シクロヘキセンのマウスを用いた
吸入による 13 週間毒性試験報告書

試験番号：０３６４

APPENDIX

APPENDIXES

APPENDIXES (CONTINUED)

APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, MOUSE : MALE

(13 - WEEK STUDY)

STUDY NO. : 0364
ANIMAL : MOUSE Crj : BDF1
REPORT TYPE : A1 13
SEX : MALE

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

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
Non Remarkable	0 ppm													
	20 ppm													
	40 ppm													
	75 ppm													
	150 ppm													
	300 ppm													

APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, MOUSE : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0364
ANIMAL : MOUSE Crj : BDF1
REPORT TYPE : A1 13
SEX : FEMALE

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

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
Non Remarkable	0 ppm													
	20 ppm													
	40 ppm													
	75 ppm													
	150 ppm													
	300 ppm													

APPENDIX B 1

BODY WEIGHT CHANGES :SUMMARY, MOUSE : MALE

(13 - WEEK STUDY)

STUDY NO. : 0364
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± 0.8	24.9± 1.0	26.0± 0.8	26.7± 0.7	27.4± 0.7	28.2± 1.0	29.2± 1.3
20ppm	23.0± 0.8	24.4± 0.9	25.7± 0.8	26.2± 1.0	26.5± 1.1	27.2± 1.2	28.1± 1.0
40ppm	23.0± 0.7	24.1± 0.9	25.0± 1.1	25.7± 1.2	25.9± 1.2*	26.7± 1.4	27.1± 1.3**
75ppm	23.0± 0.8	24.5± 0.9	24.8± 1.0	25.4± 1.0	25.6± 1.1**	26.4± 1.4	27.2± 1.2**
150ppm	23.0± 0.8	24.9± 1.0	25.4± 1.2	26.0± 1.2	26.5± 1.3	27.0± 1.3	27.6± 1.6*
300ppm	23.0± 0.8	24.2± 1.1	25.3± 0.9	25.8± 0.9	26.4± 1.0	26.7± 1.4	27.1± 1.0**

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

STUDY NO. : 0364
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	29.6± 1.4	30.4± 1.5	31.0± 1.5	31.6± 1.5	32.3± 1.6	33.0± 1.9	33.6± 1.8
20ppm	28.0± 1.1	29.1± 1.4	29.4± 1.3	30.1± 1.2	30.7± 1.4	31.8± 1.5	31.9± 1.1
40ppm	27.6± 1.5*	27.9± 1.5**	28.5± 1.8**	29.4± 2.0	29.8± 1.9*	30.3± 2.0*	30.6± 1.9**
75ppm	27.8± 1.9*	28.5± 1.8*	28.9± 1.9*	30.0± 2.4	30.7± 2.5	31.1± 2.6	30.8± 2.7**
150ppm	28.1± 1.6	28.6± 1.6	29.3± 1.9	29.9± 2.1	30.4± 2.0	31.4± 2.1	31.1± 1.9*
300ppm	27.6± 1.2*	28.1± 1.5**	28.2± 0.9**	29.2± 1.2	29.3± 1.2**	30.1± 1.0**	30.1± 1.3**

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. : 0364
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± 0.5	20.0± 0.8	21.1± 1.0	21.6± 0.9	22.2± 1.0	22.7± 0.8	23.2± 1.4
20ppm	19.1± 0.5	19.5± 0.7	21.3± 0.5	21.6± 0.7	22.1± 0.7	22.8± 1.0	23.8± 0.9
40ppm	19.1± 0.5	19.9± 0.6	20.8± 0.5	21.9± 0.8	21.7± 0.6	21.8± 0.9	22.9± 0.6
75ppm	19.1± 0.5	20.2± 0.9	21.1± 0.7	21.7± 0.6	22.2± 1.2	22.8± 1.0	23.7± 0.8
150ppm	19.1± 0.5	19.7± 0.8	20.7± 1.1	21.2± 0.7	21.6± 0.9	22.4± 0.7	23.3± 1.2
300ppm	19.1± 0.5	19.5± 0.6	20.2± 0.9	21.1± 0.9	21.3± 1.0	21.8± 0.9	22.0± 1.1*

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

STUDY NO. : 0364
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	23.3± 0.9	24.2± 1.1	24.2± 1.0	24.4± 1.5	24.4± 1.1	25.2± 1.3	25.2± 1.2
20ppm	23.7± 1.2	23.8± 0.5	24.3± 1.3	24.8± 1.1	24.8± 0.8	25.3± 0.6	25.4± 1.3
40ppm	23.0± 0.9	23.5± 0.9	23.8± 0.9	23.9± 1.0	24.2± 0.9	24.5± 0.8	24.9± 0.8
75ppm	23.7± 1.0	23.9± 1.3	24.0± 1.0	24.6± 1.1	24.4± 0.8	24.9± 1.1	25.1± 1.0
150ppm	23.1± 1.2	23.3± 0.7	23.7± 1.5	24.3± 1.4	24.5± 1.8	24.8± 1.2	24.6± 0.8
300ppm	23.3± 1.1	23.4± 1.2	23.1± 1.5	23.7± 0.9	24.3± 2.1	24.5± 1.4	24.4± 1.1

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. : 0364
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	4.1± 0.3	4.2± 0.2	4.1± 0.3	4.2± 0.4	4.2± 0.4	4.4± 0.4	4.3± 0.4
20ppm	4.2± 0.2	4.1± 0.2	4.2± 0.3	4.3± 0.3	4.5± 0.5	4.4± 0.3	4.4± 0.4
40ppm	4.1± 0.2	4.0± 0.3	4.0± 0.2	4.1± 0.2	4.3± 0.3	4.2± 0.3	4.3± 0.3
75ppm	4.2± 0.3	4.0± 0.2	4.0± 0.2	4.2± 0.3	4.2± 0.3	4.3± 0.3	4.3± 0.3
150ppm	4.3± 0.2	4.0± 0.2	4.0± 0.2	4.2± 0.2	4.2± 0.3	4.3± 0.3	4.3± 0.2
300ppm	4.1± 0.2	4.0± 0.1	4.0± 0.2	4.1± 0.2	4.0± 0.1	4.1± 0.1	4.2± 0.2

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

STUDY NO. : 0364
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	4.4± 0.4	4.4± 0.5	4.6± 0.4	4.5± 0.4	4.6± 0.4	4.5± 0.3
20ppm	4.6± 0.3	4.6± 0.3	4.6± 0.3	4.7± 0.3	4.9± 0.3	4.6± 0.3
40ppm	4.3± 0.2	4.4± 0.3	4.4± 0.3	4.3± 0.2	4.6± 0.3	4.5± 0.2
75ppm	4.4± 0.3	4.4± 0.3	4.5± 0.4	4.4± 0.3	4.5± 0.3	4.3± 0.4
150ppm	4.4± 0.3	4.5± 0.4	4.4± 0.3	4.5± 0.3	4.7± 0.3	4.5± 0.2
300ppm	4.2± 0.2	4.2± 0.1	4.2± 0.2	4.2± 0.2	4.5± 0.1	4.4± 0.2

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. : 0364
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± 0.2	3.6± 0.2	3.8± 0.1	3.8± 0.1	4.0± 0.2	4.0± 0.2
20ppm	3.6± 0.2	3.7± 0.1	3.8± 0.2*	4.1± 0.1*	4.2± 0.2**	4.3± 0.2*	4.3± 0.2
40ppm	3.5± 0.3	3.4± 0.2	3.5± 0.2	3.7± 0.2	3.8± 0.2	3.9± 0.2	4.0± 0.3
75ppm	3.5± 0.2	3.6± 0.2	3.7± 0.2	4.0± 0.3	4.1± 0.2**	4.1± 0.2	4.3± 0.2
150ppm	3.5± 0.1	3.6± 0.2	3.6± 0.2	3.9± 0.3	4.0± 0.3	4.1± 0.2	4.2± 0.4
300ppm	3.5± 0.2	3.3± 0.1*	3.5± 0.2	3.6± 0.2	3.8± 0.2	3.9± 0.2	4.0± 0.2

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

STUDY NO. : 0364
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	4.1± 0.2	4.2± 0.3	4.1± 0.3	4.1± 0.3	4.2± 0.3	4.1± 0.2
20ppm	4.3± 0.2	4.3± 0.3	4.3± 0.2	4.3± 0.1	4.6± 0.2**	4.3± 0.3
40ppm	4.2± 0.2	4.2± 0.3	4.1± 0.3	4.1± 0.2	4.4± 0.3	4.3± 0.3
75ppm	4.2± 0.3	4.3± 0.2	4.4± 0.2	4.3± 0.2	4.5± 0.2*	4.3± 0.3
150ppm	4.2± 0.3	4.2± 0.3	4.3± 0.3	4.2± 0.3	4.4± 0.2	4.4± 0.4
300ppm	4.0± 0.3	4.0± 0.3	4.1± 0.2	3.9± 0.3	4.4± 0.5	4.1± 0.2

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

APPENDIX D 1

HEMATOLOGY : SUMMARY, MOUSE : MALE

(13 - WEEK STUDY)

STUDY NO. : 0364
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 fℓ	MCH pg	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	8	10.78± 0.16	15.8± 0.2	50.9± 1.0	47.2± 0.5	14.6± 0.2	31.0± 0.3	1434± 67
20ppm	10	10.84± 0.36	15.9± 0.5	51.2± 1.5	47.3± 0.6	14.7± 0.3	31.0± 0.2	1284± 124**
40ppm	9	10.75± 0.25	15.7± 0.3	50.7± 1.8	47.1± 0.6	14.6± 0.1	30.9± 0.5	1347± 47
75ppm	10	10.80± 0.34	15.8± 0.5	50.9± 1.6	47.1± 0.6	14.7± 0.2	31.1± 0.3	1360± 79
150ppm	10	10.73± 0.29	15.8± 0.5	50.6± 1.7	47.2± 0.5	14.7± 0.2	31.1± 0.4	1357± 97
300ppm	10	10.58± 0.45	15.6± 0.7	50.4± 2.4	47.7± 0.5	14.7± 0.1	30.9± 0.3	1351± 83

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

STUDY NO. : 0364
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	8	1.85± 0.46	1± 1	14± 1	1± 1	0± 0	5± 2	79± 3	0± 0
20ppm	10	1.60± 1.07	1± 1	17± 5	1± 1	0± 0	5± 3	76± 5	0± 0
40ppm	9	1.60± 0.71	1± 1	19± 7	1± 1	0± 0	2± 1	76± 8	0± 0
75ppm	10	2.11± 1.01	1± 1	12± 2	1± 1	0± 0	4± 2	82± 3	0± 0
150ppm	10	1.71± 1.04	1± 2	18± 6	3± 3	0± 0	5± 2	74± 11	0± 0
300ppm	10	1.17± 0.73	1± 1	16± 5	1± 1	0± 0	4± 3	79± 3	0± 0

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

(HCL070)

APPENDIX D 2

HEMATOLOGY : SUMMARY, MOUSE : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0364
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 fℓ	MCH pg	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	9	10.65± 0.32	15.8± 0.5	50.5± 1.8	47.4± 0.5	14.8± 0.1	31.2± 0.4	1206± 89
20ppm	10	10.69± 0.34	15.8± 0.4	50.3± 1.4	47.1± 0.7	14.8± 0.3	31.4± 0.4	1232± 88
40ppm	10	10.51± 0.22	15.6± 0.3	49.5± 1.1	47.1± 0.4	14.9± 0.1	31.5± 0.4	1165± 39
75ppm	10	10.49± 0.23	15.5± 0.4	49.4± 1.3	47.1± 0.6	14.7± 0.2	31.3± 0.4	1226± 73
150ppm	10	10.73± 0.40	15.9± 0.6	50.8± 1.9	47.4± 0.4	14.8± 0.1	31.3± 0.4	1210± 83
300ppm	10	10.42± 0.26	15.5± 0.3	49.5± 1.2	47.5± 0.5	14.9± 0.1	31.4± 0.3	1238± 55

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

STUDY NO. : 0364
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	9	1.05±	0.55	2±	3	18±	6	1±	2	0±	0	3±	2	76±	6	0±	0
20ppm	10	1.18±	1.06	0±	1	23±	16	0±	1	0±	0	2±	2	74±	14	0±	0
40ppm	10	0.68±	0.42	0±	0	24±	10	0±	0	0±	0	6±	4	70±	12	0±	0
75ppm	10	0.76±	0.71	0±	0	16±	7	0±	0	0±	0	3±	5	81±	10	0±	0
150ppm	10	1.04±	0.97	1±	2	16±	7	1±	1	0±	0	4±	4	79±	8	0±	0
300ppm	10	0.67±	0.61	1±	2	18±	4	0±	0	0±	0	3±	4	79±	6	0±	0

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

APPENDIX E 1

BIOCHEMISTRY : SUMMARY, MOUSE : MALE

(13 - WEEK STUDY)

STUDY NO. : 0364
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	9	5.1± 0.3	2.9± 0.1	1.4± 0.1	0.15± 0.03	182± 44	80± 11	41± 19
20ppm	10	4.9± 0.1	2.9± 0.1	1.4± 0.1	0.14± 0.01	147± 37	70± 7**	23± 7
40ppm	9	4.8± 0.1	2.8± 0.1	1.4± 0.1	0.14± 0.01	152± 29	69± 5**	25± 8
75ppm	10	4.9± 0.1	2.9± 0.1	1.4± 0.1	0.14± 0.01	164± 29	68± 5**	25± 8
150ppm	10	4.9± 0.1	2.9± 0.1	1.4± 0.1	0.14± 0.01	166± 37	70± 7*	27± 10
300ppm	10	4.8± 0.1	2.8± 0.1	1.4± 0.1	0.14± 0.02	176± 27	76± 8	27± 6

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

STUDY NO. : 0364
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	9	169± 22	40± 5	18± 5	183± 90	137± 6	2± 1	46± 20
20ppm	10	146± 16*	45± 8	18± 3	176± 40	145± 14	2± 1	59± 44
40ppm	9	145± 13**	44± 3	17± 2	162± 18	137± 12	2± 1	43± 4
75ppm	10	144± 11**	42± 4	19± 2	158± 21	143± 10	1± 1	45± 17
150ppm	10	148± 14*	45± 15	20± 4	162± 28	143± 16	2± 1	40± 15
300ppm	10	152± 15	40± 6	18± 2	166± 33	143± 13	2± 1	38± 13

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

STUDY NO. : 0364
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	9	27.1± 4.4	152± 2	4.6± 0.3	123± 2	8.7± 0.4	7.1± 0.9
20ppm	10	26.6± 3.7	152± 2	4.4± 0.3	123± 2	8.7± 0.3	7.7± 1.2
40ppm	9	25.4± 1.7	152± 1	4.4± 0.1	123± 2	8.6± 0.2	7.0± 0.6
75ppm	10	24.2± 3.0	151± 1	4.7± 0.3	123± 2	8.6± 0.3	7.3± 0.9
150ppm	10	23.6± 2.5	152± 1	4.5± 0.2	123± 2	8.6± 0.3	6.6± 1.0
300ppm	10	23.3± 4.1	151± 2	4.5± 0.2	122± 1	8.5± 0.2	6.7± 0.7

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

APPENDIX E 2

BIOCHEMISTRY : SUMMARY, MOUSE : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0364
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	9	5.1± 0.2	3.2± 0.1	1.6± 0.1	0.13± 0.03	155± 20	69± 7	19± 3
20ppm	10	5.1± 0.1	3.2± 0.1	1.6± 0.1	0.13± 0.01	142± 24	71± 9	24± 13
40ppm	10	5.1± 0.2	3.2± 0.1	1.6± 0.1	0.15± 0.02	145± 27	67± 6	18± 6
75ppm	10	5.1± 0.1	3.2± 0.1	1.7± 0.1	0.13± 0.01	153± 18	67± 8	15± 5
150ppm	10	5.1± 0.2	3.2± 0.1	1.7± 0.1	0.14± 0.02	150± 30	68± 8	20± 8
300ppm	10	5.1± 0.2	3.2± 0.1	1.7± 0.1	0.14± 0.01	161± 33	70± 6	17± 5

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

STUDY NO. : 0364
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	9	139± 16	51± 10	22± 4	195± 49	230± 30	2± 1	71± 43
20ppm	10	143± 25	70± 27	24± 6	274± 124	226± 20	2± 1	119± 70
40ppm	10	132± 17	67± 23	26± 4	280± 114	231± 15	2± 1	98± 75
75ppm	10	133± 21	68± 12	28± 7	242± 75	234± 18	2± 1	102± 64
150ppm	10	139± 21	62± 13	25± 3	240± 67	235± 29	2± 1	99± 36
300ppm	10	137± 16	65± 20	26± 6	257± 103	244± 21	2± 2	101± 51

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

STUDY NO. : 0364
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	9	21.9± 2.2	151± 2	4.6± 0.2	122± 2	8.7± 0.3	6.9± 1.4
20ppm	10	20.8± 2.8	151± 2	4.5± 0.2	122± 2	8.9± 0.2	7.2± 0.9
40ppm	10	21.8± 1.9	152± 1	4.6± 0.5	124± 1	8.8± 0.3	6.9± 0.7
75ppm	10	22.2± 2.9	152± 1	4.6± 0.4	124± 2	8.8± 0.3	6.9± 0.6
150ppm	10	21.4± 2.7	151± 1	4.5± 0.4	122± 2	8.8± 0.2	7.0± 1.0
300ppm	10	22.7± 2.4	152± 2	4.6± 0.4	123± 3	8.7± 0.2	7.0± 0.9

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

APPENDIX F 1

URINALYSIS : SUMMARY, MOUSE : MALE

(13 - WEEK STUDY)

STUDY NO. : 0364
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	1	7	2		0	0	7	3	0	0		10	0	0	0	0	0		0	5	5	0	0	0		10	0	0	0	0	
20ppm	10	0	0	0	1	3	4	2		0	0	6	3	1	0		10	0	0	0	0	0		1	5	3	1	0	0		10	0	0	0	0	
40ppm	10	0	0	0	0	3	7	0		0	0	6	4	0	0		10	0	0	0	0	0		0	3	7	0	0	0		10	0	0	0	0	
75ppm	10	0	0	0	0	2	7	1		0	0	7	3	0	0		10	0	0	0	0	0		0	4	6	0	0	0		10	0	0	0	0	
150ppm	10	0	0	0	0	3	6	1		0	0	7	3	0	0		10	0	0	0	0	0		0	7	3	0	0	0		10	0	0	0	0	
300ppm	10	0	0	1	0	2	6	1		0	0	6	3	1	0		10	0	0	0	0	0		0	5	4	0	1	0		10	0	0	0	0	

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

STUDY NO. : 0364
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	
20ppm	10	10	0	0	0	0	
40ppm	10	10	0	0	0	0	
75ppm	10	10	0	0	0	0	
150ppm	10	10	0	0	0	0	
300ppm	10	10	0	0	0	0	

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

APPENDIX F 2

URINALYSIS : SUMMARY, MOUSE : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0364
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	0	0	1	2	6	1		0	0	5	5	0	0		10	0	0	0	0	0		0	8	1	1	0	0		10	0	0	0	0	
20ppm	10	0	0	0	2	4	4	0		0	0	7	3	0	0		10	0	0	0	0	0		0	5	4	1	0	0		10	0	0	0	0	
40ppm	10	0	0	0	2	6	2	0		0	0	7	3	0	0		10	0	0	0	0	0		0	6	4	0	0	0		10	0	0	0	0	
75ppm	10	0	1	1	2	2	4	0		0	3	7	0	0	0	*	10	0	0	0	0	0		1	8	1	0	0	0		10	0	0	0	0	
150ppm	10	0	0	0	1	3	6	0		0	1	8	1	0	0		10	0	0	0	0	0		0	8	1	1	0	0		10	0	0	0	0	
300ppm	10	0	0	0	1	2	7	0		0	0	8	2	0	0		10	0	0	0	0	0		1	6	3	0	0	0		10	0	0	0	0	

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

STUDY NO. : 0364
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	
20ppm	10	10	0	0	0	0	
40ppm	10	10	0	0	0	0	
75ppm	10	10	0	0	0	0	
150ppm	10	10	0	0	0	0	
300ppm	10	10	0	0	0	0	

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

APPENDIX G 1

GROSS FINDINGS : SUMMARY, MOUSE : MALE

ALL ANIMALS

(13 - WEEK STUDY)

STUDY NO. : 0364
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 (%)	20ppm 10 (%)	40ppm 10 (%)	75ppm 10 (%)
lung	nodule		1 (10)	0 (0)	0 (0)	0 (0)
spleen	black zone		0 (0)	0 (0)	2 (20)	3 (30)
kidney	white zone		1 (10)	0 (0)	0 (0)	0 (0)
	hydronephrosis		0 (0)	1 (10)	0 (0)	0 (0)

STUDY NO. : 0364
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name NO. of Animals	150ppm 10 (%)	300ppm 10 (%)
lung	nodule		0 (0)	0 (0)
spleen	black zone		2 (20)	2 (20)
kidney	white zone		0 (0)	0 (0)
	hydronephrosis		0 (0)	0 (0)

APPENDIX G 2

GROSS FINDINGS : SUMMARY, MOUSE : FEMALE

ALL ANIMALS

(13 - WEEK STUDY)

STUDY NO. : 0364
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 (%)	20ppm 10 (%)	40ppm 10 (%)	75ppm 10 (%)
spleen	black zone		2 (20)	0 (0)	1 (10)	0 (0)

STUDY NO. : 0364
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name	150ppm	300ppm
		NO. of Animals	10 (%)	10 (%)
spleen	black zone		0 (0)	0 (0)

APPENDIX H 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOUSE : MALE

(13 - WEEK STUDY)

STUDY NO. : 0364
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	30.3± 1.7	0.041± 0.007	0.010± 0.002	0.230± 0.020	0.169± 0.019	0.165± 0.010
20ppm	10	28.2± 1.3	0.035± 0.006	0.009± 0.002	0.217± 0.033	0.177± 0.017	0.162± 0.008
40ppm	10	27.4± 2.2**	0.035± 0.004	0.008± 0.002	0.227± 0.019	0.174± 0.018	0.162± 0.007
75ppm	10	28.0± 2.6*	0.038± 0.006	0.008± 0.003	0.223± 0.023	0.174± 0.018	0.165± 0.013
150ppm	10	28.3± 1.9	0.036± 0.008	0.008± 0.003	0.227± 0.026	0.169± 0.020	0.163± 0.010
300ppm	10	27.3± 1.2**	0.038± 0.005	0.008± 0.002	0.226± 0.027	0.158± 0.013	0.163± 0.010

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

STUDY NO. : 0364
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	0.480± 0.025	0.051± 0.006	1.200± 0.082	0.448± 0.013
20ppm	10	0.501± 0.035	0.049± 0.007	1.189± 0.083	0.455± 0.006
40ppm	10	0.479± 0.032	0.049± 0.006	1.145± 0.054	0.449± 0.009
75ppm	10	0.462± 0.027	0.050± 0.005	1.133± 0.090	0.444± 0.010
150ppm	10	0.492± 0.040	0.049± 0.006	1.177± 0.087	0.441± 0.009
300ppm	10	0.465± 0.031	0.047± 0.002	1.114± 0.041	0.445± 0.009

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. : 0364
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	21.6± 1.0	0.046± 0.007	0.011± 0.002	0.032± 0.008	0.138± 0.007	0.154± 0.006
20ppm	10	21.5± 1.0	0.042± 0.005	0.011± 0.002	0.040± 0.015	0.143± 0.012	0.158± 0.010
40ppm	10	21.0± 0.8	0.042± 0.005	0.010± 0.002	0.031± 0.005	0.143± 0.017	0.152± 0.011
75ppm	10	21.3± 0.8	0.042± 0.005	0.010± 0.002	0.031± 0.005	0.141± 0.010	0.161± 0.007
150ppm	10	21.2± 0.7	0.042± 0.005	0.010± 0.002	0.033± 0.006	0.146± 0.010	0.160± 0.007
300ppm	10	20.7± 0.9	0.039± 0.005	0.011± 0.002	0.028± 0.005	0.133± 0.013	0.158± 0.010

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

STUDY NO. : 0364
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	0.310± 0.022	0.058± 0.008	0.958± 0.041	0.462± 0.008
20ppm	10	0.320± 0.022	0.057± 0.009	0.962± 0.080	0.461± 0.009
40ppm	10	0.317± 0.023	0.053± 0.006	0.923± 0.070	0.458± 0.009
75ppm	10	0.317± 0.024	0.054± 0.005	0.942± 0.073	0.463± 0.020
150ppm	10	0.318± 0.019	0.055± 0.006	0.972± 0.051	0.457± 0.014
300ppm	10	0.302± 0.018	0.052± 0.004	0.890± 0.057	0.449± 0.012

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. : 0364
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	30.3± 1.7	0.136± 0.029	0.033± 0.008	0.763± 0.086	0.556± 0.060	0.546± 0.045
20ppm	10	28.2± 1.3	0.124± 0.023	0.032± 0.009	0.770± 0.131	0.626± 0.048	0.576± 0.025
40ppm	10	27.4± 2.2**	0.126± 0.014	0.029± 0.008	0.835± 0.095	0.638± 0.062*	0.592± 0.036
75ppm	10	28.0± 2.6*	0.136± 0.013	0.029± 0.010	0.802± 0.097	0.623± 0.066	0.594± 0.060
150ppm	10	28.3± 1.9	0.126± 0.025	0.030± 0.009	0.808± 0.114	0.601± 0.077	0.579± 0.037
300ppm	10	27.3± 1.2**	0.139± 0.014	0.028± 0.009	0.829± 0.112	0.578± 0.055	0.597± 0.045

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

STUDY NO. : 0364
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	1.586± 0.101	0.167± 0.017	3.959± 0.185	1.483± 0.091
20ppm	10	1.778± 0.123**	0.173± 0.021	4.213± 0.151*	1.618± 0.089*
40ppm	10	1.753± 0.126*	0.181± 0.026	4.191± 0.188*	1.648± 0.147**
75ppm	10	1.660± 0.124	0.178± 0.015	4.056± 0.149	1.597± 0.143
150ppm	10	1.741± 0.105*	0.172± 0.016	4.168± 0.244*	1.566± 0.104
300ppm	10	1.705± 0.135	0.173± 0.013	4.083± 0.118	1.633± 0.083*

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. : 0364
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	21.6± 1.0	0.211± 0.027	0.053± 0.011	0.148± 0.032	0.641± 0.043	0.713± 0.012
20ppm	10	21.5± 1.0	0.192± 0.018	0.052± 0.012	0.187± 0.068	0.663± 0.048	0.733± 0.048
40ppm	10	21.0± 0.8	0.201± 0.021	0.045± 0.011	0.148± 0.021	0.683± 0.082	0.726± 0.052
75ppm	10	21.3± 0.8	0.198± 0.022	0.048± 0.010	0.147± 0.021	0.664± 0.044	0.759± 0.055
150ppm	10	21.2± 0.7	0.200± 0.018	0.046± 0.012	0.157± 0.028	0.689± 0.054	0.754± 0.039
300ppm	10	20.7± 0.9	0.186± 0.025	0.054± 0.011	0.133± 0.022	0.643± 0.053	0.763± 0.035

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

STUDY NO. : 0364
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	1.435± 0.126	0.266± 0.028	4.435± 0.234	2.137± 0.082
20ppm	10	1.488± 0.086	0.264± 0.044	4.464± 0.254	2.143± 0.105
40ppm	10	1.509± 0.086	0.253± 0.025	4.398± 0.217	2.184± 0.067
75ppm	10	1.490± 0.123	0.255± 0.023	4.425± 0.264	2.176± 0.115
150ppm	10	1.503± 0.089	0.257± 0.025	4.595± 0.205	2.162± 0.109
300ppm	10	1.460± 0.045	0.251± 0.019	4.306± 0.185	2.172± 0.073

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

APPENDIX J 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : MALE : ALL ANIMALS

(13 - WEEK STUDY)

STUDY NO. : 0364
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
ALL ANIMALS (0- 14W)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 10				20ppm 10				40ppm 10				75ppm 10			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Hematopoietic system]																		
spleen	deposit of melanin	<10>	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	3 (30)	0 (0)	0 (0)	0 (0)
[Digestive system]																		
salivary gl	lymphocytic infiltration	<10>	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
liver	granulation	<10>	4 (40)	0 (0)	0 (0)	0 (0)	3 (30)	0 (0)	0 (0)	0 (0)	3 (30)	0 (0)	0 (0)	0 (0)	5 (50)	0 (0)	0 (0)	0 (0)
[Urinary system]																		
kidney	hydronephrosis	<10>	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Endocrine system]																		
parathyroid	cyst	< 5>	0 (0)	0 (0)	0 (0)	0 (0)	< 6> 0 (0)	0 (0)	0 (0)	0 (0)	< 9> 1 (11)	0 (0)	0 (0)	0 (0)	<10> 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

STUDY NO. : 0364
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
ALL ANIMALS (0- 14W)

Organ	Findings	Group Name	150ppm				300ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]										
spleen	deposit of melanin		<10>				<10>			
			2	0	0	0	2	0	0	0
			(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
[Digestive system]										
salivary gl	lymphocytic infiltration		<10>				<10>			
			0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
liver	granulation		<10>				<10>			
			4	0	0	0	3	0	0	0
			(40)	(0)	(0)	(0)	(30)	(0)	(0)	(0)
[Urinary system]										
kidney	hydronephrosis		<10>				<10>			
			0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Endocrine system]										
parathyroid	cyst		< 8>				< 6>			
			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

STUDY NO. : 0364
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
ALL ANIMALS (0- 14W)

Organ	Findings	Group Name	Control				20ppm				40ppm				75ppm			
		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]																		
adrenal			<10>				<10>				<10>				<10>			
	spindle-cell hyperplasia		2	0	0	0	3	0	0	0	0	0	0	0	4	0	0	0
			(20)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(40)	(0)	(0)	(0)

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

STUDY NO. : 0364
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
ALL ANIMALS (0- 14W)

Organ	Findings	Group Name	150ppm				300ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]										
adrenal			<10>				<10>			
	spindle-cell hyperplasia		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 J 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : FEMALE: ALL ANIMALS

(13 - WEEK STUDY)

STUDY NO. : 0364
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
ALL ANIMALS (0- 14W)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 10 1 (%)	Control 10 2 (%)	Control 10 3 (%)	Control 10 4 (%)	20ppm 10 1 (%)	20ppm 10 2 (%)	20ppm 10 3 (%)	20ppm 10 4 (%)	40ppm 10 1 (%)	40ppm 10 2 (%)	40ppm 10 3 (%)	40ppm 10 4 (%)	75ppm 10 1 (%)	75ppm 10 2 (%)	75ppm 10 3 (%)	75ppm 10 4 (%)
[Hematopoietic system]																		
spleen	deposit of melanin	<10>	2 (20)	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]																		
salivary gl	lymphocytic infiltration	<10>	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)
liver	necrosis:focal	<10>	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
	granulation		3 (30)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	3 (30)	0 (0)	0 (0)	0 (0)	4 (40)	0 (0)	0 (0)	0 (0)
	extramedullary hematopoiesis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Endocrine system]																		
pituitary	cyst	<10>	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	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	150ppm				300ppm			
		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	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]										
salivary gl			<10>				<10>			
	lymphocytic infiltration		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
liver			<10>				<10>			
	necrosis:focal		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	granulation		1	0	0	0	2	0	0	0
			(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	extramedullary hematopoiesis		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Endocrine system]										
pituitary			<10>				<10>			
	cyst		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

Organ	Findings	Group Name / Grade	Control				20ppm				40ppm				75ppm			
		No. of Animals on Study	10				10				10				10			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Endocrine system]																		
parathyroid			< 9>				< 8>				<10>				< 9>			
	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>				<10>				<10>				<10>			
	spindle-cell hyperplasia		7 (70)	0 (0)	0 (0)	0 (0)	8 (80)	0 (0)	0 (0)	0 (0)	5 (50)	0 (0)	0 (0)	0 (0)	8 (80)	0 (0)	0 (0)	0 (0)

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

Organ	Findings	Group Name	150ppm				300ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]										
parathyroid			< 7>				< 8>			
	cyst		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(13)	(0)	(0)	(0)
adrenal			<10>				<10>			
	spindle-cell hyperplasia		8	0	0	0	7	0	0	0
			(80)	(0)	(0)	(0)	(70)	(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 AND IMPURITY OF CYCLOHEXENE IN THE 13 - WEEK INHALATION STUDY

IDENTITY AND IMPURITY OF CYCLOHEXENE IN THE 13-WEEK INHALATION STUDY

Test Substance : Cyclohexene (Wako Pure Chemical Industries, LTD.)

Lot No. : ACJ6186

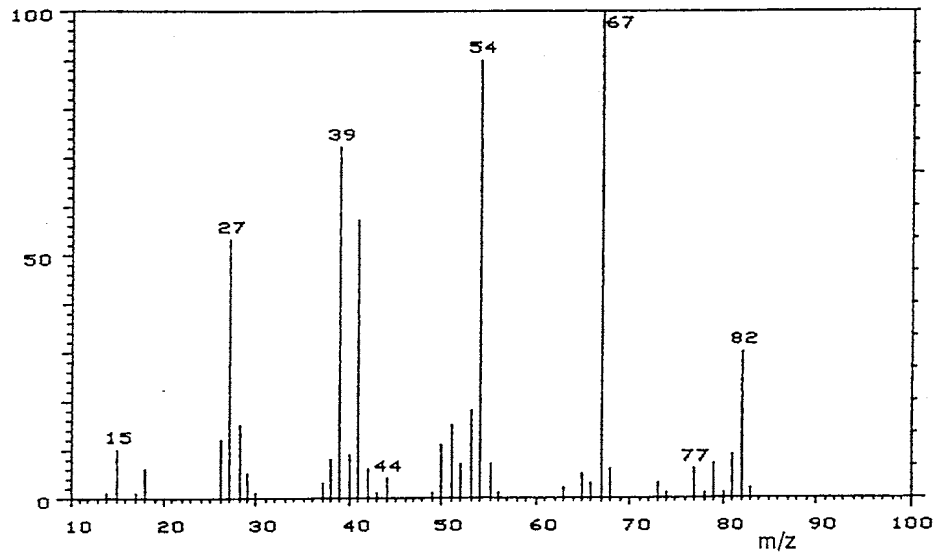
1. Spectral data

Mass Spectrometry

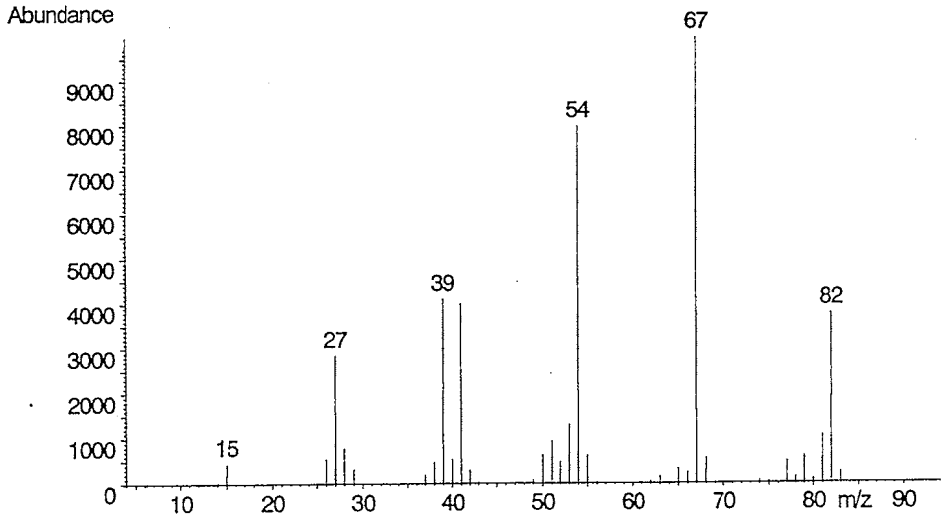
Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance



Mass Spectrum of Literature Data*

Results: The mass spectrum was consistent with literature spectrum.

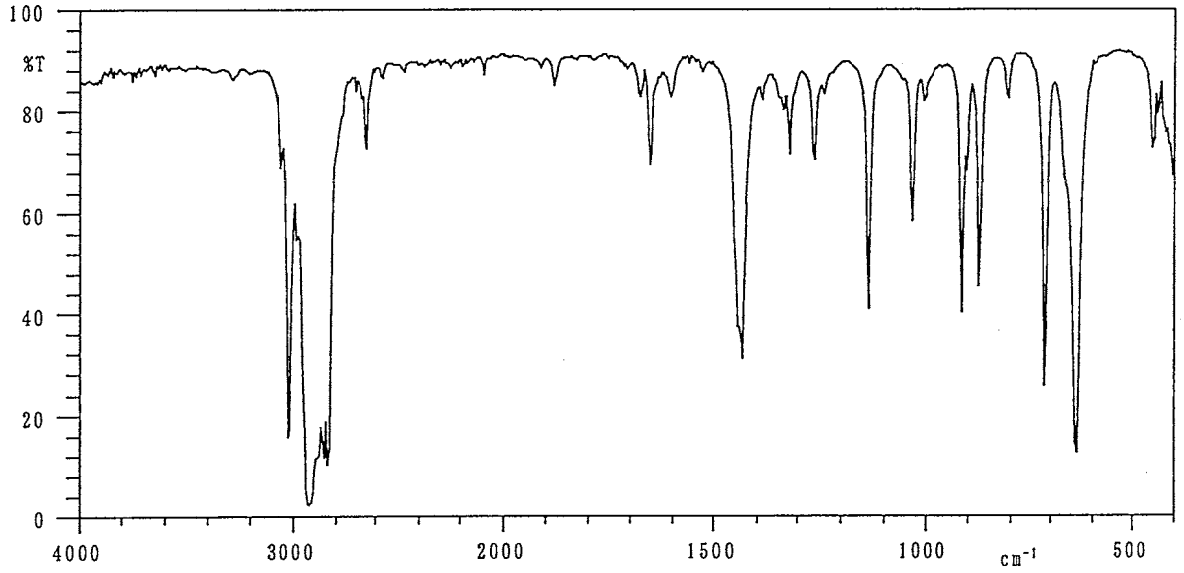
(*Fred W. McLafferty (1994) Wiley registry of mass spectral data, 6th edition. John Wiley and Sons Inc. (U.S.), Entry Number 2466)

Infrared Spectrometry

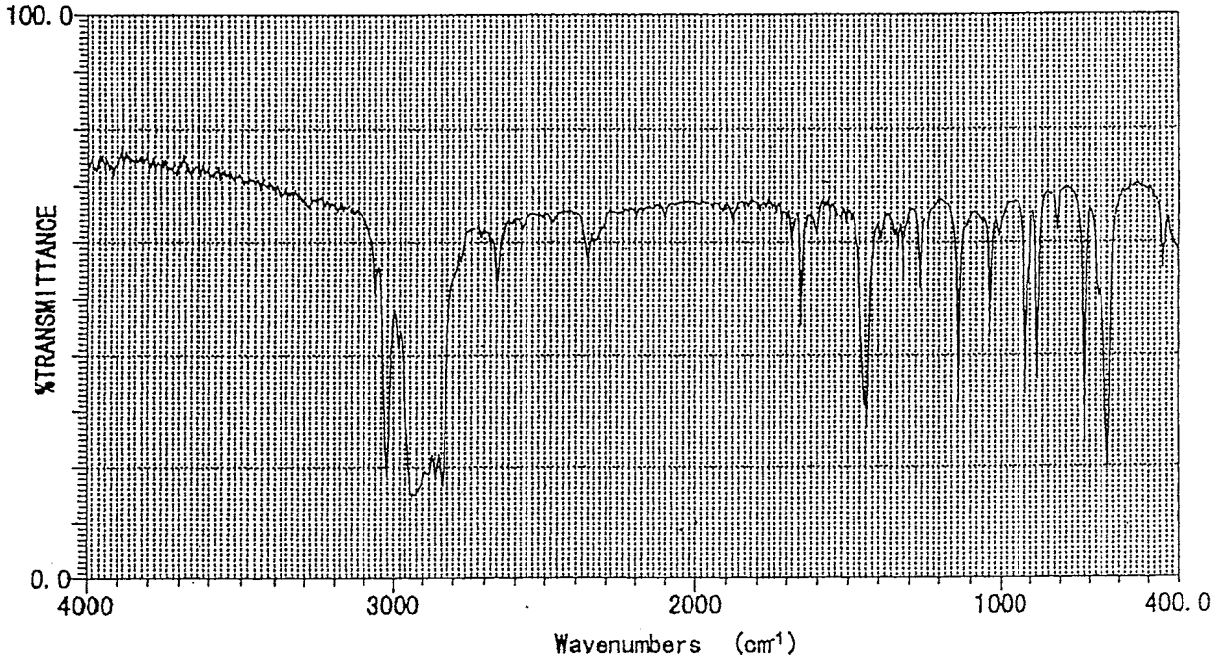
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 4 cm^{-1}



Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data*

Results: The infrared spectrum was consistent with literature spectrum.

(*Performed by the Wako Pure Chemical Industries, LTD.)

2. Impurity

Instrument	: Hewlett Packard 6890 Gas Chromatograph
Column	: Methyl Silicone (0.53 mmϕ × 60 m)
Column Temperature	: 60° C
Flow Rate	: 15 mL/min
Detector	: FID (Flame Ionization Detector)
Injection Volume	: 1 μL

Sample Name	Peak No.	Area (%)	Peak Name
Test Substance	1	0.04	1,3-Cyclodiene
	2	99.80	Cyclohexene
	3	0.16	1,4-Cyclodiene

Results: Gas chromatography indicated one major peak (peak No. 2) and two impurities. It was identified only by comparing its gas chromatograph with that of 1,3-Cyclodiene (peak No. 1) and 1,4-Cyclodiene (peak No. 3) in the Cyclohexene, the amount in the test substance were 0.04% and 0.16%.

3. Conclusions: The test substance was identified as Cyclohexene, by the mass spectrum and the infrared spectrum. Gas chromatography indicated one major peak (peak No. 2) and two impurities. It was identified only by comparing its gas chromatograph with that of 1,3-Cyclodiene and 1,4-Cyclodiene, the amount in the test substance were 0.04% and 0.16%.

APPENDIX K 2

STABILITY OF CYCLOHEXENE IN THE 13 - WEEK INHALATION STUDY

STABILITY OF CYCLOHEXENE IN THE 13-WEEK INHALATION STUDY

Test Substance : Cyclohexene (Wako Pure Chemical Industries, LTD.)

Lot No. : ACJ6186

1. Sample : This lot was used from 1998.9.8 to 1998.12.7. Test substance was stored in a dark place at room temperature.

2. Gas Chromatography

Instrument : Hewlett Packard 6890 Gas Chromatograph

Column : Methyl silicone (0.53 mmϕ × 60 m)

Column Temperature : 60° C

Flow Rate : 15 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μL

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
1998.09.03	1	7.48	0.04
	2	8.80	99.79
	3	9.67	0.16
1998.12.25	1	7.48	0.04
	2	8.81	99.80
	3	9.67	0.16

Results: Gas chromatography indicated one major peak (peak No. 2) and two impurities (peak No. 1, 3 < 0.3% of total area) analyzed at 1998.9.3 and one major peak (peak No. 2) and two impurities (peak No. 1, 3 < 0.3% of total area) analyzed at 1998.12.25. No new trace impurity peak in the test substance analyzed at 1998.12.25 was detected.

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

APPENDIX L 1

CONCENTMOUSEION OF CYCLOHEXENE IN THE INHALATION CHAMBER

OF THE 13-WEEK INHALATION STUDY

CONCENTRATION OF CYCLOHEXENE IN THE INHALATION CHAMBER OF THE 13-WEEK INHALATION STUDY

Group Name	Concentration(ppm) Mean ± S.D.
0ppm(Control)	0.0 ± 0.0
20ppm	19.8 ± 0.2
40ppm	40.0 ± 0.3
75ppm	74.9 ± 0.4
150ppm	150.1 ± 1.1
300ppm	300.1 ± 2.0

APPENDIX L 2

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE

13 - WEEK INHALATION STUDY OF CYCLOHEXENE

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 13-WEEK INHALATION STUDY OF CYCLOHEXENE

Group Name	Temperature(℃) Mean ± S.D.	Humidity(%) Mean ± S.D.	Ventilation Rate(L/min) Mean ± S.D.	Air Change(time/h) Mean
0ppm(Control)	22.5 ± 0.1	56.6 ± 0.9	104.4 ± 0.4	12.0
20ppm	22.4 ± 0.1	52.7 ± 0.8	104.3 ± 0.5	12.0
40ppm	22.1 ± 0.2	55.7 ± 1.2	104.6 ± 0.4	12.1
75ppm	22.1 ± 0.1	52.6 ± 1.1	104.5 ± 0.4	12.1
150ppm	22.4 ± 0.1	52.7 ± 0.9	104.3 ± 0.5	12.0
300ppm	22.4 ± 0.2	51.5 ± 1.2	104.6 ± 0.5	12.1

APPENDIX M 1

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS IN THE 13 - WEEK INHALATION STUDY OF CYCLOHEXENE

METHODS FOR HEMATOLOGY,BIOCHEMISTRY AND URINALYSIS IN THE 13-WEEK INHALATION STUDY OF CYCLOHEXENE

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	Enzymatic method (GLK・G-6-PDH) [3]
T-cholesterol	Enzymatic method (CE・COD・POD) [3]
Triglyceride	Enzymatic method (LPL・GK・GPO・POD) [3]
Phospholipid	Enzymatic method (PLD・COD・POD) [3]
Glutamic oxaloacetic transaminase (GOT)	UV・Rate method [3]
Glutamic pyruvic transaminase (GPT)	UV・Rate method [3]
Lactate dehydrogenase (LDH)	UV・Rate method [3]
Alkaline phosphatase (ALP)	p-Nitrophenylphosphate method [3]
γ-Glutamyl transpeptidase (γ-GTP)	L-γ-Glutamyl-p-nitroanilide method [3]
Creatine phosphokinase (CPK)	UV・Rate method [3]
Urea nitrogen	Enzymatic method (Urease・GLDH) [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	Enzymatic method (PNP・XOD・POD) [3]
Urinalysis	
pH,Protein,Glucose,Ketone body,Occult Blood, Urobilinogen	Urinalysis reagent paper method [4]

1) Automatic blood cell analyzer (Technicon H・1 : Technicon Instruments Corporation,USA)

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

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

4) Ames reagent strips for urinalysis (Uro-Labstix : Bayer-Sankyo Co.,Ltd.,Japan)

APPENDIX M 2

UNITS AND DECIMARL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13 - WEEK INHALATION STUDY OF CYCLOHEXENE

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK INHALATION STUDY OF CYCLOHEXENE

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