2,4-ジクロロ-1-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：０４１０

APPENDIXES

APPENDIXES

APPENDIXES (CONTINUED)

APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0410
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
INTERNAL MASS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1000 ppm	0	0	0	0	0	0	1	1	1	1	1	1	1
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 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
	500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1000 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	2000 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	3000 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	4000 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10

APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0410
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

Clinical sign	Group Name	Administration Week-day 1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7
INTERNAL MASS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	1000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	1	1	1	1	1	1	1
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	8000 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
	1000 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	2000 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	4000 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	6000 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	8000 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
OLIGO-STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	1000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	6000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	8000 ppm	10	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. : 0410
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 0	1	2	3	4	5	6
Control	22.9± 0.7	23.8± 0.7	24.7± 0.7	24.5± 0.9	25.4± 1.3	25.8± 1.3	26.8± 1.4
500 ppm	22.9± 0.7	23.6± 0.9	24.6± 1.0	24.7± 0.9	25.2± 1.8	26.1± 1.0	27.1± 1.4
1000 ppm	22.9± 0.7	23.4± 1.0	24.1± 1.4	25.0± 0.7	25.7± 1.2	26.4± 0.9	27.1± 1.0
2000 ppm	22.9± 0.7	23.1± 0.8	24.4± 0.9	24.6± 0.9	25.7± 1.1	26.6± 1.2	27.1± 1.3
3000 ppm	22.9± 0.7	22.4± 1.0*	23.7± 1.1	24.3± 1.2	24.8± 1.9	26.0± 1.3	26.4± 1.5
4000 ppm	22.9± 0.6	20.5± 1.7**	22.0± 1.6**	22.8± 1.7**	23.6± 2.3	25.2± 1.2	25.7± 1.1

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

STUDY NO. : 0410
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 7	8	9	10	11	12	13
Control	27.9± 1.5	28.3± 1.5	29.1± 1.6	29.8± 1.7	29.4± 2.0	31.2± 1.7	32.1± 1.9
500 ppm	27.8± 1.6	28.5± 1.4	28.8± 1.8	29.8± 2.0	30.2± 1.8	31.4± 2.2	32.0± 2.4
1000 ppm	28.0± 1.3	28.5± 1.6	29.2± 1.9	30.1± 2.1	30.3± 2.0	31.2± 2.2	31.6± 2.0
2000 ppm	28.0± 1.4	28.7± 1.7	29.3± 1.9	30.1± 2.0	30.0± 1.9	31.3± 2.0	31.9± 2.3
3000 ppm	27.3± 1.5	27.7± 1.7	28.2± 1.8	28.7± 1.8	29.0± 1.7	29.7± 1.7	30.0± 1.7
4000 ppm	26.2± 1.3	26.7± 1.1	26.9± 1.3*	27.6± 1.3*	27.8± 1.5	28.3± 1.5**	28.4± 1.7**

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. : 0410
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 0	1	2	3	4	5	6
Control	18.5± 0.7	18.8± 0.9	19.4± 0.8	19.4± 0.7	20.5± 1.1	20.1± 0.8	20.6± 0.9
1000 ppm	18.5± 0.7	18.9± 0.9	19.3± 1.0	19.4± 0.7	20.6± 1.1	20.7± 0.7	21.0± 0.8
2000 ppm	18.6± 0.7	18.6± 1.4	19.0± 0.7	19.4± 1.6	19.1± 1.3*	20.8± 0.9	20.1± 1.6
4000 ppm	18.5± 0.7	17.2± 0.7**	18.7± 0.8	19.4± 0.8	19.4± 1.4	20.3± 0.8	20.4± 0.9
6000 ppm	18.5± 0.7	15.5± 0.8**	17.3± 1.0**	18.4± 1.3	19.2± 1.1	20.3± 0.7	20.1± 0.7
8000 ppm	18.6± 0.7	13.3± 1.1**	13.8± 1.2**	14.5± 1.4**	14.2± 1.3**	15.7± 1.4**	16.5± 1.3**

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

STUDY NO. : 0410
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 7	8	9	10	11	12	13
Control	21.2± 0.8	21.4± 1.0	22.0± 1.7	21.8± 0.8	22.5± 0.7	22.3± 0.8	22.7± 0.8
1000 ppm	21.0± 0.8	21.2± 0.9	21.9± 0.9	22.2± 0.9	22.5± 1.0	22.5± 0.9	23.2± 1.2
2000 ppm	20.8± 1.7	21.2± 1.3	21.0± 1.9	21.9± 1.5	22.0± 2.2	22.1± 1.6	22.5± 1.8
4000 ppm	20.6± 0.9	21.1± 1.1	21.4± 0.8	21.9± 0.9	21.9± 1.3	21.6± 0.9	22.3± 1.3
6000 ppm	20.1± 0.8	20.1± 0.6*	20.5± 0.7	20.9± 0.8	20.8± 0.7*	20.9± 0.8*	21.4± 0.9
8000 ppm	16.6± 1.2**	16.4± 1.1**	16.4± 1.1**	16.5± 1.1**	16.1± 1.3**	16.7± 1.1**	16.9± 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. : 0410
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	3.7± 0.2	3.5± 0.4	3.6± 0.4	3.7± 0.3	3.9± 0.3	3.9± 0.3	4.0± 0.4
500 ppm	3.6± 0.3	3.5± 0.4	3.6± 0.3	3.4± 0.7	4.1± 0.6	4.0± 0.3	4.0± 0.3
1000 ppm	3.6± 0.4	3.4± 0.5	3.8± 0.3	3.6± 0.6	4.1± 0.4	4.0± 0.3	4.0± 0.3
2000 ppm	3.6± 0.2	3.6± 0.4	3.6± 0.3	3.6± 0.6	4.0± 0.4	4.0± 0.3	4.0± 0.2
3000 ppm	3.0± 0.3**	3.4± 0.2	3.5± 0.2	3.4± 0.6	3.8± 0.5	3.8± 0.2	3.8± 0.2
4000 ppm	2.3± 0.3**	3.3± 0.4	3.1± 0.3**	3.0± 0.6	3.6± 0.4	3.5± 0.3**	3.4± 0.2**

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

STUDY NO. : 0410
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	3.9± 0.2	3.9± 0.3	4.0± 0.3	3.4± 0.7	4.4± 0.4	4.0± 0.3
500 ppm	4.0± 0.3	3.8± 0.3	4.1± 0.2	3.7± 0.3	4.2± 0.3	3.9± 0.3
1000 ppm	3.9± 0.3	4.1± 0.4	4.2± 0.3	3.9± 0.2	4.2± 0.3	4.0± 0.2
2000 ppm	3.9± 0.3	3.8± 0.2	4.1± 0.3	3.5± 0.7	4.3± 0.4	3.9± 0.2
3000 ppm	3.8± 0.2	3.7± 0.2	3.9± 0.2	3.6± 0.3	4.0± 0.3*	3.8± 0.1
4000 ppm	3.4± 0.2**	3.5± 0.2**	3.6± 0.2**	3.4± 0.3	3.6± 0.2**	3.4± 0.3**

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. : 0410
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	3.3± 0.2	3.2± 0.1	3.3± 0.2	3.5± 0.2	3.3± 0.2	3.5± 0.3	3.6± 0.2
1000 ppm	3.2± 0.3	3.0± 0.3	3.2± 0.3	3.4± 0.2	3.3± 0.3	3.5± 0.3	3.5± 0.3
2000 ppm	2.8± 0.5	2.8± 0.3*	3.2± 0.4	2.6± 0.6**	3.6± 0.3*	3.2± 0.4	3.5± 0.3
4000 ppm	2.4± 0.3**	3.1± 0.4	2.8± 0.1**	2.7± 0.5**	3.1± 0.3	3.0± 0.2**	3.0± 0.3**
6000 ppm	1.8± 0.4**	2.8± 0.4	2.7± 0.3**	2.7± 0.3**	2.9± 0.2*	2.7± 0.2**	2.7± 0.2**
8000 ppm	1.2± 0.4**	2.4± 0.6**	2.5± 0.5**	2.1± 0.3**	2.5± 0.2**	2.4± 0.3**	2.2± 0.3**

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

STUDY NO. : 0410
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	3.5± 0.2	3.7± 0.4	3.5± 0.2	3.7± 0.1	3.7± 0.3	3.7± 0.3
1000 ppm	3.5± 0.2	3.6± 0.2	3.7± 0.2	3.6± 0.2	3.7± 0.3	3.7± 0.2
2000 ppm	3.5± 0.1	3.5± 0.2	3.6± 0.1	3.5± 0.5	3.6± 0.5	3.5± 0.2
4000 ppm	3.2± 0.3	3.1± 0.2**	3.2± 0.2**	3.1± 0.4*	3.1± 0.4**	3.2± 0.3**
6000 ppm	2.7± 0.2**	2.7± 0.2**	2.8± 0.2**	2.8± 0.2**	2.8± 0.2**	2.9± 0.2**
8000 ppm	2.1± 0.3**	1.9± 0.3**	1.9± 0.3**	1.8± 0.4**	2.2± 0.3**	2.1± 0.3**

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. : 0410
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
500 ppm	0.075± 0.005	0.072± 0.006	0.073± 0.007	0.067± 0.011	0.079± 0.012	0.073± 0.006	0.072± 0.008
1000 ppm	0.155± 0.013	0.140± 0.013	0.151± 0.014	0.138± 0.018	0.154± 0.013	0.148± 0.009	0.143± 0.007
2000 ppm	0.309± 0.014	0.299± 0.027	0.295± 0.021	0.277± 0.039	0.301± 0.023	0.294± 0.020	0.285± 0.012
3000 ppm	0.397± 0.026	0.428± 0.025	0.434± 0.018	0.407± 0.054	0.442± 0.047	0.435± 0.014	0.415± 0.009
4000 ppm	0.453± 0.030	0.592± 0.057	0.548± 0.035	0.508± 0.071	0.566± 0.074	0.540± 0.033	0.525± 0.025

STUDY NO. : 0410
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
500 ppm	0.070± 0.007	0.066± 0.006	0.070± 0.004	0.062± 0.008	0.068± 0.004	0.061± 0.006
1000 ppm	0.139± 0.008	0.139± 0.007	0.138± 0.008	0.128± 0.006	0.134± 0.009	0.128± 0.005
2000 ppm	0.272± 0.012	0.262± 0.012	0.271± 0.014	0.232± 0.044	0.278± 0.024	0.248± 0.017
3000 ppm	0.410± 0.009	0.396± 0.014	0.410± 0.014	0.369± 0.032	0.403± 0.026	0.377± 0.019
4000 ppm	0.513± 0.028	0.515± 0.034	0.522± 0.027	0.485± 0.029	0.504± 0.024	0.480± 0.022

APPENDIX D 2

CHEMICAL INTAKE CHANGES : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0410
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
1000 ppm	0.172± 0.011	0.157± 0.011	0.165± 0.017	0.163± 0.012	0.159± 0.017	0.166± 0.014	0.166± 0.014
2000 ppm	0.304± 0.039	0.293± 0.028	0.332± 0.028	0.276± 0.056	0.349± 0.033	0.320± 0.029	0.328± 0.032
4000 ppm	0.565± 0.078	0.650± 0.068	0.567± 0.030	0.556± 0.072	0.619± 0.079	0.588± 0.040	0.584± 0.054
6000 ppm	0.684± 0.144	0.976± 0.089	0.877± 0.062	0.842± 0.069	0.867± 0.063	0.819± 0.064	0.816± 0.056
8000 ppm	0.730± 0.197	1.414± 0.359	1.393± 0.254	1.166± 0.201	1.286± 0.130	1.187± 0.188	1.028± 0.135

STUDY NO. : 0410
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
1000 ppm	0.166± 0.010	0.163± 0.008	0.165± 0.009	0.160± 0.009	0.163± 0.012	0.159± 0.008
2000 ppm	0.328± 0.022	0.324± 0.023	0.327± 0.016	0.312± 0.039	0.320± 0.035	0.316± 0.031
4000 ppm	0.611± 0.050	0.586± 0.053	0.580± 0.042	0.562± 0.062	0.582± 0.069	0.567± 0.054
6000 ppm	0.812± 0.045	0.784± 0.052	0.803± 0.059	0.795± 0.066	0.813± 0.042	0.818± 0.055
8000 ppm	1.010± 0.172	0.929± 0.133	0.921± 0.092	0.874± 0.177	1.043± 0.116	0.978± 0.137

APPENDIX E 1

HEMATOLOGY : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0410
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

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	10.49±	0.29	15.5±	0.4	48.4±	1.3	46.1±	0.6	14.8±	0.3	32.1±	0.6	1368±	107
500 ppm	10	10.09±	0.36	14.9±	0.5*	47.1±	1.5	46.7±	0.7	14.8±	0.1	31.6±	0.4	1332±	92
1000 ppm	10	10.09±	0.41	15.0±	0.5*	47.2±	1.8	46.8±	1.1	14.8±	0.3	31.7±	0.6	1283±	87
2000 ppm	8	9.86±	0.22**	14.6±	0.3**	46.3±	1.1*	47.0±	0.4*	14.8±	0.1	31.5±	0.4	1354±	103
3000 ppm	10	9.74±	0.39**	14.7±	0.6**	46.5±	1.8	47.8±	0.6**	15.1±	0.1**	31.5±	0.4	1302±	110
4000 ppm	8	9.79±	0.34**	14.6±	0.4**	46.0±	1.8*	46.9±	0.4	14.9±	0.2	31.7±	0.5	1378±	77

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

STUDY NO. : 0410
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHER
Control	10	1.45± 0.69	0± 1	18± 5	2± 1	0± 0	4± 2	76± 5	0± 0
500 ppm	10	1.38± 0.72	0± 1	18± 7	2± 1	0± 0	4± 2	76± 7	0± 1
1000 ppm	10	1.16± 0.41	0± 0	16± 5	1± 1	0± 0	5± 2	78± 6	0± 0
2000 ppm	8	1.33± 0.27	0± 0	16± 4	1± 1	0± 0	3± 3	79± 6	0± 0
3000 ppm	10	1.46± 1.08	1± 1	16± 4	1± 1	0± 0	4± 1	78± 4	0± 1
4000 ppm	8	1.33± 0.91	0± 0	16± 4	1± 1**	0± 0	3± 2	81± 4	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. : 0410
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 $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV f ℓ	MCH p g	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	10	10.46± 0.40	15.5± 0.5	47.6± 1.8	45.5± 0.4	14.8± 0.3	32.6± 0.5	1302± 89
1000 ppm	9	10.47± 0.17	15.5± 0.3	48.4± 1.0	46.2± 0.7	14.8± 0.2	32.1± 0.4	1321± 88
2000 ppm	8	10.27± 0.88	15.0± 2.0	47.0± 5.6	45.6± 2.1	14.6± 0.9	31.9± 0.8*	1318± 312
4000 ppm	8	10.01± 0.38	14.9± 0.7	46.8± 2.0	46.7± 0.6*	14.9± 0.2	31.9± 0.4*	1253± 88
6000 ppm	9	9.77± 0.39**	14.6± 0.4**	45.8± 1.7	46.9± 1.0**	14.9± 0.3	31.8± 0.4**	1247± 109
8000 ppm	6	9.81± 0.26*	14.4± 0.4*	44.3± 1.1*	45.1± 0.9	14.7± 0.2	32.6± 0.4	1291± 53

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

STUDY NO. : 0410
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$		Differential WBC (%) N-BAND		N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHER	
Control	10	1.07±	0.37	0±	0	17±	4	1±	1	0±	0	3±	1	79±	5	0±	0
1000 ppm	9	1.19±	0.33	1±	1	16±	5	1±	1	0±	0	2±	1	80±	4	0±	0
2000 ppm	8	1.79±	0.71	0±	0	17±	5	2±	1	0±	0	2±	2	79±	6	0±	0
4000 ppm	8	1.27±	0.77	1±	1	17±	4	1±	1	0±	0	2±	1	80±	5	0±	0
6000 ppm	9	1.12±	0.42	0±	0	12±	4	0±	1	0±	0	2±	1	85±	4	0±	0
8000 ppm	6	0.97±	0.65	0±	1	18±	7	0±	1	0±	0	3±	2	78±	8	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. : 0410
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	5.0± 0.1	3.0± 0.2	1.6± 0.2	0.16± 0.02	169± 37	74± 6	29± 5
500 ppm	10	4.9± 0.1	3.0± 0.1	1.6± 0.1	0.15± 0.03	183± 48	80± 11	31± 19
1000 ppm	10	4.9± 0.1	3.0± 0.1	1.5± 0.1	0.15± 0.02	171± 34	84± 6*	30± 12
2000 ppm	8	4.9± 0.2	3.1± 0.1	1.7± 0.1	0.15± 0.02	193± 44	100± 8**	33± 16
3000 ppm	10	4.9± 0.1	3.0± 0.1	1.6± 0.1	0.16± 0.02	203± 51	103± 11**	26± 6
4000 ppm	8	5.1± 0.2	3.2± 0.1*	1.7± 0.2	0.15± 0.01	227± 36	123± 7**	31± 9

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

STUDY NO. : 0410
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	170± 10	47± 7	17± 2	230± 53	132± 13	2± 1	55± 16
500 ppm	10	171± 21	49± 15	17± 3	198± 24	124± 8	1± 1	62± 22
1000 ppm	10	180± 11	47± 6	18± 3	225± 55	121± 6	2± 1	57± 14
2000 ppm	8	203± 12**	45± 9	18± 2	251± 49	124± 16	1± 1	72± 36
3000 ppm	10	212± 21**	53± 18	16± 1	264± 40	134± 8	2± 1	82± 22
4000 ppm	8	246± 13**	43± 5	19± 5	251± 45	143± 16	1± 1	84± 28*

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

STUDY NO. : 0410
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	25.2± 3.7	151± 1	4.8± 0.3	121± 2	8.8± 0.2	7.5± 1.2
500 ppm	10	27.8± 2.9	151± 1	4.5± 0.3	121± 2	8.7± 0.1	6.9± 1.0
1000 ppm	10	27.0± 4.5	151± 1	4.5± 0.5	121± 2	8.7± 0.2	7.5± 1.2
2000 ppm	8	25.0± 2.8	151± 2	4.6± 0.4	122± 2	8.8± 0.3	6.9± 0.8
3000 ppm	10	27.5± 5.1	151± 2	4.6± 0.5	120± 2	8.8± 0.2	8.3± 1.3
4000 ppm	8	30.7± 6.0	150± 2	4.5± 0.6	120± 2	8.9± 0.2	7.3± 0.6

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

APPENDIX F 2

BIOCHEMISTRY : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0410
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	4.9±	0.1	3.2±	0.1	1.9±	0.2	0.14±	0.01	178±	30	65±	6	17±	4
1000 ppm	9	5.0±	0.3	3.4±	0.1	2.1±	0.4	0.15±	0.01	184±	13	81±	7	19±	4
2000 ppm	9	4.9±	0.3	3.3±	0.1	2.0±	0.4	0.14±	0.02	181±	29	99±	19*	25±	10
4000 ppm	9	5.0±	0.2	3.4±	0.2*	2.3±	0.5	0.15±	0.04	191±	29	105±	10**	17±	4
6000 ppm	10	5.2±	0.2*	3.7±	0.1**	2.6±	0.4**	0.17±	0.04	191±	27	129±	8**	18±	4
8000 ppm	6	5.3±	0.3**	3.8±	0.3**	2.6±	0.5**	0.17±	0.02*	119±	18**	162±	16**	18±	3

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

STUDY NO. : 0410
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	144± 12	50± 8	18± 3	232± 54	198± 17	2± 1	71± 65
1000 ppm	9	174± 18**	47± 5	18± 4	235± 54	174± 23	2± 1	107± 85
2000 ppm	9	202± 30**	47± 4	21± 5	259± 45	179± 27	1± 1	197± 289
4000 ppm	9	212± 20**	43± 6	18± 3	225± 48	182± 16	2± 2	82± 38
6000 ppm	10	256± 16**	44± 4	17± 2	271± 92	197± 20	2± 1	110± 71
8000 ppm	6	316± 20**	56± 19	23± 4*	398± 79**	245± 18**	2± 1	186± 93**

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

STUDY NO. : 0410
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	20.0±	1.5	151±	1	4.4±	0.3	121±	1	8.8±	0.2	6.0±	0.9
1000 ppm	9	20.6±	3.3	151±	2	4.7±	0.6	121±	3	8.9±	0.3	6.9±	1.6
2000 ppm	9	24.2±	5.6	151±	1	4.5±	0.4	120±	1	8.8±	0.4	6.5±	1.9
4000 ppm	9	25.0±	2.8**	151±	2	4.4±	0.6	120±	2	8.7±	0.3	7.0±	1.3
6000 ppm	10	25.1±	3.2**	151±	2	5.0±	0.7	120±	2	8.9±	0.3	7.4±	1.2
8000 ppm	6	29.0±	6.4**	151±	3	4.8±	0.5	117±	3**	8.9±	0.5	8.8±	0.6**

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

APPENDIX G 1

URINALYSIS : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0410
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	0	3	4	3		0	1	9	0	0	0		10	0	0	0	0	0		4	4	2	0	0	0		10	0	0	0	0	
500 ppm	10	0	1	0	0	4	3	2		0	4	6	0	0	0		10	0	0	0	0	0		6	4	0	0	0	0		10	0	0	0	0	
1000 ppm	10	0	0	1	0	4	5	0		0	1	9	0	0	0		10	0	0	0	0	0		3	6	1	0	0	0		10	0	0	0	0	
2000 ppm	10	0	0	0	1	3	4	2		0	4	6	0	0	0		10	0	0	0	0	0		3	7	0	0	0	0		10	0	0	0	0	
3000 ppm	10	0	0	0	1	4	5	0		0	5	5	0	0	0		10	0	0	0	0	0		5	4	1	0	0	0		10	0	0	0	0	
4000 ppm	10	0	0	1	0	2	5	2		0	8	2	0	0	0	**	10	0	0	0	0	0		6	2	2	0	0	0		10	0	0	0	0	

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

(HCL101)

STUDY NO. : 0410
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0	
500 ppm	10	10	0	0	0	0	
1000 ppm	10	10	0	0	0	0	
2000 ppm	10	10	0	0	0	0	
3000 ppm	10	10	0	0	0	0	
4000 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. : 0410
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	pH							CHI	Protein						CHI	Glucose						CHI	Ketone body						CHI	Occult blood					CHI
		5.0	6.0	6.5	7.0	7.5	8.0	8.5		−	±	+	2+	3+	4+		−	±	+	2+	3+	4+		−	±	+	2+	3+	4+		−	±	+	2+	3+	
Control	10	0	0	1	2	3	4	0		0	1	7	2	0	0		10	0	0	0	0	0		1	9	0	0	0	0		10	0	0	0	0	
1000 ppm	10	0	0	1	3	4	2	0		0	2	8	0	0	0		10	0	0	0	0	0		2	8	0	0	0	0		10	0	0	0	0	
2000 ppm	10	0	0	1	0	4	5	0		0	4	6	0	0	0		10	0	0	0	0	0		2	8	0	0	0	0		10	0	0	0	0	
4000 ppm	10	0	0	0	0	2	8	0		0	9	1	0	0	0	**	10	0	0	0	0	0		6	3	1	0	0	0	*	10	0	0	0	0	
6000 ppm	10	0	0	0	0	3	7	0		2	8	0	0	0	0	**	10	0	0	0	0	0		8	2	0	0	0	0	**	10	0	0	0	0	
8000 ppm	10	0	1	1	2	0	3	3		7	3	0	0	0	0	**	10	0	0	0	0	0		10	0	0	0	0	0	**	10	0	0	0	0	

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

STUDY NO. : 0410
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	
1000 ppm	10	10	0	0	0	0	
2000 ppm	10	10	0	0	0	0	
4000 ppm	10	10	0	0	0	0	
6000 ppm	10	10	0	0	0	0	
8000 ppm	10	10	0	0	0	0	

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

APPENDIX H 2

GROSS FINDINGS : SUMMARY, MOUSE : FEMALE ALL ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0410
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 (%)	1000 ppm 10 (%)	2000 ppm 10 (%)	4000 ppm 10 (%)
spleen	dark		0 (0)	0 (0)	0 (0)	0 (0)
	black zone		1 (10)	1 (10)	0 (0)	1 (10)
liver	dark		0 (0)	0 (0)	0 (0)	0 (0)
kidney	hydronephrosis		0 (0)	0 (0)	1 (10)	0 (0)

Organ	Findings	Group Name	6000 ppm	8000 ppm
		NO. of Animals	10 (%)	10 (%)
spleen	dark		10 (100)	10 (100)
	black zone		0 (0)	0 (0)
liver	dark		10 (100)	10 (100)
kidney	hydronephrosis		0 (0)	0 (0)

APPENDIX H 1

GROSS FINDINGS : SUMMARY, MOUSE : MALE ALL ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0410
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	500 ppm 10 (%)	1000 ppm 10 (%)	2000 ppm 10 (%)
spleen	dark		0 (0)	0 (0)	0 (0)	10 (100)
	black zone		0 (0)	0 (0)	1 (10)	0 (0)
liver	dark		0 (0)	0 (0)	0 (0)	10 (100)
kidney	hydronephrosis		0 (0)	0 (0)	1 (10)	0 (0)
testis	atrophic		0 (0)	0 (0)	0 (0)	0 (0)

STUDY NO. : 0410
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name / NO. of Animals	3000 ppm 10 (%)	4000 ppm 10 (%)
spleen	dark		10 (100)	10 (100)
	black zone		0 (0)	0 (0)
liver	dark		10 (100)	10 (100)
kidney	hydronephrosis		0 (0)	0 (0)
testis	atrophic		0 (0)	1 (10)

APPENDIX I 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0410
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	29.3± 2.0	0.038± 0.007	0.011± 0.002	0.228± 0.021	0.162± 0.013	0.160± 0.009
500 ppm	10	29.5± 2.1	0.037± 0.010	0.011± 0.003	0.224± 0.049	0.160± 0.014	0.159± 0.006
1000 ppm	10	28.9± 2.0	0.036± 0.008	0.012± 0.004	0.226± 0.025	0.162± 0.008	0.163± 0.011
2000 ppm	10	29.4± 2.1	0.035± 0.006	0.011± 0.003	0.200± 0.018	0.154± 0.010	0.161± 0.007
3000 ppm	10	27.5± 1.8	0.033± 0.005	0.011± 0.004	0.217± 0.045	0.162± 0.014	0.161± 0.011
4000 ppm	10	25.8± 1.6**	0.034± 0.007	0.010± 0.002	0.210± 0.042	0.151± 0.013	0.154± 0.007

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

STUDY NO. : 0410
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	0.403± 0.027	0.047± 0.007	1.073± 0.062	0.450± 0.013
500 ppm	10	0.399± 0.020	0.050± 0.005	1.134± 0.056	0.451± 0.015
1000 ppm	10	0.623± 0.640	0.050± 0.007	1.165± 0.084*	0.448± 0.013
2000 ppm	10	0.422± 0.037	0.060± 0.008**	1.264± 0.094**	0.446± 0.013
3000 ppm	10	0.425± 0.027	0.069± 0.012**	1.263± 0.081**	0.447± 0.013
4000 ppm	10	0.409± 0.024	0.070± 0.011**	1.254± 0.068**	0.449± 0.015

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. : 0410
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	20.5± 0.7	0.043± 0.005	0.013± 0.003	0.027± 0.005	0.118± 0.009	0.150± 0.013
1000 ppm	10	20.7± 0.9	0.043± 0.008	0.012± 0.002	0.027± 0.007	0.121± 0.006	0.154± 0.015
2000 ppm	10	20.2± 1.5	0.040± 0.006	0.013± 0.002	0.026± 0.005	0.128± 0.009*	0.151± 0.013
4000 ppm	10	19.8± 1.0	0.039± 0.007	0.010± 0.002*	0.024± 0.005	0.117± 0.009	0.144± 0.009
6000 ppm	10	19.2± 0.9*	0.040± 0.007	0.010± 0.001**	0.024± 0.004	0.109± 0.008	0.143± 0.012
8000 ppm	10	15.5± 1.0**	0.030± 0.010**	0.009± 0.001**	0.017± 0.003**	0.101± 0.008**	0.122± 0.008**

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

STUDY NO. : 0410
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	0.271± 0.009	0.048± 0.004	0.813± 0.040	0.460± 0.018
1000 ppm	10	0.278± 0.011	0.048± 0.004	0.878± 0.045	0.466± 0.016
2000 ppm	10	0.311± 0.086	0.053± 0.007	0.922± 0.084**	0.460± 0.017
4000 ppm	10	0.265± 0.015	0.058± 0.008**	0.932± 0.075**	0.451± 0.012
6000 ppm	10	0.254± 0.009	0.070± 0.005**	0.988± 0.038**	0.438± 0.019*
8000 ppm	10	0.212± 0.017**	0.042± 0.009	0.899± 0.068*	0.397± 0.018**

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. : 0410
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	29.3± 2.0	0.128± 0.022	0.037± 0.008	0.780± 0.061	0.553± 0.047	0.547± 0.037
500 ppm	10	29.5± 2.1	0.124± 0.032	0.038± 0.013	0.765± 0.180	0.545± 0.053	0.541± 0.039
1000 ppm	10	28.9± 2.0	0.123± 0.025	0.041± 0.014	0.781± 0.063	0.564± 0.048	0.565± 0.043
2000 ppm	10	29.4± 2.1	0.119± 0.014	0.037± 0.009	0.684± 0.074	0.526± 0.029	0.548± 0.036
3000 ppm	10	27.5± 1.8	0.121± 0.016	0.041± 0.014	0.791± 0.158	0.589± 0.054	0.587± 0.041
4000 ppm	10	25.8± 1.6**	0.133± 0.023	0.037± 0.008	0.811± 0.149	0.583± 0.026	0.599± 0.032*

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

STUDY NO. : 0410
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	1.379± 0.110	0.159± 0.021	3.669± 0.150	1.542± 0.116
500 ppm	10	1.358± 0.086	0.169± 0.006	3.857± 0.169	1.538± 0.111
1000 ppm	10	2.188± 2.320	0.174± 0.023	4.042± 0.206**	1.557± 0.087
2000 ppm	10	1.439± 0.103	0.204± 0.023*	4.312± 0.256**	1.523± 0.099
3000 ppm	10	1.549± 0.063**	0.250± 0.032**	4.599± 0.109**	1.632± 0.116
4000 ppm	10	1.588± 0.096**	0.273± 0.046**	4.865± 0.249**	1.744± 0.111**

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. : 0410
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	20.5± 0.7	0.212± 0.021	0.063± 0.011	0.129± 0.022	0.578± 0.051	0.731± 0.050
1000 ppm	10	20.7± 0.9	0.209± 0.034	0.059± 0.009	0.132± 0.033	0.584± 0.026	0.745± 0.060
2000 ppm	10	20.2± 1.5	0.197± 0.019	0.062± 0.011	0.128± 0.021	0.640± 0.107	0.750± 0.048
4000 ppm	10	19.8± 1.0	0.194± 0.032	0.052± 0.008*	0.121± 0.023	0.592± 0.028	0.727± 0.041
6000 ppm	10	19.2± 0.9*	0.211± 0.037	0.053± 0.005	0.123± 0.024	0.567± 0.037	0.745± 0.070
8000 ppm	10	15.5± 1.0**	0.196± 0.057	0.057± 0.010	0.112± 0.020	0.654± 0.032**	0.791± 0.047

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

STUDY NO. : 0410
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	1.324± 0.055	0.236± 0.018	3.979± 0.235	2.249± 0.078
1000 ppm	10	1.347± 0.028	0.235± 0.021	4.254± 0.252	2.256± 0.102
2000 ppm	10	1.579± 0.648	0.265± 0.040	4.558± 0.197**	2.285± 0.171
4000 ppm	10	1.338± 0.050	0.291± 0.034*	4.710± 0.207**	2.285± 0.121
6000 ppm	10	1.321± 0.058	0.365± 0.025**	5.144± 0.179**	2.280± 0.140
8000 ppm	10	1.368± 0.064	0.271± 0.047	5.823± 0.361**	2.572± 0.153**

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)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 10 1 (%)	Control 10 2 (%)	Control 10 3 (%)	Control 10 4 (%)	500 ppm 10 1 (%)	500 ppm 10 2 (%)	500 ppm 10 3 (%)	500 ppm 10 4 (%)	1000 ppm 10 1 (%)	1000 ppm 10 2 (%)	1000 ppm 10 3 (%)	1000 ppm 10 4 (%)	2000 ppm 10 1 (%)	2000 ppm 10 2 (%)	2000 ppm 10 3 (%)	2000 ppm 10 4 (%)
{Respiratory system}																		
nasal cavit			<10>				<10>				<10>				<10>			
	eosinophilic change: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)	2 (20)	0 (0)	0 (0)	0 (0)
	eosinophilic change:respiratory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	8 (80)	1 (10)	0 (0)	0 (0) **
	respiratory metaplasia: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)
	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)
	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)	4 (40)	0 (0)	0 (0)	0 (0)
nasopharynx			<10>				<10>				<10>				<10>			
	eosinophilic change		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (30)	0 (0)	0 (0)	0 (0)
{Hematopoietic system}																		
spleen			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		10 (100)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0)	1 (10)	9 (90)	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	3000 ppm				4000 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:olfactory epithelium		9	0	0	0 **	10	0	0	0 **
			(90)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	eosinophilic change:respiratory epithelium		9	1	0	0 **	10	0	0	0 **
			(90)	(10)	(0)	(0)	(100)	(0)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		5	0	0	0 *	9	0	0	0 **
			(50)	(0)	(0)	(0)	(90)	(0)	(0)	(0)
	respiratory metaplasia:gland		5	0	0	0 *	8	0	0	0 **
			(50)	(0)	(0)	(0)	(80)	(0)	(0)	(0)
	atrophy:olfactory epithelium		8	0	0	0 **	7	0	0	0 **
			(80)	(0)	(0)	(0)	(70)	(0)	(0)	(0)
nasopharynx			<10>				<10>			
	eosinophilic change		6	4	0	0 **	0	10	0	0 **
			(60)	(40)	(0)	(0)	(0)	(100)	(0)	(0)
{Hematopoietic system}										
spleen			<10>				<10>			
	deposit of hemosiderin		0	10	0	0 **	0	8	2	0 **
			(0)	(100)	(0)	(0)	(0)	(80)	(20)	(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				500 ppm 10				1000 ppm 10				2000 ppm 10			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Hematopoietic system}																		
spleen			<10>				<10>				<10>				<10>			
	deposit of melanin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	extramedullary hematopoiesis		10 (100)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0)	1 (10)	9 (90)	0 (0)	0 (0) **
{Circulatory system}																		
heart			<10>				<10>				<10>				<10>			
	vacuolic change		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
{Digestive system}																		
tongue			<10>				<10>				<10>				<10>			
	inflammatory infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
stomach			<10>				<10>				<10>				<10>			
	ulcer:forestomach		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

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	3000 ppm				4000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
spleen			<10>				<10>			
	deposit of melanin		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	extramedullary hematopoiesis		0	10	0	0 **	0	10	0	0 **
			(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
{Circulatory system}										
heart			<10>				<10>			
	vacuolic change		2	0	0	0	2	0	0	0
			(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
{Digestive system}										
tongue			<10>				<10>			
	inflammatory infiltration		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
stomach			<10>				<10>			
	ulcer:forestomach		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				500 ppm				1000 ppm				2000 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}																		
stomach			<10>				<10>				<10>				<10>			
	hyperplasia:forestomach		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
liver			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	inflammatory cell nest		7	0	0	0	7	0	0	0	7	0	0	0	7	0	0	0
			(70)	(0)	(0)	(0)	(70)	(0)	(0)	(0)	(70)	(0)	(0)	(0)	(70)	(0)	(0)	(0)
	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)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	ossification		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hydronephrosis		0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(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	3000 ppm				4000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
stomach			<10>				<10>			
	hyperplasia:forestomach		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
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		6	0	0	0	6	0	0	0
			(60)	(0)	(0)	(0)	(60)	(0)	(0)	(0)
	hepatocellular hypertrophy:central		9	1	0	0 **	2	8	0	0 **
			(90)	(10)	(0)	(0)	(20)	(80)	(0)	(0)
{Urinary system}										
kidney			<10>				<10>			
	ossification		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(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				500 ppm				1000 ppm				2000 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}																		
pituitary			< 9>				<10>				< 9>				<10>			
	Rathke pouch		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)
{Reproductive system}																		
testis			<10>				<10>				<10>				<10>			
	germ cell necrosis		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)
epididymis			<10>				<10>				<10>				<10>			
	inflammation		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)
	spermatogenic granuloma		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	decreased:sperma		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	debris of spermatic elements		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	3000 ppm				4000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Endocrine system}										
pituitary			<10>				< 9>			
	Rathke pouch		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Reproductive system}										
testis			<10>				<10>			
	germ cell necrosis		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
epididymis			<10>				<10>			
	inflammation		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	spermatogenic granuloma		0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)
	decreased:sperma		0	0	0	0	0	0	1	0
			(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)
	debris of spermatic elements		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
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				1000 ppm 10				2000 ppm 10				4000 ppm 10			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Respiratory system}																		
nasal cavit			<10>				<10>				<10>				<10>			
	eosinophilic change:olfactory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	6 (60)	0 (0)	0 (0)	0 * (0)	6 (60)	4 (40)	0 (0)	0 ** (0)
	eosinophilic change:respiratory epithelium		1 (10)	0 (0)	0 (0)	0 (0)	8 (80)	1 (10)	0 (0)	0 ** (0)	4 (40)	6 (60)	0 (0)	0 ** (0)	3 (30)	7 (70)	0 (0)	0 ** (0)
	respiratory metaplasia:olfactory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	9 (90)	1 (10)	0 (0)	0 ** (0)
	respiratory metaplasia:gland		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	4 (40)	6 (60)	0 (0)	0 ** (0)
	atrophy:olfactory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	8 (80)	0 (0)	0 (0)	0 ** (0)	10 (100)	0 (0)	0 (0)	0 ** (0)
nasopharynx			<10>				<10>				<10>				<10>			
	eosinophilic change		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	4 (40)	4 (40)	0 (0)	0 ** (0)	0 (0)	9 (90)	1 (10)	0 ** (0)
{Hematopoietic system}																		
spleen			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		10 (100)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 ** (0)	0 (0)	8 (80)	2 (20)	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	6000 ppm				8000 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:olfactory epithelium		0	10	0	0 **	0	4	6	0 **
			(0)	(100)	(0)	(0)	(0)	(40)	(60)	(0)
	eosinophilic change:respiratory epithelium		9	1	0	0 **	5	0	0	0
			(90)	(10)	(0)	(0)	(50)	(0)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		10	0	0	0 **	10	0	0	0 **
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	respiratory metaplasia:gland		0	10	0	0 **	0	10	0	0 **
			(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
	atrophy:olfactory epithelium		0	10	0	0 **	0	10	0	0 **
			(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
nasopharynx			<10>				<10>			
	eosinophilic change		0	5	5	0 **	0	3	7	0 **
			(0)	(50)	(50)	(0)	(0)	(30)	(70)	(0)
{Hematopoietic system}										
spleen			<10>				<10>			
	deposit of hemosiderin		0	0	10	0 **	0	0	10	0 **
			(0)	(0)	(100)	(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
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 10				1000 ppm 10				2000 ppm 10				4000 ppm 10			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Hematopoietic system}																		
spleen			<10>				<10>				<10>				<10>			
	deposit of melanin		1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
	extramedullary hematopoiesis		10 (100)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0)	8 (80)	2 (20)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0) **
{Circulatory system}																		
heart			<10>				<10>				<10>				<10>			
	vacuolic change		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	fibrosis:focal		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)
{Digestive system}																		
liver			<10>				<10>				<10>				<10>			
	increase in mitosis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

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	6000 ppm				8000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
spleen			<10>				<10>			
	deposit of melanin		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	extramedullary hematopoiesis		0	10	0	0 **	0	10	0	0 **
			(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
{Circulatory system}										
heart			<10>				<10>			
	vacuolic change		0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)
	fibrosis:focal		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}										
liver			<10>				<10>			
	increase in mitosis		1	0	0	0	3	0	0	0
			(10)	(0)	(0)	(0)	(30)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				1000 ppm				2000 ppm				4000 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		10	0	0	0	6	1	0	0	9	0	0	0	10	0	0	0
			(100)	(0)	(0)	(0)	(60)	(10)	(0)	(0)	(90)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	hepatocellular hypertrophy:central		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)	(90)	(0)	(0)	(0)
pancreas			<10>				<10>				<10>				<10>			
	vacuolic 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)
{Urinary system}																		
kidney			<10>				<10>				<10>				<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)
	inflammatory polyp		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)	(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	6000 ppm				8000 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	1	0	0	6	0	0	0
			(70)	(10)	(0)	(0)	(60)	(0)	(0)	(0)
	hepatocellular hypertrophy:central		1	9	0	0 **	0	10	0	0 **
			(10)	(90)	(0)	(0)	(0)	(100)	(0)	(0)
pancreas			<10>				<10>			
	vacuolic change		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Urinary system}										
kidney			<10>				<10>			
	cyst		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)	(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				1000 ppm				2000 ppm				4000 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	hydronephrosis		0	0	0	0	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)

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	6000 ppm				8000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}										
kidney			<10>				<10>			
	hydronephrosis		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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 2,4-DICHLORO-1-NITROBENZENE

IN THE 13-WEEK FEED STUDY

IDENTITY AND IMPURITY OF 2,4-DICHLORO-1-NITROBENZENE IN THE 13-WEEK FEED STUDY

Test Substance : 2,4-Dichloro-1-nitrobenzene (Wako Pure Chemical Industries, Ltd.)

Lot No. : CKK5596

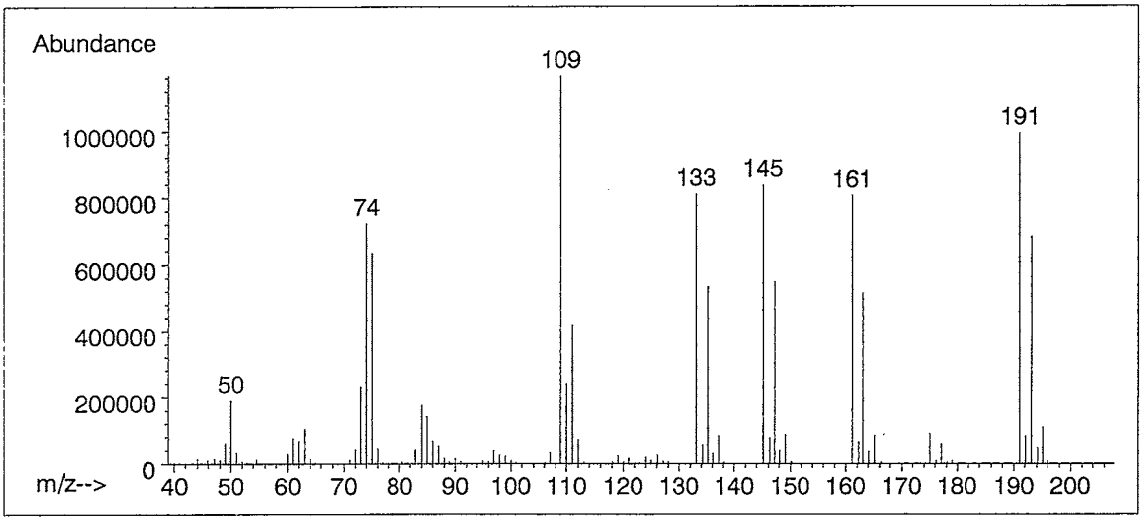
1. Spectral Data

Mass Spectrometry

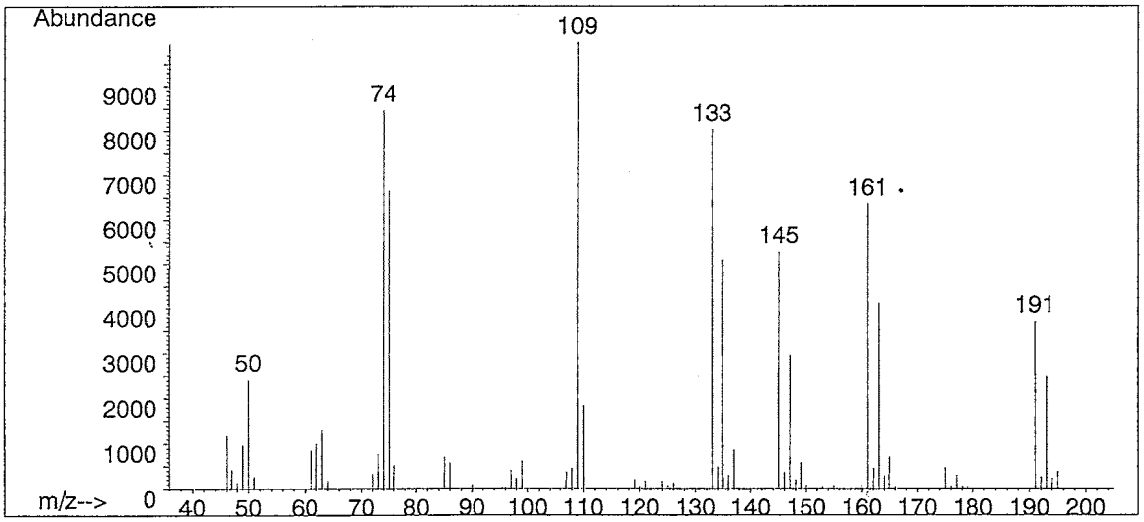
Instrument : Hewlett Packard 5989B Mass Spectrometer

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.

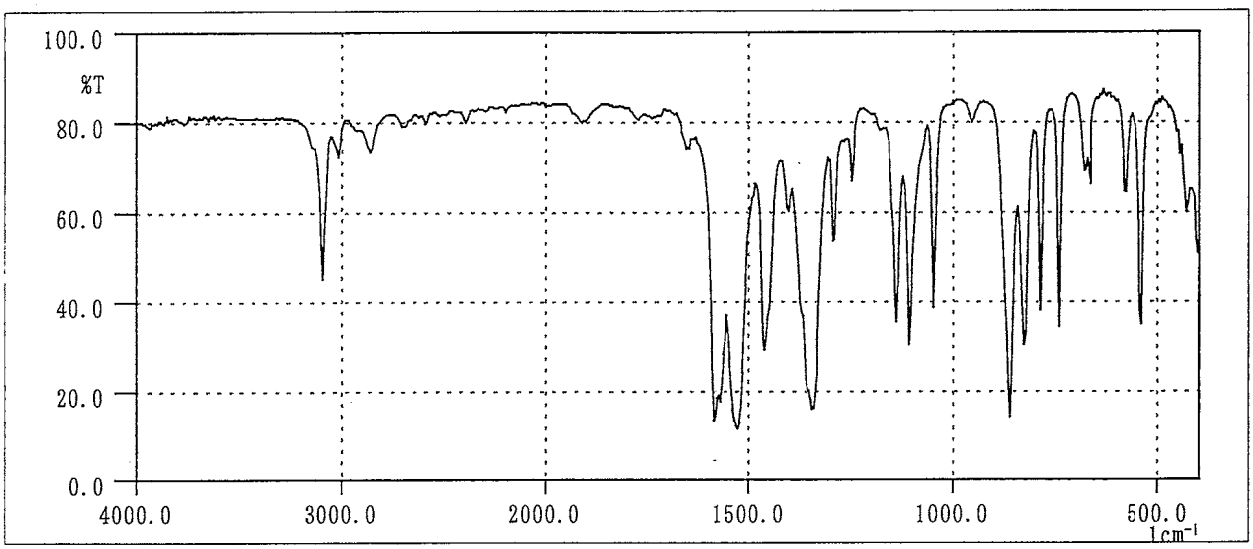
(*Fred W. McLafferty (1994) Wiley Registry of Mass Spectral Data, 6th edition. John Wiley and Sons, Inc. (U.S.), Entry Number 74218)

Infrared Spectrometry

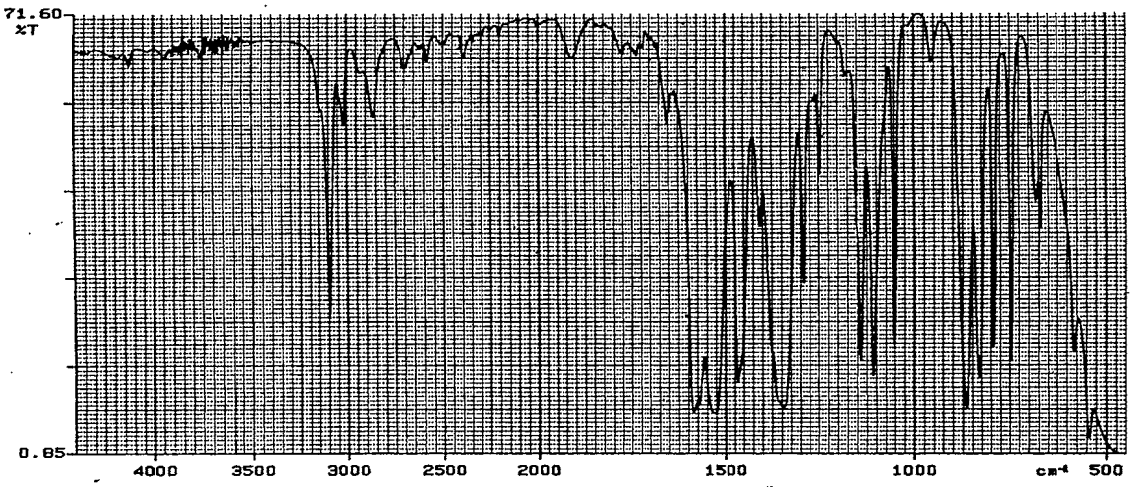
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 2 cm^{-1}



Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data*

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

2. Impurity

Instrument : Hewlett Packard 6890 Gas Chromatograph

Column : Ultra1 (0.2 mmϕ × 50 m)

Column Temperature : 160 °C (5 min) → (20 °C/min) → 260 °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	99.92	2,4-Dichloro-1-nitrobenzene
	2	0.03	1,5-Dichloro-2,3-dinitrobenzene
	3	0.05	1,2-Dichloro-4,5-dinitrobenzene

Results: Gas chromatography indicated one major peak (peak No.1) and two impurities. It was identified only by comparing its gas chromatograph with that of 1,5-dichloro-2,3-dinitrobenzene (peak No.2) and 1,2-dichloro-4,5-dinitrobenzene (peak No.3) in the 2,4-dichloro-1-nitrobenzene, the amount in the test substance were 0.03% and 0.05%.

3. Conclusions: The test substance was identified as 2,4-dichloro-1-nitrobenzene by the mass spectrum and the infrared spectrum. Gas chromatography indicated one major peak (peak No.1) and two impurities. It was identified only by comparing its gas chromatograph with that of 1,5-dichloro-2,3-dinitrobenzene and 1,2-dichloro-4,5-dinitrobenzene, the amount in the test substance were 0.03% and 0.05%.

APPENDIX L 2

STABILITY OF 2,4-DICHLORO-1-NITROBENZENE

IN THE 13-WEEK FEED STUDY

STABILITY OF 2,4-DICHLORO-1-NITROBENZENE IN THE 13-WEEK FEED STUDY

Test Substance : 2,4-Dichloro-1-nitrobenzene (Wako Pure Chemical Industries, Ltd.)

Lot No. : CKK5596

1. Sample : This lot was used from 2000.4.12 to 2000.7.13. Test substance was stored in a dark place at room temperature.

2. Gas Chromatography

Instrument : Hewlett Packard 6890 Gas Chromatograph

Column : Ultra1 (0.2 mmϕ × 50 m)

Column Temperature : 160 °C (5 min) → (20 °C/min) → 260 °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 (%)
2000.03.27	1	5.097	99.92
	2	7.549	0.03
	3	7.719	0.05
2000.07.17	1	5.103	99.92
	2	7.559	0.03
	3	7.729	0.05

Results: Gas chromatography indicated one major peak (peak No.1) and two impurities (peak No. 2, 3 < 0.1% of total area) analyzed on 2000.3.27 and one major peak (peak No.1) and two impurities (peak No.2, 3 < 0.1% of total area) analyzed on 2000.7.17. No new trace impurity peak in the test substance analyzed on 2000.7.17 was detected.

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

APPENDIX L 3

CONCENTMOUSEION OF 2,4-DICHLORO-1-NITROBENZENE

IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

CONCENTRATION OF 2,4-DICHLORO-1-NITROBENZENE IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

	Target Concentration						
Date Analyzed	500[a]	1000	2000	3000	4000	6000	8000
2000.04.04	484 (96.7)[b]	959 (95.9)	1960 (97.8)	2860 (95.4)	4020 (101)	5850 (97.5)	7820 (97.8)

[a] ppm
[b] %

Analytical method : The samples were analyzed by gas chromatography.

Instrument : Hewlett Packard 6890 Gas Chromatograph
Column : Ultra 1 (0.2 mmϕ × 50 m)
Column Temperature : 160 °C → (5 min) → (20 °C/min) → 260 °C (5 min)
Flow Rate : 1 mL/min
Detector : FID (Flame Ionization Detector)
Injection Volume : 1 μL

APPENDIX L 4

HOMOGENEITY OF 2,4-DICHLORO-1-NITROBENZENE

IN FORMULATED DIETSIN IN THE 13-WEEK FEED STUDY

HOMOGENEITY OF 2,4-DICHLORO-1-NITROBENZENE IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

	Target Concentration						
	500[a]	1000	2000	3000	4000	6000	8000
Coefficient Variation	1.84[b]	0.63	1.17	0.74	1.11	1.05	1.14

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

Analytical method : The samples were analyzed by gas chromatography.

Instrument : Hewlett Packard 6890 Gas Chromatograph
Column : Ultra 1 (0.2 mmϕ × 50 m)
Column Temperature : 160 °C → (5 min) → (20 °C/min) → 260 °C (5 min)
Flow Rate : 1 mL/min
Detector : FID (Flame Ionization Detector)
Injection Volume : 1 µL

APPENDIX L 5

STABILITY OF 2,4-DICHLORO-1-NITROBENZENE IN FORMULATED DIETS

STABILITY OF 2,4-DICHLORO-1-NITROBENZENE IN FORMULATED DIETS

Date Prepared	Date Analyzed	Target Concentration	
		200[a]	10000
1999.06.09	1999.06.09	210 (100)[b]	9900 (100)
	1999.06.18[c]	177 (84.3)	8780 (88.7)
	1999.06.24[d]	219 (104)	9010 (91.0)
	1999.07.07[d]	214 (102)	9080 (91.7)

[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 gas chromatography.

Instrument : Hewlett Packard 6890 Gas Chromatograph
Column : Ultra 1 (0.2 mmϕ × 50 m)
Column Temperature : 160 °C → (5 min) → (20 °C/min) → 260 °C (5 min)
Flow Rate : 1 mL/min
Detector : FID (Flame Ionization Detector)
Injection Volume : 1 μL

APPENDIX M 1

METHODS FOR HEMATOLOGY,BIOCHEMISTRY AND URINALYSIS IN THE 13-WEEK FEED STUDY OF 2,4-DICHLORO-1-NITROBENZENE

METHODS FOR HEMATOLOGY,BIOCHEMISTRY AND URINALYSIS IN THE 13-WEEK FEED STUDY OF 2,4-DICHLORO-1-NITROBENZENE

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 2,4-DICHLORO-1-NITROBENZENE

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY
IN THE 13-WEEK FEED STUDY OF 2,4-DICHLORO-1-NITROBENZENE

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