1，2 - ジクロロプロパンのマウスを用いた
吸 入 に よ る 1 3 週 間 毒 性 試 験 報 告 書

試験番号：0436

APPENDICES

APPENDICES

APPENDICES (CONTINUED)

APPENDICES (CONTINUED)

APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0436
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
		1	1	1	1	1	1	1	1	1	1	1	1	1
DEATH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	50ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	100ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	200ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	300ppm	1	2	2	2	2	2	2	2	2	2	2	2	2
	400ppm	6	6	6	6	6	6	6	6	6	6	6	6	6
WASTING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	50ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	100ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	200ppm	1	0	0	0	0	0	0	0	0	0	0	0	0
	300ppm	1	0	0	0	0	0	0	0	0	0	0	0	0
	400ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	50ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	100ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	200ppm	1	0	0	0	0	0	0	0	0	0	0	0	0
	300ppm	1	0	0	0	0	0	0	0	0	0	0	0	0
	400ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
INTERNAL MASS	Control	0	0	0	0	0	0	0	0	1	1	1	1	1
	50ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	100ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	200ppm	0	1	1	1	1	1	1	1	1	1	1	1	1
	300ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	400ppm	0	0	0	0	0	0	0	0	0	0	0	0	0

APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0436
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

Clinical sign	Group Name	Administration Week-day 1-7 1	2-7 1	3-7 1	4-7 1	5-7 1	6-7 1	7-7 1	8-7 1	9-7 1	10-7 1	11-7 1	12-7 1	13-7 1
DEATH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	50ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	100ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	200ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	300ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	400ppm	0	0	0	0	0	0	0	0	0	0	1	1	1
WASTING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	50ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	100ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	200ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	300ppm	2	0	0	0	0	0	0	0	0	0	0	0	0
	400ppm	3	0	0	0	0	0	0	0	0	0	0	0	0
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	50ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	100ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	200ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	300ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	400ppm	2	0	0	0	0	0	0	0	0	0	0	0	0
INTERNAL MASS	Control	0	0	0	0	0	0	0	0	1	1	1	1	1
	50ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	100ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	200ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	300ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	400ppm	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. : 0436
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	23.0± 0.9	24.6± 0.5	25.6± 1.0	26.2± 0.9	26.9± 0.8	27.7± 1.1	28.2± 1.0
50ppm	23.0± 0.8	24.8± 1.3	25.8± 1.5	27.1± 1.5	27.4± 2.1	28.2± 2.2	28.9± 1.8
100ppm	23.1± 0.8	24.7± 0.8	25.0± 0.6	26.0± 0.7	26.9± 0.9	27.0± 1.1	27.6± 1.1
200ppm	23.0± 0.8	23.5± 3.2	24.8± 1.3	25.6± 1.3	26.6± 1.0	26.8± 1.0	27.3± 1.5
300ppm	23.0± 0.8	22.5± 2.9*	24.6± 1.0	25.2± 1.1	26.3± 1.2	25.9± 1.1*	26.4± 1.1*
400ppm	23.1± 0.9	22.4± 1.7	24.6± 0.8	24.2± 1.3*	25.4± 0.5	25.6± 1.0	25.7± 0.5**

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

STUDY NO. : 0436
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	28.9± 1.0	29.6± 1.0	30.0± 1.3	30.6± 1.6	31.3± 1.7	32.0± 1.8	32.7± 1.7
50ppm	29.2± 2.3	29.6± 2.7	30.1± 2.9	30.8± 3.0	32.0± 2.9	32.4± 3.1	33.0± 2.9
100ppm	28.2± 1.6	28.9± 1.7	29.3± 1.7	29.9± 2.0	30.9± 2.2	31.2± 2.3	31.6± 2.1
200ppm	27.5± 1.5	28.2± 1.5	28.7± 1.8	28.9± 2.0	29.9± 2.0	30.1± 1.9	30.6± 1.8
300ppm	26.9± 1.2*	27.0± 1.1**	27.4± 1.3*	28.0± 1.4*	28.5± 1.6*	28.9± 1.7*	29.3± 1.4**
400ppm	25.8± 0.9**	26.7± 0.5**	27.7± 0.9	27.2± 1.0*	27.8± 1.2*	28.3± 0.6*	27.9± 1.1**

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. : 0436
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	19.0± 0.8	19.8± 0.8	20.8± 1.0	21.6± 0.7	22.0± 1.0	22.1± 0.3	22.4± 1.3
50ppm	19.0± 0.7	19.7± 0.8	21.0± 0.7	21.7± 0.6	23.2± 0.8	22.7± 0.9	23.5± 0.8
100ppm	19.0± 0.8	19.5± 0.7	20.3± 0.9	21.9± 1.3	21.8± 1.2	22.7± 0.5	23.1± 0.8
200ppm	19.0± 0.8	19.6± 0.8	20.7± 1.1	21.3± 0.9	22.8± 1.4	22.2± 0.8	23.3± 1.3
300ppm	19.0± 0.7	18.2± 2.8	20.6± 0.8	20.8± 0.7	22.6± 0.7	22.6± 0.6	22.9± 0.5
400ppm	19.0± 0.8	16.4± 3.3**	20.7± 0.8	20.5± 1.2	22.2± 0.9	22.1± 0.8	22.3± 0.5

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

STUDY NO. : 0436
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	22.9± 2.0	23.5± 1.4	22.9± 2.3	23.8± 1.5	24.6± 1.3	24.7± 1.0	25.3± 1.6
50ppm	23.8± 1.1	24.1± 0.8	24.0± 0.9	24.7± 1.2	25.2± 1.0	26.1± 0.9**	25.5± 1.2
100ppm	23.3± 1.2	23.7± 0.7	24.3± 0.9	24.3± 1.0	24.5± 1.2	24.8± 1.1	25.2± 0.7
200ppm	23.5± 1.2	24.4± 0.8	24.2± 0.5	24.6± 0.9	24.7± 1.1	25.3± 0.7	25.2± 1.7
300ppm	23.3± 0.6	23.3± 0.7	23.7± 0.9	24.0± 0.9	24.2± 1.3	24.9± 0.8	25.2± 1.2
400ppm	22.5± 0.5	22.8± 1.1	23.2± 0.7	23.3± 0.7	23.6± 0.5	24.4± 0.9	24.9± 0.6

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. : 0436
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(6)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	4.2± 0.3	4.1± 0.3	3.9± 0.3	4.1± 0.3	4.2± 0.2	4.2± 0.2	4.2± 0.2
50ppm	4.2± 0.4	4.2± 0.4	4.2± 0.4	4.3± 0.5	4.4± 0.3	4.4± 0.3	4.5± 0.4
100ppm	4.1± 0.2	4.0± 0.3	4.3± 0.3	4.4± 0.4	4.4± 0.4	4.3± 0.3	4.5± 0.3
200ppm	3.5± 0.7*	4.0± 0.4	3.8± 0.2	4.2± 0.2	4.1± 0.3	4.1± 0.3	4.3± 0.4
300ppm	3.1± 0.7**	4.2± 0.3	3.8± 0.2	4.3± 0.3	4.0± 0.2	4.3± 0.3	4.2± 0.3
400ppm	2.9± 0.4**	4.3± 0.1	3.6± 0.1	4.2± 0.2	3.9± 0.4	4.4± 0.1	4.2± 0.4

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

STUDY NO. : 0436
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	4.3± 0.2	4.3± 0.2	4.4± 0.2	4.3± 0.2	4.4± 0.2	4.3± 0.2
50ppm	4.5± 0.4	4.6± 0.4	4.6± 0.4	4.7± 0.3*	4.7± 0.4	4.6± 0.4
100ppm	4.5± 0.3	4.5± 0.4	4.6± 0.2	4.7± 0.3*	4.6± 0.1	4.5± 0.2
200ppm	4.3± 0.3	4.4± 0.3	4.3± 0.3	4.4± 0.3	4.3± 0.2	4.4± 0.3
300ppm	4.2± 0.4	4.3± 0.3	4.4± 0.3	4.4± 0.3	4.6± 0.4	4.5± 0.3
400ppm	4.5± 0.1	4.5± 0.3	4.4± 0.1	4.4± 0.4	4.4± 0.0	4.1± 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. : 0436
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(6)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	3.4± 0.2	3.5± 0.3	3.5± 0.2	3.7± 0.2	3.7± 0.3	3.8± 0.3	4.1± 0.4
50ppm	3.4± 0.2	3.7± 0.1	3.7± 0.2	3.9± 0.1	3.9± 0.1	4.0± 0.2	4.1± 0.2
100ppm	3.3± 0.2	3.6± 0.2	3.8± 0.2*	3.8± 0.2	3.9± 0.2	3.9± 0.3	4.0± 0.3
200ppm	3.1± 0.2*	3.5± 0.3	3.4± 0.3	3.9± 0.2	3.6± 0.3	3.9± 0.2	4.1± 0.3
300ppm	2.6± 0.6**	3.7± 0.4	3.3± 0.3	3.8± 0.2	3.7± 0.3	3.9± 0.3	4.0± 0.3
400ppm	2.3± 0.7**	3.8± 0.4	3.1± 0.3**	3.7± 0.3	3.5± 0.2	3.8± 0.3	3.8± 0.2

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

STUDY NO. : 0436
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	4.0± 0.4	4.0± 0.4	4.1± 0.2	4.1± 0.3	4.1± 0.3	4.2± 0.3
50ppm	4.2± 0.2	4.2± 0.2	4.3± 0.1	4.3± 0.2	4.4± 0.2*	4.2± 0.3
100ppm	4.0± 0.2	4.2± 0.2	4.2± 0.4	4.2± 0.2	4.1± 0.3	4.3± 0.2
200ppm	4.1± 0.3	4.1± 0.3	4.2± 0.3	4.1± 0.3	4.2± 0.3	4.2± 0.3
300ppm	4.0± 0.3	4.0± 0.3	4.1± 0.3	4.0± 0.4	4.2± 0.2	4.3± 0.3
400ppm	4.0± 0.2	4.1± 0.3	4.0± 0.2	3.9± 0.3	4.0± 0.3	4.0± 0.3

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

APPENDIX D 1

URINALYSIS : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0436 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	2	3	1	2	2		0	2	7	1	0	0		10	0	0	0	0	0		2	2	4	2	0	0		9	0	1	0	0	
50ppm	10	0	1	1	0	4	4	0		0	0	7	3	0	0		10	0	0	0	0	0		2	2	4	2	0	0		9	1	0	0	0	
100ppm	10	0	2	0	2	4	2	0		0	0	10	0	0	0		10	0	0	0	0	0		1	2	4	3	0	0		9	1	0	0	0	
200ppm	10	0	2	2	0	5	1	0		0	0	9	1	0	0		10	0	0	0	0	0		1	3	6	0	0	0		10	0	0	0	0	
300ppm	8	0	3	2	2	0	1	0		0	2	6	0	0	0		8	0	0	0	0	0		1	3	4	0	0	0		8	0	0	0	0	
400ppm	4	0	3	1	0	0	0	0		0	1	3	0	0	0		4	0	0	0	0	0		1	1	2	0	0	0		4	0	0	0	0	

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

STUDY NO. : 0436 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	
50ppm	10	10	0	0	0	0	
100ppm	10	10	0	0	0	0	
200ppm	10	10	0	0	0	0	
300ppm	8	8	0	0	0	0	
400ppm	4	4	0	0	0	0	

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

APPENDIX D 2

URINALYSIS : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0436
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	±	+	2+	3+	4+	CHI	Occult blood −	±	+	2+	3+	CHI
Control	10	0	1	1	1	1	4	2		0	2	7	1	0	0		10	0	0	0	0	0		1	8	1	0	0	0		10	0	0	0	0	
50ppm	10	0	0	1	2	1	6	0		0	2	8	0	0	0		10	0	0	0	0	0		0	8	2	0	0	0		10	0	0	0	0	
100ppm	10	0	0	1	1	2	6	0		0	4	6	0	0	0		10	0	0	0	0	0		0	8	2	0	0	0		10	0	0	0	0	
200ppm	10	0	0	0	2	3	5	0		0	0	6	4	0	0		10	0	0	0	0	0		0	5	3	2	0	0		10	0	0	0	0	
300ppm	10	0	0	1	0	3	4	2		0	0	4	6	0	0	*	10	0	0	0	0	0		0	0	4	6	0	0	**	10	0	0	0	0	
400ppm	9	0	3	2	2	1	1	0		0	5	3	1	0	0		9	0	0	0	0	0		0	1	5	3	0	0	**	9	0	0	0	0	

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

STUDY NO. : 0436
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	
50ppm	10	10	0	0	0	0	
100ppm	10	10	0	0	0	0	
200ppm	10	10	0	0	0	0	
300ppm	10	10	0	0	0	0	
400ppm	9	9	0	0	0	0	

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

APPENDIX E 1

HEMATOLOGY : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0436
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	10.94±	0.29	15.7±	0.3	50.4±	0.9	46.0±	0.8	14.4±	0.2	31.2±	0.4	1490±	78
50ppm	10	10.36±	0.38**	15.1±	0.6*	48.6±	1.2*	46.9±	0.7*	14.6±	0.2	31.0±	0.5	1437±	54
100ppm	10	10.28±	0.43**	15.0±	0.6*	48.6±	2.0*	47.3±	0.5**	14.6±	0.1	30.9±	0.3	1430±	52
200ppm	10	10.26±	0.39**	14.9±	0.6*	48.7±	1.4*	47.5±	0.7**	14.5±	0.2	30.6±	0.6*	1461±	70
300ppm	7	9.69±	0.47**	14.3±	0.6**	48.1±	1.5*	49.7±	1.1**	14.7±	0.3**	29.6±	0.5**	1590±	77*
400ppm	4	8.81±	0.16**	13.4±	0.3**	45.5±	0.6**	51.7±	0.5**	15.1±	0.3**	29.3±	0.6**	1772±	99**

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

STUDY NO. : 0436
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	2.52±	1.74	1±	1	12±	4	1±	1	0±	0	3±	2	84±	4	0±	0
50ppm	10	1.72±	1.06	1±	1	14±	3	1±	1	0±	0	3±	2	82±	3	0±	0
100ppm	10	1.49±	0.93	2±	2	12±	5	1±	1	0±	0	3±	3	84±	5	0±	0
200ppm	10	1.95±	1.23	1±	1	14±	3	1±	1	0±	0	3±	2	80±	4	0±	0
300ppm	7	2.24±	1.23	1±	1	17±	9	2±	2	0±	0	4±	2	76±	10	0±	0
400ppm	4	1.68±	1.20	1±	1	28±	3**	2±	1	0±	0	4±	3	66±	5**	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. : 0436
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	10.63±	0.64	15.6±	1.2	49.2±	3.1	46.3±	0.6	14.6±	0.4	31.6±	0.8	1395±	98
50ppm	10	10.49±	0.37	15.5±	0.6	49.0±	1.2	46.7±	0.7	14.8±	0.2	31.7±	0.6	1388±	172
100ppm	10	10.52±	0.30	15.5±	0.4	48.8±	1.1	46.5±	0.6	14.7±	0.2	31.7±	0.3	1300±	62
200ppm	10	10.28±	0.41	15.2±	0.7	48.9±	1.8	47.6±	0.7**	14.8±	0.2	31.2±	0.5	1256±	361
300ppm	10	9.21±	0.46**	14.1±	0.7**	46.7±	2.0*	50.7±	0.7**	15.3±	0.1**	30.3±	0.4**	1458±	51
400ppm	9	8.79±	0.44**	13.7±	0.8**	45.2±	2.2**	51.5±	0.9**	15.5±	0.3**	30.2±	0.4**	1657±	149**

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

STUDY NO. : 0436
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	1.76±	1.13	1±	1	15±	5	1±	1	0±	0	2±	1	81±	4	0±	0
50ppm	10	1.52±	0.77	1±	1	17±	6	1±	2	0±	0	2±	1	79±	5	0±	0
100ppm	10	1.55±	1.07	1±	1	18±	6	1±	1	0±	0	2±	2	78±	5	0±	0
200ppm	10	1.66±	1.55	1±	1	14±	6	1±	2	0±	0	2±	1	82±	4	0±	0
300ppm	10	1.60±	1.12	1±	1	15±	4	3±	2	0±	0	4±	2	77±	5	0±	0
400ppm	9	2.54±	1.56	2±	2	18±	4	2±	1	0±	0	4±	2*	74±	5*	0±	0

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

APPENDIX F 1

BIOCHEMISTRY : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0436
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	5.2± 0.2	3.0± 0.1	1.4± 0.1	0.15± 0.01	219± 22	83± 12	31± 9
50ppm	10	5.0± 0.1	3.0± 0.1	1.5± 0.1	0.15± 0.01	174± 38*	75± 7	20± 5
100ppm	10	5.0± 0.2**	2.9± 0.1	1.5± 0.1	0.15± 0.01	184± 43	72± 8	18± 8*
200ppm	10	4.9± 0.1**	2.9± 0.1	1.5± 0.1	0.16± 0.01	191± 32	79± 13	14± 3**
300ppm	8	5.1± 0.1	3.1± 0.1	1.6± 0.1**	0.16± 0.03	180± 32	96± 5	28± 15
400ppm	4	5.0± 0.1	3.1± 0.1	1.6± 0.1**	0.18± 0.02*	213± 33	100± 4	42± 9

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

STUDY NO. : 0436
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	179± 23	40± 4	17± 2	183± 35	141± 10	2± 1	45± 11
50ppm	10	163± 13	43± 6	16± 3	180± 27	142± 15	2± 1	41± 7
100ppm	10	155± 18*	41± 7	17± 3	218± 118	134± 10	3± 1	49± 8
200ppm	10	162± 25	39± 6	18± 3	171± 30	144± 12	2± 1	43± 16
300ppm	8	206± 8*	52± 12	21± 5	212± 50	174± 8**	1± 1	43± 11
400ppm	4	213± 17*	139± 24**	95± 37**	397± 64*	325± 45**	2± 0	86± 54

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

STUDY NO. : 0436
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	27.9± 5.7	150± 1	4.5± 0.2	120± 2	9.0± 0.3	7.9± 1.1
50ppm	10	25.0± 2.5	151± 1**	4.3± 0.2	121± 3	8.8± 0.2	7.7± 0.6
100ppm	10	26.1± 4.6	151± 1*	4.6± 0.3	122± 2	8.7± 0.1*	7.6± 0.6
200ppm	10	25.2± 3.5	150± 1	4.4± 0.3	121± 2	8.6± 0.2**	6.5± 0.6**
300ppm	8	22.3± 3.5	150± 1	4.9± 0.5	120± 2	8.9± 0.3	7.8± 0.9
400ppm	4	22.8± 1.9	151± 1	5.0± 0.3*	120± 2	8.9± 0.1	7.9± 1.7

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

APPENDIX F 2

BIOCHEMISTRY : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0436
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	5.3±	0.2	3.3±	0.1	1.7±	0.2	0.14±	0.01	168±	28	77±	12	17±	8
50ppm	10	5.2±	0.1	3.3±	0.1	1.7±	0.1	0.14±	0.03	166±	26	74±	11	16±	4
100ppm	10	5.2±	0.1	3.3±	0.1	1.7±	0.1	0.14±	0.02	155±	20	71±	7	13±	5
200ppm	10	5.2±	0.1	3.3±	0.1	1.8±	0.1	0.14±	0.00	169±	22	78±	5	12±	4
300ppm	10	5.1±	0.2	3.4±	0.1	1.9±	0.1**	0.15±	0.02	183±	29	92±	7**	18±	8
400ppm	9	5.2±	0.2	3.4±	0.1	1.9±	0.1**	0.18±	0.03**	171±	70	109±	8**	69±	56*

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

STUDY NO. : 0436
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	160± 20	53± 10	21± 4	201± 21	237± 56	1± 0	58± 22
50ppm	10	156± 17	60± 31	21± 8	233± 93	217± 27	2± 1	62± 41
100ppm	10	147± 19	54± 13	20± 3	207± 54	209± 20	2± 1	55± 23
200ppm	10	158± 15	45± 9	18± 3	226± 96	201± 28	1± 1	53± 29
300ppm	10	185± 16*	75± 45	27± 25	276± 119	195± 29	1± 1	48± 21
400ppm	9	227± 19**	206± 173*	95± 180	568± 364**	197± 16	2± 1	93± 43

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

STUDY NO. : 0436
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	29.0± 13.2	151± 2	4.2± 0.4	121± 3	9.2± 0.4	7.2± 1.2
50ppm	10	23.3± 3.4	151± 2	4.4± 0.3	122± 2	9.0± 0.3	7.1± 0.7
100ppm	10	22.4± 2.5	151± 1	4.4± 0.3	122± 2	8.9± 0.1	6.8± 1.0
200ppm	10	21.6± 2.7	151± 2	4.3± 0.3	121± 2	9.0± 0.1	6.5± 1.0
300ppm	10	19.1± 2.1**	150± 1	4.5± 0.3	120± 1	9.1± 0.2	7.4± 1.5
400ppm	9	15.7± 2.6**	152± 1	4.2± 0.3	117± 3**	9.4± 0.2	8.0± 1.8

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

APPENDIX G 1

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

(13-WEEK STUDY)

STUDY NO. : 0436
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	(%)	50ppm 0	(%)	100ppm 0	(%)	200ppm 0	(%)
thymus	atrophic		-	(-)	-	(-)	-	(-)	-	(-)
spleen	black zone		-	(-)	-	(-)	-	(-)	-	(-)
liver	pale		-	(-)	-	(-)	-	(-)	-	(-)
	accentuation of lobular structure		-	(-)	-	(-)	-	(-)	-	(-)

Organ	Findings	Group Name NO. of Animals	300ppm 2 (%)	400ppm 6 (%)
thymus	atrophic		1 (50)	1 (17)
spleen	black zone		0 (0)	1 (17)
liver	pale		1 (50)	5 (83)
	accentuation of lobular structure		1 (50)	4 (67)

APPENDIX G 2

GROSS FINDINGS : SUMMARY, MOUSE : MALE : SACRIFICED ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0436
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	50ppm 10 (%)	100ppm 10 (%)	200ppm 10 (%)
forestomach	thick		0 (0)	0 (0)	0 (0)	0 (0)
liver	black zone		0 (0)	0 (0)	0 (0)	0 (0)
kidney	hydronephrosis		1 (10)	1 (10)	0 (0)	1 (10)
testis	atrophic		1 (10)	0 (0)	0 (0)	0 (0)

Organ	Findings	Group Name NO. of Animals	300ppm 8 (%)	400ppm 4 (%)
forestomach	thick		2 (25)	4 (100)
liver	black zone		1 (13)	0 (0)
kidney	hydronephrosis		0 (0)	0 (0)
testis	atrophic		0 (0)	0 (0)

APPENDIX G 3

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

(13-WEEK STUDY)

STUDY NO. : 0436
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

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

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

STUDY NO. : 0436
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name	300ppm		400ppm	
		NO. of Animals	0	(%)	1	(%)
liver	white zone		-	(-)	1	(100)

APPENDIX G 4

GROSS FINDINGS : SUMMARY, MOUSE : FEMALE : SACRIFICED ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0436
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

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

Organ	Findings	Group Name	300ppm	400ppm
		NO. of Animals	10 (%)	9 (%)
spleen	black zone		1 (10)	0 (0)
forestomach	thick		2 (20)	9 (100)
liver	white zone		0 (0)	1 (11)
kidney	hydronephrosis		0 (0)	0 (0)

APPENDIX H 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0436
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± 1.7	0.034± 0.010	0.008± 0.002	0.202± 0.060	0.151± 0.008	0.164± 0.009
50ppm	10	29.5± 3.1	0.035± 0.006	0.009± 0.002	0.223± 0.025	0.161± 0.011	0.172± 0.015
100ppm	10	28.1± 2.1	0.030± 0.006	0.009± 0.002	0.234± 0.023	0.159± 0.013	0.173± 0.012
200ppm	10	26.6± 1.4*	0.031± 0.002	0.008± 0.002	0.229± 0.024	0.149± 0.011	0.163± 0.018
300ppm	8	25.6± 1.0**	0.034± 0.005	0.009± 0.002	0.220± 0.017	0.142± 0.004	0.160± 0.009
400ppm	4	24.1± 0.8**	0.029± 0.007	0.009± 0.001	0.210± 0.023	0.152± 0.001	0.158± 0.006

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

STUDY NO. : 0436
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	0.434± 0.041	0.047± 0.009	1.166± 0.051	0.428± 0.017
50ppm	10	0.462± 0.034	0.048± 0.008	1.209± 0.099	0.446± 0.018
100ppm	10	0.462± 0.027	0.041± 0.005	1.187± 0.057	0.438± 0.026
200ppm	10	0.450± 0.030	0.041± 0.006	1.152± 0.085	0.442± 0.018
300ppm	8	0.461± 0.022	0.043± 0.003	1.330± 0.127**	0.440± 0.016
400ppm	4	0.480± 0.012	0.052± 0.005	1.517± 0.084**	0.425± 0.012

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

APPENDIX H 2

ORGAN WEIGHT, ABSOLUTE: SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0436
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	21.7± 1.1	0.042± 0.009	0.010± 0.002	0.022± 0.006	0.136± 0.019	0.156± 0.012
50ppm	10	22.1± 1.4	0.038± 0.006	0.010± 0.002	0.025± 0.006	0.131± 0.010	0.160± 0.014
100ppm	10	21.3± 0.9	0.041± 0.005	0.011± 0.002	0.026± 0.005	0.125± 0.011	0.172± 0.013
200ppm	10	21.7± 1.3	0.040± 0.004	0.010± 0.002	0.023± 0.005	0.124± 0.007	0.159± 0.015
300ppm	10	22.0± 0.7	0.040± 0.006	0.010± 0.002	0.025± 0.005	0.139± 0.007	0.161± 0.014
400ppm	9	21.1± 0.5	0.041± 0.005	0.010± 0.003	0.023± 0.007	0.132± 0.008	0.155± 0.011

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

STUDY NO. : 0436
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	0.348± 0.166	0.052± 0.005	0.953± 0.080	0.445± 0.021
50ppm	10	0.327± 0.083	0.056± 0.015	1.012± 0.081	0.459± 0.022
100ppm	10	0.296± 0.015	0.050± 0.007	0.982± 0.052	0.456± 0.017
200ppm	10	0.306± 0.016	0.048± 0.007	1.033± 0.077	0.447± 0.022
300ppm	10	0.332± 0.010*	0.052± 0.005	1.206± 0.102**	0.448± 0.014
400ppm	9	0.350± 0.026**	0.062± 0.007	1.532± 0.151**	0.406± 0.017**

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

APPENDIX I 1

ORGAN WEIGHT, RELATIVE : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0436
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± 1.7	0.116± 0.031	0.029± 0.007	0.691± 0.208	0.518± 0.049	0.563± 0.040
50ppm	10	29.5± 3.1	0.119± 0.019	0.031± 0.006	0.764± 0.120	0.547± 0.033	0.583± 0.036
100ppm	10	28.1± 2.1	0.107± 0.014	0.030± 0.007	0.838± 0.093	0.570± 0.060*	0.616± 0.029*
200ppm	10	26.6± 1.4*	0.116± 0.010	0.030± 0.008	0.866± 0.112*	0.561± 0.035	0.611± 0.070
300ppm	8	25.6± 1.0**	0.131± 0.018	0.034± 0.009	0.859± 0.065	0.554± 0.031	0.626± 0.034*
400ppm	4	24.1± 0.8**	0.118± 0.028	0.036± 0.006	0.870± 0.076	0.632± 0.022**	0.657± 0.035**

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

STUDY NO. : 0436
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	1.487± 0.160	0.160± 0.035	3.993± 0.227	1.468± 0.128
50ppm	10	1.572± 0.084	0.163± 0.019	4.111± 0.267	1.527± 0.178
100ppm	10	1.654± 0.131**	0.145± 0.020	4.247± 0.284	1.566± 0.114
200ppm	10	1.690± 0.062**	0.154± 0.017	4.327± 0.213	1.662± 0.083**
300ppm	8	1.801± 0.114**	0.166± 0.015	5.188± 0.413**	1.719± 0.059**
400ppm	4	1.990± 0.104**	0.216± 0.026**	6.292± 0.378**	1.762± 0.076**

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

APPENDIX I 2

ORGAN WEIGHT, RELATIVE : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0436
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	21.7± 1.1	0.195± 0.046	0.048± 0.009	0.101± 0.026	0.627± 0.099	0.717± 0.058
50ppm	10	22.1± 1.4	0.171± 0.023	0.047± 0.006	0.115± 0.028	0.595± 0.058	0.722± 0.048
100ppm	10	21.3± 0.9	0.192± 0.021	0.052± 0.009	0.122± 0.019	0.587± 0.043	0.811± 0.064**
200ppm	10	21.7± 1.3	0.187± 0.020	0.048± 0.009	0.108± 0.022	0.573± 0.037	0.733± 0.076
300ppm	10	22.0± 0.7	0.181± 0.028	0.046± 0.011	0.115± 0.027	0.634± 0.041	0.732± 0.063
400ppm	9	21.1± 0.5	0.192± 0.023	0.047± 0.014	0.108± 0.033	0.626± 0.043	0.739± 0.059

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

STUDY NO. : 0436
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	1.611± 0.805	0.240± 0.027	4.383± 0.248	2.051± 0.140
50ppm	10	1.476± 0.330	0.250± 0.055	4.575± 0.258	2.083± 0.162
100ppm	10	1.391± 0.058	0.236± 0.025	4.622± 0.226	2.144± 0.089
200ppm	10	1.415± 0.084	0.220± 0.022	4.764± 0.201	2.064± 0.142
300ppm	10	1.510± 0.073	0.236± 0.022	5.477± 0.344**	2.040± 0.090
400ppm	9	1.665± 0.130**	0.293± 0.033*	7.285± 0.783**	1.927± 0.095

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

APPENDIX J 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY, MOUSE : MALE : DEAD AND MORIBUND ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0436
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				50ppm				100ppm				200ppm			
		No. of Animals on Study	0				0				0				0			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}																		
nasal cavit			< 0>				< 0>				< 0>				< 0>			
	respiratory metaplasia:olfactory epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	desquamation:olfactory epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	atrophy:olfactory epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	necrosis:olfactory epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
lung			< 0>				< 0>				< 0>				< 0>			
	congestion		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
{Hematopoietic system}																		
bone marrow			< 0>				< 0>				< 0>				< 0>			
	congestion		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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	300ppm				400ppm			
		No. of Animals on Study	2				6			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			< 2>				< 6>			
	respiratory metaplasia:olfactory epithelium		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(17)	(0)	(0)	(0)
	desquamation:olfactory epithelium		0	0	0	0	6	0	0	0
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	atrophy:olfactory epithelium		1	0	0	0	0	0	0	0
			(50)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:olfactory epithelium		2	0	0	0	0	0	0	0
			(100)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lung			< 2>				< 6>			
	congestion		1	0	0	0	3	0	0	0
			(50)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
{Hematopoietic system}										
bone marrow			< 2>				< 6>			
	congestion		1	0	0	0	1	2	3	0
			(50)	(0)	(0)	(0)	(17)	(33)	(50)	(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 / No. of Animals on Study / Grade	Control 0				50ppm 0				100ppm 0				200ppm 0			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Hematopoietic system}																		
lymph node		< a >	< 0>				< 0>				< 0>				< 0>			
	atrophy	b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	karyorrhexis	b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
thymus		< a >	< 0>				< 0>				< 0>				< 0>			
	atrophy	b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	karyorrhexis	b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
spleen		< a >	< 0>				< 0>				< 0>				< 0>			
	atrophy	b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	engorgement of erythrocyte	b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
{Circulatory system}																		
heart		< a >	< 0>				< 0>				< 0>				< 0>			
	ground glass appearance	b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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	300ppm				400ppm			
		No. of Animals on Study	2				6			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
lymph node			< 2>				< 5>			
	atrophy		0	0	1	0	0	0	0	0
			(0)	(0)	(50)	(0)	(0)	(0)	(0)	(0)
	karyorrhexis		0	0	0	0	1	4	0	0
			(0)	(0)	(0)	(0)	(20)	(80)	(0)	(0)
thymus			< 2>				< 6>			
	atrophy		0	0	1	0	0	0	1	0
			(0)	(0)	(50)	(0)	(0)	(0)	(17)	(0)
	karyorrhexis		1	0	0	0	2	3	0	0
			(50)	(0)	(0)	(0)	(33)	(50)	(0)	(0)
spleen			< 2>				< 5>			
	atrophy		0	0	1	0	3	2	0	0
			(0)	(0)	(50)	(0)	(60)	(40)	(0)	(0)
	engorgement of erythrocyte		1	0	0	0	1	0	0	0
			(50)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
{Circulatory system}										
heart			< 2>				< 6>			
	ground glass appearance		0	0	1	0	0	5	1	0
			(0)	(0)	(50)	(0)	(0)	(83)	(17)	(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	Control				50ppm				100ppm				200ppm			
		No. of Animals on Study	0				0				0				0			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
liver			< 0>				< 0>				< 0>				< 0>			
	congestion		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	necrosis:central		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	fatty change:central		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	mineralization:central		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	vacuolic change:central		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
{Urinary system}																		
kidney			< 0>				< 0>				< 0>				< 0>			
	hyaline cast:urinary tubule		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
{Endocrine system}																		
pituitary			< 0>				< 0>				< 0>				< 0>			
	congestion		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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	300ppm				400ppm			
		No. of Animals on Study	2				6			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
liver			< 2>				< 6>			
	congestion		1	0	0	0	0	0	0	0
			(50)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:central		0	0	1	0	0	0	2	0
			(0)	(0)	(50)	(0)	(0)	(0)	(33)	(0)
	fatty change:central		1	0	0	0	1	4	0	0
			(50)	(0)	(0)	(0)	(17)	(67)	(0)	(0)
	mineralization:central		0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(17)	(0)	(0)
	vacuolic change:central		0	0	0	0	0	1	4	0
			(0)	(0)	(0)	(0)	(0)	(17)	(67)	(0)
{Urinary system}										
kidney			< 2>				< 6>			
	hyaline cast:urinary tubule		2	0	0	0	0	0	0	0
			(100)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Endocrine system}										
pituitary			< 2>				< 6>			
	congestion		1	0	0	0	6	0	0	0
			(50)	(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	Control				50ppm				100ppm				200ppm			
		No. of Animals on Study	0				0				0				0			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Endocrine system}																		
adrenal			< 0>				< 0>				< 0>				< 0>			
	congestion		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
{Reproductive system}																		
testis			< 0>				< 0>				< 0>				< 0>			
	germ cell necrosis		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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	300ppm				400ppm			
		No. of Animals on Study	2				6			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Endocrine system}										
adrenal			< 2>				< 6>			
	congestion		1	0	0	0	6	0	0	0
			(50)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Reproductive system}										
testis			< 2>				< 6>			
	germ cell necrosis		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(33)	(0)	(0)	(0)

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

APPENDIX J 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY, MOUSE : MALE : SACRIFICED ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0436
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control				50ppm				100ppm				200ppm			
		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>			
	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)
	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)
	necrosis: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)
lung			<10>				<10>				<10>				<10>			
	congestion		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Hematopoietic system}																		
bone marrow			<10>				<10>				<10>				<10>			
	erythropoiesis:increased		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen			<10>				<10>				<10>				<10>			
	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)

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	300ppm				400ppm			
		No. of Animals on Study	8				4			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			< 8>				< 4>			
	respiratory metaplasia:olfactory epithelium		3	0	0	0	2	0	0	0
			(38)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
	atrophy:olfactory epithelium		6	0	0	0 **	4	0	0	0 **
			(75)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	necrosis:olfactory epithelium		2	0	0	0	1	0	0	0
			(25)	(0)	(0)	(0)	(25)	(0)	(0)	(0)
lung			< 8>				< 4>			
	congestion		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}										
bone marrow			< 8>				< 4>			
	erythropoiesis:increased		3	0	0	0	2	0	0	0
			(38)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
spleen			< 8>				< 4>			
	deposit of hemosiderin		0	0	0	0	4	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	Control				50ppm				100ppm				200ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}																		
spleen			<10>				<10>				<10>				<10>			
	deposit of melanin		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	increased extramedullary hematopoiesis		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)
	megakaryocyte:increased		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Circulatory system}																		
heart			<10>				<10>				<10>				<10>			
	ground glass appearance		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}																		
stomach			<10>				<10>				<10>				<10>			
	hyperplasia:forestomach		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	300ppm				400ppm			
		No. of Animals on Study	8				4			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
spleen			< 8>				< 4>			
	deposit of melanin		1	0	0	0	0	0	0	0
			(13)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	increased extramedullary hematopoiesis		3	0	0	0	0	4	0	0 **
			(38)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
	megakaryocyte:increased		3	0	0	0	4	0	0	0 **
			(38)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Circulatory system}										
heart			< 8>				< 4>			
	ground glass appearance		2	0	0	0	3	0	0	0 *
			(25)	(0)	(0)	(0)	(75)	(0)	(0)	(0)
{Digestive system}										
stomach			< 8>				< 4>			
	hyperplasia:forestomach		2	0	0	0	2	2	0	0 **
			(25)	(0)	(0)	(0)	(50)	(50)	(0)	(0)

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

Organ	Findings	Group Name	Control				50ppm				100ppm				200ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
liver			<10>				<10>				<10>				<10>			
	necrosis:central		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	swelling:central		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization: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)
	vacuolic change: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>			
	basophilic change		1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	inflammatory polyp		0	1	0	0	0	1	0	0	0	0	0	0	0	1	0	0
			(0)	(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)
	vacuolization of proximal tubule		5	3	0	0	6	4	0	0	7	1	2	0	8	0	0	0
			(50)	(30)	(0)	(0)	(60)	(40)	(0)	(0)	(70)	(10)	(20)	(0)	(80)	(0)	(0)	(0)

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

Organ	Findings	Group Name	300ppm				400ppm			
		No. of Animals on Study	8				4			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
liver			< 8>				< 4>			
	necrosis:central		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(25)	(0)	(0)	(0)
	swelling:central		8	0	0	0 **	2	1	1	0 **
			(100)	(0)	(0)	(0)	(50)	(25)	(25)	(0)
	mineralization:central		0	0	0	0	1	2	0	0 **
			(0)	(0)	(0)	(0)	(25)	(50)	(0)	(0)
	vacuolic change:central		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
{Urinary system}										
kidney			< 8>				< 4>			
	basophilic change		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)
	vacuolization of proximal tubule		5	0	0	0	0	0	0	0 *
			(63)	(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				50ppm				100ppm				200ppm			
		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	1	0	0	0	1	0	0	0	0	0	0	0	1	0
			(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)
	tubular necrosis:proximale tubule		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyaline cast:urinary tubule		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Endocrine system}																		
thyroid			<10>				<10>				<10>				<10>			
	ultimibranchial body remanet		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>			
	hypoplasia		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)

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	300ppm				400ppm			
		No. of Animals on Study	8				4			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}										
kidney			< 8>				< 4>			
	hydronephrosis		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	tubular necrosis:proximale tubule		1	0	0	0	0	0	0	0
			(13)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyaline cast:urinary tubule		1	0	0	0	0	0	0	0
			(13)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Endocrine system}										
thyroid			< 8>				< 4>			
	ultimibranchial body remanet		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Reproductive system}										
testis			< 8>				< 4>			
	hypoplasia		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 J 3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY, MOUSE : FEMALE : DEAD AND MORIBUND ANIMALS

(13-WEEK STUDY)

Organ	Findings	Group Name	Control				50ppm				100ppm				200ppm			
		No. of Animals on Study	0				0				0				0			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}																		
nasal cavit			< 0>				< 0>				< 0>				< 0>			
	atrophy:olfactory epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	necrosis:olfactory epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
lung			< 0>				< 0>				< 0>				< 0>			
	congestion		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
{Hematopoietic system}																		
bone marrow			< 0>				< 0>				< 0>				< 0>			
	erythropoiesis:increased		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
spleen			< 0>				< 0>				< 0>				< 0>			
	deposit of hemosiderin		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	increased extramedullary hematopoiesis		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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	300ppm				400ppm			
		No. of Animals on Study	0				1			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			< 0>				< 1>			
	atrophy:olfactory epithelium		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
	necrosis:olfactory epithelium		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
lung			< 0>				< 1>			
	congestion		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
{Hematopoietic system}										
bone marrow			< 0>				< 1>			
	erythropoiesis:increased		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
spleen			< 0>				< 1>			
	deposit of hemosiderin		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
	increased extramedullary hematopoiesis		-	-	-	-	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	Control				50ppm				100ppm				200ppm			
		No. of Animals on Study	0				0				0				0			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}																		
spleen			< 0>				< 0>				< 0>				< 0>			
	engorgement of erythrocyte		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
{Circulatory system}																		
heart			< 0>				< 0>				< 0>				< 0>			
	ground glass appearance		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	mineralization		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
{Digestive system}																		
stomach			< 0>				< 0>				< 0>				< 0>			
	inflammation:foreign body		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	hyperplasia:forestomach		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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	300ppm				400ppm			
		No. of Animals on Study	0				1			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
spleen			< 0>				< 1>			
	engorgement of erythrocyte		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
{Circulatory system}										
heart			< 0>				< 1>			
	ground glass appearance		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
	mineralization		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
{Digestive system}										
stomach			< 0>				< 1>			
	inflammation:foreign body		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
	hyperplasia:forestomach		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)

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

Organ	Findings	Group Name	Control				50ppm				100ppm				200ppm			
		No. of Animals on Study	0				0				0				0			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
liver			< 0>				< 0>				< 0>				< 0>			
	mineralization:central		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	vacuolic change: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	300ppm				400ppm			
		No. of Animals on Study	0				1			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Digestive system}										
liver			< 0>				< 1>			
	mineralization:central		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
	vacuolic change:central		-	-	-	-	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

APPENDIX J 4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY, MOUSE : FEMALE : SACRIFICED ANIMALS

(13-WEEK STUDY)

Organ	Findings	Group Name	Control				50ppm				100ppm				200ppm			
		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>			
	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)
	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)
	necrosis: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}																		
bone marrow			<10>				<10>				<10>				<10>			
	erythropoiesis:increased		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	deposit of melanin		0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)

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	300ppm				400ppm			
		No. of Animals on Study	10				9			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			<10>				< 9>			
	respiratory metaplasia:olfactory epithelium		4	0	0	0	3	0	0	0
			(40)	(0)	(0)	(0)	(33)	(0)	(0)	(0)
	atrophy:olfactory epithelium		7	0	0	0 **	8	0	0	0 **
			(70)	(0)	(0)	(0)	(89)	(0)	(0)	(0)
	necrosis:olfactory epithelium		4	0	0	0	1	0	0	0
			(40)	(0)	(0)	(0)	(11)	(0)	(0)	(0)
{Hematopoietic system}										
bone marrow			<10>				< 9>			
	erythropoiesis:increased		4	0	0	0	3	0	0	0
			(40)	(0)	(0)	(0)	(33)	(0)	(0)	(0)
spleen			<10>				< 9>			
	deposit of hemosiderin		0	0	0	0	9	0	0	0 **
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	deposit of melanin		1	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(11)	(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				50ppm				100ppm				200ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}																		
spleen			<10>				<10>				<10>				<10>			
	increased extramedullary hematopoiesis		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)
	engorgement of erythrocyte		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)
	megakaryocyte:increased		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)
{Circulatory system}																		
heart			<10>				<10>				<10>				<10>			
	ground glass appearance		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}																		
stomach			<10>				<10>				<10>				<10>			
	inflammation:foreign body		0	0	0	0	0	0	0	0	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	300ppm				400ppm			
		No. of Animals on Study	10				9			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
spleen			<10>				< 9>			
	increased extramedullary hematopoiesis		5	0	0	0 *	4	5	0	0 **
			(50)	(0)	(0)	(0)	(44)	(56)	(0)	(0)
	engorgement of erythrocyte		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	megakaryocyte:increased		3	0	0	0	9	0	0	0 **
			(30)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Circulatory system}										
heart			<10>				< 9>			
	ground glass appearance		3	0	0	0	4	1	3	0 **
			(30)	(0)	(0)	(0)	(44)	(11)	(33)	(0)
	mineralization		0	0	0	0	8	1	0	0 **
			(0)	(0)	(0)	(0)	(89)	(11)	(0)	(0)
{Digestive system}										
stomach			<10>				< 9>			
	inflammation:foreign body		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(22)	(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				50ppm				100ppm				200ppm			
		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	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
liver			<10>				<10>				<10>				<10>			
	necrosis:focal		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	swelling:central		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization: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>			
	hydronephrosis		0	0	2	0	0	0	1	0	0	0	0	0	0	0	0	0
			(0)	(0)	(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Endocrine system}																		
pituitary			<10>				<10>				<10>				<10>			
	congestion		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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	300ppm				400ppm			
		No. of Animals on Study	10				9			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
stomach			<10>				< 9>			
	hyperplasia:forestomach		5	5	0	0 **	4	3	2	0 **
			(50)	(50)	(0)	(0)	(44)	(33)	(22)	(0)
liver			<10>				< 9>			
	necrosis:focal		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(11)	(0)	(0)	(0)
	swelling:central		7	0	0	0 **	8	1	0	0 **
			(70)	(0)	(0)	(0)	(89)	(11)	(0)	(0)
	mineralization:central		0	0	0	0	2	6	0	0 **
			(0)	(0)	(0)	(0)	(22)	(67)	(0)	(0)
{Urinary system}										
kidney			<10>				< 9>			
	hydronephrosis		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Endocrine system}										
pituitary			<10>				< 9>			
	congestion		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(11)	(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 1 (%)	Control 10 2 (%)	Control 10 3 (%)	Control 10 4 (%)	50ppm 10 1 (%)	50ppm 10 2 (%)	50ppm 10 3 (%)	50ppm 10 4 (%)	100ppm 10 1 (%)	100ppm 10 2 (%)	100ppm 10 3 (%)	100ppm 10 4 (%)	200ppm 10 1 (%)	200ppm 10 2 (%)	200ppm 10 3 (%)	200ppm 10 4 (%)
{Endocrine system}																		
thyroid		<10>																
	ultimibranchial body remanet		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
parathyroid		<10>																
	cyst		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
adrenal		<10>																
	congestion		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

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	300ppm				400ppm			
		No. of Animals on Study	10				9			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Endocrine system}										
thyroid			<10>				< 9>			
	ultimibranchial body remanet		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
parathyroid			<10>				< 9>			
	cyst		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
adrenal			<10>				< 9>			
	congestion		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(11)	(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 1

IDENTITY OF 1,2-DICHLOROPROPANE IN THE 13-WEEK INHALATION STUDY

IDENTITY OF 1,2-DICHLOROPROPANE IN THE 13-WEEK INHALATION STUDY

Test Substance : 1,2-Dichloropropane (Wako Pure Chemical Industries, Ltd.)

Lot No. : LDL5937

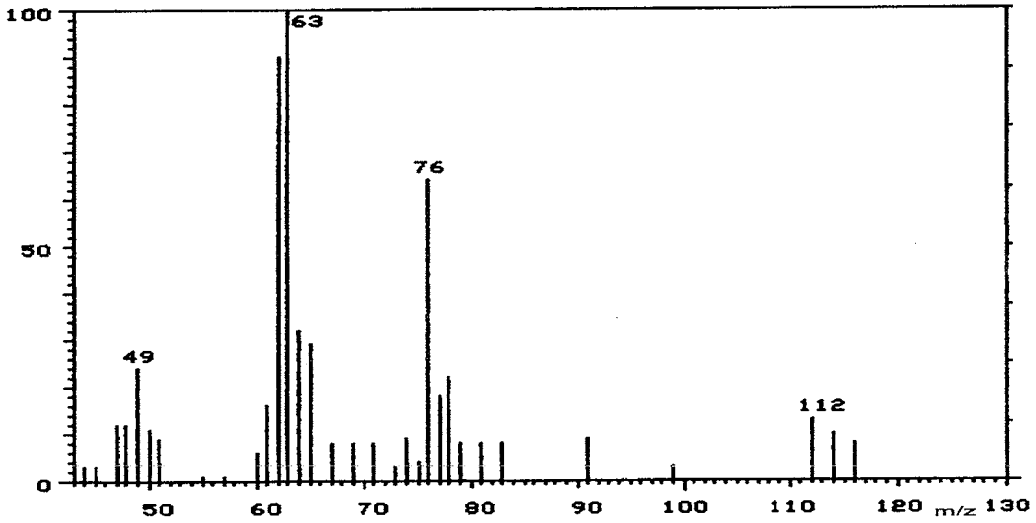
1. Spectral Data

Mass Spectrometry

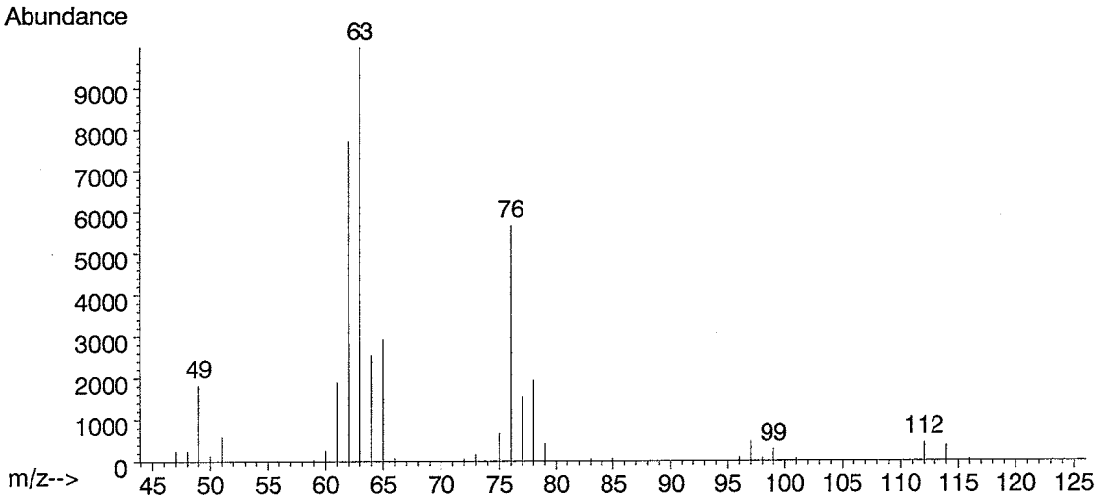
Instrument : Hitachi M-80B Mass Spectrometer

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.

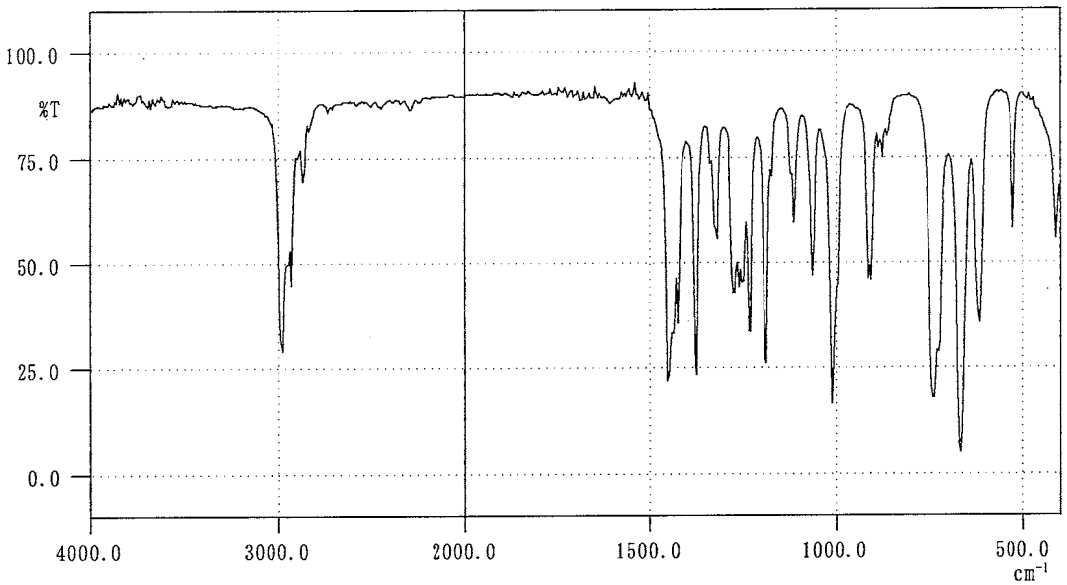
(*McLafferty F. W. (1994)
Wiley Registry of Mass Spectral Data, (6th edition), Entry Number 10229.
John Wiley and Sons, New York, NY)

Infrared Spectrometry

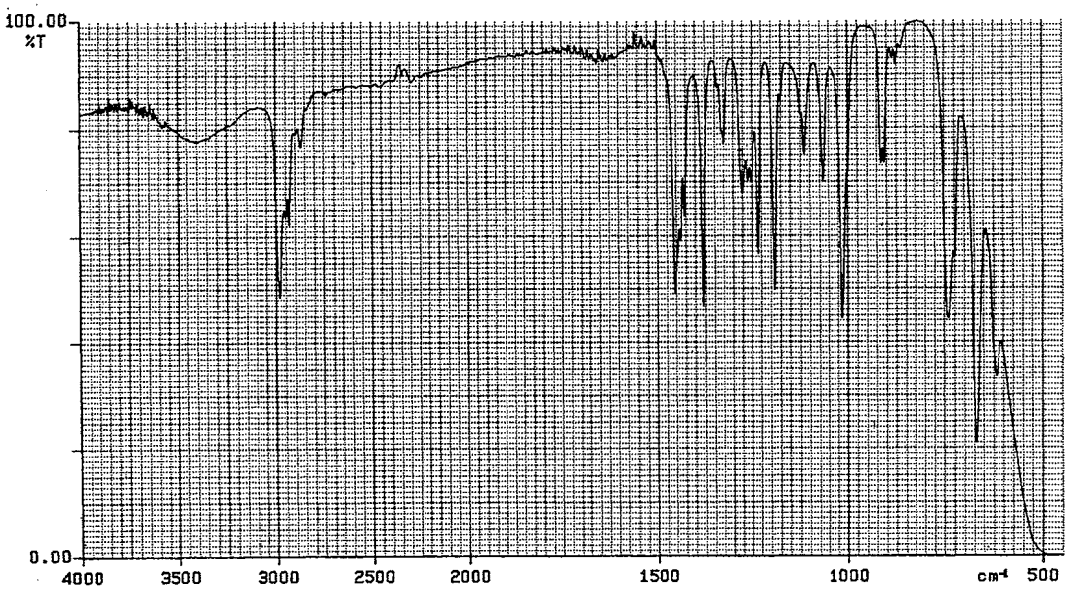
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 4 cm^{-1}



Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data*

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

2. Conclusion: The test substance was identified as 1,2-dichloropropane by the mass spectrum and the infrared spectrum.

APPENDIX K 2

STABILITY OF 1,2-DICHLOROPROPANE IN THE 13-WEEK INHALATION STUDY

STABILITY OF 1,2-DICHLOROPROPANE IN THE 13-WEEK INHALATION STUDY

Test Substance : 1,2-Dichloropropane (Wako Pure Chemical Industries, Ltd.)

Lot No. : LDL5937

1. Sample : This lot was used from 2001.9.12 to 2001.12.11. Test substance was stored in a dark place at room temperature.

2. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : Methyl Silicone (0.53 mmϕ × 60 m)

Column Temperature: 100° C

Flow Rate : 15 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μL

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
2001.08.21	1	3.348	99.72
	2	4.659	0.28
2001.12.17	1	3.347	99.71
	2	4.658	0.29

Result: Gas chromatography indicated one major peak (peak No.1) and one impurity (peak No.2 < 0.3% of total area) analyzed on 2001.8.21 and one major peak (peak No.1) and one impurity (peak No.2 < 0.3% of total area) analyzed on 2001.12.17. No new trace impurity peak in the test substance analyzed on 2001.12.17 was detected.

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

APPENDIX L 1

CONCENTRATION OF 1,2-DICHLOROPROPANE IN THE INHALATION CHAMBER OF THE 13-WEEK INHALATION STUDY

CONCENTRATION OF 1,2-DICHLOROPROPANE IN THE INHALATION CHAMBER
OF THE 13-WEEK INHALATION STUDY

Group Name	Concentration(ppm) Mean ± S.D.
Control	0.0 ± 0.0
50 ppm	50.0 ± 0.3
100 ppm	100.1 ± 0.8
200 ppm	200.0 ± 1.2
300 ppm	300.2 ± 1.4
400 ppm	399.9 ± 2.6

APPENDIX L 2

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 13-WEEK INHALATION STUDY OF 1,2-DICHLOROPROPANE

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 13-WEEK INHALATION STUDY OF 1,2-DICHLOROPROPANE

Group Name	Temperature(℃) Mean ± S.D.	Humidity(%) Mean ± S.D.	Ventilation Rate(L/min) Mean ± S.D.	Air Change(time/h) Mean
Control	22.3 ± 0.1	57.8 ± 1.0	104.5 ± 0.3	12.1
50ppm	22.4 ± 0.1	57.8 ± 0.9	104.3 ± 0.5	12.0
100ppm	22.3 ± 0.1	57.6 ± 0.8	104.2 ± 0.4	12.0
200ppm	22.2 ± 0.1	56.4 ± 1.0	104.4 ± 0.5	12.0
300ppm	22.4 ± 0.1	56.0 ± 1.1	104.5 ± 0.5	12.1
400ppm	22.1 ± 0.1	55.6 ± 1.3	104.8 ± 0.4	12.1

APPENDIX M 1

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS IN THE 13-WEEK INHALATION STUDY OF 1,2-DICHLOROPROPANE

METHODS FOR HEMATOLOGY,BIOCHEMISTRY AND URINALYSIS IN THE 13-WEEK INHALATION STUDY OF 1,2-DICHLOROPROPANE

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 M 2

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK INHALATION STUDY OF 1,2-DICHLOROPROPANE

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK INHALATION STUDY OF 1,2-DICHLOROPROPANE

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