p-ニトロアニソールのマウスを用いた経口投与による
１３ 週 間 毒 性 試 験（混 餌 試 験 ）報 告 書

試験番号：０３７０

APPENDIX

APPENDIXES

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1 14

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7	14-7
DEATH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30000 ppm	0	0	2	4	5	5	5	5	5	5	5	5	5	5
HUNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30000 ppm	0	0	1	0	0	0	0	0	0	0	0	0	0	0
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30000 ppm	0	0	1	0	0	0	0	0	0	0	0	0	0	0
GUM	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	1	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
IRREGULAR BREATHING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30000 ppm	0	0	1	0	0	0	0	0	0	0	0	0	0	0
ABNORMAL RESPIRATION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30000 ppm	0	0	1	0	0	0	0	0	0	0	0	0	0	0

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1 14

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7	14-7
YELLOW URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	10	10	10	10	10	10	10
	5000 ppm	0	0	0	0	0	0	0	10	10	10	10	10	10	10
	10000 ppm	0	0	0	0	0	0	0	10	10	10	10	10	10	10
	20000 ppm	0	10	10	10	10	10	10	10	10	10	10	10	10	10
	30000 ppm	0	10	8	6	5	5	5	5	5	5	5	5	5	5
SMALL STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30000 ppm	0	0	1	0	0	0	0	0	0	0	0	0	0	0

APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1 14

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

Clinical sign	Group Name	Administration Week-day 1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7	14-7
DEATH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30000 ppm	0	1	4	7	7	7	7	7	7	7	7	7	7	7
HUNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30000 ppm	0	0	2	0	0	0	0	0	0	0	0	0	0	0
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30000 ppm	0	0	3	0	0	0	0	0	0	0	0	0	0	0
IRREGULAR BREATHING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30000 ppm	0	0	1	0	0	0	0	0	0	0	0	0	0	0
ABNORMAL RESPIRATION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30000 ppm	0	0	1	0	0	0	0	0	0	0	0	0	0	0
YELLOW URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	10	10	10	10	10	10	10
	5000 ppm	0	0	0	0	0	0	0	10	10	10	10	10	10	10
	10000 ppm	0	0	0	0	0	0	0	10	10	10	10	10	10	10
	20000 ppm	0	10	10	10	10	10	10	10	10	10	10	10	10	10
	30000 ppm	0	9	6	3	3	3	3	3	3	3	3	3	3	3

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1 14

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

Clinical sign	Group Name	Administration Week-day 1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7	14-7
SMALL STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30000 ppm	0	0	1	0	0	0	0	0	0	0	0	0	0	0

APPENDIX B 1

BODY WEIGHT CHANGES : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 14
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 0	1	2	3	4	5	6
Control	23.2± 0.6	23.8± 0.5	24.4± 1.1	25.8± 0.8	26.9± 0.9	27.1± 0.9	28.2± 1.2
2500 ppm	23.1± 0.6	23.6± 0.9	24.2± 0.8	25.2± 0.8	25.9± 1.2	26.8± 1.3	27.6± 1.6
5000 ppm	23.1± 0.6	23.5± 0.9	24.1± 1.0	25.5± 1.1	26.4± 1.4	27.5± 1.5	28.1± 1.6
10000 ppm	23.1± 0.7	23.9± 0.8	24.3± 0.9	25.7± 0.8	26.1± 1.1	26.8± 1.3	27.1± 1.2
20000 ppm	23.2± 0.6	23.7± 0.7	22.3± 0.9**	24.9± 1.0	25.6± 1.9	25.8± 1.3	26.4± 1.0*
30000 ppm	23.1± 0.7	23.1± 0.8	18.2± 0.8**	17.3± 1.5**	18.1± 1.8**	20.1± 1.6**	21.3± 1.7**

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

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 14
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 7	8	9	10	11	12	13
Control	28.0± 1.2	28.9± 1.4	29.7± 1.7	30.0± 1.7	31.1± 1.6	31.3± 1.5	31.9± 1.5
2500 ppm	27.3± 1.5	28.2± 1.9	28.5± 2.4	28.9± 2.1	29.9± 2.1	29.9± 2.1	30.8± 2.5
5000 ppm	27.4± 1.5	28.3± 1.8	28.8± 2.3	29.2± 2.4	30.1± 2.4	30.0± 2.3	30.7± 2.4
10000 ppm	26.6± 1.3	27.8± 1.4	28.1± 1.4	28.1± 1.5	28.8± 1.7*	28.7± 1.6**	28.9± 2.3**
20000 ppm	25.9± 1.1**	26.8± 0.9*	27.0± 0.9**	27.3± 1.0**	27.3± 1.0**	27.3± 1.0**	28.0± 1.0**
30000 ppm	22.4± 1.4**	22.7± 1.6**	23.7± 1.9**	24.2± 1.1**	24.4± 1.4**	24.2± 1.4**	24.6± 1.3**

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

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 14
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 14
Control	32.4± 1.5
2500 ppm	31.5± 2.7
5000 ppm	31.6± 2.4
10000 ppm	29.5± 2.7
20000 ppm	28.3± 0.9**
30000 ppm	25.0± 1.8**

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

APPENDIX B 2

BODY WEIGHT CHANGES : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 14
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 0	1	2	3	4	5	6
Control	18.3± 0.4	18.4± 0.6	19.0± 0.6	19.7± 0.5	19.6± 0.7	21.1± 0.9	21.0± 0.8
2500 ppm	18.3± 0.4	18.5± 0.4	19.1± 0.8	19.8± 0.5	20.2± 0.4	20.6± 0.9	21.1± 0.6
5000 ppm	18.3± 0.4	18.5± 0.7	19.1± 0.6	19.8± 0.5	20.1± 0.6	20.7± 0.5	21.6± 0.8
10000 ppm	18.3± 0.4	18.7± 0.6	19.0± 0.5	19.8± 0.6	20.3± 0.6	20.8± 0.6	21.6± 0.7
20000 ppm	18.3± 0.4	18.5± 0.8	17.3± 0.6**	19.8± 1.0	21.0± 0.9**	21.6± 1.1	21.4± 1.0
30000 ppm	18.3± 0.4	18.5± 0.8	14.5± 0.9**	12.9± 1.4*	16.2± 0.9**	18.0± 2.1	19.6± 2.0*

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

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 14
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 7	8	9	10	11	12	13
Control	20.7± 0.6	21.3± 1.1	21.3± 0.7	22.1± 1.1	21.5± 0.8	22.1± 1.1	22.3± 1.1
2500 ppm	20.9± 0.8	21.3± 1.1	21.2± 0.7	21.8± 1.0	21.7± 1.3	21.6± 0.8	22.0± 1.0
5000 ppm	20.2± 0.4	21.3± 1.0	21.5± 0.4	22.0± 0.5	21.7± 0.7	22.3± 1.0	22.5± 0.6
10000 ppm	20.9± 0.8	22.1± 0.8	21.8± 0.8	22.2± 0.7	22.8± 1.1	22.7± 1.0	23.4± 0.5*
20000 ppm	20.6± 1.1	21.4± 1.1	21.7± 0.9	21.7± 0.9	21.8± 0.7	22.0± 1.0	22.2± 1.0
30000 ppm	20.7± 1.8	22.2± 1.4	22.3± 1.3	22.5± 1.4	22.4± 1.4	22.2± 0.7	22.5± 0.8

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

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 14
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 14
Control	22.4± 0.9
2500 ppm	22.1± 0.9
5000 ppm	22.8± 0.8
10000 ppm	23.5± 0.5*
20000 ppm	22.3± 0.8
30000 ppm	22.4± 0.9

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

APPENDIX C 1

FOOD CONSUMPTION CHANGES : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 14
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(7)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	4.2± 0.3	3.8± 0.5	4.2± 0.4	3.9± 0.5	4.0± 0.5	4.0± 0.4	4.1± 0.2
2500 ppm	4.0± 0.3	3.7± 0.4	4.0± 0.4	4.0± 0.4	3.9± 0.3	4.0± 0.4	3.9± 0.3
5000 ppm	4.1± 0.2	3.8± 0.3	4.0± 0.2	4.0± 0.3	4.0± 0.3	4.0± 0.3	3.8± 0.3
10000 ppm	4.0± 0.2	3.8± 0.3	3.9± 0.5	3.8± 0.5	3.8± 0.4	3.9± 0.4	3.9± 0.4
20000 ppm	4.2± 0.4	3.9± 1.2	4.7± 1.1	4.2± 1.2	4.4± 1.0	4.3± 1.1	4.4± 0.8
30000 ppm	3.9± 0.3	2.0± 0.4**	2.4± 0.6**	3.1± 1.1	3.7± 1.1	4.1± 1.3	4.5± 1.4

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

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 14
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)	14-7(7)
Control	3.9± 0.3	4.1± 0.4	4.1± 0.3	4.2± 0.3	3.9± 0.3	4.0± 0.4	4.1± 0.3
2500 ppm	4.0± 0.4	4.0± 0.3	4.0± 0.3	4.1± 0.4	3.9± 0.4	4.0± 0.4	4.2± 0.3
5000 ppm	4.1± 0.3	3.9± 0.6	4.0± 0.4	4.0± 0.3	3.8± 0.3	4.0± 0.4	4.2± 0.3
10000 ppm	4.0± 0.4	4.0± 0.3	3.9± 0.4	4.1± 0.3	4.0± 0.4	3.7± 0.5	4.1± 0.4
20000 ppm	4.6± 0.9	4.3± 0.5	4.2± 0.6	4.1± 0.5	4.2± 0.8	4.3± 0.7	4.4± 0.7
30000 ppm	4.5± 1.5	4.5± 1.7	4.2± 1.1	4.0± 1.0	4.1± 1.2	4.8± 0.9*	4.8± 0.9

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

APPENDIX C 2

FOOD CONSUMPTION CHANGES : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 14
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(7)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	3.7± 0.5	3.5± 0.3	3.5± 0.3	3.5± 0.2	3.6± 0.3	3.5± 0.3	3.5± 0.1
2500 ppm	3.6± 0.3	3.4± 0.3	3.4± 0.2	3.3± 0.2	3.6± 0.2	3.5± 0.3	3.5± 0.2
5000 ppm	3.6± 0.1	3.4± 0.2	3.4± 0.2	3.5± 0.2	3.6± 0.3	3.5± 0.3	3.5± 0.2
10000 ppm	3.6± 0.2	3.3± 0.2	3.5± 0.4	3.5± 0.4	3.6± 0.4	3.6± 0.4	3.5± 0.5
20000 ppm	3.5± 0.2	3.3± 0.7	3.8± 0.7	3.5± 0.7	3.4± 0.8	3.1± 0.3**	3.2± 0.4
30000 ppm	3.5± 0.2	3.0± 1.3	3.1± 2.2	3.5± 1.5	3.0± 0.8	3.2± 0.6	3.4± 0.6

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

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 14
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)	14-7(7)
Control	3.7± 0.2	3.7± 0.2	3.8± 0.3	3.7± 0.2	3.7± 0.3	3.8± 0.2	3.7± 0.2
2500 ppm	3.7± 0.3	3.7± 0.2	3.7± 0.3	3.8± 0.3	3.5± 0.3	3.7± 0.4	3.7± 0.2
5000 ppm	3.8± 0.3	3.8± 0.2	3.7± 0.2	3.8± 0.4	3.8± 0.3	3.8± 0.4	3.8± 0.3
10000 ppm	3.7± 0.5	3.6± 0.4	3.7± 0.5	3.9± 0.6	3.7± 0.5	3.9± 0.5	3.7± 0.5
20000 ppm	3.4± 0.4	3.4± 0.3*	3.5± 0.5	3.7± 0.5	3.6± 0.7	3.7± 0.5	3.6± 0.3
30000 ppm	3.3± 0.3	3.3± 0.7	3.5± 0.7	4.1± 1.7	4.1± 2.1	4.3± 2.0	3.9± 1.2

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

APPENDIX D 1

CHEMICAL INTAKE CHANGES : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
UNIT : g/kg/day
REPORT TYPE : A1 14
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 2	3	4	5	6	7	8
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
2500 ppm	0.383± 0.037	0.398± 0.034	0.387± 0.030	0.362± 0.026	0.367± 0.024	0.359± 0.021	0.353± 0.020
5000 ppm	0.790± 0.083	0.776± 0.039	0.762± 0.031	0.722± 0.056	0.707± 0.026	0.702± 0.047	0.718± 0.029
10000 ppm	1.571± 0.097	1.528± 0.164	1.441± 0.144	1.419± 0.118	1.439± 0.117	1.456± 0.108	1.454± 0.106
20000 ppm	3.487± 1.021	3.799± 0.815	3.227± 0.782	3.381± 0.755	3.233± 0.835	3.402± 0.631	3.452± 0.684
30000 ppm	3.329± 0.644	4.130± 0.840	5.148± 1.441	5.420± 1.423	5.639± 1.454	5.958± 1.566	5.919± 1.779

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
UNIT : g／kg／d a y
REPORT TYPE : A1 14
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 9	10	11	12	13	14
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
2500 ppm	0.350± 0.020	0.346± 0.023	0.339± 0.027	0.328± 0.032	0.325± 0.021	0.333± 0.024
5000 ppm	0.675± 0.097	0.683± 0.033	0.668± 0.032	0.642± 0.025	0.647± 0.046	0.665± 0.030
10000 ppm	1.426± 0.099	1.385± 0.086	1.411± 0.111	1.378± 0.109	1.266± 0.121	1.384± 0.142
20000 ppm	3.147± 0.414	3.053± 0.449	3.040± 0.367	3.064± 0.555	3.060± 0.463	3.110± 0.468
30000 ppm	5.776± 1.957	5.179± 1.273	5.003± 1.134	5.097± 1.383	5.916± 1.390	5.820± 1.244

APPENDIX D 2

CHEMICAL INTAKE CHANGES : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
UNIT : g/kg/day
REPORT TYPE : A1 14
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 2	3	4	5	6	7	8
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
2500 ppm	0.444± 0.033	0.435± 0.026	0.412± 0.027	0.440± 0.031	0.412± 0.031	0.422± 0.018	0.435± 0.020
5000 ppm	0.885± 0.059	0.862± 0.053	0.858± 0.043	0.876± 0.068	0.821± 0.042	0.862± 0.048	0.896± 0.050
10000 ppm	1.714± 0.112	1.781± 0.172	1.702± 0.182	1.719± 0.213	1.654± 0.183	1.681± 0.193	1.681± 0.161
20000 ppm	3.856± 0.841	3.836± 0.714	3.291± 0.595	3.125± 0.679	2.871± 0.206	3.082± 0.260	3.160± 0.244
30000 ppm	6.263± 2.635	7.052± 4.799	6.332± 2.459	4.936± 0.802	4.889± 0.510	4.957± 0.583	4.470± 0.384

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
UNIT : g／kg／d a y
REPORT TYPE : A1 14
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 9	10	11	12	13	14
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
2500 ppm	0.434± 0.035	0.419± 0.025	0.435± 0.029	0.409± 0.031	0.423± 0.035	0.413± 0.019
5000 ppm	0.876± 0.050	0.843± 0.041	0.865± 0.071	0.845± 0.045	0.833± 0.084	0.824± 0.045
10000 ppm	1.666± 0.162	1.689± 0.208	1.707± 0.257	1.650± 0.207	1.666± 0.187	1.560± 0.224
20000 ppm	3.096± 0.243	3.255± 0.366	3.420± 0.466	3.284± 0.555	3.309± 0.405	3.249± 0.264
30000 ppm	4.466± 0.670	4.633± 0.667	5.373± 2.009	5.458± 2.714	5.756± 2.506	5.242± 1.396

APPENDIX E 1

HEMATOLOGY : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (15W)

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	10.69±	0.28	15.5±	0.3	49.8±	1.3	46.6±	0.5	14.5±	0.2	31.1±	0.4	1368±	87
2500 ppm	9	10.76±	0.28	15.5±	0.2	49.9±	1.0	46.4±	0.5	14.5±	0.3	31.2±	0.5	1382±	105
5000 ppm	10	10.70±	0.30	15.7±	0.3	50.3±	1.5	47.0±	0.7	14.6±	0.2	31.1±	0.6	1369±	158
10000 ppm	9	10.49±	0.34	15.6±	0.5	49.4±	1.7	47.1±	0.7	14.9±	0.3*	31.5±	0.4	1456±	96
20000 ppm	10	9.63±	0.36**	15.5±	0.7	45.2±	1.6**	46.9±	0.5	16.1±	0.4**	34.2±	0.6**	1514±	65*
30000 ppm	5	10.23±	0.38*	14.9±	0.3	46.7±	1.2**	45.6±	0.6*	14.6±	0.3	31.9±	0.3*	1528±	95*

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

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (15W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHER
Control	10	1.23± 0.48	1± 1	17± 3	2± 1	0± 0	4± 2	77± 4	0± 0
2500 ppm	9	1.47± 0.59	1± 1	15± 5	1± 1	0± 0	4± 3	79± 6	0± 0
5000 ppm	10	1.22± 0.50	0± 1	16± 5	1± 1	0± 0	3± 1	80± 5	0± 0
10000 ppm	9	1.43± 0.70	1± 2	17± 5	1± 1	0± 0	3± 2	78± 5	0± 0
20000 ppm	10	1.28± 0.61	1± 2	16± 5	0± 1	0± 0	2± 2	81± 5	0± 0
30000 ppm	5	0.71± 0.39	0± 0	14± 4	1± 1	0± 0	6± 2	79± 3	0± 0

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

APPENDIX E 2

HEMATOLOGY : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (15W)

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	11.05± 0.37	16.0± 0.6	50.7± 1.9	45.9± 0.5	14.5± 0.2	31.5± 0.5	1223± 77
2500 ppm	10	11.08± 0.26	16.1± 0.4	51.0± 1.4	46.0± 0.4	14.5± 0.2	31.6± 0.4	1307± 120
5000 ppm	10	10.89± 0.28	16.0± 0.4	50.0± 1.2	46.0± 0.8	14.7± 0.2	31.9± 0.6	1322± 92
10000 ppm	10	10.69± 0.37*	15.9± 0.5	50.3± 1.4	47.0± 0.7**	14.8± 0.3**	31.6± 0.5	1358± 102*
20000 ppm	10	9.82± 0.24**	15.3± 0.4*	46.8± 1.2**	47.7± 0.6**	15.6± 0.2**	32.7± 0.3**	1385± 84**
30000 ppm	3	9.49± 0.16**	14.2± 0.1**	43.5± 1.0**	45.8± 0.8	15.0± 0.2**	32.7± 0.5**	1430± 15**

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

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (15W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$		Differential WBC (%) N-BAND		N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHER	
Control	10	1.24±	0.45	1±	1	17±	8	1±	1	0±	0	3±	2	80±	8	0±	0
2500 ppm	10	1.19±	0.79	0±	0	17±	10	1±	2	0±	0	3±	2	78±	10	0±	0
5000 ppm	10	1.27±	0.43	0±	1	18±	5	1±	1	0±	0	4±	4	77±	5	0±	0
10000 ppm	10	1.10±	0.53	1±	3	18±	7	1±	1	0±	0	2±	2	78±	8	0±	0
20000 ppm	10	1.58±	0.40	0±	1	15±	5	1±	1	0±	0	4±	2	80±	6	0±	0
30000 ppm	3	3.52±	2.58	0±	1	13±	2	1±	1	0±	0	4±	2	81±	3	0±	0

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

APPENDIX F 1

BIOCHEMISTRY : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (15W)

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	4.7± 0.2	2.7± 0.1	1.3± 0.1	0.16± 0.02	171± 23	79± 10	52± 18
2500 ppm	10	4.9± 0.2	2.8± 0.2	1.3± 0.1	0.16± 0.01	172± 37	81± 13	52± 31
5000 ppm	10	5.0± 0.2**	2.9± 0.1**	1.4± 0.1	0.16± 0.02	184± 28	81± 6	45± 15
10000 ppm	10	5.1± 0.2**	2.9± 0.1*	1.3± 0.1	0.18± 0.04	183± 45	103± 21	42± 19
20000 ppm	10	5.4± 0.2**	3.1± 0.1**	1.4± 0.1	0.17± 0.01	242± 52**	189± 17**	82± 32*
30000 ppm	5	5.8± 0.2**	3.4± 0.1**	1.4± 0.0	0.18± 0.01	308± 47**	262± 17**	65± 23

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

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (15W)

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	172± 17	43± 6	19± 3	194± 29	130± 11	2± 1	61± 16
2500 ppm	10	169± 23	44± 5	19± 3	209± 66	136± 10	1± 1	65± 28
5000 ppm	10	164± 11	42± 4	19± 3	204± 47	139± 8	2± 1	64± 17
10000 ppm	10	183± 31	45± 9	24± 7	269± 119	147± 20	1± 1	78± 36
20000 ppm	10	293± 28**	47± 7	35± 10**	230± 52	177± 19**	1± 1	82± 32
30000 ppm	5	387± 22**	137± 52**	146± 57**	386± 86**	285± 21**	4± 2**	120± 59

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

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (15W)

Group Name	NO. of Animals	UREA NITROGEN mg/dℓ		SODIUM mEq/ℓ		POTASSIUM mEq/ℓ		CHLORIDE mEq/ℓ		CALCIUM mg/dℓ		INORGANIC PHOSPHORUS mg/dℓ	
Control	10	23.8±	3.6	151±	1	4.8±	0.5	123±	2	8.5±	0.5	7.7±	0.5
2500 ppm	10	26.0±	5.2	152±	1	4.7±	0.6	122±	3	8.8±	0.3	8.1±	0.8
5000 ppm	10	29.4±	5.4	152±	1	4.7±	0.5	122±	2	8.8±	0.2	7.7±	0.9
10000 ppm	10	32.2±	6.5**	151±	1	4.6±	0.7	122±	2	8.7±	0.3	7.5±	1.2
20000 ppm	10	30.7±	3.6*	150±	2	4.3±	0.5	120±	2*	9.1±	0.2**	6.9±	0.6
30000 ppm	5	31.8±	3.1*	149±	1**	4.6±	0.3	116±	2**	9.4±	0.1**	7.8±	0.5

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

APPENDIX F 2

BIOCHEMISTRY : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (15W)

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	5.0±	0.1	3.1±	0.1	1.6±	0.1	0.15±	0.01	147±	22	77±	4	35±	17
2500 ppm	10	5.0±	0.1	3.1±	0.1	1.6±	0.1	0.14±	0.01	143±	18	69±	9	24±	8
5000 ppm	10	5.0±	0.2	3.0±	0.1	1.6±	0.1	0.15±	0.01	159±	28	81±	12	24±	11
10000 ppm	10	5.0±	0.2	3.1±	0.1	1.6±	0.1	0.14±	0.01	167±	25	100±	7*	26±	12
20000 ppm	10	5.2±	0.1**	3.1±	0.1	1.5±	0.0**	0.14±	0.01	226±	26**	192±	17**	48±	18
30000 ppm	3	5.7±	0.2**	3.4±	0.1**	1.5±	0.1	0.16±	0.01	261±	7**	208±	12**	58±	9

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

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (15W)

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	160±	10	50±	5	19±	3	188±	20	197±	14	2±	2	84±	39
2500 ppm	10	142±	22	52±	7	25±	15	209±	30	202±	14	1±	1	95±	28
5000 ppm	10	158±	26	51±	8	20±	3	203±	37	200±	23	1±	1	104±	63
10000 ppm	10	178±	12	50±	10	24±	6	204±	57	196±	19	2±	1	90±	33
20000 ppm	10	313±	27**	75±	18**	47±	12**	225±	30*	201±	13	2±	1	88±	27
30000 ppm	3	347±	15**	202±	97*	182±	81**	405±	141**	201±	20	7±	1**	118±	61

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

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (15W)

Group Name	NO. of Animals	UREA NITROGEN mg/dℓ		SODIUM mEq/ℓ		POTASSIUM mEq/ℓ		CHLORIDE mEq/ℓ		CALCIUM mg/dℓ		INORGANIC PHOSPHORUS mg/dℓ	
Control	10	18.1±	2.4	151±	1	4.7±	0.3	121±	2	8.8±	0.2	6.9±	1.2
2500 ppm	10	20.6±	2.5	151±	2	4.8±	0.3	122±	1	8.6±	0.2	6.7±	0.7
5000 ppm	10	20.9±	2.2	151±	2	4.7±	0.2	122±	2	8.8±	0.2	6.5±	0.6
10000 ppm	10	22.4±	2.5**	151±	2	4.7±	0.4	123±	2	8.9±	0.2	6.3±	0.7
20000 ppm	10	25.0±	4.0**	150±	1	4.2±	0.5**	120±	2	9.2±	0.2**	6.5±	0.7
30000 ppm	3	26.1±	2.1**	149±	2	5.4±	0.7	116±	2**	9.5±	0.2**	6.4±	0.8

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

APPENDIX G 1

URINALYSIS : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	±	+	2+	3+	4+	CHI	Occult blood −	±	+	2+	3+	CHI
Control	10	0	0	0	1	8	1	0		0	0	10	0	0	0		10	0	0	0	0	0		1	9	0	0	0	0		10	0	0	0	0	
2500 ppm	10	0	0	0	0	3	7	0	*	0	0	10	0	0	0		10	0	0	0	0	0		2	8	0	0	0	0		10	0	0	0	0	
5000 ppm	10	0	0	0	0	6	4	0		0	0	7	3	0	0		10	0	0	0	0	0		4	6	0	0	0	0		10	0	0	0	0	
10000 ppm	10	0	0	0	3	5	2	0		0	0	10	0	0	0		10	0	0	0	0	0		3	7	0	0	0	0		10	0	0	0	0	
20000 ppm	9	0	7	1	1	0	0	0	**	0	1	8	0	0	0		9	0	0	0	0	0		4	5	0	0	0	0		9	0	0	0	0	
30000 ppm	4	0	2	1	1	0	0	0	*	0	0	4	0	0	0		4	0	0	0	0	0		0	4	0	0	0	0		4	0	0	0	0	

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

STUDY NO. : 0370 URINALYSIS
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

Group Name	NO. of Animals	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0	
2500 ppm	10	10	0	0	0	0	
5000 ppm	10	10	0	0	0	0	
10000 ppm	10	10	0	0	0	0	
20000 ppm	9	9	0	0	0	0	
30000 ppm	4	4	0	0	0	0	

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

APPENDIX G 2

URINALYSIS : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0370 URINALYSIS
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	±	+	2+	3+	4+	CHI	Occult blood −	±	+	2+	3+	CHI
Control	10	0	1	3	2	2	2	0		0	5	5	0	0	0		10	0	0	0	0	0		0	8	2	0	0	0		10	0	0	0	0	
2500 ppm	10	0	0	1	3	4	2	0		0	5	5	0	0	0		10	0	0	0	0	0		1	8	1	0	0	0		10	0	0	0	0	
5000 ppm	10	0	0	1	4	3	2	0		0	6	4	0	0	0		10	0	0	0	0	0		1	9	0	0	0	0		10	0	0	0	0	
10000 ppm	10	0	1	6	2	1	0	0		0	8	2	0	0	0		10	0	0	0	0	0		1	9	0	0	0	0		10	0	0	0	0	
20000 ppm	10	0	6	3	1	0	0	0		1	8	1	0	0	0		10	0	0	0	0	0		1	9	0	0	0	0		10	0	0	0	0	
30000 ppm	3	0	3	0	0	0	0	0		0	2	1	0	0	0		3	0	0	0	0	0		0	3	0	0	0	0		3	0	0	0	0	

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

URINALYSIS

Group Name	NO. of Animals	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0	
2500 ppm	10	10	0	0	0	0	
5000 ppm	10	10	0	0	0	0	
10000 ppm	10	10	0	0	0	0	
20000 ppm	10	10	0	0	0	0	
30000 ppm	3	3	0	0	0	0	

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

APPENDIX H 1

GROSS FINDINGS : SUMMARY, MOUSE : MALE ALL ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
ALL ANIMALS (0- 15W)

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	2500 ppm 10 (%)	5000 ppm 10 (%)	10000 ppm 10 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)

Organ	Findings	Group Name	20000 ppm	30000 ppm
		NO. of Animals	10 (%)	10 (%)
thymus	atrophic		0 (0)	5 (50)

APPENDIX H 2

GROSS FINDINGS : SUMMARY, MOUSE : FEMALE ALL ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
ALL ANIMALS (0- 15W)

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	2500 ppm 10 (%)	5000 ppm 10 (%)	10000 ppm 10 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)

Organ	Findings	Group Name NO. of Animals	20000 ppm 10 (%)	30000 ppm 10 (%)
thymus	atrophic		0 (0)	7 (70)

APPENDIX H 3

GROSS FINDINGS : SUMMARY, MOUSE : MALE

DEAD AND MORIBUND ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 15W)

Organ	Findings	Group Name NO. of Animals	Control 0 (%)	2500 ppm 0 (%)	5000 ppm 0 (%)	10000 ppm 0 (%)
thymus	atrophic		- (-)	- (-)	- (-)	- (-)

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 15W)

Organ	Findings	Group Name NO. of Animals	20000 ppm 0 (%)	30000 ppm 5 (%)
thymus	atrophic		- (-)	5 (100)

APPENDIX H 4

GROSS FINDINGS : SUMMARY, MOUSE : FEMALE

DEAD AND MORIBUND ANIMALS

(13-WEEK STUDY)

Organ	Findings	Group Name NO. of Animals	Control 0 (%)	2500 ppm 0 (%)	5000 ppm 0 (%)	10000 ppm 0 (%)
thymus	atrophic		- (-)	- (-)	- (-)	- (-)

Organ	Findings	Group Name NO. of Animals	20000 ppm 0 (%)	30000 ppm 7 (%)
thymus	atrophic		- (-)	7 (100)

APPENDIX I 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (15W)

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	30.0± 1.9	0.035± 0.007	0.017± 0.005	0.195± 0.018	0.159± 0.018	0.159± 0.009
2500 ppm	10	29.2± 2.6	0.032± 0.005	0.014± 0.004	0.222± 0.015	0.149± 0.011	0.157± 0.009
5000 ppm	10	29.0± 2.5	0.034± 0.008	0.014± 0.003	0.226± 0.032	0.153± 0.012	0.159± 0.014
10000 ppm	10	27.6± 1.8*	0.030± 0.006	0.014± 0.003	0.210± 0.045	0.151± 0.013	0.159± 0.012
20000 ppm	10	26.0± 1.2**	0.030± 0.004	0.013± 0.004	0.218± 0.025	0.139± 0.013**	0.155± 0.005
30000 ppm	5	23.2± 1.8**	0.032± 0.003	0.014± 0.003	0.207± 0.023	0.119± 0.009**	0.140± 0.007**

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

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (15W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.412± 0.032	0.043± 0.005	1.078± 0.073	0.441± 0.019
2500 ppm	10	0.406± 0.030	0.045± 0.004	1.132± 0.076	0.441± 0.015
5000 ppm	10	0.420± 0.035	0.047± 0.003	1.178± 0.080	0.447± 0.022
10000 ppm	10	0.410± 0.027	0.051± 0.004*	1.318± 0.100**	0.453± 0.016
20000 ppm	10	0.385± 0.017	0.092± 0.018**	1.925± 0.214**	0.435± 0.012
30000 ppm	5	0.329± 0.021**	0.057± 0.011*	2.508± 0.287**	0.424± 0.014

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

APPENDIX I 2

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (15W)

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	20.5± 1.1	0.038± 0.006	0.015± 0.004	0.041± 0.019	0.120± 0.008	0.150± 0.008
2500 ppm	10	19.6± 0.7	0.036± 0.005	0.014± 0.005	0.032± 0.006	0.121± 0.009	0.148± 0.011
5000 ppm	10	20.2± 0.8	0.035± 0.005	0.012± 0.002	0.036± 0.007	0.122± 0.007	0.153± 0.010
10000 ppm	10	20.2± 0.5	0.034± 0.003	0.013± 0.003	0.034± 0.006	0.120± 0.006	0.149± 0.010
20000 ppm	10	20.5± 0.9	0.036± 0.005	0.014± 0.003	0.033± 0.011	0.120± 0.010	0.147± 0.010
30000 ppm	3	20.9± 0.9	0.042± 0.010	0.014± 0.001	0.037± 0.008	0.127± 0.017	0.145± 0.008

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

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (15W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.282± 0.017	0.050± 0.006	0.878± 0.061	0.448± 0.014
2500 ppm	10	0.279± 0.017	0.046± 0.006	0.823± 0.050	0.451± 0.015
5000 ppm	10	0.280± 0.011	0.051± 0.005	0.895± 0.048	0.457± 0.019
10000 ppm	10	0.283± 0.016	0.055± 0.006	0.980± 0.059	0.466± 0.013
20000 ppm	10	0.279± 0.013	0.083± 0.011**	1.489± 0.127**	0.442± 0.018
30000 ppm	3	0.295± 0.010	0.080± 0.008**	2.116± 0.121**	0.424± 0.017

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

APPENDIX J 1

ORGAN WEIGHT, RELATIVE : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (15W)

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	30.0± 1.9	0.115± 0.022	0.056± 0.015	0.652± 0.070	0.530± 0.046	0.531± 0.031
2500 ppm	10	29.2± 2.6	0.109± 0.013	0.048± 0.015	0.765± 0.064	0.512± 0.027	0.541± 0.039
5000 ppm	10	29.0± 2.5	0.116± 0.024	0.049± 0.009	0.783± 0.132*	0.529± 0.026	0.550± 0.034
10000 ppm	10	27.6± 1.8*	0.109± 0.025	0.050± 0.013	0.758± 0.146	0.549± 0.041	0.577± 0.032*
20000 ppm	10	26.0± 1.2**	0.114± 0.016	0.050± 0.016	0.839± 0.094**	0.535± 0.055	0.597± 0.033**
30000 ppm	5	23.2± 1.8**	0.139± 0.018	0.062± 0.022	0.895± 0.130**	0.514± 0.031	0.603± 0.046**

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

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (15W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.375± 0.109	0.142± 0.013	3.590± 0.116	1.473± 0.092
2500 ppm	10	1.396± 0.094	0.154± 0.013	3.889± 0.227	1.517± 0.112
5000 ppm	10	1.454± 0.119	0.164± 0.012	4.067± 0.177	1.548± 0.131
10000 ppm	10	1.488± 0.096	0.183± 0.015**	4.792± 0.431**	1.646± 0.089**
20000 ppm	10	1.482± 0.076	0.352± 0.061**	7.385± 0.631**	1.673± 0.065**
30000 ppm	5	1.419± 0.096	0.245± 0.038**	10.776± 0.670**	1.830± 0.118**

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

APPENDIX J 2

ORGAN WEIGHT, RELATIVE : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (15W)

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	20.5± 1.1	0.185± 0.023	0.072± 0.016	0.198± 0.081	0.583± 0.029	0.732± 0.030
2500 ppm	10	19.6± 0.7	0.184± 0.029	0.074± 0.024	0.161± 0.033	0.618± 0.034	0.757± 0.041
5000 ppm	10	20.2± 0.8	0.172± 0.025	0.059± 0.012	0.175± 0.031	0.605± 0.033	0.758± 0.049
10000 ppm	10	20.2± 0.5	0.167± 0.018	0.062± 0.015	0.165± 0.028	0.592± 0.028	0.734± 0.050
20000 ppm	10	20.5± 0.9	0.174± 0.022	0.066± 0.014	0.160± 0.053	0.587± 0.056	0.718± 0.041
30000 ppm	3	20.9± 0.9	0.199± 0.040	0.067± 0.002	0.177± 0.036	0.613± 0.104	0.697± 0.029

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

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (15W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.373± 0.045	0.245± 0.023	4.280± 0.153	2.189± 0.094
2500 ppm	10	1.425± 0.072	0.234± 0.030	4.198± 0.149	2.305± 0.101
5000 ppm	10	1.385± 0.059	0.251± 0.020	4.428± 0.224	2.264± 0.146
10000 ppm	10	1.397± 0.071	0.271± 0.026	4.841± 0.240**	2.302± 0.072
20000 ppm	10	1.366± 0.088	0.403± 0.044**	7.265± 0.367**	2.161± 0.063
30000 ppm	3	1.413± 0.071	0.383± 0.026**	10.136± 0.160**	2.034± 0.110

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

APPENDIX K 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : MALE : ALL ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
ALL ANIMALS (0- 15W)

Organ	Findings	Group Name	Control				2500 ppm				5000 ppm				10000 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
[Respiratory system]																		
nasal cavit			<10>				<10>				<10>				<10>			
	eosinophilic change:respiratory epithelium		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		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)
	respiratory metaplasia:gland		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
[Hematopoietic system]																		
bone marrow			<10>				<10>				<10>				<10>			
	congestion		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thymus			<10>				<10>				<10>				<10>			
	atrophy		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen			<10>				<10>				<10>				<10>			
	atrophy		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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	20000 ppm				30000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
nasal cavit			<10>				<10>			
	eosinophilic change:respiratory epithelium		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	respiratory metaplasia:gland		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Hematopoietic system]										
bone marrow			<10>				<10>			
	congestion		0	0	0	0	4	0	0	0
			(0)	(0)	(0)	(0)	(40)	(0)	(0)	(0)
thymus			<10>				<10>			
	atrophy		0	0	0	0	0	0	5	0 *
			(0)	(0)	(0)	(0)	(0)	(0)	(50)	(0)
spleen			<10>				<10>			
	atrophy		0	0	0	0	0	5	0	0 *
			(0)	(0)	(0)	(0)	(0)	(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				2500 ppm				5000 ppm				10000 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>			
	extramedullary hematopoiesis		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]																		
liver			<10>				<10>				<10>				<10>			
	granulation		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	hepatocellular hypertrophy:central		0	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0 *
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
[Urinary system]																		
kidney			<10>				<10>				<10>				<10>			
	vacuolic change:proximal tubule		7	0	0	0	5	0	0	0	5	0	0	0	1	0	0	0 *
			(70)	(0)	(0)	(0)	(50)	(0)	(0)	(0)	(50)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
[Reproductive system]																		
epididymis			<10>				<10>				<10>				<10>			
	debris of spermatic elements		0	0	0	0	0	0	0	0	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	20000 ppm				30000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]										
spleen			<10>				<10>			
	extramedullary hematopoiesis		6	0	0	0 *	3	0	0	0
			(60)	(0)	(0)	(0)	(30)	(0)	(0)	(0)
[Digestive system]										
liver			<10>				<10>			
	granulation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hepatocellular hypertrophy:central		2	8	0	0 **	0	5	0	0 *
			(20)	(80)	(0)	(0)	(0)	(50)	(0)	(0)
[Urinary system]										
kidney			<10>				<10>			
	vacuolic change:proximal tubule		0	0	0	0 **	0	0	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Reproductive system]										
epididymis			<10>				<10>			
	debris of spermatic elements		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

APPENDIX K 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : FEMALE : ALL ANIMALS

(13-WEEK STUDY)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 10 1 (%)	Control 10 2 (%)	Control 10 3 (%)	Control 10 4 (%)	2500 ppm 10 1 (%)	2500 ppm 10 2 (%)	2500 ppm 10 3 (%)	2500 ppm 10 4 (%)	5000 ppm 10 1 (%)	5000 ppm 10 2 (%)	5000 ppm 10 3 (%)	5000 ppm 10 4 (%)	10000 ppm 10 1 (%)	10000 ppm 10 2 (%)	10000 ppm 10 3 (%)	10000 ppm 10 4 (%)
[Respiratory system]																		
nasal cavit			<10>				<10>				<10>				<10>			
	eosinophilic change:respiratory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:gland		0 (0)	0 (0)	0 (0)	0 (0)	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			<10>				<10>				<10>				<10>			
	congestion		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
thymus			<10>				<10>				<10>				<10>			
	atrophy		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
spleen			<10>				<10>				<10>				<10>			
	atrophy		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	extramedullary hematopoiesis		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)

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	20000 ppm				30000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
nasal cavit			<10>				<10>			
	eosinophilic change:respiratory epithelium		3	0	0	0	0	0	0	0
			(30)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	respiratory metaplasia:gland		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Hematopoietic system]										
bone marrow			<10>				<10>			
	congestion		0	0	0	0	6	0	0	0 *
			(0)	(0)	(0)	(0)	(60)	(0)	(0)	(0)
thymus			<10>				<10>			
	atrophy		0	0	0	0	0	1	6	0 **
			(0)	(0)	(0)	(0)	(0)	(10)	(60)	(0)
spleen			<10>				<10>			
	atrophy		0	0	0	0	0	7	0	0 **
			(0)	(0)	(0)	(0)	(0)	(70)	(0)	(0)
	extramedullary hematopoiesis		6	0	0	0 *	3	0	0	0
			(60)	(0)	(0)	(0)	(30)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				2500 ppm				5000 ppm				10000 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>			
	hepatocellular hypertrophy: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)
	amphophilic cell focus		0	0	0	0	0	0	0	0	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>			
	basophilic change		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	20000 ppm				30000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]										
liver			<10>				<10>			
	hepatocellular hypertrophy:central		9	0	0	0 **	0	3	0	0
			(90)	(0)	(0)	(0)	(0)	(30)	(0)	(0)
	amphophilic cell focus		3	0	0	0	1	0	0	0
			(30)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
[Urinary system]										
kidney			<10>				<10>			
	basophilic change		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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 K 3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : MALE : DEAD AND MORIBUND ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 15W)

Organ	Findings	Group Name	Control				2500 ppm				5000 ppm				10000 ppm			
		No. of Animals on Study	0				0				0				0			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
bone marrow			< 0>				< 0>				< 0>				< 0>			
	congestion		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
thymus			< 0>				< 0>				< 0>				< 0>			
	atrophy		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
spleen			< 0>				< 0>				< 0>				< 0>			
	atrophy		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Reproductive system]																		
epididymis			< 0>				< 0>				< 0>				< 0>			
	debris of spermatic elements		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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

Organ	Findings	Group Name	20000 ppm				30000 ppm			
		No. of Animals on Study	0				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]										
bone marrow			< 0>				< 5>			
	congestion		-	-	-	-	4	0	0	0
			(-)	(-)	(-)	(-)	(80)	(0)	(0)	(0)
thymus			< 0>				< 5>			
	atrophy		-	-	-	-	0	0	5	0
			(-)	(-)	(-)	(-)	(0)	(0)	(100)	(0)
spleen			< 0>				< 5>			
	atrophy		-	-	-	-	0	5	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
[Reproductive system]										
epididymis			< 0>				< 5>			
	debris of spermatic elements		-	-	-	-	1	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

APPENDIX K 4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : FEMALE : DEAD AND MORIBUND ANIMALS

(13-WEEK STUDY)

Organ	Findings	Group Name	Control				2500 ppm				5000 ppm				10000 ppm			
		No. of Animals on Study	0				0				0				0			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
bone marrow			< 0>				< 0>				< 0>				< 0>			
	congestion		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
thymus			< 0>				< 0>				< 0>				< 0>			
	atrophy		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
spleen			< 0>				< 0>				< 0>				< 0>			
	atrophy		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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

Organ	Findings	Group Name	20000 ppm				30000 ppm			
		No. of Animals on Study	0				7			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]										
bone marrow			< 0>				< 7>			
	congestion		-	-	-	-	6	0	0	0
			(-)	(-)	(-)	(-)	(86)	(0)	(0)	(0)
thymus			< 0>				< 7>			
	atrophy		-	-	-	-	0	1	6	0
			(-)	(-)	(-)	(-)	(0)	(14)	(86)	(0)
spleen			< 0>				< 7>			
	atrophy		-	-	-	-	0	7	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)

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

APPENDIX K 5

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : MALE : SACRIFICED ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (15W)

Organ	Findings	Group Name	Control				2500 ppm				5000 ppm				10000 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
nasal cavit			<10>				<10>				<10>				<10>			
	eosinophilic change:respiratory epithelium		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		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)
	respiratory metaplasia:gland		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
[Hematopoietic system]																		
spleen			<10>				<10>				<10>				<10>			
	extramedullary hematopoiesis		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]																		
liver			<10>				<10>				<10>				<10>			
	granulation		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)

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	20000 ppm				30000 ppm			
		No. of Animals on Study	10				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
nasal cavit			<10>				< 5>			
	eosinophilic change:respiratory epithelium		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	respiratory metaplasia:gland		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Hematopoietic system]										
spleen			<10>				< 5>			
	extramedullary hematopoiesis		6	0	0	0 *	3	0	0	0 *
			(60)	(0)	(0)	(0)	(60)	(0)	(0)	(0)
[Digestive system]										
liver			<10>				< 5>			
	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				2500 ppm				5000 ppm				10000 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>			
	hepatocellular hypertrophy:central		0	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0 *
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
[Urinary system]																		
kidney			<10>				<10>				<10>				<10>			
	vacuolic change:proximal tubule		7	0	0	0	5	0	0	0	5	0	0	0	1	0	0	0 *
			(70)	(0)	(0)	(0)	(50)	(0)	(0)	(0)	(50)	(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	20000 ppm				30000 ppm			
		No. of Animals on Study	10				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]										
liver			<10>				< 5>			
	hepatocellular hypertrophy:central		2	8	0	0 **	0	5	0	0 **
			(20)	(80)	(0)	(0)	(0)	(100)	(0)	(0)
[Urinary system]										
kidney			<10>				< 5>			
	vacuolic change:proximal tubule		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 K 6

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : MALE : SACRIFICED ANIMALS

(13-WEEK STUDY)

Organ	Findings	Group Name	Control				2500 ppm				5000 ppm				10000 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
nasal cavit			<10>				<10>				<10>				<10>			
	eosinophilic change:respiratory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	respiratory metaplasia:gland		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Hematopoietic system]																		
spleen			<10>				<10>				<10>				<10>			
	extramedullary hematopoiesis		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)
[Digestive system]																		
liver			<10>				<10>				<10>				<10>			
	hepatocellular hypertrophy: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)
	amphophilic cell focus		0	0	0	0	0	0	0	0	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	20000 ppm				30000 ppm			
		No. of Animals on Study	10				3			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
nasal cavit			<10>				< 3>			
	eosinophilic change:respiratory epithelium		3	0	0	0	0	0	0	0
			(30)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	respiratory metaplasia:gland		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Hematopoietic system]										
spleen			<10>				< 3>			
	extramedullary hematopoiesis		6	0	0	0 *	3	0	0	0 **
			(60)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
[Digestive system]										
liver			<10>				< 3>			
	hepatocellular hypertrophy:central		9	0	0	0 **	0	3	0	0 **
			(90)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
	amphophilic cell focus		3	0	0	0	1	0	0	0
			(30)	(0)	(0)	(0)	(33)	(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				2500 ppm				5000 ppm				10000 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																		
kidney			<10>				<10>				<10>				<10>			
	basophilic change		0	0	0	0	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	20000 ppm				30000 ppm			
		No. of Animals on Study	10				3			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]										
kidney			<10>				< 3>			
	basophilic change		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 L 1

IDENTITY AND IMPURITY OF p-NITROANISOLE

IN THE 13-WEEK FEED STUDY

IDENTITY AND IMPURITY OF p-NITROANISOLE IN THE 13-WEEK FEED STUDY

Test Substance : p-Nitroanisole (Wako Pure Chemical Industries, LTD.)

Lot No. : ACG7156

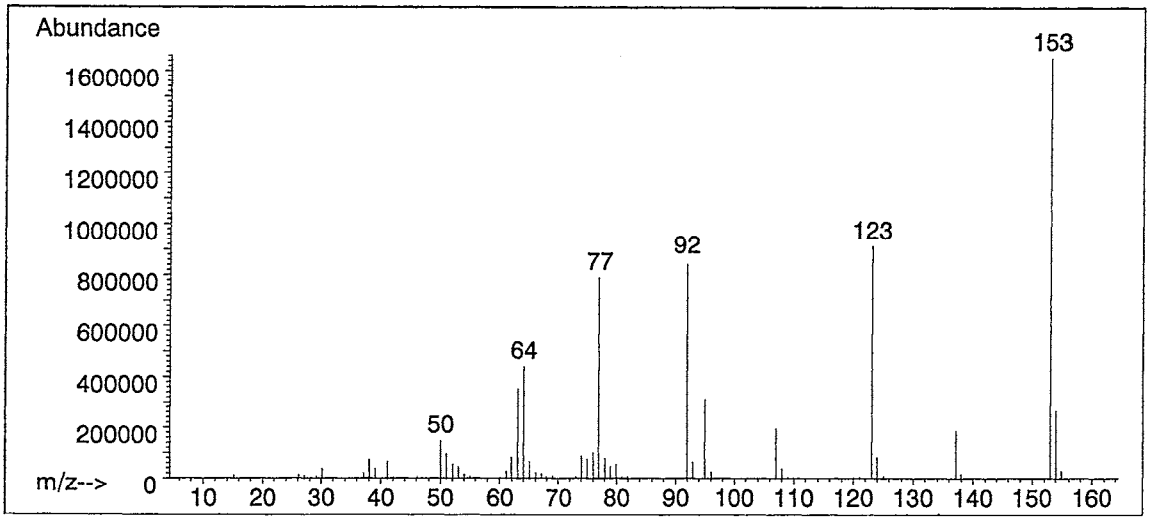
1. Spectral data

Mass Spectrometry

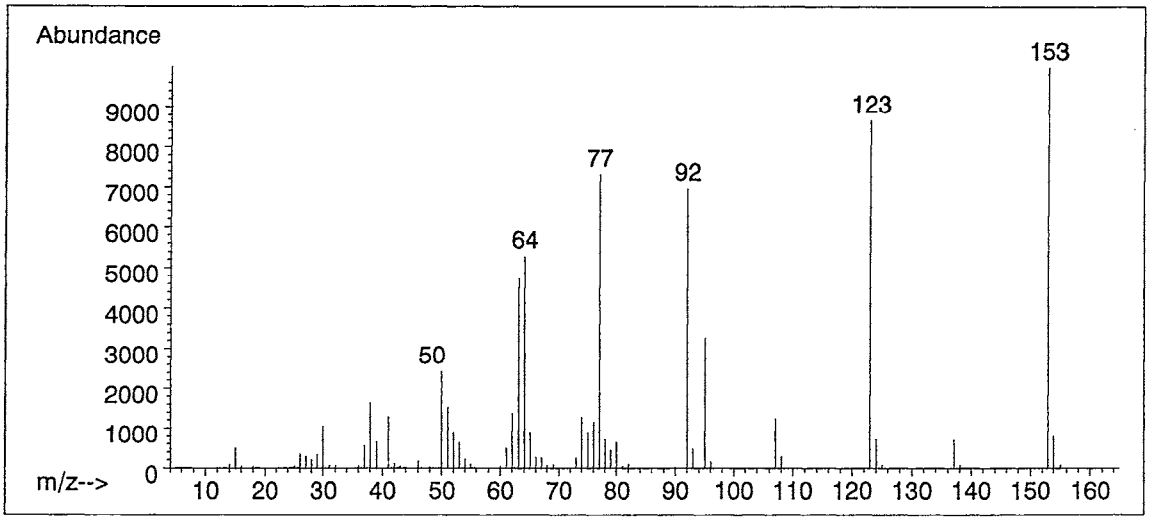
Instrument : Hewlett Packard 5989B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance



Mass Spectrum of Literature Data*

Results: The mass spectrum was consistent with literature spectrum.

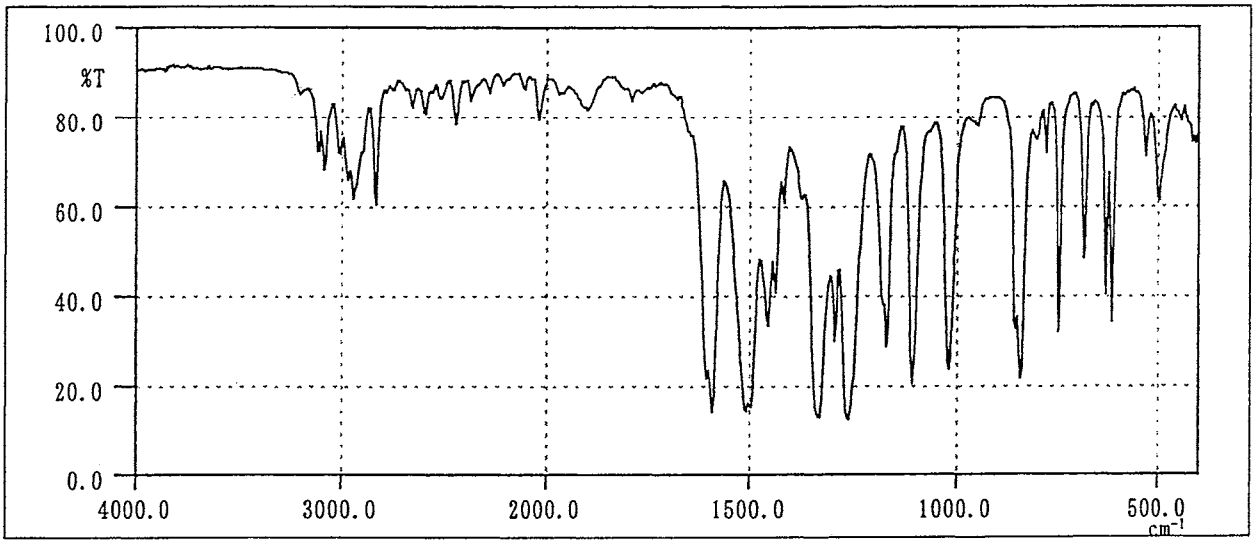
(*Fred W. McLafferty (1994) Wiley Registry of Mass Spectral Data, 6th edition. John Wiley and Sons, Inc. (U.S.), Entry Number 38330)

Infrared Spectrometry

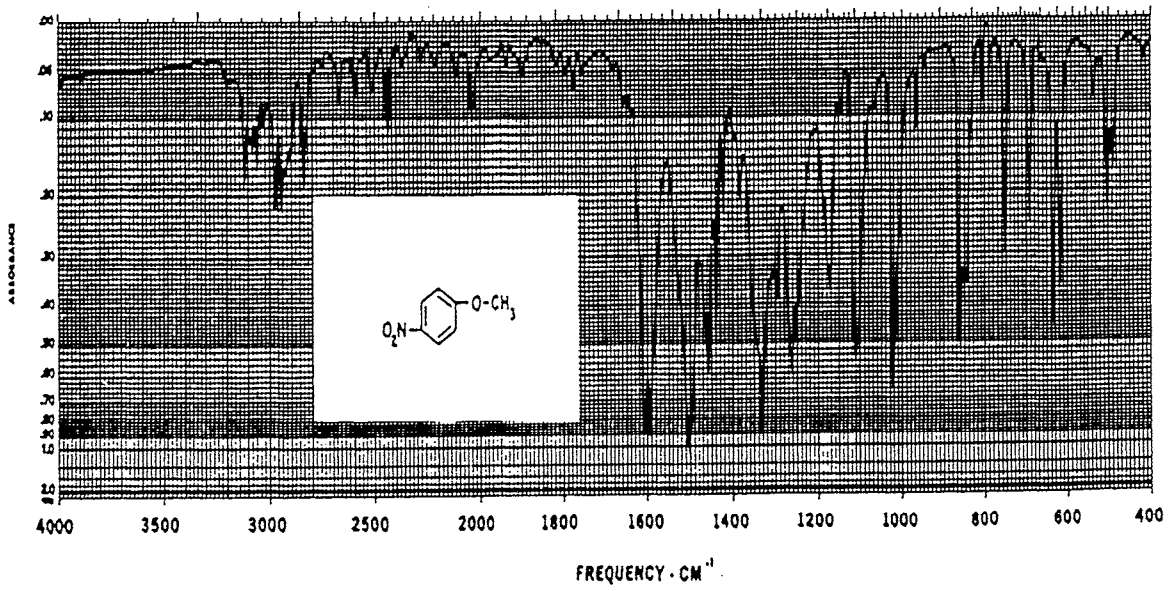
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 2.0 cm^{-1}



Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data*

Results: The infrared spectrum was consistent with literature spectrum.

(*William W. Simons (1978) The Sadtler Handbook of Infrared Spectra. Sadtler Research Laboratories, Inc. (U.K.), pp.443)

2. Impurity

Instrument	: Hewlett Packard 5890A Gas Chromatograph
Column	: INNOWAX (0.2 mmϕ × 50 m)
Column Temperature	: 80 °C → (15 °C/min) → 280 °C (5 min)
Flow Rate	: 1 mL/min
Detector	: FID (Flame Ionization Detector)
Injection Volume	: 1 μL

Sample Name	Peak No.	Area (%)	Peak Name
Test Substance	1	0.01	m-Chloronitrobenzene
	2	99.99	p-Nitroanisole

Results: Gas chromatography indicated one major peak (peak No.2) and one impurity. It was identified only by comparing its gas chromatograph with that of m-chloronitrobenzene (peak No.1) in the p-nitroanisole, the amount in the test substance were 0.01%.

3. Conclusions: The test substance was identified as p-nitroanisole, by the mass spectrum and the infrared spectrum. Gas chromatography indicated one major peak (peak No.2) and one impurity. It was identified only by comparing its gas chromatograph with that of m-chloronitrobenzene, the amount in the test substance were 0.01%.

APPENDIX L 2

STABILITY OF p-NITROANISOLE IN THE 13-WEEK FEED STUDY

STABILITY OF p-NITROANISOLE IN THE 13-WEEK FEED STUDY

Test Substance : p-Nitroanisole (Wako Pure Chemical Industries, LTD.)

Lot No. : ACG7156

1. Sample : This lot was used from 1998.11.6 to 1999.2.8. Test substance was stored in a dark place at room temperature.

2. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : INNOWAX (0.2 mmϕ × 50 m)

Column Temperature : 80 °C → (15 °C/min) → 280 °C (5 min)

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μL

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
1998.10.26	1	10.248	0.01
	2	13.132	99.99
1999.02.24	1	10.251	0.01
	2	13.139	99.99

Results: Gas chromatography indicated one major peak (peak No.2) and one impurity (peak No.1 < 0.02% of total area) analyzed at 1998.10.26 and one major peak (peak No.2) and one impurity (peak No.1 < 0.02% of total area) analyzed at 1999.2.24. No new trace impurity peak in the test substance analyzed at 1999.2.24 was detected.

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

APPENDIX L 3

CONCENTMOUSEION OF p-NITROANISOLE IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

CONCENTRATION OF p-NITROANISOLE IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

	Target Concentration				
Date Analyzed	2500[a]	5000	10000	20000	30000
1998.10.29	2430 (97.2)[b]	4760 (95.2)	9430 (94.3)	19200 (96.0)	29500 (98.3)

[a] ppm
[b] %

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

Instrument : Hewlett Packard 1090 High Performance Liquid Chromatograph
Column : TSK GEL ODS-80TM (4.6 mmϕ × 15 cm)
Column Temperature : Room Temperature
Flow Rate : 1 mL/min
Mobile Phase : Distilled Water : Acetonitrile = 1 : 1
Detector : UV (295 nm)
Injection Volume : 20 µL

APPENDIX L 4

STABILITY OF p-NITROANISOLE IN FORMULATED DIETS

IN THE 13-WEEK FEED STUDY

STABILITY OF p-NITROANISOLE IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

		Target Concentration	
Date Prepared	Date Analyzed	300[a]	40000
1998.09.24	1998.09.24	314 (100)[b]	40500 (100)
	1998.10.02[c]	264 (84.1)	37700 (93.1)
	1998.10.29[d]	304 (96.8)	39400 (97.3)

[a] ppm
[b] % (Percentage was based on the concentration on date of preparation.)
[c] Animal room samples
[d] Cold storage samples

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

Instrument : Hewlett Packard 1090 High Performance Liquid Chromatograph
Column : TSK GEL ODS-80TM (4.6 mmϕ $\times$ 15 cm)
Column Temperature : Room Temperature
Flow Rate : 1 mL/min
Mobile Phase : Distilled Water : Acetonitrile = 1 : 1
Detector : UV (295 nm)
Injection Volume : 20 μL

APPENDIX M 1

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALSIS IN THE 13-WEEK FEED STUDY OF p-NITROANISOLE

METHODS FOR HEMATOLOGY,BIOCHEMISTRY AND URINALYSIS IN THE 13-WEEK FEED STUDY OF p-NITROANISOLE

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]
White blood cell (WBC)	Light scattering method [1]
Differential WBC	Pattern recognition method [2] (Wright staining)
Biochemistry	
Total protein (TP)	Biuret method [3]
Albumin (Alb)	BCG method [3]
A/G ratio	Calculated as Alb/(TP−Alb) [3]
T-bilirubin	Alkaline azobilirubin method [3]
Glucose	GlcK・G-6-PDH method [3]
T-cholesterol	CE・COD・POD method [3]
Triglyceride	LPL・GK・GPO・POD method [3]
Phospholipid	PLD・ChOD・POD method [3]
Glutamic oxaloacetic transaminase (GOT)	JSCC method [3]
Glutamic pyruvic transaminase (GPT)	JSCC method [3]
Lactate dehydrogenase (LDH)	SFBC method [3]
Alkaline phosphatase (ALP)	GSCC method [3]
γ-Glutamyl transpeptidase (γ-GTP)	L-γ-Glutamyl-p-nitroanilide method [3]
Creatine phosphokinase (CPK)	JSCC method [3]
Urea nitrogen	Urease・GLDH method [3]
Sodium	Ion selective electrode method [3]
Potassium	Ion selective electrode method [3]
Chloride	Ion selective electrode method [3]
Calcium	OCPC method [3]
Inorganic phosphorus	PNP・XOD・POD method [3]
Urinalysis	
pH,Protein,Glucose,Ketone body,Occult Blood, Urobilinogen	Urinalysis reagent paper method [4]

1) Automatic blood cell analyzer (Technicon H・1 : Bayer Corporation)

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

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

4) Ames reagent strips for urinalysis (Uro-Labstix : Bayer Corporation)

APPENDIX N 1

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK FEED STUDY OF p-NITROANISOLE

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY
IN THE 13-WEEK FEED STUDY OF p-NITROANISOLE

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