o－クロロニトロベンゼンのマウスを用いた
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：　０４４０

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APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0440
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7
DEATH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	78 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	313 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	0	0	0	1	1	1	1	1	1	1	1	1	1
	2500 ppm	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
EXTERNAL MASS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	78 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	313 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	0	0	1	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
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
INTERNAL MASS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	78 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	313 ppm	1	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	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
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
M. BREAST	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	78 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	313 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	0	0	1	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
	5000 ppm	0	0	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
	78 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	313 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	10	10	10	9	9	9	9	9	9	9	9	9	9
	2500 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	5000 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
SMALL STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	78 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	313 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	0	0	1	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
	5000 ppm	1	1	0	0	0	0	0	0	0	0	0	0	0

STUDY NO. : 0440
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7
OLIGO-STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	78 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	313 ppm	1	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	1	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
	5000 ppm	2	2	0	0	0	0	0	0	0	0	0	0	0
NON REMARKABLE	Control	10	10	10	10	10	10	10	10	10	10	10	10	10
	78 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	313 ppm	9	10	10	10	10	10	10	10	10	10	10	10	10
	1250 ppm	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
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0

APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

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
INTERNAL MASS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	78 ppm	0	0	0	0	0	1	1	1	1	1	1	1	1
	313 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	0	0	0	0	0	0	0	0	1	0	0	0	0
	2500 ppm	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
YELLOW URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	78 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	313 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	2500 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	5000 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
SMALL STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	78 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	313 ppm	0	0	0	0	0	0	0	0	1	0	0	0	0
	1250 ppm	1	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
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
NON REMARKABLE	Control	10	10	10	10	10	10	10	10	10	10	10	10	10
	78 ppm	10	10	10	10	10	9	9	9	9	9	9	9	9
	313 ppm	10	10	10	10	10	10	10	10	9	10	10	10	10
	1250 ppm	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
	5000 ppm	0	0	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. : 0440
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7
Control	22.8± 0.8	24.2± 0.9	25.1± 1.5	25.9± 1.2	26.5± 1.1	27.3± 1.1	27.9± 1.3
78 ppm	22.8± 0.8	23.7± 0.7	24.9± 1.2	25.9± 1.2	26.7± 1.4	27.2± 1.7	28.1± 1.7
313 ppm	22.8± 0.8	23.1± 1.5	25.1± 1.0	25.7± 1.4	26.5± 1.2	27.3± 1.4	28.2± 1.5
1250 ppm	22.8± 0.8	24.1± 1.9	25.3± 1.6	25.8± 2.3	27.6± 1.0	28.2± 0.9	28.9± 1.0
2500 ppm	22.8± 0.8	24.2± 0.9	25.8± 0.9	26.7± 0.9	27.5± 0.9	28.0± 0.8	28.7± 1.0
5000 ppm	22.8± 0.8	21.2± 0.8**	22.9± 1.1**	24.4± 2.0	25.1± 1.9	26.1± 1.9	26.7± 1.5

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

STUDY NO. : 0440
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 7-7	8-7	9-7	10-7	11-7	12-7	13-7
Control	28.7± 1.3	28.7± 1.6	29.5± 1.4	30.2± 1.7	30.6± 1.9	31.4± 1.8	32.0± 1.8
78 ppm	28.8± 1.5	29.5± 2.0	30.1± 2.2	31.0± 2.4	31.7± 2.5	32.8± 2.8	33.3± 2.8
313 ppm	28.9± 1.8	29.8± 2.0	30.1± 1.8	30.8± 2.2	31.8± 2.2	32.6± 2.4	33.0± 2.3
1250 ppm	29.7± 1.4	30.0± 1.5	30.5± 1.9	31.0± 1.7	31.8± 2.0	32.6± 1.9	33.1± 1.9
2500 ppm	29.2± 1.0	29.5± 1.3	30.0± 1.5	30.7± 1.5	31.0± 1.5	31.5± 1.6	31.9± 1.2
5000 ppm	27.1± 1.3*	27.5± 1.3	28.0± 1.2	28.9± 1.2	29.1± 1.4	29.6± 1.2	29.9± 1.6

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. : 0440
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7
Control	18.4± 0.7	18.8± 0.8	19.7± 1.1	19.9± 1.1	20.6± 1.2	21.1± 1.3	21.6± 1.3
78 ppm	18.4± 0.7	19.1± 0.7	19.6± 0.7	20.1± 0.6	20.2± 0.9	20.8± 0.9	21.4± 0.9
313 ppm	18.4± 0.7	19.0± 0.9	19.9± 0.9	20.4± 1.1	20.5± 0.9	21.4± 1.4	21.9± 1.4
1250 ppm	18.4± 0.7	19.4± 1.0	20.2± 0.7	20.8± 0.7	21.2± 0.7	21.9± 0.7	22.6± 0.8
2500 ppm	18.4± 0.7	19.4± 0.9	20.3± 1.0	20.9± 0.9	21.4± 1.1	21.7± 0.8	22.9± 0.9*
5000 ppm	18.4± 0.7	18.3± 0.8	20.0± 0.9	21.9± 0.9**	22.7± 1.3**	22.8± 1.0**	23.1± 1.0*

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

STUDY NO. : 0440
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 7-7	8-7	9-7	10-7	11-7	12-7	13-7
Control	21.9± 1.3	21.8± 1.3	22.3± 1.0	22.5± 1.3	22.8± 1.2	23.2± 1.4	23.3± 1.6
78 ppm	21.6± 1.4	21.9± 1.2	22.3± 1.3	22.7± 1.2	22.8± 1.4	23.8± 1.6	23.9± 2.3
313 ppm	22.7± 1.2	22.8± 1.7	23.1± 1.6	23.0± 1.9	23.4± 2.3	24.6± 2.4	24.4± 2.5
1250 ppm	22.7± 0.9	22.9± 1.2	23.7± 1.3	23.3± 1.1	24.3± 1.2	25.3± 1.5	25.7± 2.1
2500 ppm	23.2± 1.0*	23.2± 1.0	23.9± 1.2*	24.2± 1.4	24.7± 1.8*	24.9± 1.2	25.0± 1.2
5000 ppm	22.9± 0.9	22.8± 1.1	23.4± 1.2	23.8± 1.3	23.9± 1.3	24.8± 1.5	24.9± 1.3

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. : 0440
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(7)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	4.1± 0.3	3.8± 0.4	3.8± 0.2	3.8± 0.2	3.8± 0.2	3.9± 0.2	3.8± 0.2
78 ppm	4.0± 0.2	3.9± 0.5	4.0± 0.3	4.0± 0.2	3.8± 0.4	4.0± 0.3	4.1± 0.3
313 ppm	3.9± 0.5	4.1± 0.5	4.1± 0.6	4.1± 0.6	4.1± 0.7	4.3± 0.7	4.1± 0.5
1250 ppm	4.0± 0.4	3.9± 0.5	4.0± 0.4	4.0± 0.4	3.9± 0.4	4.1± 0.4	4.1± 0.5
2500 ppm	4.2± 0.7	4.6± 1.0	3.8± 0.6	3.8± 0.5	3.7± 0.3	3.8± 0.3	3.8± 0.3
5000 ppm	3.1± 0.4**	3.8± 0.4	3.9± 0.6	3.5± 0.4	3.5± 0.3	3.7± 0.3	3.6± 0.3

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

STUDY NO. : 0440
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)
Control	3.7± 0.2	3.8± 0.2	4.0± 0.2	4.0± 0.2	3.9± 0.2	4.1± 0.2
78 ppm	4.0± 0.3	3.9± 0.3	4.0± 0.2	4.1± 0.3	4.1± 0.3	4.1± 0.3
313 ppm	4.1± 0.5	4.0± 0.6	4.1± 0.4	4.2± 0.5	4.1± 0.6	4.1± 0.4
1250 ppm	3.9± 0.5	3.9± 0.4	3.9± 0.4	4.1± 0.4	4.0± 0.4	4.1± 0.3
2500 ppm	3.9± 0.4	3.8± 0.4	3.8± 0.3	3.9± 0.4	3.8± 0.2	3.9± 0.2
5000 ppm	3.6± 0.3	3.7± 0.2	3.8± 0.3	3.9± 0.3	3.9± 0.4	4.0± 0.5

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. : 0440
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(7)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	3.6± 0.1	3.5± 0.2	3.5± 0.2	3.5± 0.3	3.6± 0.2	3.6± 0.2	3.5± 0.3
78 ppm	3.6± 0.3	3.3± 0.3	3.3± 0.2	3.3± 0.3	3.4± 0.3	3.6± 0.2	3.6± 0.4
313 ppm	3.5± 0.2	3.5± 0.1	3.5± 0.2	3.4± 0.3	3.6± 0.3	3.7± 0.2	3.7± 0.3
1250 ppm	3.5± 0.2	3.4± 0.2	3.5± 0.2	3.4± 0.3	3.5± 0.3	3.6± 0.2	3.6± 0.2
2500 ppm	3.4± 0.2	3.3± 0.2	3.5± 0.3	3.4± 0.2	3.4± 0.2	3.6± 0.2	3.7± 0.2
5000 ppm	3.5± 1.1	3.8± 0.9	4.0± 0.8	3.4± 0.5	3.3± 0.2	3.3± 0.3*	3.3± 0.2

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

STUDY NO. : 0440
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)
Control	3.6± 0.3	3.7± 0.4	3.7± 0.3	3.8± 0.3	3.8± 0.2	3.8± 0.3
78 ppm	3.5± 0.3	3.7± 0.4	3.6± 0.2	3.6± 0.3	3.8± 0.3	3.8± 0.5
313 ppm	3.6± 0.3	3.7± 0.2	3.6± 0.3	3.7± 0.2	3.8± 0.4	3.9± 0.5
1250 ppm	3.5± 0.3	3.6± 0.3	3.6± 0.3	3.7± 0.2	3.8± 0.3	4.0± 0.7
2500 ppm	3.7± 0.3	3.7± 0.3	3.7± 0.3	3.8± 0.4	3.7± 0.4	3.9± 0.5
5000 ppm	3.3± 0.3	3.4± 0.3	3.4± 0.3	3.5± 0.2	3.6± 0.2	3.7± 0.2

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. : 0440
ANIMAL : MOUSE Crj:BDF1
UNIT : g／kg／d a y
REPORT TYPE : A1 13
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2	3	4	5	6	7
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
78 ppm	0.013± 0.001	0.013± 0.001	0.012± 0.001	0.012± 0.001	0.011± 0.001	0.011± 0.001	0.011± 0.001
313 ppm	0.053± 0.004	0.051± 0.005	0.051± 0.008	0.048± 0.007	0.048± 0.007	0.047± 0.007	0.045± 0.005
1250 ppm	0.207± 0.012	0.195± 0.036	0.197± 0.037	0.181± 0.015	0.175± 0.014	0.176± 0.016	0.173± 0.018
2500 ppm	0.430± 0.064	0.442± 0.089	0.359± 0.052	0.344± 0.039	0.330± 0.027	0.335± 0.022	0.328± 0.019
5000 ppm	0.734± 0.104	0.820± 0.096	0.797± 0.120	0.710± 0.130	0.685± 0.099	0.686± 0.087	0.661± 0.056

STUDY NO. : 0440
ANIMAL : MOUSE Crj:BDF1
UNIT : g／kg／d a y
REPORT TYPE : A1 13
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 8	9	10	11	12	13
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
78 ppm	0.011± 0.001	0.010± 0.001	0.010± 0.001	0.010± 0.001	0.010± 0.001	0.010± 0.001
313 ppm	0.044± 0.006	0.041± 0.006	0.042± 0.004	0.042± 0.005	0.040± 0.006	0.039± 0.004
1250 ppm	0.161± 0.017	0.159± 0.012	0.159± 0.014	0.162± 0.014	0.153± 0.013	0.154± 0.010
2500 ppm	0.329± 0.028	0.319± 0.027	0.311± 0.024	0.313± 0.030	0.300± 0.018	0.302± 0.015
5000 ppm	0.654± 0.052	0.661± 0.053	0.652± 0.054	0.665± 0.053	0.657± 0.068	0.675± 0.074

APPENDIX D 2

CHEMICAL INTAKE CHANGES : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0440
ANIMAL : MOUSE Crj:BDF1
UNIT : g／kg／d a y
REPORT TYPE : A1 13
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2	3	4	5	6	7
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
78 ppm	0.015± 0.001	0.013± 0.001	0.013± 0.001	0.013± 0.001	0.013± 0.001	0.013± 0.001	0.013± 0.001
313 ppm	0.059± 0.002	0.055± 0.002	0.053± 0.003	0.052± 0.003	0.052± 0.003	0.052± 0.003	0.051± 0.003
1250 ppm	0.226± 0.012	0.213± 0.016	0.211± 0.016	0.203± 0.018	0.199± 0.018	0.200± 0.016	0.198± 0.018
2500 ppm	0.434± 0.026	0.402± 0.019	0.413± 0.032	0.400± 0.024	0.388± 0.023	0.397± 0.022	0.395± 0.015
5000 ppm	0.969± 0.299	0.951± 0.224	0.904± 0.167	0.742± 0.091	0.714± 0.042	0.715± 0.064	0.711± 0.059

STUDY NO. : 0440
ANIMAL : MOUSE Crj:BDF1
UNIT : g／kg／d a y
REPORT TYPE : A1 13
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 8	9	10	11	12	13
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
78 ppm	0.013± 0.001	0.013± 0.001	0.012± 0.001	0.012± 0.001	0.012± 0.001	0.013± 0.001
313 ppm	0.049± 0.002	0.050± 0.003	0.049± 0.004	0.050± 0.003	0.049± 0.002	0.050± 0.004
1250 ppm	0.193± 0.015	0.191± 0.013	0.191± 0.018	0.192± 0.014	0.188± 0.015	0.193± 0.027
2500 ppm	0.400± 0.034	0.390± 0.025	0.381± 0.029	0.389± 0.030	0.372± 0.041	0.393± 0.046
5000 ppm	0.729± 0.046	0.722± 0.052	0.722± 0.045	0.742± 0.042	0.730± 0.021	0.744± 0.022

APPENDIX E 1

HEMATOLOGY : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0440
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : I
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu L$	HEMOGLOBIN g/dL	HEMATOCRIT %	MCV fL	MCH pg	MCHC g/dL	PLATELET $10^3/\mu L$
Control	10	10.82± 0.27	15.5± 0.3	48.7± 1.1	45.0± 0.6	14.4± 0.2	31.9± 0.3	1481± 139
78 ppm	10	10.77± 0.32	15.5± 0.5	48.7± 1.4	45.2± 0.7	14.4± 0.3	31.9± 0.5	1488± 101
313 ppm	9	10.58± 0.26	15.2± 0.3	48.3± 0.8	45.6± 0.7	14.3± 0.2	31.4± 0.4*	1478± 65
1250 ppm	9	10.20± 0.11**	14.9± 0.2**	47.0± 0.7**	46.0± 0.5**	14.6± 0.1	31.8± 0.3	1534± 70
2500 ppm	10	9.95± 0.26**	14.6± 0.3**	45.2± 1.3**	45.5± 0.5	14.7± 0.3*	32.2± 0.5	1559± 58
5000 ppm	10	9.57± 0.20**	15.6± 0.3!	42.5± 1.1**	44.4± 0.9	16.3± 0.4!	36.6± 0.6!	1454± 52

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

! : Significant test is not applied to this group.

STUDY NO. : 0440
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	WBC $10^3/\mu L$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHER
Control	10	1.79± 0.99	1± 1	15± 3	2± 1	0± 0	3± 1	79± 4	0± 0
78 ppm	10	1.88± 0.81	1± 1	14± 4	2± 1	0± 0	3± 1	81± 4	0± 0
313 ppm	9	1.54± 0.63	1± 1	14± 2	1± 1	0± 0	3± 2	82± 3	0± 0
1250 ppm	9	1.38± 0.68	1± 1	12± 2	2± 2	0± 0	2± 1	84± 3*	0± 0
2500 ppm	10	1.32± 0.70	1± 1	10± 4**	0± 1*	0± 0	2± 1	87± 4**	0± 0
5000 ppm	10	2.14± 0.89	1± 1	11± 2*	1± 1*	0± 0	2± 1	87± 2**	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. : 0440
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	WBC $10^3/\mu L$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHER
Control	10	1.09± 0.40	1± 1	15± 5	1± 1	0± 0	2± 1	81± 5	0± 0
78 ppm	10	1.24± 0.90	1± 2	16± 6	1± 1	0± 0	3± 2	79± 7	0± 0
313 ppm	10	1.22± 1.00	2± 2	13± 4	2± 1	0± 0	2± 2	82± 5	0± 0
1250 ppm	10	1.28± 0.64	0± 0	13± 4	2± 2	0± 0	2± 1	83± 3	0± 0
2500 ppm	10	1.56± 0.82	0± 1	15± 4	1± 1	0± 0	1± 1	83± 5	0± 0
5000 ppm	10	1.75± 0.97	1± 1	11± 3	0± 1	0± 0	2± 1	86± 3	0± 0

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

STUDY NO. : 0440
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu L$	HEMOGLOBIN g/dL	HEMATOCRIT %	MCV fL	MCH pg	MCHC g/dL	PLATELET $10^3/\mu L$
Control	10	10.60± 0.25	15.6± 0.4	47.7± 1.0	45.0± 0.5	14.7± 0.2	32.7± 0.4	1376± 75
78 ppm	10	10.81± 0.35	15.8± 0.4	49.1± 1.6*	45.4± 0.7	14.6± 0.3	32.1± 0.8	1358± 89
313 ppm	10	10.59± 0.27	15.7± 0.5	48.4± 1.1	45.8± 0.5*	14.9± 0.1	32.5± 0.5	1390± 66
1250 ppm	10	10.17± 0.18**	15.0± 0.3*	47.0± 0.6	46.2± 0.7**	14.8± 0.3	32.0± 0.4*	1353± 84
2500 ppm	10	9.90± 0.25**	14.7± 0.4**	45.0± 1.0**	45.5± 0.6	14.9± 0.3	32.8± 0.6	1399± 100
5000 ppm	10	9.71± 0.20**	16.2± 0.5!	44.1± 0.9**	45.5± 0.7	16.7± 0.3!	36.8± 0.9!	1313± 90

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

! : Significant test is not applied to this group.

APPENDIX F 1

BIOCHEMISTRY : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0440
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

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	5.1± 0.2	3.1± 0.1	1.6± 0.1	0.18± 0.03	175± 40	89± 12	37± 13
78 ppm	10	5.2± 0.2	3.2± 0.1	1.6± 0.1	0.19± 0.07	183± 57	98± 14	41± 18
313 ppm	10	5.4± 0.2*	3.2± 0.1	1.5± 0.1	0.18± 0.05	193± 47	126± 14	43± 15
1250 ppm	9	5.5± 0.2**	3.4± 0.1**	1.5± 0.1	0.17± 0.01	215± 35	223± 20**	58± 21*
2500 ppm	10	5.7± 0.2**	3.4± 0.1**	1.5± 0.1	0.18± 0.02	227± 28*	306± 27**	52± 14
5000 ppm	10	5.8± 0.3**	3.5± 0.2**	1.5± 0.0	0.20± 0.02	219± 24	393± 44**	37± 6

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

STUDY NO. : 0440
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

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	188±	20	46±	5	19±	5	296±	72	137±	10	2±	1	62±	21
78 ppm	10	197±	21	44±	7	19±	3	319±	140	135±	13	2±	1	54±	18
313 ppm	10	242±	21	44±	6	25±	6	320±	113	133±	11	2±	2	55±	21
1250 ppm	9	367±	27**	37±	6*	26±	4	291±	43	131±	11	3±	2	49±	8
2500 ppm	10	467±	31**	38±	5	39±	8**	330±	38	170±	17	4±	2	53±	20
5000 ppm	10	601±	54**	52±	12	65±	14**	354±	114	322±	37**	36±	12**	59±	14

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

STUDY NO. : 0440
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

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	26.4± 5.9	152± 2	4.2± 0.6	120± 3	8.9± 0.2	6.5± 0.7
78 ppm	10	26.7± 4.5	153± 2	4.4± 0.8	121± 3	9.1± 0.4	7.1± 1.3
313 ppm	10	29.3± 4.4	152± 2	4.1± 0.4	120± 1	9.1± 0.3	7.0± 1.0
1250 ppm	9	30.1± 3.3	151± 1	4.0± 0.3	120± 2	9.3± 0.1*	7.2± 1.0
2500 ppm	10	32.1± 3.2*	151± 1	4.1± 0.5	118± 2	9.4± 0.2**	7.4± 0.6
5000 ppm	10	32.2± 3.8*	151± 1	4.1± 0.3	117± 2**	9.6± 0.3**	7.5± 1.1

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

APPENDIX F 2

BIOCHEMISTRY : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0440
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

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	3.4± 0.2	2.0± 0.3	0.18± 0.02	123± 31	74± 8	23± 11
78 ppm	10	5.3± 0.2	3.5± 0.2	2.0± 0.3	0.17± 0.02	132± 23	87± 10	23± 14
313 ppm	10	5.3± 0.2	3.5± 0.2	1.9± 0.2	0.17± 0.01	126± 27	102± 12	23± 11
1250 ppm	10	5.4± 0.1**	3.5± 0.1	1.9± 0.2	0.17± 0.03	139± 16	163± 15**	34± 16
2500 ppm	10	5.6± 0.2**	3.6± 0.1*	1.9± 0.2	0.20± 0.05	151± 19*	236± 18**	39± 11*
5000 ppm	10	5.8± 0.2**	3.7± 0.2**	1.8± 0.3	0.25± 0.07**	166± 19**	325± 34**	32± 9

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

STUDY NO. : 0440
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

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	159± 23	56± 8	20± 2	320± 58	214± 17	2± 2	56± 12
78 ppm	10	178± 20	54± 14	21± 4	324± 98	203± 17	3± 2	69± 41
313 ppm	10	201± 24**	54± 8	22± 2	357± 77	182± 19*	2± 2	77± 38
1250 ppm	10	291± 23**	51± 13	32± 7*	352± 84	171± 15**	2± 1	67± 25
2500 ppm	10	377± 24**	54± 9	51± 12**	420± 141	178± 10*	4± 2	56± 9
5000 ppm	10	522± 39**	71± 32	65± 39**	514± 196	268± 39	35± 8**	101± 114

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

STUDY NO. : 0440
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

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	21.3± 3.3	153± 2	4.3± 0.4	121± 2	9.0± 0.4	5.8± 0.7
78 ppm	10	22.2± 4.5	153± 2	4.3± 0.5	122± 2	9.2± 0.2	5.9± 1.1
313 ppm	10	20.2± 2.8	153± 3	4.0± 0.4	121± 2	9.1± 0.2	6.0± 0.5
1250 ppm	10	22.5± 2.3	154± 2	3.7± 0.4**	122± 2	9.4± 0.2**	6.3± 1.1
2500 ppm	10	24.5± 3.0	154± 2	3.9± 0.5	121± 2	9.6± 0.2**	6.4± 1.0
5000 ppm	10	28.3± 3.6**	154± 2	4.0± 0.4	118± 3**	9.7± 0.3**	7.6± 1.2**

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

APPENDIX G 1

URINALYSIS : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0440 URINALYSIS
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
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	1	2	2	5		0	0	10	0	0	0		10	0	0	0	0	0		4	5	1	0	0	0		10	0	0	0	0	
78 ppm	10	0	0	0	0	5	4	1		0	0	10	0	0	0		10	0	0	0	0	0		0	8	2	0	0	0		10	0	0	0	0	
313 ppm	10	0	0	0	2	5	1	2		0	1	8	1	0	0		10	0	0	0	0	0		2	6	2	0	0	0		10	0	0	0	0	
1250 ppm	9	0	0	0	0	3	4	2		0	0	9	0	0	0		9	0	0	0	0	0		0	9	0	0	0	0	*	9	0	0	0	0	
2500 ppm	10	0	0	0	1	3	5	1		0	2	8	0	0	0		10	0	0	0	0	0		2	7	1	0	0	0		10	0	0	0	0	
5000 ppm	10	0	0	0	1	4	2	3		0	3	7	0	0	0		10	0	0	0	0	0		1	7	2	0	0	0		10	0	0	0	0	

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

STUDY NO. : 0440 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	
78 ppm	10	10	0	0	0	0	
313 ppm	10	10	0	0	0	0	
1250 ppm	9	9	0	0	0	0	
2500 ppm	10	10	0	0	0	0	
5000 ppm	10	10	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. : 0440 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	0	0	5	0	5	0		0	2	7	1	0	0		10	0	0	0	0	0		1	8	1	0	0	0		10	0	0	0	0	
78 ppm	10	0	0	0	3	3	4	0		0	3	7	0	0	0		10	0	0	0	0	0		2	8	0	0	0	0		10	0	0	0	0	
313 ppm	10	0	0	1	2	2	5	0		0	3	7	0	0	0		10	0	0	0	0	0		1	8	1	0	0	0		10	0	0	0	0	
1250 ppm	10	0	0	0	4	2	4	0		0	7	3	0	0	0		10	0	0	0	0	0		0	10	0	0	0	0		10	0	0	0	0	
2500 ppm	10	0	0	1	0	2	7	0	*	0	3	7	0	0	0		10	0	0	0	0	0		0	9	1	0	0	0		10	0	0	0	0	
5000 ppm	10	0	0	0	1	1	7	1		0	7	3	0	0	0		10	0	0	0	0	0		1	7	2	0	0	0		10	0	0	0	0	

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

STUDY NO. : 0440
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0	
78 ppm	10	10	0	0	0	0	
313 ppm	10	10	0	0	0	0	
1250 ppm	10	10	0	0	0	0	
2500 ppm	10	10	0	0	0	0	
5000 ppm	10	10	0	0	0	0	

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

APPENDIX H 1

GROSS FINDINGS : SUMMARY, MOUSE : MALE : SACRIFICED ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0440
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	78 ppm 10 (%)	313 ppm 10 (%)	1250 ppm 9 (%)
spleen	dark		0 (0)	0 (0)	0 (0)	0 (0)
	black zone		1 (10)	0 (0)	0 (0)	0 (0)
liver	dark		0 (0)	0 (0)	0 (0)	0 (0)
kidney	hydronephrosis		1 (10)	1 (10)	1 (10)	0 (0)

STUDY NO. : 0440
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name / NO. of Animals	2500 ppm 10 (%)	5000 ppm 10 (%)
spleen	dark		0 (0)	10 (100)
	black zone		0 (0)	0 (0)
liver	dark		0 (0)	10 (100)
kidney	hydronephrosis		0 (0)	1 (10)

APPENDIX H 2

GROSS FINDINGS : SUMMARY, MOUSE : MALE : DEAD AND MORIBUND ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0440
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name / NO. of Animals	Control 0 (%)	78 ppm 0 (%)	313 ppm 0 (%)	1250 ppm 1 (%)
thymus	atrophic		- (-)	- (-)	- (-)	1 (100)
kidney	hydronephrosis		- (-)	- (-)	- (-)	1 (100)

STUDY NO. : 0440
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name / NO. of Animals	2500 ppm 0 (%)	5000 ppm 0 (%)
thymus	atrophic		- (-)	- (-)
kidney	hydronephrosis		- (-)	- (-)

APPENDIX H 3

GROSS FINDINGS : SUMMARY, MOUSE : FEMALE : ALL ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0440
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	78 ppm 10 (%)	313 ppm 10 (%)	1250 ppm 10 (%)
spleen	dark		0 (0)	0 (0)	0 (0)	0 (0)
liver	dark		0 (0)	0 (0)	0 (0)	0 (0)
kidney	hydronephrosis		0 (0)	1 (10)	0 (0)	0 (0)

Organ	Findings	Group Name NO. of Animals	2500 ppm 10 (%)	5000 ppm 10 (%)
spleen	dark		0 (0)	10 (100)
liver	dark		0 (0)	10 (100)
kidney	hydronephrosis		0 (0)	0 (0)

APPENDIX I 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0440
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	29.5± 1.8	0.040± 0.007	0.017± 0.003	0.218± 0.040	0.155± 0.009	0.158± 0.015
78 ppm	10	31.1± 2.8	0.045± 0.006	0.019± 0.003	0.231± 0.034	0.155± 0.012	0.164± 0.012
313 ppm	10	30.5± 2.4	0.046± 0.007	0.019± 0.006	0.218± 0.015	0.159± 0.015	0.160± 0.014
1250 ppm	9	30.2± 2.1	0.044± 0.010	0.018± 0.003	0.232± 0.014	0.159± 0.014	0.158± 0.015
2500 ppm	10	29.0± 1.2	0.040± 0.004	0.015± 0.003	0.237± 0.009	0.161± 0.013	0.161± 0.017
5000 ppm	10	26.7± 1.2*	0.036± 0.006	0.011± 0.002**	0.211± 0.031	0.159± 0.009	0.163± 0.012

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

STUDY NO. : 0440
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.597± 0.640	0.052± 0.007	1.120± 0.043	0.452± 0.012
78 ppm	10	0.435± 0.072	0.053± 0.006	1.207± 0.081	0.449± 0.015
313 ppm	10	0.495± 0.269	0.055± 0.010	1.328± 0.114	0.449± 0.017
1250 ppm	9	0.431± 0.028	0.060± 0.007	1.739± 0.171**	0.453± 0.018
2500 ppm	10	0.451± 0.033*	0.077± 0.007**	2.240± 0.145**	0.448± 0.010
5000 ppm	10	0.524± 0.178**	0.135± 0.017**	2.978± 0.142**	0.441± 0.013

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. : 0440
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	21.1± 1.7	0.045± 0.003	0.013± 0.002	0.026± 0.004	0.123± 0.010	0.150± 0.013
78 ppm	10	21.3± 1.7	0.043± 0.008	0.014± 0.003	0.025± 0.003	0.123± 0.005	0.153± 0.013
313 ppm	10	21.9± 2.3	0.043± 0.008	0.014± 0.003	0.027± 0.004	0.124± 0.007	0.153± 0.009
1250 ppm	10	22.9± 1.9	0.045± 0.008	0.015± 0.003	0.026± 0.004	0.132± 0.008	0.155± 0.013
2500 ppm	10	22.2± 0.9	0.045± 0.005	0.013± 0.001	0.029± 0.006	0.131± 0.009	0.158± 0.013
5000 ppm	10	21.7± 1.2	0.042± 0.006	0.013± 0.002	0.022± 0.003	0.133± 0.007*	0.147± 0.013

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

STUDY NO. : 0440
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.282± 0.010	0.055± 0.007	0.889± 0.074	0.458± 0.012
78 ppm	10	0.316± 0.120	0.055± 0.011	0.928± 0.063	0.458± 0.011
313 ppm	10	0.287± 0.019	0.053± 0.005	0.997± 0.070	0.457± 0.013
1250 ppm	10	0.296± 0.017	0.070± 0.010	1.330± 0.120**	0.459± 0.015
2500 ppm	10	0.313± 0.014**	0.094± 0.008**	1.685± 0.078**	0.462± 0.010
5000 ppm	10	0.330± 0.018**	0.171± 0.024**	2.291± 0.162**	0.443± 0.012*

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. : 0440
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	29.5± 1.8	0.137± 0.026	0.057± 0.009	0.741± 0.139	0.527± 0.047	0.536± 0.037
78 ppm	10	31.1± 2.8	0.145± 0.018	0.063± 0.010	0.744± 0.110	0.501± 0.053	0.531± 0.063
313 ppm	10	30.5± 2.4	0.152± 0.022	0.063± 0.018	0.720± 0.087	0.523± 0.043	0.528± 0.056
1250 ppm	9	30.2± 2.1	0.144± 0.026	0.059± 0.011	0.771± 0.049	0.528± 0.037	0.524± 0.034
2500 ppm	10	29.0± 1.2	0.139± 0.018	0.051± 0.010	0.817± 0.034	0.555± 0.038	0.556± 0.064
5000 ppm	10	26.7± 1.2*	0.133± 0.024	0.042± 0.007*	0.790± 0.118	0.595± 0.041**	0.609± 0.041**

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

STUDY NO. : 0440
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	2.035± 2.196	0.177± 0.023	3.810± 0.146	1.538± 0.087
78 ppm	10	1.405± 0.225	0.171± 0.020	3.891± 0.197	1.451± 0.110
313 ppm	10	1.646± 0.964	0.179± 0.029	4.359± 0.203	1.481± 0.112
1250 ppm	9	1.430± 0.030	0.199± 0.015	5.757± 0.322**	1.507± 0.114
2500 ppm	10	1.555± 0.082	0.266± 0.023**	7.723± 0.277**	1.546± 0.064
5000 ppm	10	1.955± 0.618**	0.505± 0.055**	11.150± 0.528**	1.651± 0.061*

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. : 0440
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	21.1± 1.7	0.215± 0.019	0.061± 0.008	0.126± 0.020	0.585± 0.062	0.716± 0.086
78 ppm	10	21.3± 1.7	0.200± 0.038	0.063± 0.011	0.115± 0.014	0.579± 0.057	0.720± 0.071
313 ppm	10	21.9± 2.3	0.197± 0.041	0.064± 0.007	0.125± 0.023	0.569± 0.062	0.704± 0.078
1250 ppm	10	22.9± 1.9	0.196± 0.037	0.065± 0.012	0.114± 0.019	0.578± 0.036	0.681± 0.055
2500 ppm	10	22.2± 0.9	0.203± 0.023	0.059± 0.007	0.131± 0.027	0.588± 0.031	0.712± 0.061
5000 ppm	10	21.7± 1.2	0.194± 0.021	0.058± 0.008	0.102± 0.014	0.612± 0.032	0.674± 0.037

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

STUDY NO. : 0440
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.341± 0.095	0.260± 0.037	4.221± 0.313	2.179± 0.160
78 ppm	10	1.485± 0.562	0.256± 0.049	4.354± 0.150	2.158± 0.168
313 ppm	10	1.320± 0.100	0.245± 0.030	4.576± 0.272*	2.109± 0.214
1250 ppm	10	1.298± 0.074	0.306± 0.030	5.813± 0.260**	2.013± 0.139
2500 ppm	10	1.407± 0.078	0.423± 0.045**	7.581± 0.263**	2.079± 0.077
5000 ppm	10	1.518± 0.049**	0.784± 0.086**	10.539± 0.400**	2.041± 0.101

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

APPENDIX K 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : MALE : SACRIFICED ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0440
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control				78 ppm				313 ppm				1250 ppm			
		No. of Animals on Study	10				10				10				9			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}																		
nasal cavit			<10>				<10>				<10>				< 9>			
	atrophy: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)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}																		
spleen			<10>				<10>				<10>				< 9>			
	deposit of hemosiderin		0	0	0	0	0	0	0	0	5	0	0	0 *	9	0	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	deposit of melanin		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	increased extramedullary hematopoiesis		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)	(56)	(0)	(0)	(0)
	engorgement of erythrocyte		0	0	0	0	0	0	0	0	0	0	0	0	7	0	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(78)	(0)	(0)	(0)
{Digestive system}																		
liver			<10>				<10>				<10>				< 9>			
	deposit of hemosiderin		0	0	0	0	0	0	0	0	0	0	0	0	9	0	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(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	2500 ppm				5000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			<10>				<10>			
	atrophy:olfactory epithelium		7	0	0	0 **	10	0	0	0 **
			(70)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Hematopoietic system}										
spleen			<10>				<10>			
	deposit of hemosiderin		10	0	0	0 **	0	10	0	0 **
			(100)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
	deposit of melanin		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	increased extramedullary hematopoiesis		9	1	0	0 **	1	9	0	0 **
			(90)	(10)	(0)	(0)	(10)	(90)	(0)	(0)
	engorgement of erythrocyte		10	0	0	0 **	7	3	0	0 **
			(100)	(0)	(0)	(0)	(70)	(30)	(0)	(0)
{Digestive system}										
liver			<10>				<10>			
	deposit of hemosiderin		10	0	0	0 **	10	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 / No. of Animals on Study / Grade	Control 10				78 ppm 10				313 ppm 10				1250 ppm 9			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Digestive system}																		
liver			<10>				<10>				<10>				< 9>			
	inflammatory cell nest		2 (20)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	1 (11)	0 (0)	0 (0)	0 (0)
	hepatocellular hypertrophy:central		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 ** (0)	0 (0)	0 (0)	9 (100)	0 ** (0)
	nuclear atypia:central		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	6 (60)	0 (0)	0 (0)	0 * (0)	0 (0)	9 (100)	0 (0)	0 ** (0)
{Urinary system}																		
kidney			<10>				<10>				<10>				< 9>			
	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)
	inflammatory polyp		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)	0 (0)	0 (0)	0 (0)
	hydronephrosis		0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
{Endocrine system}																		
parathyroid			< 9>				< 9>				< 9>				< 8>			
	cyst		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (11)	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	2500 ppm				5000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
liver			<10>				<10>			
	inflammatory cell nest		1	0	0	0	2	0	0	0
			(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	hepatocellular hypertrophy:central		0	0	10	0 **	0	0	10	0 **
			(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)
	nuclear atypia:central		0	10	0	0 **	0	10	0	0 **
			(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
{Urinary system}										
kidney			<10>				<10>			
	deposit of hemosiderin		0	0	0	0	10	0	0	0 **
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	inflammatory polyp		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hydronephrosis		0	0	0	0	0	0	1	0
			(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)
{Endocrine system}										
parathyroid			< 9>				< 9>			
	cyst		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 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : MALE : DEAD AND MORIBUND ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0440
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control				78 ppm				313 ppm				1250 ppm			
		No. of Animals on Study	0				0				0				1			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Hematopoietic system}																		
thymus	atrophy		< 0>				< 0>				< 0>				< 1>			
			-	-	-	-	-	-	-	-	-	-	-	-	0	0	1	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(0)	(0)	(100)	(0)
spleen	deposit of hemosiderin		< 0>				< 0>				< 0>				< 1>			
			-	-	-	-	-	-	-	-	-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
{Circulatory system}																		
heart	thrombus		< 0>				< 0>				< 0>				< 1>			
			-	-	-	-	-	-	-	-	-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
	necrosis		-	-	-	-	-	-	-	-	-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
{Digestive system}																		
liver	nuclear atypia:central		< 0>				< 0>				< 0>				< 1>			
			-	-	-	-	-	-	-	-	-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)

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

Organ	Findings	Group Name	2500 ppm				5000 ppm			
		No. of Animals on Study	0				0			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
thymus			< 0>				< 0>			
	atrophy		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
spleen			< 0>				< 0>			
	deposit of hemosiderin		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
{Circulatory system}										
heart			< 0>				< 0>			
	thrombus		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	necrosis		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
{Digestive system}										
liver			< 0>				< 0>			
	nuclear atypia:central		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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

Organ	Findings	Group Name	Control				78 ppm				313 ppm				1250 ppm			
		No. of Animals on Study	0				0				0				1			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}																		
kidney			< 0>				< 0>				< 0>				< 1>			
	inflammatory polyp		-	-	-	-	-	-	-	-	-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
	hydronephrosis		-	-	-	-	-	-	-	-	-	-	-	-	0	0	1	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(0)	(0)	(100)	(0)

Grade 1 : Slight 2 : Moderate 3 : 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	2500 ppm				5000 ppm			
		No. of Animals on Study	0				0			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Urinary system)										
kidney			< 0>				< 0>			
	inflammatory polyp		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	hydronephrosis		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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 3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : FEMALE : ALL ANIMALS

(13-WEEK STUDY)

Organ	Findings	Group Name	Control				78 ppm				313 ppm				1250 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>			
	atrophy: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)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}																		
spleen			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		0	0	0	0	0	0	0	0	5	0	0	0 *	10	0	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	deposit of melanin		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mastcell hyperplasia		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	increased extramedullary hematopoiesis		0	0	0	0	0	0	0	0	0	0	0	0	6	0	0	0 *
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(60)	(0)	(0)	(0)
	engorgement of erythrocyte		0	0	0	0	0	0	0	0	0	0	0	0	10	0	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Digestive system}																		
stomach			<10>				<10>				<10>				<10>			
	mastcell hyperplasia		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(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	2500 ppm				5000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Respiratory system)										
nasal cavit			<10>				<10>			
	atrophy:olfactory epithelium		8	0	0	0 **	10	0	0	0 **
			(80)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
(Hematopoietic system)										
spleen			<10>				<10>			
	deposit of hemosiderin		1	9	0	0 **	0	10	0	0 **
			(10)	(90)	(0)	(0)	(0)	(100)	(0)	(0)
	deposit of melanin		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mastcell hyperplasia		0	1	0	0	0	0	0	0
			(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)
	increased extramedullary hematopoiesis		3	7	0	0 **	0	10	0	0 **
			(30)	(70)	(0)	(0)	(0)	(100)	(0)	(0)
	engorgement of erythrocyte		10	0	0	0 **	0	10	0	0 **
			(100)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
(Digestive system)										
stomach			<10>				<10>			
	mastcell hyperplasia		0	1	0	0	0	0	0	0
			(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				78 ppm				313 ppm				1250 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	10	0	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	inflammatory cell nest		2	0	0	0	2	0	0	0	2	0	0	0	4	0	0	0
			(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(40)	(0)	(0)	(0)
	hepatocellular hypertrophy:central		0	0	0	0	0	0	0	0	1	0	0	0	0	4	6	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(40)	(60)	(0)
	nuclear atypia:central		0	0	0	0	0	0	0	0	0	0	0	0	9	1	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(90)	(10)	(0)	(0)
{Urinary system}																		
kidney			<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)
	inflammatory polyp		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hydronephrosis		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)	(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	2500 ppm				5000 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)
	inflammatory cell nest		7	0	0	0	5	0	0	0
			(70)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
	hepatocellular hypertrophy:central		0	0	10	0 **	0	0	10	0 **
			(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)
	nuclear atypia:central		3	7	0	0 **	10	0	0	0 **
			(30)	(70)	(0)	(0)	(100)	(0)	(0)	(0)
(Urinary system)										
kidney			<10>				<10>			
	deposit of hemosiderin		0	0	0	0	10	0	0	0 **
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	inflammatory polyp		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hydronephrosis		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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				78 ppm				313 ppm				1250 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Endocrine system)																		
parathyroid			< 9>				< 8>				< 6>				<10>			
	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	2500 ppm				5000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Endocrine system}										
parathyroid			<10>				<10>			
	cyst		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 OF *o* -CHLORONITROBENZENE IN THE 13-WEEK FEED STUDY

IDENTITY OF *o*-CHLORONITROBENZENE IN THE 13-WEEK FEED STUDY

Test Substance : *o*-Chloronitrobenzene (Wako Pure Chemical Industries, Ltd.)

Lot No. : SEF9795

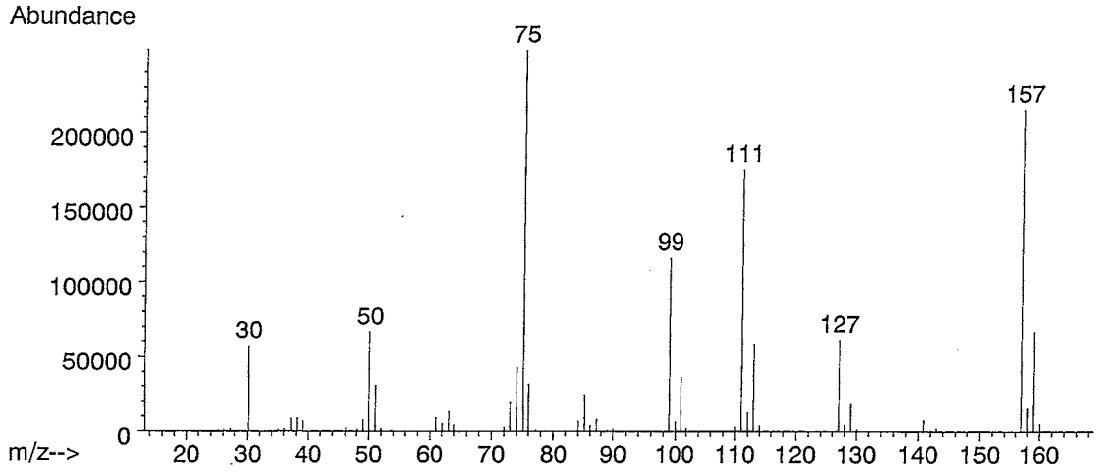
1. Spectral Data

Mass Spectrometry

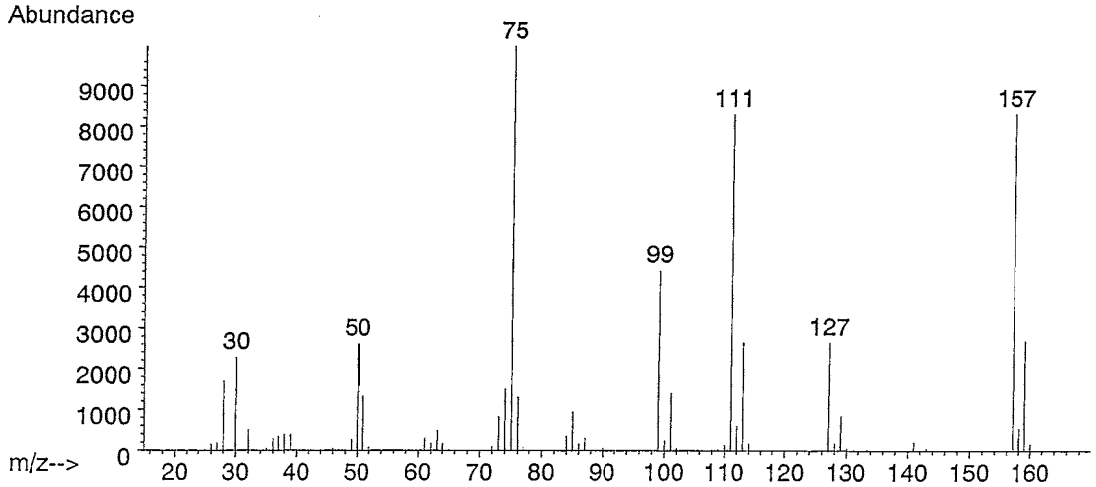
Instrument : Hewlett Packard 5989B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance



Mass Spectrum of Literature Data*

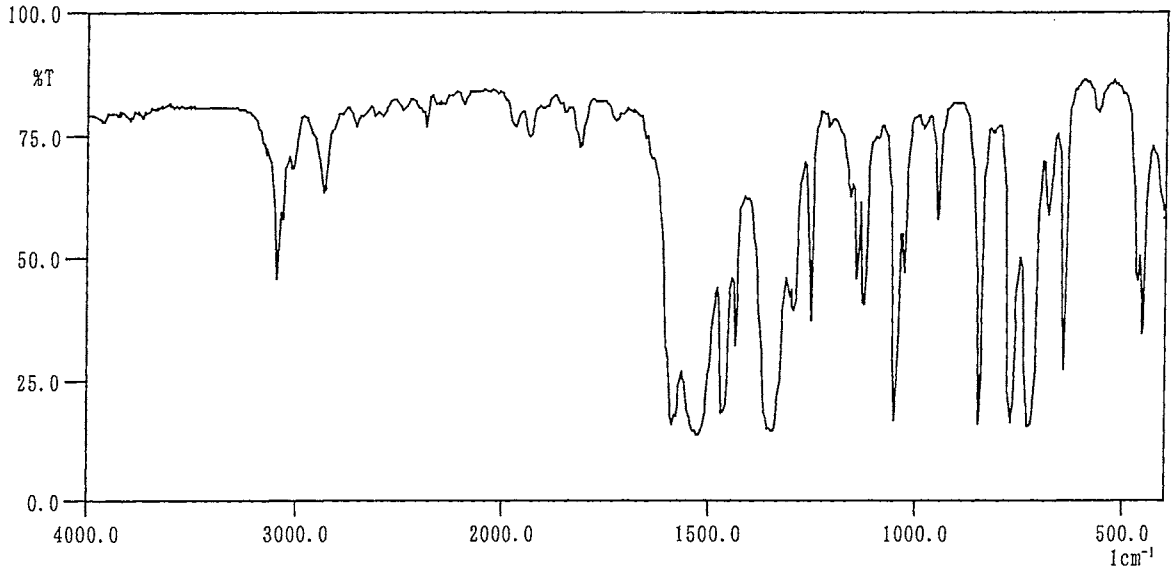
Result: The mass spectrum was consistent with literature spectrum.
(*McLafferty, FW. 1994. Wiley Registry of Mass Spectral Data, 6th ed. New York:John Wiley and Sons.)

Infrared Spectrometry

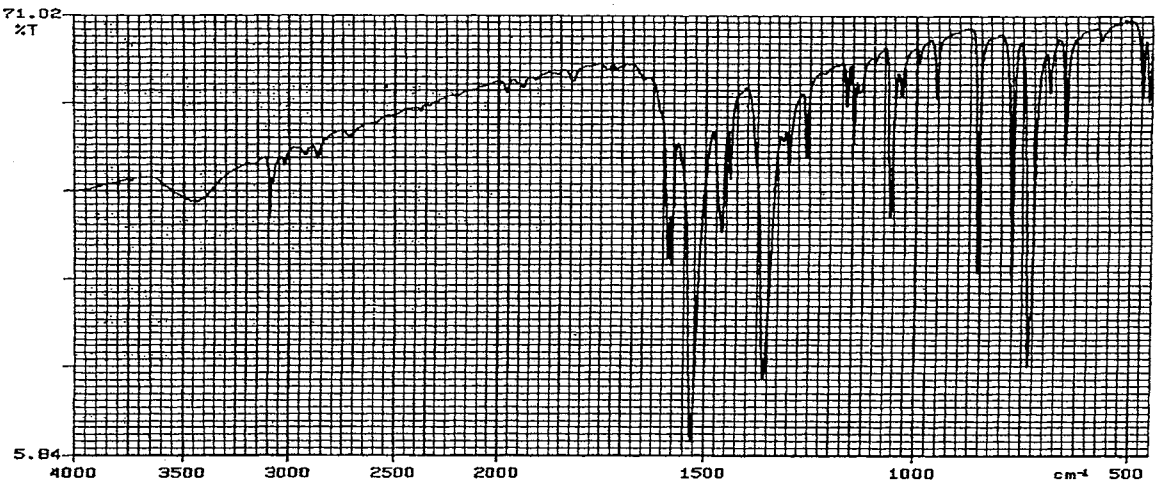
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr

Resolution : 2 cm^{-1}



Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data*

Result: The infrared spectrum was consistent with literature spectrum.
(*Performed by Wako Pure Chemical Industries, Ltd.)

2. Conclusion: The test substance was identified as *o*-chloronitrobenzene by mass spectrum and infrared spectrum.

APPENDIX L 2

STABILITY OF *o* -CHLORONITROBENZENE IN THE 13-WEEK FEED STUDY

STABILITY OF *o*-CHLORONITROBENZENE IN THE 13-WEEK FEED STUDY

Test Substance : *o*-Chloronitrobenzene (Wako Pure Chemical Industries, Ltd.)

Lot No. : SEF9795

1. Sample : This lot was used from 2001.12.14 to 2002.3.18. Test substance was stored in cold storage in a dark place.

2. 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

Mobile Phase : Acetonitrile : Distilled Water = 1 : 1

Flow Rate : 1 mL/min

Detector : UV (254 nm)

Injection Volume : 20 μL

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
2001.12.03	1	7.064	100
2002.03.26	1	7.022	100

Result: Gas chromatography indicated one major peak (peak No.1) analyzed on 2001.12.3 and one major peak (peak No.1) analyzed on 2002.3.26. No new trace impurity peak in the test substance analyzed on 2002.3.26 was detected.

3. Conclusion: The test substance was stable for about 4 months in cold storage in a dark place.

APPENDIX L 3

CONCENTRATION OF *o* -CHLORONITROBENZENE IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

CONCENTRATION OF *o*-CHLORONITROBENZENE IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

	Target Concentration				
Date Analyzed	78[a]	313	1250	2500	5000
2001.12.13	74.1 (95.0)[b]	301 (96.2)	1230 (98.4)	2520 (101)	4910 (98.2)

[a] ppm
[b] %

Analytical Method : The samples were analyzed by 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
Mobile Phase : Acetonitrile : Distilled Water = 1 : 1
Flow Rate : 1 mL/min
Detector : UV (254 nm)
Injection Volume : 20 µL

APPENDIX L 4

HOMOGENITY OF *o* -CHLORONITROBENZENE IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

HOMOGENEITY OF *o*-CHLORONITROBENZENE IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

	Target Concentration				
	78[a]	313	1250	2500	5000
Coefficient Variation	1.59[b]	2.05	1.48	1.67	2.32

[a] ppm
[b] % (n=7)

Analytical Method : The samples were analyzed by 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
Mobile Phase : Acetonitrile : Distilled Water = 1 : 1
Flow Rate : 1 mL/min
Detector : UV (254 nm)
Injection Volume : 20 µL

APPENDIX L 5

STABILITY OF *o* -CHLORONITROBENZENE IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

STABILITY OF *o*-CHLORONITROBENZENE IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

		Target Concentration	
Date Prepared	Date Analyzed	50[a]	5000
2001.10.11	2001.10.11	50.3 (100)[b]	4840 (100)
	2001.10.19[c]	44.2 (89.7)	3900 (80.6)
	2001.11.30[d]	52.2 (104)	4810 (99.4)

[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 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
Mobile Phase : Acetonitrile : Distilled Water = 1 : 1
Flow Rate : 1 mL/min
Detector : UV (254 nm)
Injection Volume : 20 µL

APPENDIX M 1

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS IN THE 13-WEEK FEED STUDY OF *o* -CHLORONITROBENZENE

METHOD FOR HEMATOLOGY,BIOCHEMISTRY AND URINALYSIS IN THE 13-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

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 (ADVIA120 : 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 *o* -CHLORONITROBENZENE

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY
IN THE 13-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

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 transaminase (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

APPENDIX O 1

METHEMOGLOBIN CONCENTRATION OF MICE IN THE 13-WEEK FEED STUDY OF *o* -CHLORONITROBENZENE

METHEMOGLOBIN CONCENTRATION OF MICE IN THE 13-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

Male

Group Name	Control	78 ppm	313 ppm	1250 ppm	2500 ppm	5000 ppm
No. of examined animals	10	10	9	9	10	10
Methemoglobin (%)	0.3 ± 0.0	0.3 ± 0.0	0.3 ± 0.0	0.4 ± 0.2	0.9 ± 0.4 **	1.7 ± 1.0 **

Female

Group Name	Control	78 ppm	313 ppm	1250 ppm	2500 ppm	5000 ppm
No. of examined animals	10	9	10	10	9	10
Methemoglobin (%)	0.3 ± 0.0	0.3 ± 0.0	0.3 ± 0.1	0.6 ± 0.3	0.9 ± 0.5 **	2.0 ± 1.3 **

Mean ± S.D.

*) Significant difference, $p<0.05$ (Test of Dunnett)

**) Significant difference, $p<0.01$ (Test of Dunnett)

Instrument : CO-oximeter (CIBA·CORNING 270: Bayer Corporation)

Analytical method : Multiple-wavelength spectrophotometric method.