data Base (1978) Vol. 1, p. 20.)

Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

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})
650～ 680	650～ 680
850～ 890	850～ 890
920～1030	
1030～1150	1030～1150
1220～1280	1220～1280
1350～1430	1350～1430
1430～1480	1430～1480
1480～1540	1480～1540
1600～1760	1600～1760
2800～3000	2800～3000
3100～3650	3100～3700

(*Performed by the WAKO PURE CHEMICAL INDUSTRIES, LTD.)

2. Conclusions: The test substance was identified as *N,N*-Dimethylformamide, by the mass spectrum and the infrared spectrum.

APPENDIX B 10-2

STABILITY OF *N,N*-DIMETHYLFORMAMIDE

(THIRTEEN - WEEK STUDY)

STABILITY OF *N,N*-DIMETHYLFORMAMIDE(THIRTEEN-WEEK STUDIES)

Lot no. CAL4288

1. Sample: This lot was used from 1994.9.7 to 1994.12.12. Test substance was stored at room temperature .

2. Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium

Results: The result of infrared spectrum did not change when before and after studies.

1994.09.06(date analyzed)	1994.12.14(date analyzed)
Wave Number(cm^{-1})	Wave Number(cm^{-1})
650～ 680	650～ 680
850～ 890	850～ 890
920～1030	920～1030
1030～1150	1030～1150
1220～1280	1220～1280
1350～1430	1350～1430
1430～1480	1430～1480
1480～1540	1480～1540
1600～1760	1600～1760
2800～3000	2800～3000
3100～3650	3100～3650

3. Gas Chromatography

Instrument: Hewlett Packard 5890A Gas Chromatograph

Column: INNOWax(0.2mm ϕ × 50m)

Column Temperature: 150°C

Flow Rate: 1 ml/min

Detector: FID(Flame Ionization Detector)

Injection Volume: 1 μl

Results: Gas chromatography indicated one major peak(peak No.1) analyzed at 1994.9.6 and one major peak(peak No.1) analyzed at 1994.12.14. No new treace impurity peak in the test substance analyzed at 1994.12.14 was detected.

Date	Peak No.	Retention Time(min)	Area Count
1994.09.06 (date analyzed)	1	6.013	28353
1994.12.14 (date a.alyzed)	1	6.013	28450

4. Conclusions: The test substance was stable for about 3 months in the dark at room temperature.

APPENDIX B 11-1

CONCENTRATION OF *N,N*-DIMETHYLFORMAMIDE IN INHALATION CHAMBER

(THIRTEEN - WEEK STUDY)

CONCENTRATION OF *N,N*-DIMETHYLFORMAMIDE
IN INHALTION CHAMBER
(RAT : THIRTEEN-WEEK STUDY)

Group Name	Concentration (ppm) Mean ± S.D.
Control	0.0 ± 0.0
50ppm	49.6 ± 0.7
100ppm	100.1 ± 0.8
200ppm	199.5 ± 1.9
400ppm	399.7 ± 3.2
800ppm	795.6 ± 9.3

CONCENTRATION OF *N,N*-DIMETHYLFORMAMIDE
IN INHALTION CHAMBER
(MOUSE : THIRTEEN-WEEK STUDY)

Group Name	Concentration (ppm) Mean ± S.D.
Control	0.0 ± 0.0
50ppm	50.1 ± 0.7
100ppm	100.3 ± 1.3
200ppm	199.2 ± 1.7
400ppm	400.2 ± 1.7
800ppm	796.3 ± 5.7

APPENDIX B 11-2

ENVIRONMENT OF INHALATION CHAMBER

(THIRTEEN - WEEK STUDY)

ENVIRONMENT OF INHALATION CHAMBER (RAT : THIRTEEN-WEEK STUDY)

Group Name	Temperature(℃) Mean ± S.D.	Humidity(%) Mean ± S.D.	Ventilation Rate(L/min) Mean ± S.D.	Room Air Change(time/h) Mean
Control	22.4 ± 0.1	57.0 ± 0.4	212.0 ± 0.6	12.0
50ppm	21.8 ± 0.4	57.0 ± 0.6	211.8 ± 0.5	12.0
100ppm	22.6 ± 0.2	56.6 ± 0.8	211.1 ± 0.7	11.9
200ppm	22.3 ± 0.1	51.9 ± 0.7	211.9 ± 0.6	12.0
400ppm	22.8 ± 0.1	49.3 ± 1.0	210.9 ± 0.7	11.9
800ppm	22.6 ± 0.1	53.5 ± 1.1	212.1 ± 0.7	12.0

ENVIRONMENT OF INHALATION CHAMBER (MOUSE : THIRTEEN-WEEK STUDY)

Group Name	Temperature(℃) Mean ± S.D.	Humidity(%) Mean ± S.D.	Ventilation Rate(L/min) Mean ± S.D.	Room Air Change(time/h) Mean
Control	21.2 ± 0.2	58.1 ± 1.2	104.1 ± 0.3	12.0
50ppm	21.1 ± 0.2	53.4 ± 0.7	104.1 ± 0.3	12.0
100ppm	21.4 ± 0.2	55.3 ± 0.9	104.5 ± 0.3	12.1
200ppm	21.9 ± 0.1	54.0 ± 1.2	103.9 ± 0.3	12.0
400ppm	22.7 ± 0.1	52.1 ± 1.1	104.3 ± 0.4	12.0
800ppm	22.1 ± 0.1	50.2 ± 1.2	104.4 ± 0.3	12.0

APPENDIX B 12

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS

(THIRTEEN - WEEK STUDY)

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS (THIRTEEN WEEK STUDIES)

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)	IFCC method [4]
Glutamic pyruvic transaminase(GPT)	IFCC method [4]
Lactate dehydrogenase (LDH)	Wroblewski-LaDue method [4]
Alkaline phosphatase (ALP)	GSCC method [4]
γ-Glutamyl transpeptidase (G-GTP)	L-γ-Glutamyl-p-nitroanilide substrate method [4]
Creatine phosphokinase (CPK)	GSCC method [4]
Urea nitrogen	Enzymatic method (Urease·GLDH) [4]
Creatinine	Jaffe metod [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 metod [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 : Miles-Sankyo Co., Ltd., Japan)

APPENDIX C 1

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)	×106/μL	2
Hemoglobin (Hgb)	g/dL	1
Hematocrit (Hct)	%	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	×103/μL	0
White blood cell (WBC)	×103/μL	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 (G-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