シクロヘキセンのラットを用いた
吸入による 13 週間毒性試験報告書

試験番号：０３６３

APPENDIX

APPENDIXES

APPENDIXES (CONTINUED)

APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, RAT : MALE

(13 - WEEK STUDY)

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
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													
	150 ppm													
	300 ppm													
	600 ppm													
	1200 ppm													
	2400 ppm													

APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
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													
	150 ppm													
	300 ppm													
	600 ppm													
	1200 ppm													
	2400 ppm													

APPENDIX B 1

BODY WEIGHT CHANGES :SUMMARY, RAT : MALE

(13 - WEEK STUDY)

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
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	115± 4	139± 4	166± 5	189± 7	211± 9	225± 11	239± 12
150ppm	115± 4	142± 7	165± 9	188± 9	210± 10	224± 10	237± 10
300ppm	115± 4	143± 6	171± 10	192± 13	214± 16	228± 15	242± 15
600ppm	115± 4	140± 6	166± 9	189± 11	210± 11	226± 11	242± 12
1200ppm	115± 4	134± 6	156± 7*	178± 10	196± 10*	209± 12**	223± 13*
2400ppm	115± 4	137± 6	163± 6	178± 8	197± 9*	211± 10*	224± 10*

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

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
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	251± 14	263± 15	273± 18	282± 19	289± 18	295± 22	300± 20
150ppm	250± 10	262± 10	273± 9	282± 8	290± 9	296± 11	302± 12
300ppm	258± 15	270± 17	278± 16	286± 19	293± 17	300± 16	305± 19
600ppm	255± 12	265± 14	277± 14	286± 15	292± 15	298± 16	301± 15
1200ppm	235± 13*	246± 13*	258± 13	267± 15	273± 14	279± 14	284± 14
2400ppm	238± 9	251± 9	263± 7	272± 8	280± 7	288± 9	292± 8

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

APPENDIX B 2

BODY WEIGHT CHANGES : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
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	95± 3	108± 3	119± 5	126± 5	134± 6	140± 7	147± 8
150ppm	95± 4	108± 3	118± 5	127± 6	136± 9	140± 7	148± 7
300ppm	95± 4	111± 4	123± 4	129± 4	139± 4	143± 5	149± 6
600ppm	95± 4	107± 5	118± 5	128± 6	138± 8	143± 9	148± 8
1200ppm	95± 4	106± 3	117± 3	125± 4	133± 5	138± 6	140± 7
2400ppm	95± 4	107± 4	117± 4	123± 4	130± 6	135± 6	140± 7

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

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
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	148± 8	155± 9	159± 10	161± 10	165± 10	166± 11	167± 10
150ppm	150± 9	157± 9	160± 10	165± 12	169± 14	169± 13	172± 13
300ppm	153± 7	156± 7	161± 7	165± 7	170± 7	170± 7	172± 7
600ppm	151± 9	156± 11	159± 10	164± 11	168± 12	169± 12	171± 12
1200ppm	145± 7	148± 9	152± 9	157± 9	159± 11	161± 9	161± 9
2400ppm	143± 6	149± 7	152± 7	156± 7	157± 6	160± 7	161± 7

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

APPENDIX C 1

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : MALE

(13 - WEEK STUDY)

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
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	13.5± 0.8	14.1± 0.5	15.1± 0.6	16.0± 1.0	16.0± 0.9	15.4± 1.0	15.3± 1.0
150ppm	13.7± 1.0	14.2± 0.8	14.5± 0.9	15.5± 0.8	15.2± 0.8	15.5± 0.9	15.2± 0.6
300ppm	13.1± 0.7	15.0± 1.1	15.8± 1.2	15.8± 1.5	16.1± 1.3	16.1± 1.1	15.4± 1.1
600ppm	13.0± 0.9	14.4± 0.9	15.1± 1.1	15.8± 1.0	15.6± 1.0	15.6± 1.0	15.6± 1.1
1200ppm	12.6± 0.8	14.0± 0.8	14.7± 1.0	15.9± 0.9	15.1± 0.9	15.6± 0.9	15.2± 1.0
2400ppm	12.3± 0.4**	14.5± 0.7	15.8± 0.8	15.7± 0.6	15.4± 0.4	15.7± 0.7	15.5± 0.5

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

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
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	15.3± 1.0	15.3± 1.2	15.2± 1.2	15.4± 1.0	15.6± 1.2	15.2± 0.9
150ppm	15.3± 0.5	15.4± 0.6	15.6± 0.5	15.4± 0.5	15.7± 0.7	15.1± 0.8
300ppm	15.7± 1.0	15.4± 1.1	15.4± 1.1	15.4± 1.1	15.6± 1.0	15.8± 1.2
600ppm	15.8± 1.0	15.6± 1.1	15.8± 1.1	15.4± 1.1	15.6± 1.2	15.5± 0.9
1200ppm	15.3± 0.9	15.2± 0.5	15.2± 0.7	15.2± 1.1	15.5± 0.8	14.9± 1.0
2400ppm	16.1± 0.5	16.0± 0.7	15.8± 0.7	15.8± 0.5	16.1± 0.6	15.8± 0.7

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

APPENDIX C 2

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
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	10.3± 0.4	10.3± 0.6	10.1± 0.7	10.5± 0.5	10.3± 0.6	10.3± 0.6	10.0± 0.7
150ppm	10.6± 0.8	10.2± 0.7	10.5± 1.0	10.7± 1.1	10.5± 0.9	10.5± 0.4	10.3± 1.0
300ppm	10.9± 0.6	11.2± 0.4**	11.3± 0.4**	11.3± 0.4*	10.6± 0.5	10.9± 0.7	10.5± 0.7
600ppm	10.8± 0.8	10.8± 0.6	11.3± 0.9**	11.3± 0.8	10.8± 0.8	10.9± 0.8	10.5± 0.7
1200ppm	10.2± 1.1	10.1± 0.5	10.5± 0.4	11.0± 0.6	10.1± 0.6	10.4± 0.5	9.9± 0.5
2400ppm	9.9± 0.6	10.5± 0.6	10.9± 0.5*	10.8± 0.5	10.4± 0.7	10.3± 0.7	9.9± 0.6

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

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
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	9.9± 0.6	10.2± 0.8	10.1± 0.6	10.3± 0.7	10.0± 0.6	10.0± 0.7
150ppm	10.4± 0.9	10.4± 0.8	10.5± 1.0	11.4± 1.7	10.5± 1.1	10.4± 1.1
300ppm	10.2± 0.6	10.6± 0.7	10.4± 0.5	11.1± 0.5	10.6± 0.5	10.5± 0.4
600ppm	10.5± 1.1	10.4± 0.5	10.3± 0.8	10.8± 1.1	11.0± 1.6	10.6± 1.0
1200ppm	9.9± 0.6	10.0± 0.7	9.9± 0.7	10.2± 0.8	10.1± 0.7	9.9± 0.6
2400ppm	10.1± 0.6	9.9± 0.5	9.9± 0.7	9.8± 0.4	10.0± 0.6	9.9± 0.7

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

APPENDIX D 1

HEMATOLOGY : SUMMARY, RAT : MALE

(13 - WEEK STUDY)

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
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	10	9.36± 0.25	16.0± 0.4	45.8± 1.3	48.9± 0.2	17.1± 0.1	34.9± 0.3	711± 39
150ppm	10	9.37± 0.16	16.0± 0.3	46.2± 1.0	49.3± 0.4	17.0± 0.1	34.6± 0.5	707± 27
300ppm	10	9.31± 0.27	15.9± 0.4	45.9± 1.4	49.2± 0.4	17.1± 0.2	34.6± 0.4	715± 47
600ppm	10	9.31± 0.29	15.9± 0.5	45.9± 1.5	49.2± 0.6	17.1± 0.2	34.7± 0.6	745± 24
1200ppm	10	9.25± 0.21	15.9± 0.2	45.6± 1.1	49.3± 0.4	17.2± 0.3	34.8± 0.4	718± 42
2400ppm	10	9.19± 0.23	15.9± 0.2	45.9± 0.8	50.0± 0.7**	17.3± 0.3	34.6± 0.3	750± 23

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

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RETICULOCYTE ‰		PROTHROMBIN TIME sec		APTT sec	
Control	10	15±	4	15.3±	1.2	19.6±	3.4
150ppm	10	17±	3	15.7±	1.7	19.5±	3.5
300ppm	10	17±	5	14.9±	2.0	18.7±	1.2
600ppm	10	18±	3	14.1±	1.4	16.7±	3.4
1200ppm	10	19±	5	14.7±	2.0	17.8±	3.5
2400ppm	10	21±	7	14.0±	0.8	17.2±	1.5

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

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
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	5.80± 1.77	1± 1	25± 4	1± 1	0± 0	4± 1	69± 4	0± 0
150ppm	10	5.36± 1.64	2± 1	27± 9	1± 1	0± 0	5± 3	66± 9	0± 0
300ppm	10	5.50± 2.39	1± 1	27± 7	1± 1	0± 0	4± 3	68± 7	0± 0
600ppm	10	5.49± 2.11	1± 1	26± 7	1± 1	0± 0	4± 2	68± 8	0± 0
1200ppm	10	5.02± 1.22	1± 1	24± 4	1± 1	0± 0	4± 2	69± 6	0± 0
2400ppm	10	5.27± 1.18	0± 1	27± 5	1± 1	0± 0	4± 2	67± 6	0± 0

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

APPENDIX D 2

HEMATOLOGY : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
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	8.56± 0.11	15.7± 0.2	44.4± 0.4	51.9± 0.5	18.4± 0.1	35.4± 0.3	811± 42
150ppm	10	8.65± 0.15	16.0± 0.3	45.1± 0.8	52.1± 0.5	18.5± 0.2	35.4± 0.2	773± 41
300ppm	10	8.61± 0.16	15.9± 0.3	44.9± 1.0	52.1± 0.4	18.5± 0.2	35.4± 0.4	792± 50
600ppm	10	8.46± 0.22	15.7± 0.4	44.2± 1.4	52.2± 0.5	18.6± 0.2	35.6± 0.3	815± 39
1200ppm	10	8.44± 0.25	15.6± 0.4	44.0± 1.1	52.2± 0.7	18.5± 0.2	35.5± 0.5	782± 33
2400ppm	9	8.53± 0.17	15.7± 0.3	44.6± 1.1	52.2± 0.5	18.4± 0.2	35.3± 0.3	815± 47

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

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RETICULOCYTE ‰		PROTHROMBIN TIME sec		APTT sec	
Control	9	16±	4	13.6±	0.6	14.9±	2.4
150ppm	10	17±	4	13.7±	0.5	14.6±	1.4
300ppm	10	15±	3	13.8±	0.5	14.8±	2.0
600ppm	10	18±	6	13.9±	0.5	15.0±	1.0
1200ppm	10	18±	7	13.9±	0.3	14.2±	2.0
2400ppm	9	22±	3*	14.4±	0.3**	15.0±	1.1

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

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
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	3.10± 1.19	1± 1	26± 8	1± 1	0± 0	5± 2	67± 8	0± 0
150ppm	10	2.47± 0.72	1± 1	27± 10	2± 1	0± 0	5± 2	66± 11	0± 0
300ppm	10	2.93± 0.95	0± 0	25± 5	2± 1	0± 0	4± 2	69± 5	0± 0
600ppm	10	2.79± 1.34	0± 1	27± 6	1± 1	0± 0	4± 2	68± 6	0± 0
1200ppm	10	3.51± 1.47	1± 1	24± 7	1± 1	0± 0	3± 1	71± 8	0± 0
2400ppm	9	3.08± 1.16	1± 1	27± 7	2± 1	0± 0	4± 2	67± 8	0± 0

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

APPENDIX E 1

BIOCHEMISTRY : SUMMARY, RAT : MALE

(13 - WEEK STUDY)

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
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	6.2± 0.1	3.9± 0.1	1.7± 0.1	0.12± 0.01	181± 14	59± 3	67± 15
150ppm	10	6.3± 0.1	3.9± 0.1	1.6± 0.1	0.11± 0.01	183± 12	59± 4	54± 9
300ppm	10	6.4± 0.1	4.0± 0.1*	1.7± 0.1	0.12± 0.01	180± 13	63± 4	60± 23
600ppm	10	6.3± 0.1	4.0± 0.1	1.7± 0.1	0.12± 0.01	189± 13	64± 5*	54± 14
1200ppm	10	6.4± 0.1	4.0± 0.1**	1.7± 0.1	0.12± 0.01	182± 11	63± 4	61± 14
2400ppm	10	6.5± 0.2**	4.1± 0.1**	1.7± 0.1	0.12± 0.01	185± 11	61± 3	56± 15

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

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
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	108± 8	64± 10	40± 4	152± 42	243± 18	1± 1	98± 14
150ppm	10	106± 6	66± 15	43± 10	158± 24	247± 12	1± 1	103± 8
300ppm	10	112± 7	70± 19	42± 8	169± 53	248± 25	2± 1	98± 17
600ppm	10	113± 8	67± 21	40± 7	178± 78	232± 11	1± 1	100± 29
1200ppm	10	113± 8	62± 17	41± 12	155± 45	242± 20	2± 1	103± 12
2400ppm	10	109± 6	52± 5	34± 4	127± 17	236± 19	2± 1	93± 9

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

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	UREA NITROGEN mg/dℓ	CREATININE mg/dℓ	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dℓ	INORGANIC PHOSPHORUS mg/dℓ
Control	10	18.9± 1.5	0.5± 0.0	141± 1	3.5± 0.2	103± 1	10.2± 0.2	5.7± 0.6
150ppm	10	18.6± 0.8	0.6± 0.1	140± 1	3.3± 0.2	103± 1	10.1± 0.2	5.6± 0.8
300ppm	10	19.5± 1.1	0.6± 0.1	141± 1	3.4± 0.3	103± 1	10.2± 0.2	5.6± 1.0
600ppm	10	20.0± 0.8	0.5± 0.0	140± 1	3.4± 0.2	103± 1	10.1± 0.3	5.7± 0.8
1200ppm	10	19.0± 1.7	0.6± 0.1	141± 1	3.4± 0.3	103± 1	10.2± 0.2	5.8± 0.7
2400ppm	10	20.0± 1.4	0.6± 0.1	140± 1	3.5± 0.1	102± 1**	10.3± 0.1	6.1± 0.9

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

APPENDIX E 2

BIOCHEMISTRY : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
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	6.1± 0.1	3.8± 0.1	1.7± 0.1	0.13± 0.01	134± 18	69± 7	14± 5
150ppm	10	6.1± 0.2	3.8± 0.1	1.7± 0.1	0.13± 0.01	135± 15	68± 7	11± 2
300ppm	10	6.1± 0.2	3.8± 0.1	1.6± 0.1	0.13± 0.01	141± 7	64± 7	14± 3
600ppm	10	6.1± 0.2	3.8± 0.1	1.6± 0.1	0.13± 0.01	142± 13	66± 10	14± 3
1200ppm	10	6.0± 0.2	3.7± 0.1	1.7± 0.1	0.14± 0.01	138± 15	61± 6	15± 3
2400ppm	9	6.0± 0.1	3.8± 0.1	1.7± 0.1	0.13± 0.02	132± 15	64± 8	15± 3

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

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
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	126± 10	69± 23	39± 22	238± 119	184± 16	2± 1	117± 34
150ppm	10	124± 14	69± 11	39± 7	208± 85	185± 15	2± 1	117± 27
300ppm	10	122± 12	68± 13	37± 9	222± 114	200± 21	2± 1	118± 32
600ppm	10	124± 17	63± 5	36± 4	172± 79	188± 24	2± 1	104± 24
1200ppm	10	118± 10	65± 6	33± 4	180± 65	191± 35	2± 1	104± 21
2400ppm	9	122± 12	63± 4	32± 4	226± 131	202± 20	2± 1	116± 42

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

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	UREA NITROGEN mg/dℓ	CREATININE mg/dℓ	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dℓ	INORGANIC PHOSPHORUS mg/dℓ
Control	9	18.2± 1.4	0.6± 0.1	139± 1	3.3± 0.3	105± 2	9.8± 0.3	5.0± 1.4
150ppm	10	18.8± 0.9	0.6± 0.1	140± 2	3.3± 0.2	105± 2	9.8± 0.2	5.4± 1.3
300ppm	10	19.5± 2.0	0.6± 0.1	140± 1	3.5± 0.2	104± 2	9.8± 0.2	5.5± 1.0
600ppm	10	18.8± 1.5	0.6± 0.1	139± 1	3.3± 0.1	104± 1	9.9± 0.2	5.4± 1.0
1200ppm	10	18.7± 1.6	0.6± 0.1	139± 1	3.4± 0.2	105± 1	9.7± 0.2	5.3± 1.2
2400ppm	9	18.6± 1.3	0.6± 0.1	140± 1	3.6± 0.2	105± 1	9.7± 0.1	5.4± 0.9

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

APPENDIX F 1

URINALYSIS : SUMMARY, RAT : MALE

(13 - WEEK STUDY)

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
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	Bilirubin −	+	2+	3+	CHI
Control	10	0	0	0	0	2	2	6		0	2	5	3	0	0		10	0	0	0	0	0		3	3	4	0	0	0		10	0	0	0	
150ppm	10	0	0	0	1	2	3	4		0	6	3	1	0	0		10	0	0	0	0	0		7	2	1	0	0	0		10	0	0	0	
300ppm	10	0	0	0	1	2	2	5		0	4	3	3	0	0		10	0	0	0	0	0		9	0	1	0	0	0	*	10	0	0	0	
600ppm	10	0	0	0	0	2	5	3		1	1	4	4	0	0		10	0	0	0	0	0		5	3	2	0	0	0		10	0	0	0	
1200ppm	10	0	0	0	0	2	4	4		0	2	3	5	0	0		10	0	0	0	0	0		4	2	4	0	0	0		10	0	0	0	
2400ppm	10	0	0	0	0	4	1	5		0	3	6	1	0	0		10	0	0	0	0	0		7	1	2	0	0	0		10	0	0	0	

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

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	Occult blood −	±	+	2+	3+	CHI	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	9	1	0	0	0		10	0	0	0	0	
150ppm	10	9	1	0	0	0		10	0	0	0	0	
300ppm	10	9	0	1	0	0		10	0	0	0	0	
600ppm	10	9	1	0	0	0		10	0	0	0	0	
1200ppm	10	10	0	0	0	0		10	0	0	0	0	
2400ppm	10	10	0	0	0	0		10	0	0	0	0	

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

APPENDIX F 2

URINALYSIS : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
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	Bilirubin −	+	2+	3+	CHI
Control	10	0	0	0	0	2	7	1		0	4	6	0	0	0		10	0	0	0	0	0		6	4	0	0	0	0		10	0	0	0	
150ppm	10	0	0	0	1	1	7	1		0	9	1	0	0	0	*	10	0	0	0	0	0		10	0	0	0	0	0	*	10	0	0	0	
300ppm	10	0	0	0	0	0	7	3		0	9	1	0	0	0	*	10	0	0	0	0	0		9	1	0	0	0	0		10	0	0	0	
600ppm	10	0	0	0	0	2	7	1		0	9	1	0	0	0	*	10	0	0	0	0	0		9	1	0	0	0	0		10	0	0	0	
1200ppm	10	0	0	0	0	0	9	1		0	7	2	1	0	0		10	0	0	0	0	0		8	2	0	0	0	0		10	0	0	0	
2400ppm	10	0	0	0	0	3	4	3		0	7	3	0	0	0		10	0	0	0	0	0		8	2	0	0	0	0		10	0	0	0	

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

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	Occult blood −	±	+	2+	3+	CHI	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0		10	0	0	0	0	
150ppm	10	10	0	0	0	0		10	0	0	0	0	
300ppm	10	10	0	0	0	0		10	0	0	0	0	
600ppm	10	10	0	0	0	0		10	0	0	0	0	
1200ppm	10	10	0	0	0	0		10	0	0	0	0	
2400ppm	10	10	0	0	0	0		10	0	0	0	0	

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

APPENDIX G 1

GROSS FINDINGS : SUMMARY, RAT : MALE :ALL ANIMALS

(13 - WEEK STUDY)

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	150ppm 10 (%)	300ppm 10 (%)	600ppm 10 (%)
liver	herniation		1 (10)	2 (20)	0 (0)	0 (0)

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	1200ppm	2400ppm
		NO. of Animals	10 (%)	10 (%)
liver	herniation		3 (30)	0 (0)

APPENDIX G 2

GROSS FINDINGS : SUMMARY, RAT : FEMALE :ALL ANIMALS

(13 - WEEK STUDY)

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	150ppm 10 (%)	300ppm 10 (%)	600ppm 10 (%)
liver	herniation		0 (0)	1 (10)	4 (40)	0 (0)

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name	1200ppm	2400ppm
		NO. of Animals	10 (%)	10 (%)
liver	herniation		1 (10)	0 (0)

APPENDIX H 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : MALE

(13 - WEEK STUDY)

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
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	280± 19	0.242± 0.043	0.051± 0.006	2.975± 0.134	0.876± 0.058	0.963± 0.056
150ppm	10	281± 11	0.248± 0.036	0.053± 0.008	2.960± 0.106	0.871± 0.031	0.972± 0.043
300ppm	10	286± 18	0.234± 0.032	0.049± 0.003	3.036± 0.118	0.892± 0.056	0.993± 0.060
600ppm	10	281± 15	0.231± 0.036	0.051± 0.007	3.034± 0.130	0.882± 0.066	0.982± 0.048
1200ppm	10	265± 14	0.223± 0.026	0.052± 0.006	2.959± 0.153	0.844± 0.045	0.959± 0.055
2400ppm	10	272± 8	0.233± 0.042	0.052± 0.006	2.943± 0.151	0.862± 0.044	0.973± 0.058

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

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
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	1.725± 0.108	0.518± 0.038	6.997± 0.610	1.828± 0.038
150ppm	10	1.718± 0.077	0.522± 0.031	7.084± 0.386	1.820± 0.043
300ppm	10	1.776± 0.127	0.531± 0.032	7.198± 0.554	1.843± 0.052
600ppm	10	1.814± 0.110	0.512± 0.027	7.309± 0.583	1.857± 0.064
1200ppm	10	1.713± 0.098	0.495± 0.017	7.044± 0.340	1.795± 0.059
2400ppm	10	1.803± 0.075	0.512± 0.034	7.535± 0.234	1.813± 0.062

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

APPENDIX H 2

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
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	155± 9	0.172± 0.026	0.054± 0.006	0.100± 0.011	0.565± 0.039	0.714± 0.039
150ppm	10	158± 12	0.187± 0.022	0.056± 0.003	0.094± 0.009	0.560± 0.031	0.706± 0.045
300ppm	10	158± 7	0.187± 0.011	0.055± 0.004	0.104± 0.015	0.569± 0.017	0.700± 0.032
600ppm	10	158± 11	0.186± 0.028	0.058± 0.005	0.099± 0.007	0.570± 0.022	0.708± 0.049
1200ppm	10	149± 9	0.172± 0.033	0.058± 0.007	0.095± 0.009	0.542± 0.032	0.720± 0.029
2400ppm	10	149± 6	0.171± 0.015	0.058± 0.006	0.097± 0.009	0.539± 0.022	0.697± 0.036

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

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
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	1.045± 0.033	0.343± 0.014	3.697± 0.219	1.701± 0.030
150ppm	10	1.039± 0.041	0.349± 0.025	3.704± 0.252	1.677± 0.035
300ppm	10	1.060± 0.042	0.355± 0.016	3.739± 0.158	1.701± 0.034
600ppm	10	1.065± 0.062	0.359± 0.028	3.785± 0.225	1.678± 0.051
1200ppm	10	1.057± 0.039	0.339± 0.025	3.670± 0.224	1.681± 0.032
2400ppm	10	1.075± 0.049	0.337± 0.021	3.754± 0.229	1.669± 0.059

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

APPENDIX I 1

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : MALE

(13 - WEEK STUDY)

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
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	280± 19	0.086± 0.011	0.018± 0.003	1.067± 0.070	0.313± 0.012	0.345± 0.013
150ppm	10	281± 11	0.088± 0.010	0.019± 0.003	1.056± 0.053	0.310± 0.012	0.346± 0.011
300ppm	10	286± 18	0.082± 0.009	0.017± 0.001	1.064± 0.045	0.313± 0.016	0.348± 0.014
600ppm	10	281± 15	0.082± 0.009	0.018± 0.002	1.082± 0.052	0.314± 0.016	0.350± 0.015
1200ppm	10	265± 14	0.084± 0.008	0.020± 0.002	1.118± 0.033	0.319± 0.010	0.363± 0.018
2400ppm	10	272± 8	0.086± 0.016	0.019± 0.002	1.082± 0.049	0.317± 0.016	0.358± 0.020

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

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.617± 0.023	0.185± 0.006	2.499± 0.064	0.656± 0.037
150ppm	10	0.612± 0.020	0.186± 0.009	2.523± 0.073	0.649± 0.030
300ppm	10	0.621± 0.029	0.186± 0.005	2.517± 0.092	0.646± 0.031
600ppm	10	0.646± 0.015*	0.183± 0.010	2.599± 0.094*	0.662± 0.030
1200ppm	10	0.647± 0.011*	0.187± 0.007	2.663± 0.071**	0.679± 0.018
2400ppm	10	0.663± 0.026**	0.188± 0.009	2.771± 0.064**	0.667± 0.028

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

APPENDIX I 2

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
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	155± 9	0.111± 0.012	0.035± 0.004	0.065± 0.007	0.366± 0.016	0.464± 0.034
150ppm	10	158± 12	0.119± 0.012	0.035± 0.003	0.060± 0.004	0.356± 0.018	0.449± 0.028
300ppm	10	158± 7	0.119± 0.008	0.035± 0.002	0.066± 0.010	0.360± 0.016	0.444± 0.026
600ppm	10	158± 11	0.118± 0.014	0.037± 0.004	0.063± 0.005	0.363± 0.019	0.449± 0.019
1200ppm	10	149± 9	0.115± 0.018	0.039± 0.005	0.064± 0.005	0.365± 0.010	0.485± 0.025
2400ppm	10	149± 6	0.115± 0.010	0.039± 0.003	0.066± 0.006	0.363± 0.012	0.470± 0.012

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

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.678± 0.034	0.222± 0.012	2.395± 0.090	1.104± 0.060
150ppm	10	0.661± 0.037	0.222± 0.012	2.352± 0.103	1.069± 0.076
300ppm	10	0.672± 0.029	0.225± 0.014	2.368± 0.087	1.078± 0.049
600ppm	10	0.676± 0.017	0.228± 0.012	2.404± 0.070	1.069± 0.060
1200ppm	10	0.712± 0.026*	0.228± 0.013	2.469± 0.059	1.134± 0.060
2400ppm	10	0.724± 0.017**	0.227± 0.009	2.527± 0.096**	1.126± 0.056

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

APPENDIX J 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : ALL ANIMALS

(13 - WEEK STUDY)

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control				150ppm				300ppm				600ppm			
		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>			
	inflammation:respiratory epithelium		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)
[Circulatory system]																		
heart			<10>				<10>				<10>				<10>			
	inflammatory cell nest		1	0	0	0	2	0	0	0	1	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
[Digestive system]																		
liver			<10>				<10>				<10>				<10>			
	herniation		1	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:focal		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)
	granulation		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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	1200ppm				2400ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
nasal cavit			<10>				<10>			
	inflammation:respiratory epithelium		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Circulatory system]										
heart			<10>				<10>			
	inflammatory cell nest		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]										
liver			<10>				<10>			
	herniation		3	0	0	0	0	0	0	0
			(30)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:focal		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	granulation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control				150ppm				300ppm				600ppm			
		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>			
	perivascular inflammation		0	0	0	0	3	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
pancreas			<10>				<10>				<10>				<10>			
	atrophy		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
[Urinary system]																		
kidney			<10>				<10>				<10>				<10>			
	basophilic change		0	0	0	0	0	0	0	0	1	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	eosinophilic body		2	8	0	0	2	8	0	0	1	9	0	0	1	9	0	0
			(20)	(80)	(0)	(0)	(20)	(80)	(0)	(0)	(10)	(90)	(0)	(0)	(10)	(90)	(0)	(0)
	mineralization:cortico-medullary junction		0	0	0	0	0	0	0	0	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:papilla		0	0	0	0	0	0	0	0	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	1200ppm				2400ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]										
liver			<10>				<10>			
	perivascular inflammation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
pancreas			<10>				<10>			
	atrophy		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Urinary system]										
kidney			<10>				<10>			
	basophilic change		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	eosinophilic body		2	8	0	0	2	8	0	0
			(20)	(80)	(0)	(0)	(20)	(80)	(0)	(0)
	mineralization:cortico-medullary junction		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:papilla		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

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
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 1 (%)	Control 10 2 (%)	Control 10 3 (%)	Control 10 4 (%)	150ppm 10 1 (%)	150ppm 10 2 (%)	150ppm 10 3 (%)	150ppm 10 4 (%)	300ppm 10 1 (%)	300ppm 10 2 (%)	300ppm 10 3 (%)	300ppm 10 4 (%)	600ppm 10 1 (%)	600ppm 10 2 (%)	600ppm 10 3 (%)	600ppm 10 4 (%)
[Endocrine system]																		
pituitary	Rathke pouch	<10>	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
thyroid	ultimibranchial body remanet	<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)	0 (0)	0 (0)	0 (0)	0 (0)
[Reproductive system]																		
prostate	inflammation	<10>	0 (0)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Special sense organs/appendage]																		
eye	retinal atrophy	<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)
Harder gl	lymphocytic infiltration	<10>	1 (10)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (20)	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	1200ppm				2400ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]										
pituitary			<10>				<10>			
	Rathke pouch		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
thyroid			<10>				<10>			
	ultimibranchial body remanet		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Reproductive system]										
prostate			<10>				<10>			
	inflammation		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
[Special sense organs/appendage]										
eye			<10>				<10>			
	retinal atrophy		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
Harder gl			<10>				<10>			
	lymphocytic infiltration		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)

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

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control				150ppm				300ppm				600ppm			
		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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Special sense organs/appendage]																		
Harder gl			<10>				<10>				<10>				<10>			
	granulation		1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(10)	(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

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	1200ppm				2400ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Special sense organs/appendage]										
Harder gl			<10>				<10>			
	granulation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

APPENDIX J 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE: ALL ANIMALS

(13 - WEEK STUDY)

STUDY NO. : 0363
ANIMAL : RAT F344/DuCrj
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				150ppm				300ppm				600ppm			
			10				10				10				10			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
nasal cavit			<10>				<10>				<10>				<10>			
	inflammation:respiratory epithelium		1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
larynx			<10>				<10>				<10>				<10>			
	inflammation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Hematopoietic system]																		
bone marrow			<10>				<10>				<10>				<10>			
	granulation		2 (20)	1 (10)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	3 (30)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)
[Circulatory system]																		
heart			<10>				<10>				<10>				<10>			
	inflammatory cell nest		2 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Digestive system]																		
liver			<10>				<10>				<10>				<10>			
	herniation		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	5 (50)	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	1200ppm				2400ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
nasal cavit			<10>				<10>			
	inflammation:respiratory epithelium		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
larynx			<10>				<10>			
	inflammation		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
[Hematopoietic system]										
bone marrow			<10>				<10>			
	granulation		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Circulatory system]										
heart			<10>				<10>			
	inflammatory cell nest		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]										
liver			<10>				<10>			
	herniation		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	Control				150ppm				300ppm				600ppm			
		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>			
	granulation		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)
	perivascular inflammation		0	0	0	0	1	0	0	0	0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
[Urinary system]																		
kidney			<10>				<10>				<10>				<10>			
	mineralization:cortico-medullary junction		1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:papilla		0	0	0	0	0	0	0	0	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			<10>				<10>				<10>				<10>			
	Rathke pouch		0	0	0	0	0	0	0	0	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	1200ppm				2400ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]										
liver			<10>				<10>			
	granulation		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	perivascular inflammation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Urinary system]										
kidney			<10>				<10>			
	mineralization:cortico-medullary junction		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:papilla		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Endocrine system]										
pituitary			<10>				<10>			
	Rathke pouch		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	Control				150ppm				300ppm				600ppm			
		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]																		
thyroid			<10>				<10>				<10>				<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)
[Special sense organs/appendage]																		
eye			<10>				<10>				<10>				<10>			
	retinal atrophy		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)
Harder gl			<10>				<10>				<10>				<10>			
	lymphocytic infiltration		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)	(0)	(0)	(0)	(0)
	granulation		1	0	0	0	1	1	0	0	2	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(10)	(10)	(0)	(0)	(20)	(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	1200ppm				2400ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]										
thyroid			<10>				<10>			
	ultimibranchial body remanet		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Special sense organs/appendage]										
eye			<10>				<10>			
	retinal atrophy		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
Harder gl			<10>				<10>			
	lymphocytic infiltration		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	granulation		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)

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

APPENDIX K 1

IDENTITY 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. : ACM4092

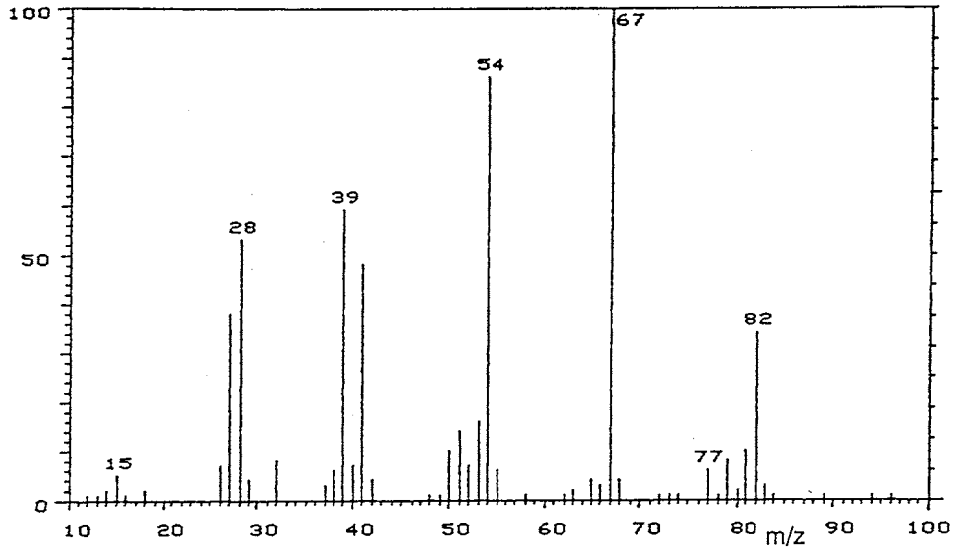
1. Spectral data

Mass Spectrometry

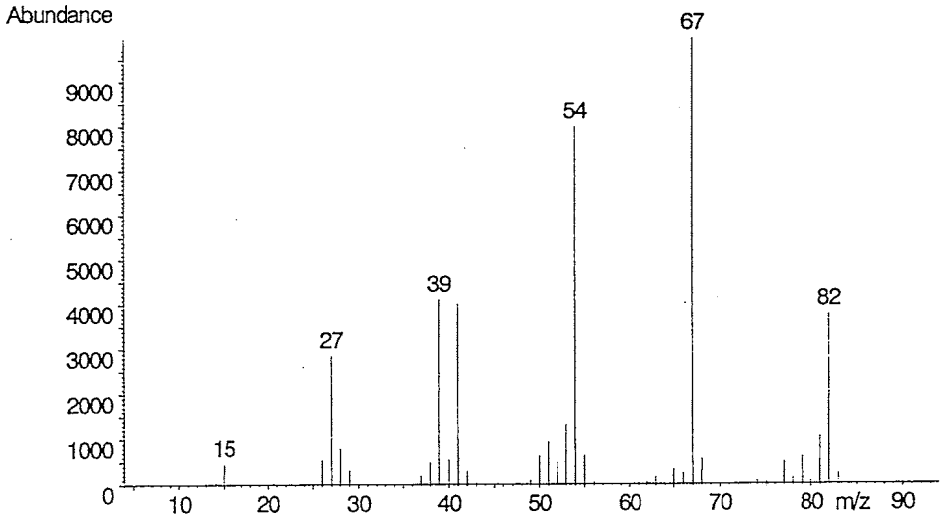
Instrument : Hitachi M-80B Mass Spectrometer

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.

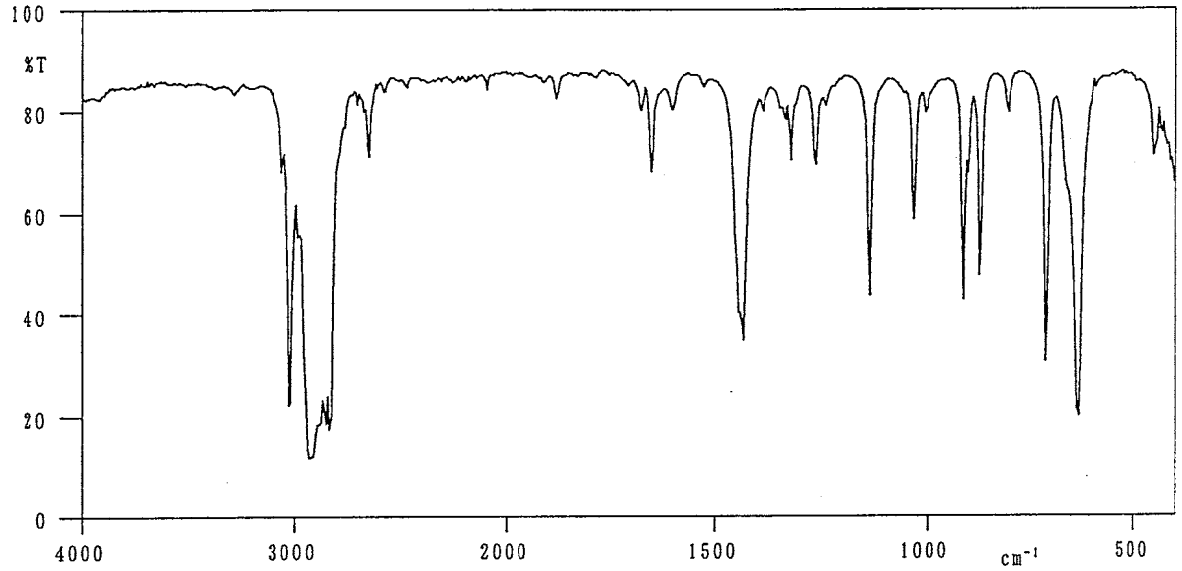
(*Fred W. McLafferty (1994) Wiley registry of mass spectral data, 6th edition. John Wiley and Sons Inc. (U.S.), Entry Number 2466)

Infrared Spectrometry

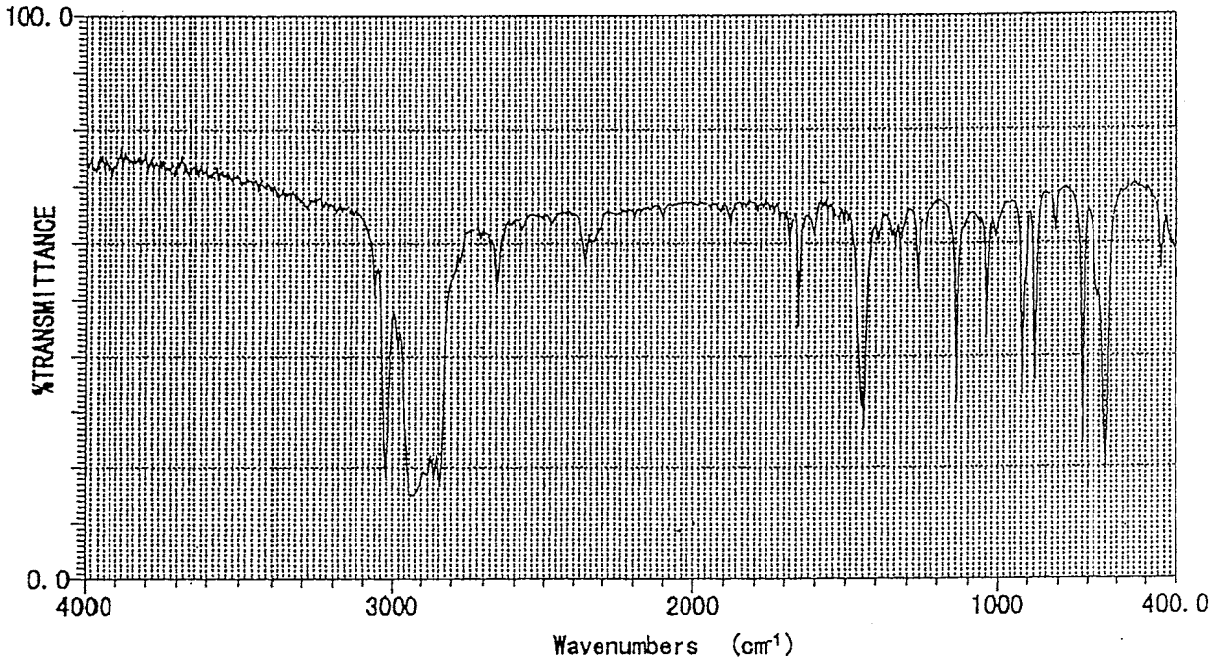
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

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	0.05	1,3-Cyclodiene
	2	99.80	Cyclohexene
	3	0.15	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 0.05% and 0.15%.

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 0.05% and 0.15%.

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. : ACM4092

1. Sample : This lot was used from 1998.9.16 to 1998.12.15. 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	0.05
	2	8.80	99.80
	3	9.67	0.15
1998.12.25	1	7.48	0.05
	2	8.80	99.80
	3	9.67	0.15

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

CONCENTRATION 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
150ppm	150.1 ± 1.0
300ppm	300.2 ± 1.4
600ppm	600.1 ± 3.4
1200ppm	1202.3 ± 7.2
2400ppm	2403.6 ± 19.2

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)	22.8 ± 0.2	54.6 ± 1.1	212.2 ± 0.7	12.0
150ppm	22.6 ± 0.3	58.1 ± 1.6	212.1 ± 0.8	12.0
300ppm	22.8 ± 0.2	56.3 ± 1.3	212.4 ± 0.6	12.0
600ppm	22.6 ± 0.3	52.7 ± 1.2	212.5 ± 0.7	12.0
1200ppm	22.7 ± 0.2	54.0 ± 0.8	212.7 ± 0.7	12.0
2400ppm	22.9 ± 0.2	54.0 ± 1.1	212.8 ± 0.7	12.0

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]
Reticulocyte	Pattern recognition method [3] (New methyleneblue staining)
Prothrombin time	Quick one stage method [2]
Activated partial thromboplastin time (APTT)	Ellagic acid activaterd method [2]
White blood cell (WBC)	Light scattering method [1]
Differential WBC	Pattern recognition method [3] (Wright staining)
Biochemistry	
Total protein (TP)	Biuret method [4]
Albumin (Alb)	BCG method [4]
A/G ratio	Calculated as Alb/(TP−Alb) [4]
T-bilirubin	Alkaline azobilirubin method [4]
Glucose	Enzymatic method (GLK・G-6-PDH) [4]
T-cholesterol	Enzymatic method (CE・COD・POD) [4]
Triglyceride	Enzymatic method (LPL・GK・GPO・POD) [4]
Phospholipid	Enzymatic method (PLD・COD・POD) [4]
Glutamic oxaloacetic transaminase (GOT)	UV・Rate method [4]
Glutamic pyruvic transaminase (GPT)	UV・Rate method [4]
Lactate dehydrogenase (LDH)	UV・Rate method [4]
Alkaline phosphatase (ALP)	p-Nitrophenylphosphate method [4]
γ-Glutamyl transpeptidase (γ-GTP)	L-γ-Glutamyl-p-nitroanilide method [4]
Creatine phosphokinase (CPK)	UV・Rate method [4]
Urea nitrogen	Enzymatic method (Urease・GLDH) [4]
Creatinine	Jaffe method [4]
Sodium	Ion selective electrode method [4]
Potassium	Ion selective electrode method [4]
Chloride	Ion selective electrode method [4]
Calcium	OCPC method [4]
Inorganic phosphorus	Enzymatic method (PNP・XOD・POD) [4]
Urinalysis	
pH,Protein,Glucose,Ketone body,Bilirubin,Occult Blood, Urobilinogen	Urinalysis reagent paper method [5]

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

2) Automatic coagulometer (Sysmex CA-5000 : Toa Medical Electronics Co.,Ltd.,Japan)

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

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

5) Ames reagent strips for urinalysis (Multistix : 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
Reticulocyte	‰	0
Prothrombin time	sec	1
Activated partial thromboplastin time (APTT)	sec	1
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
Creatinine	mg/dL	1
Sodium	mEq/L	0
Potassium	mEq/L	1
Chloride	mEq/L	0
Calcium	mg/dL	1
Inorganic phosphorus	mg/dL	1