ブチル 2,3-エポキシプロピル エーテルのラット
を用いた吸入による 13 週間毒性試験報告書

試験番号：0415

APPENDICES

APPENDICES

APPENDICES (CONTINUED)

APPENDIX A 1

BODY WEIGHT CHANGES :SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0415
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	121± 4	153± 6	176± 8	200± 12	220± 12	235± 12	252± 12
12.5ppm	121± 4	149± 6	169± 7	188± 10	203± 12**	218± 14*	231± 15**
25ppm	121± 4	150± 6	177± 10	197± 12	216± 16	230± 17	242± 17
50ppm	121± 4	149± 8	174± 9	195± 12	211± 13	222± 12	235± 14*
100ppm	121± 4	145± 6*	170± 7	192± 7	209± 8	220± 9*	229± 9**
200ppm	121± 4	134± 6**	146± 6**	158± 7**	175± 7**	175± 6**	182± 6**

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

STUDY NO. : 0415
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	261± 11	271± 11	279± 12	289± 11	293± 12	298± 12	305± 10
12.5ppm	242± 16**	254± 17*	261± 15*	268± 16**	275± 16*	278± 14*	285± 14*
25ppm	255± 16	264± 16	267± 19	272± 21*	279± 21	284± 22	289± 23
50ppm	245± 14*	254± 14*	258± 14**	265± 13**	272± 14**	278± 15*	284± 14**
100ppm	238± 9**	247± 12**	242± 11**	247± 12**	254± 13**	254± 12**	257± 12**
200ppm	183± 7**	192± 7**	190± 7**	193± 7**	197± 8**	196± 9**	199± 9**

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

APPENDIX A 2

BODY WEIGHT CHANGES : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0415
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	111± 3	120± 3	130± 4	137± 5	143± 6	149± 8
12.5ppm	95± 3	109± 5	119± 5	127± 6	133± 7	140± 8	145± 9
25ppm	95± 3	110± 5	121± 4	128± 4	135± 5	140± 4	143± 4
50ppm	95± 3	111± 3	122± 3	128± 4	136± 4	139± 5	145± 6
100ppm	95± 3	107± 3	117± 5	125± 6	133± 8	137± 9	142± 10
200ppm	95± 3	103± 3**	108± 4**	114± 4**	123± 5**	122± 6**	125± 7**

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

STUDY NO. : 0415
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	152± 7	155± 8	160± 9	162± 10	164± 9	164± 9	168± 10
12.5ppm	149± 9	152± 9	155± 10	159± 9	162± 9	162± 8	164± 9
25ppm	148± 6	150± 6	153± 6	156± 7	159± 6	160± 7	163± 7
50ppm	147± 6	150± 6	152± 5	156± 6	160± 6	163± 6	165± 7
100ppm	145± 9	149± 9	149± 9**	152± 9*	153± 9**	155± 9*	156± 8**
200ppm	126± 7**	132± 6**	130± 6**	133± 7**	137± 7**	136± 6**	139± 7**

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

APPENDIX B 1

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0415
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	14.5± 0.7	15.5± 0.9	16.0± 1.3	16.6± 1.1	16.3± 1.0	16.3± 1.0	16.5± 0.9
12.5ppm	13.9± 0.8	14.6± 0.7*	14.5± 1.0**	14.9± 0.9**	15.1± 1.5	14.8± 1.3**	14.9± 1.3**
25ppm	14.0± 0.8	14.8± 0.9	15.8± 0.9	15.6± 1.2*	15.3± 1.1	15.1± 1.2*	15.5± 0.9
50ppm	13.6± 0.8	14.4± 0.8**	15.3± 0.9	15.5± 0.6*	15.0± 0.9	15.2± 1.0	15.2± 0.8*
100ppm	12.8± 0.8**	13.8± 0.6**	15.2± 0.9	15.0± 0.7**	14.6± 0.9*	14.1± 0.7**	14.3± 0.7**
200ppm	10.8± 0.5**	10.8± 0.6**	11.4± 0.6**	11.9± 0.5**	11.1± 0.4**	11.2± 0.5**	11.2± 0.7**

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

STUDY NO. : 0415
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	16.3± 0.7	16.0± 1.1	15.3± 0.7	15.5± 0.6	15.8± 0.6	15.7± 0.7
12.5ppm	14.7± 1.2**	14.7± 1.1*	14.7± 1.0	14.8± 1.1	14.0± 1.0*	14.2± 1.0
25ppm	15.6± 0.9	16.0± 1.1	14.3± 1.2	14.5± 1.2	14.2± 1.3	14.3± 1.2
50ppm	15.3± 0.9*	15.3± 0.7	14.2± 0.7	13.9± 1.0*	14.2± 0.9	14.4± 0.7
100ppm	14.5± 0.8**	13.9± 0.9**	13.4± 0.7**	13.7± 0.8**	12.9± 0.8**	13.2± 0.4**
200ppm	12.0± 0.5**	11.6± 0.5**	11.2± 0.3**	12.1± 0.5**	11.1± 0.3**	11.4± 0.5**

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

APPENDIX B 2

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0415
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	10.8± 0.5	11.0± 0.6	11.3± 0.6	11.4± 0.8	11.2± 0.9	11.3± 1.3	11.1± 1.4
12.5ppm	10.5± 0.7	10.6± 0.5	11.1± 0.7	10.8± 0.7	11.0± 0.7	11.2± 0.9	10.6± 0.7
25ppm	10.9± 0.7	11.1± 0.5	11.4± 0.5	11.6± 0.6	11.1± 0.5	10.6± 0.4	10.7± 0.4
50ppm	10.9± 0.5	10.8± 0.5	11.3± 1.0	11.2± 0.7	10.5± 0.4	10.8± 1.0	10.4± 0.9
100ppm	9.9± 0.7*	10.2± 0.7**	10.8± 0.7	11.3± 1.1	10.5± 0.8	10.5± 1.1	10.4± 1.0
200ppm	8.9± 0.6**	8.6± 0.5**	9.1± 0.6**	9.4± 0.6**	8.8± 0.7**	8.6± 0.6**	8.7± 0.4**

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

STUDY NO. : 0415
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	10.7± 1.2	10.7± 0.9	10.7± 1.6	10.6± 1.2	10.4± 1.1	10.8± 1.6
12.5ppm	10.2± 0.9	10.6± 0.9	10.4± 0.9	10.6± 1.2	9.5± 0.9	10.0± 0.8
25ppm	10.0± 0.7	10.3± 0.7	9.8± 0.7	9.8± 0.6	9.8± 0.8	10.1± 0.6
50ppm	9.9± 0.6	10.2± 0.5	9.9± 0.8	10.1± 0.6	10.3± 0.8	10.1± 0.9
100ppm	10.1± 0.7	9.6± 0.5**	9.4± 0.6	10.1± 0.8	9.5± 0.7	9.6± 0.5
200ppm	9.0± 0.6**	8.8± 0.5**	8.2± 0.6**	9.0± 0.5**	8.4± 0.4**	8.7± 0.6**

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

APPENDIX C 1

URINALYSIS : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0415
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	1	1	7	1		0	4	3	3	0	0		10	0	0	0	0	0		8	0	2	0	0	0		10	0	0	0	
12.5ppm	10	0	0	0	0	2	5	3		0	1	5	4	0	0		10	0	0	0	0	0		6	3	0	1	0	0		10	0	0	0	
25ppm	10	0	0	0	0	4	6	0		0	4	4	2	0	0		10	0	0	0	0	0		6	3	1	0	0	0		10	0	0	0	
50ppm	10	0	0	0	0	4	4	2		0	4	4	2	0	0		10	0	0	0	0	0		6	4	0	0	0	0		10	0	0	0	
100ppm	10	0	0	0	1	0	7	2		0	3	4	2	1	0		10	0	0	0	0	0		4	3	3	0	0	0		10	0	0	0	
200ppm	10	0	0	0	0	1	7	2		0	2	4	3	1	0		10	0	0	0	0	0		2	5	2	1	0	0	*	10	0	0	0	

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

STUDY NO. : 0415
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	10	0	0	0	0		10	0	0	0	0	
12.5ppm	10	10	0	0	0	0		10	0	0	0	0	
25ppm	10	10	0	0	0	0		10	0	0	0	0	
50ppm	10	10	0	0	0	0		10	0	0	0	0	
100ppm	10	10	0	0	0	0		10	0	0	0	0	
200ppm	10	8	0	0	0	2		10	0	0	0	0	

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

APPENDIX C 2

URINALYSIS : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0415
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	6	2		4	4	2	0	0	0		10	0	0	0	0	0		9	1	0	0	0	0		10	0	0	0	
12.5ppm	10	0	0	0	1	2	7	0		5	5	0	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
25ppm	10	0	0	0	0	3	4	3		5	5	0	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
50ppm	10	0	0	0	0	0	5	5		3	6	1	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
100ppm	10	0	0	0	0	2	5	3		5	5	0	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
200ppm	10	0	0	0	1	1	2	6		1	1	6	2	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. : 0415 URINALYSIS
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

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	
12.5ppm	10	10	0	0	0	0		10	0	0	0	0	
25ppm	10	10	0	0	0	0		10	0	0	0	0	
50ppm	10	10	0	0	0	0		10	0	0	0	0	
100ppm	10	10	0	0	0	0		10	0	0	0	0	
200ppm	10	10	0	0	0	0		10	0	0	0	0	

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

APPENDIX D 1

HEMATOLOGY : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0415
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 $10^5/\mu\ell$		HEMOGLOBIN g/dℓ		HEMATOCRIT %		MCV fℓ		MCH pg		MCHC g/dℓ		PLATELET $10^3/\mu\ell$	
Control	10	9.25±	0.12	16.0±	0.3	45.6±	0.7	49.3±	0.4	17.3±	0.4	35.2±	0.6	795±	68
12.5ppm	10	9.42±	0.21	16.4±	0.3*	46.8±	0.9*	49.7±	0.6	17.4±	0.4	35.0±	0.6	751±	32
25ppm	10	9.23±	0.17	16.1±	0.3	45.7±	0.3	49.6±	0.7	17.4±	0.4	35.1±	0.5	762±	46
50ppm	10	9.20±	0.20	16.1±	0.3	45.6±	1.0	49.6±	0.5	17.5±	0.2	35.3±	0.4	786±	51
100ppm	10	9.19±	0.16	16.3±	0.3	45.7±	1.0	49.8±	0.3	17.7±	0.3	35.5±	0.7	740±	44
200ppm	10	8.86±	0.20**	16.0±	0.3	45.1±	1.2	50.9±	0.5**	18.1±	0.4**	35.5±	0.9	690±	60**

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

STUDY NO. : 0415
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	21±	4	14.5±	1.1	21.3±	4.0
12.5ppm	10	18±	5	16.1±	2.7	22.0±	3.7
25ppm	10	23±	6	15.5±	2.2	22.9±	3.3
50ppm	10	21±	5	15.2±	1.9	21.6±	4.6
100ppm	10	24±	7	13.5±	0.8	18.0±	3.7
200ppm	10	22±	5	14.0±	1.4	18.9±	3.8

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

STUDY NO. : 0415
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	5.42± 1.78	0± 1	25± 7	1± 1	0± 0	4± 2	70± 7	0± 0
12.5ppm	10	5.42± 1.40	0± 0	28± 6	1± 1	0± 0	5± 2	66± 6	0± 0
25ppm	10	4.38± 1.59	1± 1	26± 4	1± 1	0± 0	4± 2	69± 4	0± 0
50ppm	10	4.86± 1.42	0± 1	25± 4	1± 1	0± 0	3± 2	70± 4	0± 0
100ppm	10	4.94± 1.45	0± 1	28± 7	2± 1	0± 0	2± 1	68± 7	0± 0
200ppm	10	3.85± 1.53	1± 1	40± 8**	1± 1	0± 0	5± 2	54± 9**	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. : 0415
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 f ℓ	MCH p g	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	10	8.57± 0.25	16.2± 0.4	45.0± 1.3	52.6± 0.5	18.9± 0.5	35.9± 0.9	817± 55
12.5ppm	10	8.60± 0.15	16.2± 0.3	45.0± 1.0	52.3± 0.5	18.9± 0.4	36.1± 0.9	772± 40
25ppm	10	8.67± 0.22	16.2± 0.5	45.3± 1.2	52.3± 0.4	18.7± 0.3	35.8± 0.6	791± 40
50ppm	10	8.65± 0.29	16.3± 0.5	45.4± 1.8	52.5± 0.5	18.8± 0.3	35.9± 0.8	784± 64
100ppm	10	8.47± 0.26	15.9± 0.6	44.2± 1.4	52.2± 0.4	18.7± 0.4	36.0± 0.9	795± 72
200ppm	10	8.56± 0.22	16.0± 0.3	44.7± 1.4	52.2± 0.7	18.7± 0.4	35.8± 1.1	691± 63**

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

STUDY NO. : 0415
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	10	16±	4	13.7±	0.8	15.5±	2.4
12.5ppm	10	18±	3	13.5±	1.2	16.4±	2.9
25ppm	10	18±	5	13.8±	0.7	16.1±	1.0
50ppm	10	20±	3	13.6±	0.8	15.1±	2.3
100ppm	10	23±	4**	14.2±	0.5	16.8±	1.9
200ppm	10	20±	4	14.2±	0.7	16.7±	2.3

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

(HCL070)

STUDY NO. : 0415
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	10	2.31±	0.51	1±	0	27±	3	2±	1	0±	0	3±	1	67±	3	0±	1
12.5ppm	10	2.01±	0.63	1±	1	27±	8	2±	1	0±	0	3±	1	67±	7	0±	0
25ppm	10	2.53±	1.00	1±	1	29±	6	1±	1	0±	0	3±	1	65±	7	0±	1
50ppm	10	3.24±	1.72	0±	1	27±	5	1±	1	0±	0	4±	1	68±	5	0±	0
100ppm	10	3.28±	0.84	1±	1	29±	9	1±	1	0±	0	3±	2	67±	8	0±	0
200ppm	10	2.81±	0.73	1±	1	34±	6	1±	1	0±	0	4±	1	60±	6	1±	1

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

APPENDIX E 1

BIOCHEMISTRY : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0415
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	6.4±	0.1	3.9±	0.1	1.6±	0.1	0.11±	0.01	181±	12	59±	4	53±	13
12.5ppm	10	6.4±	0.2	3.9±	0.1	1.6±	0.0	0.11±	0.01	184±	14	60±	5	61±	12
25ppm	10	6.4±	0.1	3.9±	0.1	1.6±	0.1	0.11±	0.02	180±	11	59±	6	50±	12
50ppm	10	6.4±	0.1	3.9±	0.1	1.6±	0.1	0.11±	0.02	174±	12	60±	4	49±	19
100ppm	10	6.3±	0.1	3.8±	0.1	1.5±	0.0	0.11±	0.01	170±	11	60±	4	35±	11*
200ppm	10	6.4±	0.2	3.8±	0.1	1.5±	0.1	0.12±	0.01	163±	12**	60±	4	25±	11**

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

STUDY NO. : 0415
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	116± 7	66± 15	46± 7	187± 33	257± 23	2± 1	111± 14
12.5ppm	10	120± 8	75± 28	47± 10	218± 35	265± 24	2± 1	115± 12
25ppm	10	117± 7	63± 11	43± 3	186± 49	246± 19	2± 1	121± 22
50ppm	10	113± 6	67± 7	43± 5	181± 52	248± 25	2± 1	105± 16
100ppm	10	115± 7	59± 13	37± 4**	172± 51	236± 19	2± 1	100± 17
200ppm	10	117± 7	59± 6	36± 3**	187± 68	274± 25	1± 1	105± 17

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

STUDY NO. : 0415
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	19.1± 1.9	0.5± 0.1	141± 1	3.4± 0.3	103± 1	10.2± 0.2	5.6± 1.1
12.5ppm	10	19.1± 1.3	0.5± 0.1	140± 1	3.5± 0.4	104± 2	10.0± 0.2	5.5± 1.1
25ppm	10	18.9± 0.9	0.5± 0.1	141± 1	3.6± 0.2	103± 2	10.2± 0.2	5.6± 1.0
50ppm	10	19.7± 1.5	0.5± 0.1	140± 1	3.6± 0.3	103± 1	10.1± 0.3	6.0± 0.7
100ppm	10	20.6± 1.5	0.5± 0.1	139± 1**	3.7± 0.4	102± 2	10.1± 0.3	5.8± 1.0
200ppm	10	20.6± 2.3	0.5± 0.0	138± 1**	3.8± 0.3	102± 2	9.9± 0.2	5.9± 0.7

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

APPENDIX E 2

BIOCHEMISTRY : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0415
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	10	6.2± 0.2	3.8± 0.1	1.5± 0.0	0.13± 0.01	134± 17	70± 10	13± 2
12.5ppm	10	6.3± 0.1	3.7± 0.1	1.5± 0.1	0.14± 0.02	137± 12	66± 9	13± 1
25ppm	10	6.1± 0.1	3.7± 0.1	1.5± 0.1	0.14± 0.02	130± 11	66± 6	13± 2
50ppm	10	6.2± 0.2	3.7± 0.1	1.5± 0.1	0.14± 0.03	135± 17	66± 6	13± 4
100ppm	10	6.0± 0.1*	3.6± 0.1**	1.5± 0.1	0.14± 0.01	133± 12	67± 6	14± 4
200ppm	10	5.9± 0.1**	3.5± 0.1**	1.5± 0.1	0.15± 0.02	134± 13	65± 4	14± 2

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

STUDY NO. : 0415
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	10	139± 13	67± 6	35± 5	261± 102	198± 14	3± 1	151± 48
12.5ppm	10	135± 13	75± 12	41± 11	332± 176	196± 20	2± 1	147± 48
25ppm	10	135± 10	69± 12	39± 18	325± 164	195± 20	3± 1	148± 42
50ppm	10	133± 10	73± 12	37± 9	295± 121	195± 11	2± 1	132± 31
100ppm	10	134± 9	63± 4	31± 4	270± 84	196± 18	2± 1	129± 23
200ppm	10	129± 9	68± 3	35± 3	299± 103	256± 26**	4± 1	126± 27

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

STUDY NO. : 0415
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	10	18.8± 1.4	0.6± 0.1	139± 1	3.5± 0.3	105± 2	9.8± 0.2	4.9± 1.2
12.5ppm	10	20.1± 2.1	0.6± 0.1	139± 1	3.6± 0.3	105± 2	9.8± 0.3	5.2± 1.2
25ppm	10	20.2± 1.2	0.6± 0.1	139± 1	3.7± 0.3	105± 1	9.8± 0.1	5.6± 0.9
50ppm	10	19.8± 1.8	0.6± 0.1	139± 1	3.6± 0.4	105± 1	9.9± 0.2	5.5± 1.1
100ppm	10	20.3± 1.5	0.6± 0.1	138± 1**	3.8± 0.4	105± 1	9.7± 0.2	6.0± 0.8
200ppm	10	21.6± 3.2	0.6± 0.1	137± 1**	3.8± 0.3	103± 1	9.7± 0.2	6.1± 0.9

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

APPENDIX F 1

GROSS FINDINGS : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0415
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control	12.5ppm	25ppm	50ppm
		NO. of Animals	10 (%)	10 (%)	10 (%)	10 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)
liver	herniation		1 (10)	0 (0)	0 (0)	1 (10)

STUDY NO. : 0415
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	100ppm		200ppm	
		NO. of Animals	10	(%)	10	(%)
thymus	atrophic		0	(0)	8	(80)
liver	herniation		0	(0)	0	(0)

APPENDIX F 2

GROSS FINDINGS : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0415
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 (%)	12.5ppm 10 (%)	25ppm 10 (%)	50ppm 10 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)
spleen	adhesion		0 (0)	1 (10)	0 (0)	0 (0)
liver	herniation		2 (20)	0 (0)	0 (0)	2 (20)
ovary	cyst		1 (10)	0 (0)	0 (0)	0 (0)

STUDY NO. : 0415
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name	100ppm		200ppm	
		NO. of Animals	10	(%)	10	(%)
thymus	atrophic		0	(0)	5	(50)
spleen	adhesion		0	(0)	0	(0)
liver	herniation		2	(20)	2	(20)
ovary	cyst		0	(0)	0	(0)

APPENDIX G 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0415
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	284± 10	0.213± 0.026	0.048± 0.006	2.914± 0.086	0.914± 0.029	0.983± 0.032
12.5ppm	10	265± 13**	0.203± 0.029	0.047± 0.008	2.765± 0.457	0.853± 0.037**	0.934± 0.052*
25ppm	10	269± 20	0.207± 0.027	0.049± 0.008	2.911± 0.145	0.862± 0.057*	0.957± 0.045
50ppm	10	264± 12**	0.204± 0.020	0.045± 0.004	2.937± 0.132	0.872± 0.043	0.952± 0.033
100ppm	10	238± 11**	0.154± 0.016**	0.047± 0.007	2.852± 0.130	0.812± 0.031**	0.910± 0.036**
200ppm	10	183± 8**	0.111± 0.018**	0.048± 0.006	2.383± 0.304**	0.700± 0.039**	0.800± 0.037**

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

STUDY NO. : 0415
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	1.729± 0.056	0.548± 0.051	6.932± 0.195	1.866± 0.066
12.5ppm	10	1.626± 0.062	0.500± 0.026	6.501± 0.410*	1.831± 0.043
25ppm	10	1.678± 0.127	0.501± 0.041	6.528± 0.501*	1.875± 0.033
50ppm	10	1.650± 0.084	0.514± 0.037	6.446± 0.325*	1.871± 0.065
100ppm	10	1.599± 0.047**	0.442± 0.017**	6.029± 0.281**	1.805± 0.067
200ppm	10	1.442± 0.066**	0.337± 0.025**	4.877± 0.268**	1.738± 0.049**

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

APPENDIX G 2

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0415
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	0.169± 0.014	0.048± 0.003	0.089± 0.014	0.581± 0.029	0.715± 0.043
12.5ppm	10	150± 9	0.163± 0.012	0.050± 0.006	0.085± 0.007	0.573± 0.033	0.688± 0.037
25ppm	10	149± 7	0.165± 0.012	0.051± 0.006	0.087± 0.010	0.558± 0.028	0.682± 0.040
50ppm	10	151± 6	0.164± 0.019	0.050± 0.004	0.080± 0.009	0.573± 0.023	0.706± 0.026
100ppm	10	141± 9**	0.153± 0.020	0.054± 0.006*	0.081± 0.008	0.553± 0.042	0.703± 0.047
200ppm	10	127± 5**	0.119± 0.012**	0.054± 0.004*	0.073± 0.009**	0.530± 0.026**	0.639± 0.023**

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

STUDY NO. : 0415
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	1.025± 0.057	0.347± 0.033	3.769± 0.251	1.712± 0.045
12.5ppm	10	0.997± 0.039	0.344± 0.022	3.655± 0.223	1.740± 0.046
25ppm	10	1.005± 0.041	0.332± 0.027	3.607± 0.167	1.698± 0.033
50ppm	10	1.028± 0.031	0.341± 0.026	3.712± 0.241	1.688± 0.064
100ppm	10	1.024± 0.050	0.328± 0.026	3.638± 0.208	1.696± 0.030
200ppm	10	1.020± 0.031	0.272± 0.018**	3.404± 0.188**	1.623± 0.030**

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

APPENDIX H 1

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0415
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	284± 10	0.075± 0.009	0.017± 0.002	1.028± 0.038	0.322± 0.007	0.347± 0.014
12.5ppm	10	265± 13**	0.077± 0.009	0.018± 0.003	1.051± 0.192	0.323± 0.007	0.353± 0.015
25ppm	10	269± 20	0.077± 0.008	0.018± 0.002	1.086± 0.050	0.321± 0.008	0.357± 0.016
50ppm	10	264± 12**	0.077± 0.007	0.017± 0.002	1.116± 0.072	0.331± 0.011	0.362± 0.012
100ppm	10	238± 11**	0.065± 0.005*	0.020± 0.003	1.200± 0.035**	0.342± 0.015*	0.383± 0.018**
200ppm	10	183± 8**	0.060± 0.008**	0.026± 0.003**	1.303± 0.176**	0.383± 0.018**	0.437± 0.020**

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

STUDY NO. : 0415
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	0.610± 0.021	0.193± 0.016	2.445± 0.068	0.658± 0.022
12.5ppm	10	0.615± 0.016	0.189± 0.009	2.455± 0.054	0.693± 0.026
25ppm	10	0.625± 0.022	0.187± 0.012	2.430± 0.051	0.701± 0.044*
50ppm	10	0.626± 0.017	0.195± 0.010	2.445± 0.044	0.711± 0.043**
100ppm	10	0.674± 0.030**	0.186± 0.007	2.537± 0.082**	0.761± 0.041**
200ppm	10	0.788± 0.028**	0.184± 0.010	2.661± 0.069**	0.950± 0.035**

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

APPENDIX H 2

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0415
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	0.109± 0.008	0.031± 0.002	0.058± 0.009	0.375± 0.018	0.461± 0.018
12.5ppm	10	150± 9	0.109± 0.009	0.033± 0.003	0.057± 0.004	0.382± 0.019	0.459± 0.010
25ppm	10	149± 7	0.110± 0.005	0.034± 0.004	0.058± 0.005	0.374± 0.021	0.457± 0.020
50ppm	10	151± 6	0.109± 0.011	0.033± 0.003	0.053± 0.007	0.379± 0.013	0.467± 0.024
100ppm	10	141± 9**	0.108± 0.011	0.038± 0.004**	0.058± 0.005	0.391± 0.013	0.497± 0.019**
200ppm	10	127± 5**	0.094± 0.009**	0.042± 0.003**	0.058± 0.008	0.420± 0.024**	0.506± 0.023**

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

STUDY NO. : 0415
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	0.661± 0.033	0.224± 0.016	2.431± 0.124	1.107± 0.075
12.5ppm	10	0.665± 0.019	0.230± 0.014	2.436± 0.078	1.162± 0.051
25ppm	10	0.673± 0.023	0.222± 0.013	2.415± 0.089	1.138± 0.047
50ppm	10	0.680± 0.027	0.225± 0.014	2.454± 0.119	1.118± 0.066
100ppm	10	0.725± 0.023**	0.232± 0.015	2.574± 0.063*	1.203± 0.069**
200ppm	10	0.807± 0.021**	0.215± 0.007	2.692± 0.116**	1.286± 0.062**

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

APPENDIX I 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE

(13-WEEK STUDY)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 10 1 (%)	Control 10 2 (%)	Control 10 3 (%)	Control 10 4 (%)	12.5ppm 10 1 (%)	12.5ppm 10 2 (%)	12.5ppm 10 3 (%)	12.5ppm 10 4 (%)	25ppm 10 1 (%)	25ppm 10 2 (%)	25ppm 10 3 (%)	25ppm 10 4 (%)	50ppm 10 1 (%)	50ppm 10 2 (%)	50ppm 10 3 (%)	50ppm 10 4 (%)
{Respiratory system}																		
nasal cavit			<10>				<10>				<10>				<10>			
	adhesion		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	inflammation:respiratory 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)
	inflammation:olfactory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia: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)
	inflammation:transitional epithelium		1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)
	squamous cell metaplasia:respiratory 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)

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	100ppm				200ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			<10>				<10>			
	adhesion		0	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(30)	(0)	(0)	(0)
	inflammation:respiratory epithelium		10	0	0	0 **	10	0	0	0 **
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	inflammation:olfactory epithelium		0	0	0	0	8	0	0	0 **
			(0)	(0)	(0)	(0)	(80)	(0)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		0	0	0	0	10	0	0	0 **
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	inflammation:transitional epithelium		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	squamous cell metaplasia:respiratory epithelium		0	0	0	0	5	5	0	0 **
			(0)	(0)	(0)	(0)	(50)	(50)	(0)	(0)
	atrophy:olfactory epithelium		0	10	0	0 **	0	0	10	0 **
			(0)	(100)	(0)	(0)	(0)	(0)	(100)	(0)
	necrosis:olfactory epithelium		1	0	0	0	7	3	0	0 **
			(10)	(0)	(0)	(0)	(70)	(30)	(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 (%)	2 (%)	3 (%)	4 (%)	12.5ppm 10 1 (%)	2 (%)	3 (%)	4 (%)	25ppm 10 1 (%)	2 (%)	3 (%)	4 (%)	50ppm 10 1 (%)	2 (%)	3 (%)	4 (%)
{Respiratory system}																		
nasal cavit	necrosis:respiratory epithelium	<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)
	hyperplasia:respiratory 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)	10 (100)	0 (0)	0 (0)	0 ** (0)
lung	accumulation of foamy cells	<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)
{Hematopoietic system}																		
bone marrow	granulation	<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)
thymus	atrophy	<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)
{Circulatory system}																		
heart	inflammatory cell nest	<10>	3 (30)	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)

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	100ppm				200ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			<10>				<10>			
	necrosis:respiratory epithelium		8	0	0	0 **	9	1	0	0 **
			(80)	(0)	(0)	(0)	(90)	(10)	(0)	(0)
	hyperplasia:respiratory epithelium		0	10	0	0 **	0	0	10	0 **
			(0)	(100)	(0)	(0)	(0)	(0)	(100)	(0)
lung			<10>				<10>			
	accumulation of foamy cells		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Hematopoietic system}										
bone marrow			<10>				<10>			
	granulation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thymus			<10>				<10>			
	atrophy		0	0	0	0	8	0	0	0 **
			(0)	(0)	(0)	(0)	(80)	(0)	(0)	(0)
{Circulatory system}										
heart			<10>				<10>			
	inflammatory cell nest		3	0	0	0	2	0	0	0
			(30)	(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	Control				12.5ppm				25ppm				50ppm			
		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>			
	herniation		1 (10)	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)
	granulation		1 (10)	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)
	perivascular inflammation		1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	eosinophilic body		1 (10)	9 (90)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	1 (10)	9 (90)	0 (0)	0 (0)	1 (10)	9 (90)	0 (0)	0 (0)
	mineralization:papilla		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)
	hemorrhage: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)	2 (20)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)

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

Organ	Findings	Group Name	100ppm				200ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
liver			<10>				<10>			
	herniation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	granulation		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	perivascular inflammation		3	0	0	0	0	0	0	0
			(30)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Urinary system}										
kidney			<10>				<10>			
	eosinophilic body		0	10	0	0	9	1	0	0 **
			(0)	(100)	(0)	(0)	(90)	(10)	(0)	(0)
	mineralization:papilla		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hemorrhage:papilla		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Endocrine system}										
pituitary			<10>				<10>			
	Rathke pouch		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 / No. of Animals on Study / Grade	Control 10				12.5ppm 10				25ppm 10				50ppm 10			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Reproductive system}																		
testis			<10>				<10>				<10>				<10>			
	germ cell necrosis		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)	0 (0)	0 (0)
epididymis			<10>				<10>				<10>				<10>			
	decreased:sperma		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)	0 (0)	0 (0)
	debris of spermatic elements		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)
prostate			<10>				<10>				<10>				<10>			
	inflammation		0 (0)	0 (0)	0 (0)	0 (0)	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		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)
	vascularization:cornea		0 (0)	0 (0)	0 (0)	0 (0)	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	100ppm				200ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Reproductive system}										
testis			<10>				<10>			
	germ cell necrosis		0	1	0	0	5	2	1	0 **
			(0)	(10)	(0)	(0)	(50)	(20)	(10)	(0)
epididymis			<10>				<10>			
	decreased:sperma		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	debris of spermatic elements		0	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(30)	(0)	(0)	(0)
prostate			<10>				<10>			
	inflammation		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)
	vascularization:cornea		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

Organ	Findings	Group Name	Control				12.5ppm				25ppm				50ppm			
		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>			
	lymphocytic infiltration		0	1	0	0	1	0	0	0	1	0	0	0	2	0	0	0
			(0)	(10)	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(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	100ppm				200ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Special sense organs/appendage}										
Harder gl			<10>				<10>			
	lymphocytic infiltration		2	0	0	0	0	0	0	0
			(20)	(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 I 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE

(13-WEEK STUDY)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 10				12.5ppm 10				25ppm 10				50ppm 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>			
	adhesion		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	inflammation:respiratory 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)
	inflammation:olfactory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia: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)
	inflammation:transitional epithelium		3 (30)	0 (0)	0 (0)	0 (0)	5 (50)	0 (0)	0 (0)	0 (0)	6 (60)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)
	squamous cell metaplasia:respiratory 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)

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	100ppm				200ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			<10>				<10>			
	adhesion		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	inflammation:respiratory epithelium		10	0	0	0 **	10	0	0	0 **
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	inflammation:olfactory epithelium		0	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(30)	(0)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		0	0	0	0	6	0	0	0 *
			(0)	(0)	(0)	(0)	(60)	(0)	(0)	(0)
	inflammation:transitional epithelium		2	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	squamous cell metaplasia:respiratory epithelium		0	0	0	0	4	6	0	0 **
			(0)	(0)	(0)	(0)	(40)	(60)	(0)	(0)
	atrophy:olfactory epithelium		6	4	0	0 **	0	4	6	0 **
			(60)	(40)	(0)	(0)	(0)	(40)	(60)	(0)
	necrosis:olfactory epithelium		1	0	0	0	9	1	0	0 **
			(10)	(0)	(0)	(0)	(90)	(10)	(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				12.5ppm				25ppm				50ppm			
		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>			
	necrosis:respiratory 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)
	hyperplasia:respiratory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(30)	(0)	(0)	(0)
lung			<10>				<10>				<10>				<10>			
	accumulation of foamy cells		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)
{Hematopoietic system}																		
bone marrow			<10>				<10>				<10>				<10>			
	granulation		1	1	0	0	2	2	0	0	2	1	0	0	3	0	0	0
			(10)	(10)	(0)	(0)	(20)	(20)	(0)	(0)	(20)	(10)	(0)	(0)	(30)	(0)	(0)	(0)
thymus			<10>				<10>				<10>				<10>			
	atrophy		0	0	0	0	0	0	0	0	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>			
	capsule hyperplasia		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	100ppm				200ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			<10>				<10>			
	necrosis:respiratory epithelium		0	0	0	0	9	0	0	0 **
			(0)	(0)	(0)	(0)	(90)	(0)	(0)	(0)
	hyperplasia:respiratory epithelium		0	10	0	0 **	0	4	6	0 **
			(0)	(100)	(0)	(0)	(0)	(40)	(60)	(0)
lung			<10>				<10>			
	accumulation of foamy cells		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}										
bone marrow			<10>				<10>			
	granulation		2	3	0	0	0	1	0	0
			(20)	(30)	(0)	(0)	(0)	(10)	(0)	(0)
thymus			<10>				<10>			
	atrophy		0	0	0	0	5	0	0	0 *
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
spleen			<10>				<10>			
	capsule hyperplasia		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				12.5ppm				25ppm				50ppm			
		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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Circulatory system}																		
heart			<10>				<10>				<10>				<10>			
	inflammatory cell nest		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)
{Digestive system}																		
liver			<10>				<10>				<10>				<10>			
	herniation		2	0	0	0	0	0	0	0	2	0	0	0	2	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	granulation		1	0	0	0	3	0	0	0	3	0	0	0	2	0	0	0
			(10)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	perivascular inflammation		2	0	0	0	3	0	0	0	2	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	mineralization:cortico-medullary junction		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)

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	100ppm				200ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Circulatory system}										
heart			<10>				<10>			
	inflammatory cell nest		1	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Digestive system}										
liver			<10>				<10>			
	herniation		2	0	0	0	2	0	0	0
			(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	granulation		2	0	0	0	2	0	0	0
			(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	perivascular inflammation		1	0	0	0	2	0	0	0
			(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
{Urinary system}										
kidney			<10>				<10>			
	mineralization:cortico-medullary junction		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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 10				12.5ppm 10				25ppm 10				50ppm 10			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Urinary system}																		
kidney	mineralization:papilla		<10>				<10>				<10>				<10>			
			1	0	0	0	1	0	0	0	2	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Endocrine system}																		
pituitary	Rathke pouch		<10>				<10>				<10>				<10>			
			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)
thyroid	ultimibranchial body remanet		<10>				<10>				<10>				<10>			
			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)
{Reproductive system}																		
ovary	cyst		< 9>				<10>				<10>				<10>			
			1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(11)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Special sense organs/appendage}																		
eye	vascularization:cornea		<10>				<10>				<10>				<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	100ppm				200ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}										
kidney			<10>				<10>			
	mineralization:papilla		1	0	0	0	2	0	0	0
			(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
{Endocrine system}										
pituitary			<10>				<10>			
	Rathke pouch		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thyroid			<10>				<10>			
	ultimibranchial body remanet		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Reproductive system}										
ovary			<10>				<10>			
	cyst		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Special sense organs/appendage}										
eye			<10>				<10>			
	vascularization:cornea		0	0	0	0	2	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	Control				12.5ppm				25ppm				50ppm			
		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>			
	lymphocytic infiltration		2	1	0	0	3	0	0	0	3	0	0	0	1	0	0	0
			(20)	(10)	(0)	(0)	(30)	(0)	(0)	(0)	(30)	(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	100ppm				200ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Special sense organs/appendage}										
Harder gl			<10>				<10>			
	lymphocytic infiltration		2	1	0	0	1	0	0	0
			(20)	(10)	(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 J 1

IDENTITY OF BUTY2,3-EPOXYPROPYL ETHER IN THE 13-WEEK INHALATION STUDY

IDENTITY OF BUTYL 2,3-EPOXYPROPYL ETHER IN THE 13-WEEK INHALATION STUDY

Test Substance : Butyl 2,3-epoxypropyl ether (Wako Pure Chemical Industries, Ltd.)

Lot No. : SEK5971

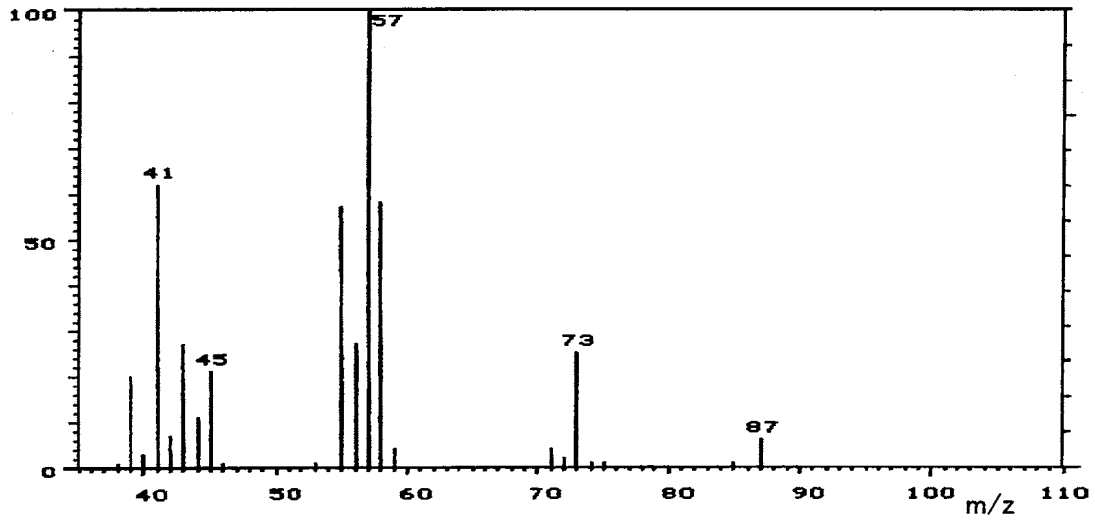
1. Spectral Data

Mass Spectrometry

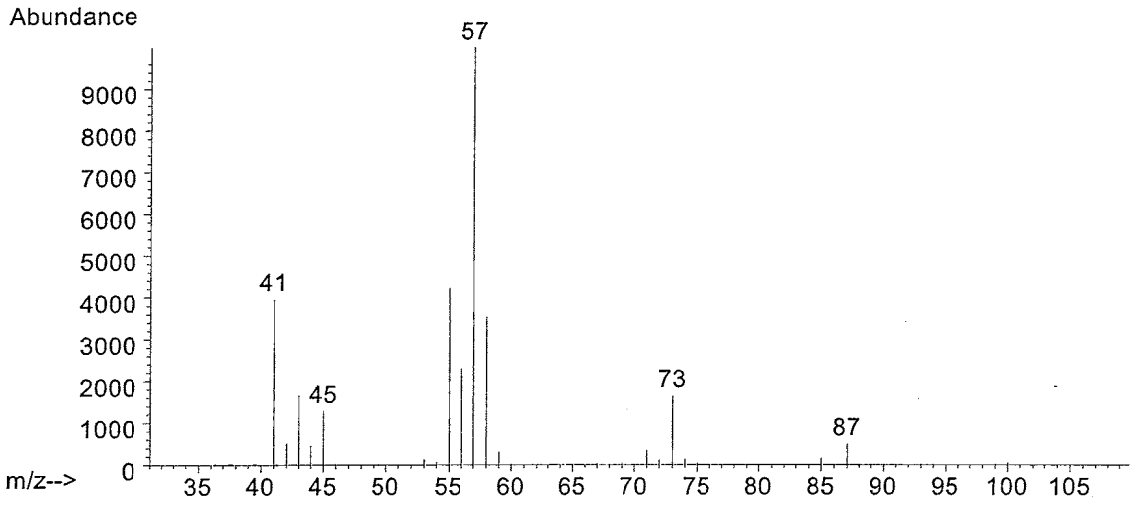
Instrument : Hitachi M-80B Mass Spectrometer

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.

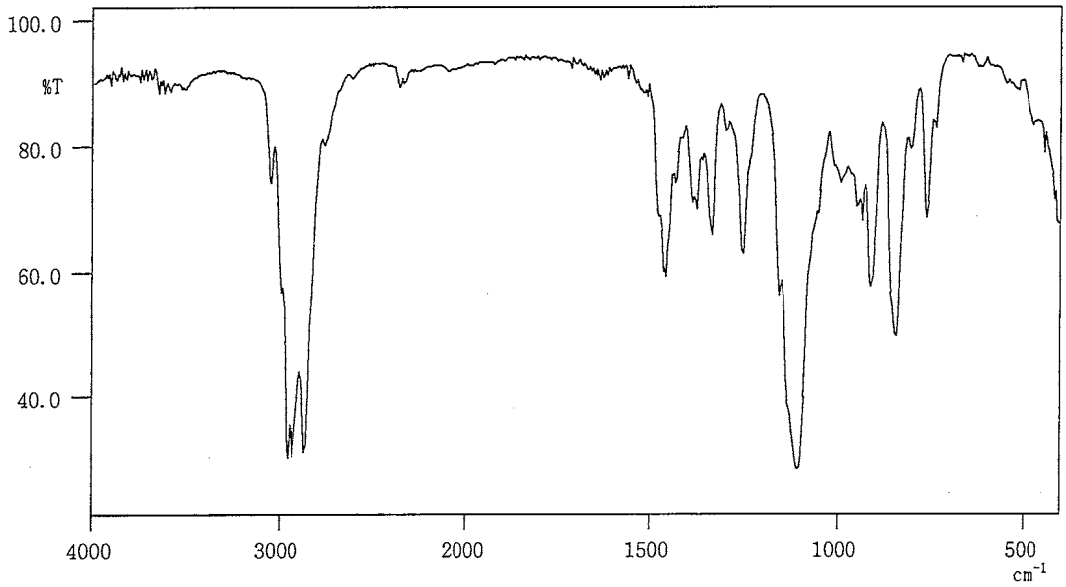
(*Fred W. McLafferty (1994)
Wiley Registry of Mass Spectral Data, 6th edition. Entry Number 20313
John Wiley and Sons, Inc. New York)

Infrared Spectrometry

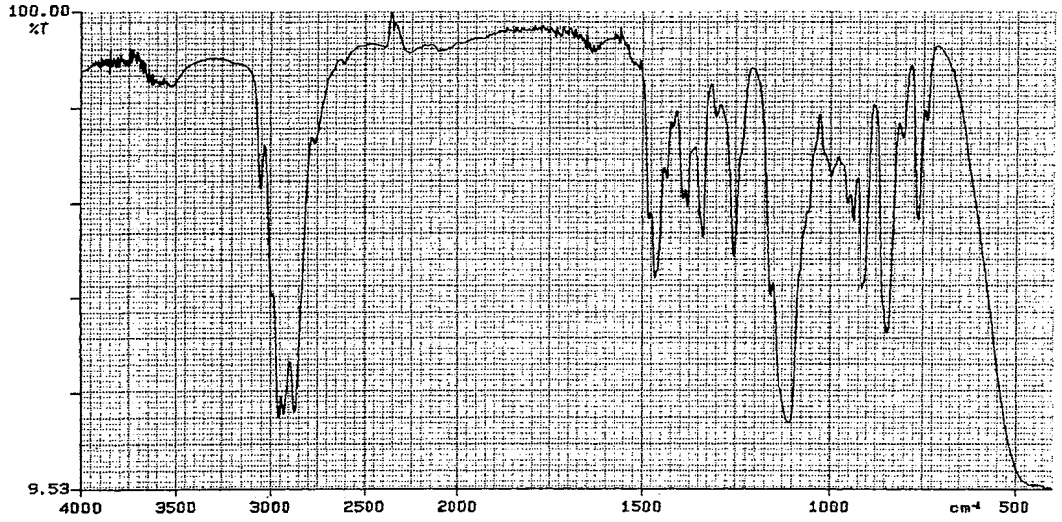
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

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 Wako Pure Chemical Industries, Ltd.)

2. Conclusion: The test substance was identified as butyl 2,3-epoxypropyl ether by mass spectrum and infrared spectrum.

APPENDIX J 2

STABILITY OF BUTY2,3-EPOXYPROPYL ETHER IN THE 13-WEEK INHALATION STUDY

STABILITY OF BUTYL 2,3-EPOXYPROPYL ETHER IN THE 13-WEEK INHALATION STUDY

Test Substance : Butyl 2,3-epoxypropyl ether (Wako Pure Chemical Industries, Ltd.)

Lot No. : SEK5971

1. Sample : This lot was used from 2000.9.13 to 2000.12.12. 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 mm ϕ × 60 m)

Column Temperature: 160° C

Flow Rate : 20 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μL

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
2000.09.12	1	2.859	100
2000.12.22	1	2.855	100

Result: Gas chromatography indicated one major peak (peak No.1) analyzed on 2000.9.12 and one major peak (peak No.1) analyzed on 2000.12.22. No new trace impurity peak in the test substance analyzed on 2000.12.22 was detected.

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

APPENDIX K 1

CONCENTRATION OF BUTY2,3-EPOXYPROPYL ETHER

IN THE INHALATION CHAMBER

OF THE 13-WEEK INHALATION STUDY

CONCENTRATION OF BUTYL 2,3-EPOXYPROPYL ETHER IN THE INHALATION CHAMBER
OF THE 13-WEEK INHALATION STUDY

Group Name	Concentration(ppm) Mean ± S.D.
Control	0.0 ± 0.0
12.5ppm	12.6 ± 0.1
25ppm	25.2 ± 0.2
50ppm	50.3 ± 0.2
100ppm	100.4 ± 0.6
200ppm	200.2 ± 1.2

APPENDIX K 2

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 13-WEEK INHALATION STUDY OF BUTY2,3-EPOXYPROPYL ETHER

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 13-WEEK INHALATION STUDY OF BUTYL 2,3-EPOXYPROPYL ETHER

Group Name	Temperature(℃) Mean ± S.D.	Humidity(%) Mean ± S.D.	Ventilation Rate(L/min) Mean ± S.D.	Air Change(time/h) Mean
Control	22.5 ± 0.2	55.7 ± 1.1	212.3 ± 0.4	12.0
12.5ppm	22.2 ± 0.2	55.9 ± 1.7	212.4 ± 0.5	12.0
25ppm	22.5 ± 0.3	54.7 ± 1.4	211.8 ± 0.5	12.0
50ppm	22.4 ± 0.3	54.4 ± 2.3	211.7 ± 1.2	12.0
100ppm	22.6 ± 0.3	53.6 ± 2.6	212.0 ± 0.5	12.0
200ppm	22.6 ± 0.2	54.2 ± 3.0	212.2 ± 0.4	12.0

APPENDIX L 1

METHODS FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK INHALATION STUDY OF BUTY2,3-EPOXYPROPYL ETHER

METHOD FOR HEMATOLOGY,BIOCHEMISTRY AND URINALYSIS IN THE 13-WEEK INHALATION STUDY OF BUTYL 2,3-EPOXYPROPYL ETHER

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	GlcK･G-6-PDH method [4]
T-cholesterol	CE･COD･POD method [4]
Triglyceride	LPL･GK･GPO･POD method [4]
Phospholipid	PLD･ChOD･POD method [4]
Glutamic oxaloacetic transaminase (GOT)	JSCC method [4]
Glutamic pyruvic transaminase (GPT)	JSCC method [4]
Lactate dehydrogenase (LDH)	SFBC method [4]
Alkaline phosphatase (ALP)	GSCC method [4]
γ-Glutamyl transpeptidase (γ-GTP)	L-γ-Glutamyl-p-nitroanilide method [4]
Creatine phosphokinase (CPK)	JSCC method [4]
Urea nitrogen	Urease･GLDH method [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	PNP･XOD･POD method [4]
Urinalysis	
pH,Protein,Glucose,Ketone body,Bilirubin,Occult Blood, Urobilinogen	Urinalysis reagent paper method [5]

1) Automatic blood cell analyzer (Technicon H･1 : Bayer Corporation)
2) Automatic coagulometer (Sysmex CA-5000 : Sysmex Corporation)
3) Automatic blood cell differential analyzer (MICROX HEG-120NA : OMRON Corporation)
4) Automatic analyzer (Hitachi 7070 : Hitachi,Ltd.)
5) Ames reagent strips for urinalysis (Multistix : Bayer Corporation)

APPENDIX L 2

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK INHALATION STUDY OF BUTY2,3-EPOXYPROPYL ETHER

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK INHALATION STUDY OF BUTYL 2,3 - EPOXYPROPYL ETHER

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