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

試験番号：0416

APPENDICES

APPENDICES

APPENDICES (CONTINUED)

APPENDIX A 1

BODY WEIGHT CHANGES :SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7
Control	23.3± 0.7	25.2± 0.9	26.0± 1.0	26.4± 1.2	27.1± 1.1	27.5± 1.0	28.7± 1.1
12.5ppm	23.3± 0.8	24.3± 0.9	24.8± 0.8*	25.1± 0.8*	25.7± 1.0	26.3± 0.8**	26.8± 0.7
25ppm	23.3± 0.8	24.3± 1.1	25.1± 1.0	25.4± 1.1	26.4± 1.4	26.8± 0.9	27.0± 1.3
50ppm	23.3± 0.8	24.3± 1.2	24.5± 1.2**	24.5± 1.2**	25.1± 1.4	25.2± 1.2**	25.5± 1.5**
100ppm	23.3± 0.8	23.4± 0.8**	22.8± 0.7**	23.2± 0.8**	23.5± 0.6**	23.6± 0.6**	23.9± 0.8**
200ppm	23.3± 0.8	21.3± 0.6**	22.0± 0.6**	22.4± 0.6**	23.1± 0.4**	23.2± 0.5**	23.5± 0.6**

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

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 7-7	8-7	9-7	10-7	11-7	12-7	13-7
Control	29.1± 1.3	29.6± 1.2	29.8± 1.2	30.6± 1.4	31.3± 1.4	31.7± 1.3	32.4± 1.5
12.5ppm	27.4± 0.7**	27.7± 0.8	28.5± 0.9*	29.0± 0.9	29.5± 0.9**	30.1± 1.1	30.3± 1.2**
25ppm	27.8± 1.3*	28.7± 1.5	28.8± 1.6	29.6± 1.6	29.9± 1.2*	30.0± 2.1	30.6± 2.0*
50ppm	25.9± 1.4**	25.9± 1.2**	25.8± 1.3**	26.3± 1.2**	26.1± 1.1**	26.4± 1.3**	26.8± 1.2**
100ppm	24.4± 0.8**	24.7± 0.9**	24.6± 0.9**	24.8± 0.6**	25.1± 0.9**	25.1± 0.7**	25.7± 0.9**
200ppm	24.0± 0.6**	24.0± 0.5**	24.2± 0.5**	24.5± 0.7**	24.9± 0.5**	25.0± 0.8**	25.3± 1.0**

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

APPENDIX A 2

BODY WEIGHT CHANGES : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7
Control	18.8± 0.6	20.1± 1.2	20.9± 0.9	21.3± 1.3	22.1± 1.4	22.8± 1.2	23.5± 1.1
12.5ppm	18.7± 0.7	19.9± 1.0	20.6± 0.7	21.0± 0.9	21.9± 0.6	22.4± 1.2	23.4± 1.3
25ppm	18.8± 0.7	19.6± 0.6	20.5± 0.7	20.9± 0.6	22.1± 0.6	22.1± 0.5	22.8± 0.8
50ppm	18.7± 0.6	19.5± 1.0	20.0± 0.5*	20.4± 1.2	21.5± 1.4	21.7± 0.8	22.1± 0.8**
100ppm	18.7± 0.7	19.3± 0.8	19.4± 0.7**	19.3± 0.6**	20.1± 0.7**	20.1± 0.7**	19.9± 0.5**
200ppm	18.7± 0.6	17.0± 0.7**	18.0± 0.6**	18.6± 0.6**	19.3± 0.3**	19.3± 0.5**	19.4± 0.6**

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

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 7-7	8-7	9-7	10-7	11-7	12-7	13-7
Control	23.8± 1.6	24.0± 1.1	24.6± 1.6	24.1± 1.3	24.2± 1.5	24.8± 1.5	24.8± 1.5
12.5ppm	23.5± 0.9	23.4± 1.1	23.6± 1.3	24.4± 1.4	24.5± 1.5	25.0± 1.8	24.9± 1.3
25ppm	23.0± 0.9	23.6± 0.8	23.6± 0.8	23.8± 0.7	23.8± 0.7	24.3± 1.1	24.8± 1.0
50ppm	22.5± 0.9*	22.6± 1.0**	23.0± 1.1	23.4± 1.4	22.7± 1.0*	23.3± 1.1*	23.5± 1.1*
100ppm	20.4± 0.8**	20.6± 0.9**	20.6± 0.7**	21.2± 0.7**	21.2± 0.9**	21.4± 0.8**	21.8± 0.8**
200ppm	19.7± 0.8**	19.9± 0.6**	20.1± 0.6**	20.4± 0.9**	20.5± 0.8**	20.5± 1.0**	20.6± 0.8**

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

APPENDIX B 1

FOOD CONSUMPTION CHANGES : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(6)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	4.5± 0.3	4.2± 0.2	4.2± 0.3	4.4± 0.4	4.3± 0.4	4.5± 0.5	4.3± 0.4
12.5ppm	4.3± 0.2	4.1± 0.2	4.2± 0.2	4.3± 0.2	4.2± 0.2	4.3± 0.2	4.3± 0.2
25ppm	4.4± 0.3	4.1± 0.4	4.2± 0.4	4.4± 0.4	4.3± 0.4	4.3± 0.4	4.4± 0.3
50ppm	4.3± 0.3	3.8± 0.3	3.8± 0.2	4.0± 0.2	3.9± 0.2	3.8± 0.2*	4.1± 0.2
100ppm	3.7± 0.3**	3.2± 0.2**	3.3± 0.2**	3.4± 0.1**	3.4± 0.1**	3.3± 0.1**	3.5± 0.1**
200ppm	2.9± 0.2**	3.2± 0.1**	3.2± 0.1**	3.4± 0.1**	3.2± 0.2**	3.1± 0.2**	3.3± 0.1**

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

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)
Control	4.5± 0.3	4.5± 0.3	4.5± 0.4	4.5± 0.3	4.6± 0.3	4.6± 0.4
12.5ppm	4.5± 0.2	4.5± 0.3	4.5± 0.1	4.5± 0.1	4.5± 0.2	4.4± 0.2
25ppm	4.5± 0.5	4.4± 0.3	4.6± 0.3	4.4± 0.3	4.4± 0.4	4.5± 0.3
50ppm	3.9± 0.2	3.9± 0.2**	4.1± 0.2	3.8± 0.2*	4.0± 0.2*	4.0± 0.2**
100ppm	3.5± 0.1**	3.5± 0.2**	3.6± 0.2**	3.6± 0.1**	3.6± 0.1**	3.6± 0.2**
200ppm	3.3± 0.1**	3.2± 0.2**	3.4± 0.2**	3.3± 0.1**	3.4± 0.2**	3.3± 0.4**

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

APPENDIX B 2

FOOD CONSUMPTION CHANGES : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(6)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	3.9± 0.3	3.6± 0.2	3.8± 0.3	4.1± 0.2	4.2± 0.2	4.4± 0.3	4.2± 0.2
12.5ppm	4.0± 0.3	3.9± 0.2	4.0± 0.3	4.4± 0.3	4.4± 0.4	4.4± 0.4	4.5± 0.3*
25ppm	3.7± 0.2	3.5± 0.3	3.7± 0.2	3.9± 0.2	3.9± 0.2	4.0± 0.2	4.0± 0.2
50ppm	3.7± 0.3	3.6± 0.1	3.6± 0.3	3.8± 0.3	3.8± 0.3	3.7± 0.3*	3.8± 0.3**
100ppm	3.2± 0.3**	2.9± 0.1**	3.0± 0.1**	3.2± 0.1**	3.1± 0.1**	3.1± 0.2**	3.3± 0.2**
200ppm	2.6± 0.3**	2.8± 0.2**	2.9± 0.1**	3.1± 0.1**	2.9± 0.2**	2.9± 0.1**	3.0± 0.2**

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

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)
Control	4.4± 0.1	4.3± 0.3	4.2± 0.2	4.3± 0.2	4.5± 0.3	4.4± 0.3
12.5ppm	4.5± 0.4	4.5± 0.3	4.5± 0.2	4.5± 0.4	4.7± 0.5	4.6± 0.6
25ppm	4.1± 0.2	4.1± 0.2	4.1± 0.2	4.1± 0.1	4.2± 0.2	4.2± 0.2
50ppm	3.8± 0.2*	3.8± 0.3**	3.9± 0.2**	3.7± 0.2*	3.9± 0.3	3.7± 0.3*
100ppm	3.3± 0.2**	3.3± 0.2**	3.5± 0.2**	3.3± 0.2**	3.5± 0.2**	3.5± 0.2**
200ppm	3.0± 0.2**	3.0± 0.2**	3.1± 0.2**	3.1± 0.2**	3.1± 0.2**	3.1± 0.2**

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

APPENDIX C 1

URINALYSIS : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0416 URINALYSIS
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	±	+	2+	3+	4+	CHI	Occult blood −	±	+	2+	3+	CHI
Control	10	0	0	1	1	2	4	2		0	1	8	1	0	0		10	0	0	0	0	0		4	6	0	0	0	0		10	0	0	0	0	
12.5ppm	10	0	1	0	2	4	2	1		0	0	9	1	0	0		10	0	0	0	0	0		3	6	1	0	0	0		10	0	0	0	0	
25ppm	10	0	0	0	4	1	5	0		0	0	9	1	0	0		10	0	0	0	0	0		2	2	6	0	0	0	*	10	0	0	0	0	
50ppm	10	0	0	0	1	0	5	4		0	0	9	1	0	0		10	0	0	0	0	0		4	3	2	1	0	0		10	0	0	0	0	
100ppm	10	0	0	0	0	2	5	3		0	0	10	0	0	0		10	0	0	0	0	0		0	2	8	0	0	0	**	10	0	0	0	0	
200ppm	10	0	0	1	0	1	5	3		0	1	9	0	0	0		10	0	0	0	0	0		0	8	1	1	0	0		10	0	0	0	0	

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

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0	
12.5ppm	10	10	0	0	0	0	
25ppm	10	10	0	0	0	0	
50ppm	10	10	0	0	0	0	
100ppm	10	10	0	0	0	0	
200ppm	10	10	0	0	0	0	

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

APPENDIX C 2

URINALYSIS : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0416 URINALYSIS
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	±	+	2+	3+	4+	CHI	Occult blood −	±	+	2+	3+	CHI
Control	10	0	0	0	1	3	6	0		0	2	5	3	0	0		10	0	0	0	0	0		1	7	1	1	0	0		10	0	0	0	0	
12.5ppm	10	0	0	0	1	1	7	1		0	2	5	3	0	0		10	0	0	0	0	0		1	5	4	0	0	0		10	0	0	0	0	
25ppm	9	0	0	0	0	3	6	0		0	0	6	3	0	0		9	0	0	0	0	0		0	6	3	0	0	0		9	0	0	0	0	
50ppm	10	0	0	0	0	1	8	1		0	0	5	5	0	0		10	0	0	0	0	0		0	4	4	2	0	0		10	0	0	0	0	
100ppm	10	0	0	0	0	0	6	4	*	0	2	4	4	0	0		10	0	0	0	0	0		0	7	2	1	0	0		10	0	0	0	0	
200ppm	10	0	0	0	1	0	8	1		0	0	3	7	0	0		10	0	0	0	0	0		0	2	5	3	0	0		10	0	0	0	0	

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

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0	
12.5ppm	10	10	0	0	0	0	
25ppm	9	9	0	0	0	0	
50ppm	10	10	0	0	0	0	
100ppm	10	10	0	0	0	0	
200ppm	10	10	0	0	0	0	

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

APPENDIX D 1

HEMATOLOGY : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV f ℓ	MCH p g	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	9	10.59± 0.38	15.8± 0.6	50.0± 2.0	47.3± 0.4	14.9± 0.2	31.6± 0.6	1428± 103
12.5ppm	10	10.72± 0.37	16.0± 0.5	50.5± 1.7	47.1± 0.5	14.9± 0.3	31.7± 0.5	1442± 97
25ppm	10	10.76± 0.16	15.9± 0.3	50.4± 0.9	46.8± 0.4	14.8± 0.1	31.6± 0.3	1368± 108
50ppm	9	10.83± 0.35	16.1± 0.5	51.0± 1.4	47.1± 0.7	14.9± 0.2	31.6± 0.4	1416± 85
100ppm	10	10.60± 0.32	16.0± 0.3	50.1± 1.2	47.3± 0.6	15.1± 0.2	31.9± 0.5	1465± 95
200ppm	10	10.49± 0.22	16.0± 0.2	50.2± 1.5	47.9± 0.8	15.3± 0.3*	31.9± 0.9	1456± 69

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

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$		Differential WBC (%) N-BAND		N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHER	
Control	9	1.37±	0.77	1±	1	15±	6	2±	2	0±	0	2±	1	81±	6	0±	0
12.5ppm	10	1.41±	1.03	0±	0	18±	4	2±	1	0±	0	3±	2	77±	4	0±	0
25ppm	10	0.96±	0.83	1±	1	17±	7	1±	1	0±	0	3±	2	78±	8	0±	0
50ppm	9	1.27±	0.79	1±	1	15±	3	2±	2	0±	0	2±	1	80±	4	0±	0
100ppm	10	0.86±	0.56	1±	1	21±	5	2±	1	0±	0	3±	1	73±	6	0±	0
200ppm	10	0.89±	0.40	1±	1	19±	7	2±	3	0±	0	5±	3	74±	8	0±	0

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

(HCL070)

APPENDIX D 2

HEMATOLOGY : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV f ℓ	MCH p g	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	10	10.57± 0.46	16.0± 0.5	49.6± 2.1	47.0± 0.6	15.1± 0.2	32.1± 0.4	1263± 87
12.5ppm	9	10.72± 0.23	16.3± 0.4	50.7± 0.9	47.3± 0.6	15.3± 0.2	32.2± 0.3	1356± 84
25ppm	9	10.74± 0.29	16.3± 0.4	50.6± 1.7	47.1± 0.6	15.2± 0.3	32.2± 0.6	1324± 47
50ppm	10	10.66± 0.46	16.2± 0.6	50.5± 2.3	47.4± 0.4	15.2± 0.2	32.1± 0.4	1253± 74
100ppm	9	10.39± 0.18	16.0± 0.5	49.8± 1.3	47.9± 0.6**	15.4± 0.2*	32.1± 0.2	1233± 142
200ppm	9	10.11± 0.26	15.6± 0.4	48.9± 1.4	48.4± 0.5**	15.4± 0.3*	31.8± 0.5	1237± 85

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

(HCL070)

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$		Differential WBC (%) N-BAND		N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHER	
Control	10	0.84±	0.91	1±	1	18±	10	1±	1	0±	0	3±	3	78±	10	0±	0
12.5ppm	9	0.70±	0.53	1±	1	18±	7	1±	1	0±	0	2±	1	79±	7	0±	0
25ppm	9	1.03±	0.75	1±	1	15±	5	1±	1	0±	0	2±	1	82±	6	0±	0
50ppm	10	1.35±	1.20	1±	1	17±	9	1±	1	0±	0	3±	3	78±	9	0±	0
100ppm	9	0.80±	0.71	1±	3	33±	15**	1±	2	0±	0	2±	2	62±	15**	0±	1
200ppm	9	0.71±	0.46	4±	4	23±	7	2±	2	0±	0	2±	1	69±	10	0±	0

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

(HCL070)

APPENDIX E 1

BIOCHEMISTRY : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	TOTAL PROTEIN g/dl	ALBUMIN g/dl	A/G RATIO	T-BILIRUBIN mg/dl	GLUCOSE mg/dl	T-CHOLESTEROL mg/dl	TRIGLYCERIDE mg/dl
Control	9	5.0± 0.2	3.0± 0.1	1.5± 0.1	0.14± 0.01	212± 41	82± 9	29± 13
12.5ppm	10	5.0± 0.1	3.0± 0.1	1.6± 0.1	0.15± 0.02	175± 39	72± 6*	19± 6
25ppm	10	5.0± 0.2	3.1± 0.2	1.6± 0.2	0.14± 0.01	180± 35	74± 10	20± 7
50ppm	10	5.0± 0.1	3.2± 0.1	1.8± 0.2*	0.18± 0.02**	184± 33	67± 5**	13± 3**
100ppm	10	5.1± 0.2	3.2± 0.1	1.7± 0.1*	0.18± 0.02**	161± 39	74± 9	14± 4**
200ppm	10	5.3± 0.2*	3.3± 0.2**	1.8± 0.3*	0.18± 0.03**	172± 43	77± 7	17± 9*

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

(HCL074)

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	PHOSPHOLIPID mg/dℓ	GOT IU/ℓ	GPT IU/ℓ	LDH IU/ℓ	ALP IU/ℓ	G-GTP IU/ℓ	CPK IU/ℓ
Control	9	176± 16	39± 3	16± 1	177± 27	148± 12	1± 1	61± 22
12.5ppm	10	160± 17	45± 8	19± 5	213± 43	146± 9	1± 1	69± 21
25ppm	10	164± 18	46± 9	20± 8	217± 62	145± 7	2± 1	62± 25
50ppm	10	145± 10**	42± 4	17± 2	217± 87	156± 13	2± 1	70± 24
100ppm	10	150± 18**	39± 5	17± 2	198± 35	196± 11**	1± 1	69± 26
200ppm	10	157± 12*	41± 6	18± 3	213± 46	207± 21**	1± 1	70± 28

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

(HCL074)

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	UREA NITROGEN mg/dl	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dl	INORGANIC PHOSPHORUS mg/dl
Control	9	29.8± 4.4	149± 1	4.8± 0.3	119± 2	8.8± 0.3	7.6± 0.7
12.5ppm	10	29.0± 2.3	150± 1	4.5± 0.5	121± 1	8.6± 0.2	7.5± 0.8
25ppm	10	28.7± 2.3	150± 1	4.5± 0.5	121± 2	8.7± 0.3	7.6± 1.0
50ppm	10	28.6± 3.9	150± 1	4.9± 0.4	120± 2	8.6± 0.3	6.7± 1.0
100ppm	10	27.9± 3.4	150± 2	4.9± 0.5	118± 1	8.9± 0.4	7.6± 1.2
200ppm	10	22.8± 3.2**	149± 1	5.2± 0.6	118± 2	8.9± 0.3	8.9± 1.7

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

(HCL074)

APPENDIX E 2

BIOCHEMISTRY : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	TOTAL PROTEIN g/dℓ	ALBUMIN g/dℓ	A/G RATIO	T-BILIRUBIN mg/dℓ	GLUCOSE mg/dℓ	T-CHOLESTEROL mg/dℓ	TRIGLYCERIDE mg/dℓ
Control	10	5.1± 0.2	3.3± 0.2	1.9± 0.2	0.14± 0.02	163± 22	70± 7	15± 5
12.5ppm	10	5.2± 0.2	3.4± 0.1	1.9± 0.2	0.15± 0.03	157± 27	69± 5	12± 4
25ppm	9	5.2± 0.2	3.4± 0.1	1.9± 0.1	0.13± 0.02	156± 21	75± 6	17± 4
50ppm	10	5.2± 0.1	3.4± 0.1	1.9± 0.1	0.16± 0.01	163± 19	70± 7	12± 3
100ppm	10	5.2± 0.3	3.5± 0.2	2.1± 0.3	0.16± 0.02	160± 23	74± 6	12± 4
200ppm	10	5.1± 0.2	3.5± 0.1	2.1± 0.3	0.17± 0.03**	152± 28	73± 5	14± 4

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

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	PHOSPHOLIPID mg/dℓ	GOT IU/ℓ	GPT IU/ℓ	LDH IU/ℓ	ALP IU/ℓ	G-GTP IU/ℓ	CPK IU/ℓ
Control	10	148± 19	64± 27	25± 9	269± 85	235± 26	2± 1	105± 62
12.5ppm	10	143± 22	65± 19	24± 6	271± 115	248± 28	2± 1	87± 58
25ppm	9	162± 13	56± 8	22± 3	201± 40	230± 24	2± 1	61± 20
50ppm	10	142± 17	52± 11	22± 3	215± 59	251± 38	1± 1	58± 28
100ppm	10	142± 14	61± 29	22± 7	305± 205	349± 65**	2± 1	100± 95
200ppm	10	144± 12	52± 11	21± 3	258± 87	377± 31**	1± 1	72± 21

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

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	UREA NITROGEN mg/dℓ		SODIUM mEq/ℓ		POTASSIUM mEq/ℓ		CHLORIDE mEq/ℓ		CALCIUM mg/dℓ		INORGANIC PHOSPHORUS mg/dℓ	
Control	10	23.0±	4.3	150±	1	4.3±	0.5	121±	1	8.7±	0.3	7.3±	0.9
12.5ppm	10	24.5±	5.7	150±	2	4.5±	0.3	121±	1	8.7±	0.2	6.8±	1.1
25ppm	9	23.6±	2.3	151±	2	4.6±	0.2	120±	1	9.0±	0.3	7.3±	1.1
50ppm	10	24.3±	2.5	149±	2	4.4±	0.4	119±	2	8.8±	0.2	6.8±	0.8
100ppm	10	25.8±	6.0	150±	4	4.7±	0.5	119±	4	8.9±	0.2	7.4±	1.9
200ppm	10	21.8±	3.7	150±	1	4.5±	0.4	119±	2	8.8±	0.3	7.4±	0.8

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

APPENDIX F 1

GROSS FINDINGS : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
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 (%)
spleen	black zone		1 (10)	1 (10)	1 (10)	1 (10)
kidney	hydronephrosis		0 (0)	0 (0)	0 (0)	0 (0)

Organ	Findings	Group Name	100ppm		200ppm	
		NO. of Animals	10	(%)	10	(%)
spleen	black zone		0	(0)	0	(0)
kidney	hydronephrosis		1	(10)	0	(0)

APPENDIX F 2

GROSS FINDINGS : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name / NO. of Animals	Control 10	(%)	12.5ppm 10	(%)	25ppm 9	(%)	50ppm 10	(%)
spleen	black zone		0	(0)	0	(0)	1	(11)	0	(0)

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name	100ppm		200ppm	
		NO. of Animals	10	(%)	10	(%)
spleen	black zone		0	(0)	1	(10)

APPENDIX G 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	29.0± 1.4	0.034± 0.008	0.010± 0.003	0.223± 0.035	0.169± 0.013	0.162± 0.010
12.5ppm	10	26.6± 1.1**	0.028± 0.006	0.009± 0.003	0.204± 0.031	0.167± 0.020	0.156± 0.012
25ppm	10	26.8± 1.8**	0.032± 0.007	0.009± 0.004	0.228± 0.020	0.172± 0.011	0.159± 0.012
50ppm	10	23.3± 1.0**	0.023± 0.007**	0.009± 0.003	0.215± 0.026	0.152± 0.011*	0.157± 0.009
100ppm	10	22.3± 0.7**	0.025± 0.006**	0.008± 0.003	0.215± 0.025	0.137± 0.010**	0.149± 0.011*
200ppm	10	22.4± 1.1**	0.025± 0.005**	0.009± 0.004	0.190± 0.019*	0.138± 0.010**	0.146± 0.010**

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

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.451± 0.032	0.045± 0.009	1.189± 0.074	0.438± 0.018
12.5ppm	10	0.446± 0.034	0.045± 0.009	1.130± 0.061	0.434± 0.014
25ppm	10	0.444± 0.030	0.041± 0.003	1.129± 0.067	0.438± 0.009
50ppm	10	0.402± 0.028	0.035± 0.006	0.958± 0.047**	0.424± 0.020
100ppm	10	0.427± 0.145**	0.031± 0.006**	0.900± 0.046**	0.422± 0.010
200ppm	10	0.382± 0.035**	0.032± 0.007**	0.916± 0.084**	0.407± 0.009**

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

APPENDIX G 2

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	21.0± 1.4	0.038± 0.007	0.010± 0.004	0.033± 0.008	0.131± 0.012	0.155± 0.011
12.5ppm	10	20.6± 1.0	0.032± 0.008	0.011± 0.003	0.031± 0.006	0.133± 0.009	0.156± 0.011
25ppm	9	20.8± 0.7	0.038± 0.008	0.010± 0.004	0.035± 0.004	0.132± 0.011	0.155± 0.012
50ppm	10	19.7± 0.8*	0.038± 0.009	0.010± 0.001	0.033± 0.007	0.126± 0.009	0.156± 0.012
100ppm	10	18.1± 0.7**	0.029± 0.010	0.010± 0.005	0.024± 0.007*	0.116± 0.009**	0.144± 0.015
200ppm	10	17.6± 0.8**	0.026± 0.006**	0.010± 0.003	0.026± 0.008	0.115± 0.012**	0.141± 0.013

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

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.302± 0.015	0.052± 0.010	0.924± 0.078	0.455± 0.017
12.5ppm	10	0.299± 0.017	0.048± 0.006	0.916± 0.101	0.449± 0.009
25ppm	9	0.306± 0.019	0.054± 0.005	0.929± 0.063	0.455± 0.014
50ppm	10	0.289± 0.012	0.049± 0.010	0.830± 0.080*	0.439± 0.014
100ppm	10	0.276± 0.014**	0.035± 0.007**	0.748± 0.052**	0.419± 0.018**
200ppm	10	0.283± 0.016*	0.033± 0.011**	0.762± 0.037**	0.410± 0.008**

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

(HCL040)

APPENDIX H 1

ORGAN WEIGHT, RELATIVE : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	29.0± 1.4	0.118± 0.025	0.033± 0.010	0.771± 0.120	0.581± 0.041	0.559± 0.061
12.5ppm	10	26.6± 1.1**	0.106± 0.022	0.035± 0.011	0.766± 0.110	0.629± 0.074	0.587± 0.044
25ppm	10	26.8± 1.8**	0.118± 0.022	0.034± 0.015	0.853± 0.088	0.646± 0.056*	0.596± 0.045
50ppm	10	23.3± 1.0**	0.099± 0.026	0.040± 0.015	0.927± 0.111**	0.652± 0.048*	0.675± 0.038**
100ppm	10	22.3± 0.7**	0.110± 0.028	0.038± 0.014	0.966± 0.109**	0.616± 0.032	0.671± 0.057**
200ppm	10	22.4± 1.1**	0.110± 0.025	0.040± 0.016	0.849± 0.082	0.617± 0.036	0.651± 0.049**

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

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.558± 0.133	0.154± 0.030	4.098± 0.211	1.514± 0.104
12.5ppm	10	1.679± 0.124	0.171± 0.032	4.253± 0.213	1.637± 0.104*
25ppm	10	1.662± 0.120	0.155± 0.013	4.229± 0.251	1.643± 0.107**
50ppm	10	1.728± 0.084*	0.150± 0.026	4.124± 0.174	1.824± 0.050**
100ppm	10	1.919± 0.661*	0.139± 0.026	4.045± 0.171	1.896± 0.060**
200ppm	10	1.701± 0.102	0.144± 0.034	4.077± 0.249	1.818± 0.072**

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

APPENDIX H 2

ORGAN WEIGHT, RELATIVE : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	21.0± 1.4	0.180± 0.028	0.049± 0.022	0.154± 0.032	0.625± 0.036	0.741± 0.052
12.5ppm	10	20.6± 1.0	0.156± 0.034	0.051± 0.013	0.148± 0.026	0.647± 0.046	0.758± 0.058
25ppm	9	20.8± 0.7	0.185± 0.037	0.048± 0.019	0.170± 0.019	0.632± 0.041	0.745± 0.062
50ppm	10	19.7± 0.8*	0.190± 0.039	0.048± 0.007	0.165± 0.036	0.641± 0.043	0.792± 0.069
100ppm	10	18.1± 0.7**	0.160± 0.051	0.057± 0.028	0.134± 0.037	0.642± 0.044	0.799± 0.083
200ppm	10	17.6± 0.8**	0.150± 0.030	0.055± 0.016	0.147± 0.041	0.653± 0.043	0.802± 0.058

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

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.441± 0.064	0.249± 0.039	4.400± 0.154	2.173± 0.127
12.5ppm	10	1.448± 0.040	0.233± 0.031	4.435± 0.366	2.179± 0.118
25ppm	9	1.470± 0.083	0.260± 0.028	4.458± 0.172	2.186± 0.104
50ppm	10	1.465± 0.071	0.247± 0.047	4.204± 0.299	2.232± 0.121
100ppm	10	1.527± 0.087*	0.195± 0.038*	4.133± 0.160*	2.320± 0.109*
200ppm	10	1.612± 0.067**	0.188± 0.057**	4.345± 0.116	2.340± 0.125*

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

(HCL042)

APPENDIX I 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0416
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 10 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>			
	polyp		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:olfactory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	5 (50)	0 (0)	0 (0)	0 * (0)	8 (80)	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)	8 (80)	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)	1 (10)	0 (0)	0 (0)	0 (0)
	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)	5 (50)	0 (0)	0 (0)	0 * (0)
{Hematopoietic system}																		
spleen		<10>					<10>				<10>				<10>			
	deposit of melanin		1 (10)	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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			<10>				<10>			
	polyp		10	0	0	0 **	10	0	0	0 **
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		7	0	0	0 **	9	0	0	0 **
			(70)	(0)	(0)	(0)	(90)	(0)	(0)	(0)
	squamous cell metaplasia:respiratory epithelium		0	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(30)	(0)	(0)	(0)
	atrophy:olfactory epithelium		7	3	0	0 **	0	10	0	0 **
			(70)	(30)	(0)	(0)	(0)	(100)	(0)	(0)
	necrosis:olfactory epithelium		4	0	0	0	9	1	0	0 **
			(40)	(0)	(0)	(0)	(90)	(10)	(0)	(0)
	necrosis:respiratory epithelium		10	0	0	0 **	10	0	0	0 **
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Hematopoietic system}										
spleen			<10>				<10>			
	deposit of melanin		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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
salivary gl			<10>				<10>				<10>				<10>			
	lymphocytic infiltration		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)
stomach			<10>				<10>				<10>				<10>			
	erosion:forestomach		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)
	ulcer:forestomach		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyperplasia:forestomach		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
liver			<10>				<10>				<10>				<10>			
	inflammatory cell nest		4	0	0	0	4	0	0	0	3	0	0	0	2	0	0	0
			(40)	(0)	(0)	(0)	(40)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	hydronephrosis		0	0	0	0	0	0	0	0	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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
salivary gl			<10>				<10>			
	lymphocytic infiltration		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
stomach			<10>				<10>			
	erosion:forestomach		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	ulcer:forestomach		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	hyperplasia:forestomach		1	0	0	0	5	3	0	0 **
			(10)	(0)	(0)	(0)	(50)	(30)	(0)	(0)
liver			<10>				<10>			
	inflammatory cell nest		1	0	0	0	2	0	0	0
			(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
{Urinary system}										
kidney			<10>				<10>			
	hydronephrosis		0	0	1	0	0	0	0	0
			(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	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)
{Endocrine system}																		
pituitary			<10>				<10>				<10>				<10>			
	Rathke pouch		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	100ppm				200ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{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)
{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

APPENDIX I 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : FEMALE

(13-WEEK STUDY)

Organ	Findings	Group Name / Grade	Control				12.5ppm				25ppm				50ppm			
		No. of Animals on Study	10				10				9				10			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Respiratory system}																		
nasal cavit			<10>				<10>				< 9>				<10>			
	polyp		0	0	0	0	0	0	0	0	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	6	0	0	0 **	8	0	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(67)	(0)	(0)	(0)	(80)	(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	10	0	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(100)	(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)
	necrosis:respiratory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	7	0	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(70)	(0)	(0)	(0)
lung			<10>				<10>				< 9>				<10>			
	accumulation of foamy cells		0	0	0	0	0	0	0	0	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}																		
thymus			<10>				<10>				< 9>				<10>			
	atrophy		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>			
	polyp		9	0	0	0 **	7	0	0	0 **
			(90)	(0)	(0)	(0)	(70)	(0)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		9	0	0	0 **	6	0	0	0 *
			(90)	(0)	(0)	(0)	(60)	(0)	(0)	(0)
	squamous cell metaplasia:respiratory epithelium		0	0	0	0	9	0	0	0 **
			(0)	(0)	(0)	(0)	(90)	(0)	(0)	(0)
	atrophy:olfactory epithelium		10	0	0	0 **	0	10	0	0 **
			(100)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
	necrosis:olfactory epithelium		2	0	0	0	9	1	0	0 **
			(20)	(0)	(0)	(0)	(90)	(10)	(0)	(0)
	necrosis:respiratory epithelium		10	0	0	0 **	9	1	0	0 **
			(100)	(0)	(0)	(0)	(90)	(10)	(0)	(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}										
thymus			<10>				<10>			
	atrophy		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 9				50ppm 10			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Hematopoietic system}																		
thymus			<10>				<10>				< 9>				<10>			
	karyorrhexis		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)
spleen			<10>				<10>				< 9>				<10>			
	deposit of melanin		0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(11)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Digestive system}																		
salivary gl			<10>				<10>				< 9>				<10>			
	lymphocytic infiltration		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
stomach			<10>				<10>				< 9>				<10>			
	erosion:forestomach		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyperplasia:forestomach		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
liver			<10>				<10>				< 9>				<10>			
	inflammatory cell nest		2	0	0	0	3	0	0	0	2	0	0	0	4	0	0	0
			(20)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(22)	(0)	(0)	(0)	(40)	(0)	(0)	(0)

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

Organ	Findings	Group Name	100ppm				200ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
thymus			<10>				<10>			
	karyorrhexis		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen			<10>				<10>			
	deposit of melanin		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Digestive system}										
salivary gl			<10>				<10>			
	lymphocytic infiltration		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
stomach			<10>				<10>			
	erosion:forestomach		0	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(30)	(0)	(0)	(0)
	hyperplasia:forestomach		6	2	0	0 **	6	2	0	0 **
			(60)	(20)	(0)	(0)	(60)	(20)	(0)	(0)
liver			<10>				<10>			
	inflammatory cell nest		2	0	0	0	1	0	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

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

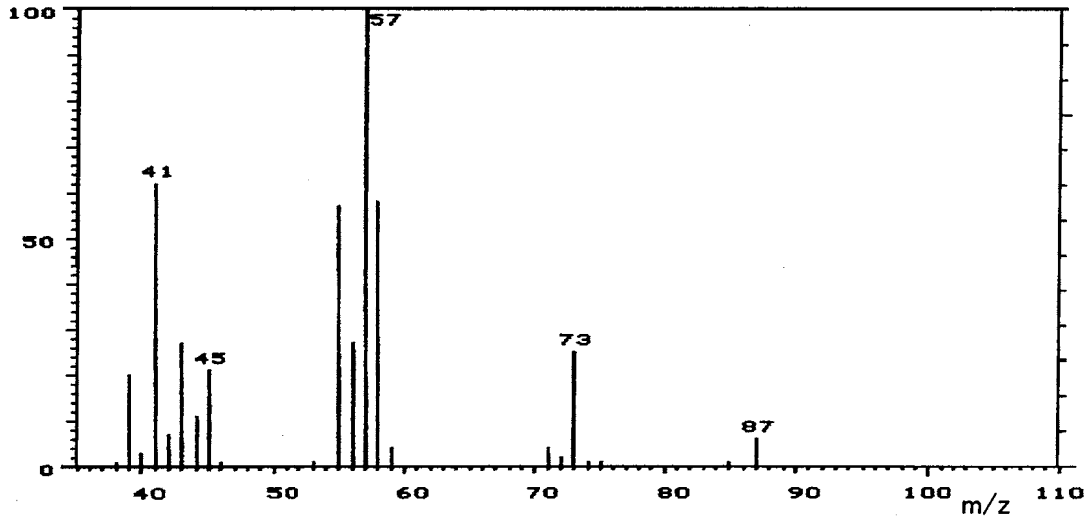
1. Spectral Data

Mass Spectrometry

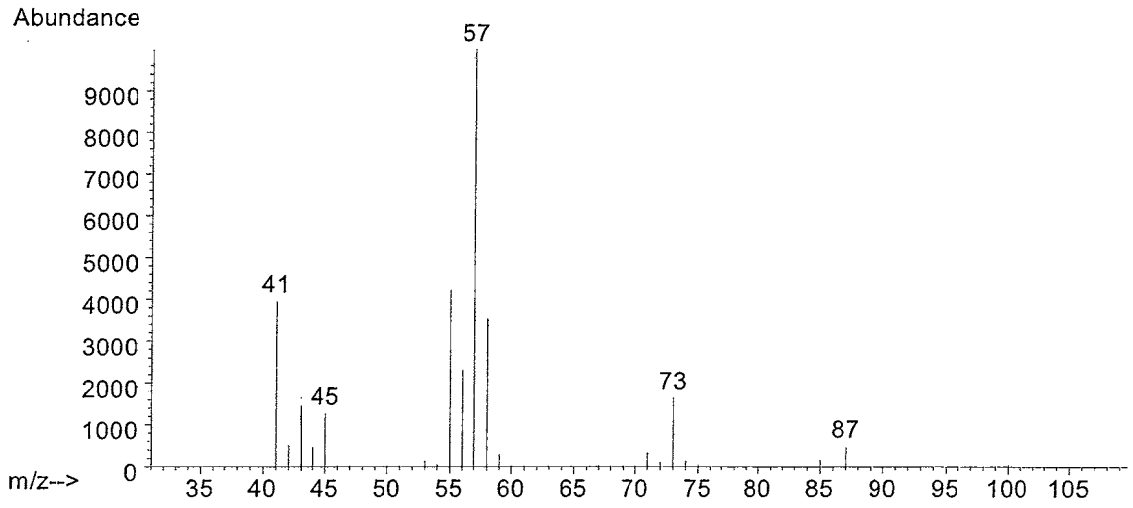
Instrument : Hitachi M-80B Mass Spectrometer

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.

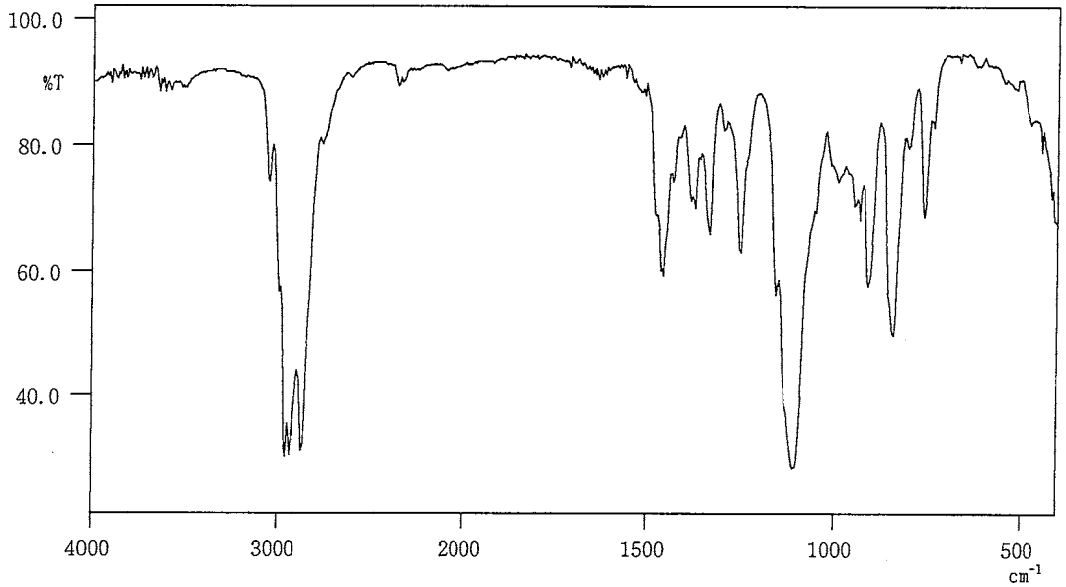
(*Fred W. McLafferty (1994)
Wiley Registry of Mass Spectral Data, 6th edition. Entry Number 20313
John Wiley and Sons, Inc. New York)

Infrared Spectrometry

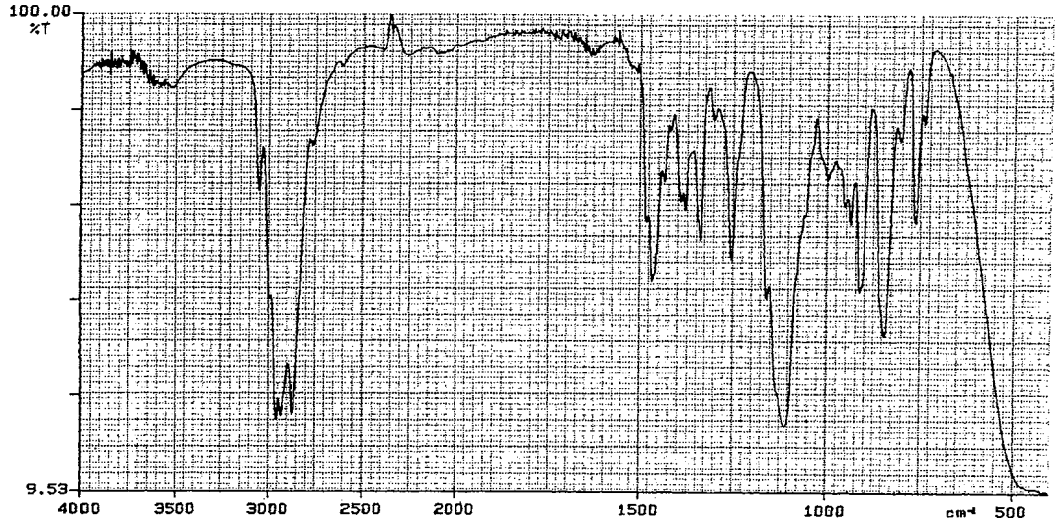
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

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 2000.9.19 to 2000.12.18. Test substance was stored in a dark place at room temperature.

2. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : Methyl Silicone (0.53 mmϕ × 60 m)

Column Temperature: 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

CONCENTMOUSEION 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	25.1 ± 0.2
50ppm	50.1 ± 0.4
100ppm	100.3 ± 0.5
200ppm	200.7 ± 1.0

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	22.1 ± 0.1	51.7 ± 1.5	104.2 ± 0.2	12.0
12.5ppm	21.8 ± 0.2	52.3 ± 0.8	104.3 ± 0.2	12.0
25ppm	22.0 ± 0.2	55.6 ± 1.1	104.4 ± 0.2	12.0
50ppm	22.3 ± 0.2	53.4 ± 1.4	104.5 ± 0.3	12.1
100ppm	22.3 ± 0.3	52.1 ± 1.6	104.5 ± 0.3	12.1
200ppm	21.8 ± 0.2	51.9 ± 2.3	104.5 ± 0.3	12.1

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]
White blood cell (WBC)	Light scattering method [1]
Differential WBC	Pattern recognition method [2] (Wright staining)
Biochemistry	
Total protein (TP)	Biuret method [3]
Albumin (Alb)	BCG method [3]
A/G ratio	Calculated as Alb/(TP－Alb) [3]
T-bilirubin	Alkaline azobilirubin method [3]
Glucose	GlcK･G-6-PDH method [3]
T-cholesterol	CE･COD･POD method [3]
Triglyceride	LPL･GK･GPO･POD method [3]
Phospholipid	PLD･ChOD･POD method [3]
Glutamic oxaloacetic transaminase (GOT)	JSCC method [3]
Glutamic pyruvic transaminase (GPT)	JSCC method [3]
Lactate dehydrogenase (LDH)	SFBC method [3]
Alkaline phosphatase (ALP)	GSCC method [3]
γ-Glutamyl transpeptidase (γ-GTP)	L-γ-Glutamyl-p-nitroanilide method [3]
Creatine phosphokinase (CPK)	JSCC method [3]
Urea nitrogen	Urease･GLDH method [3]
Sodium	Ion selective electrode method [3]
Potassium	Ion selective electrode method [3]
Chloride	Ion selective electrode method [3]
Calcium	OCPC method [3]
Inorganic phosphorus	PNP･XOD･POD method [3]
Urinalysis	
pH,Protein,Glucose,Ketone body,Occult Blood, Urobilinogen	Urinalysis reagent paper method [4]

1) Automatic blood cell analyzer (Technicon H･1 : Bayer Corporation)

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

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

4) Ames reagent strips for urinalysis (Uro-Labstix : Bayer Corporation)

APPENDIX 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
White blood cell (WBC)	$\times 10^3/\mu L$	2
Differential WBC	%	0
Biochemistry		
Total protein	g/dL	1
Albumin	g/dL	1
A/G ratio	–	1
T-bilirubin	mg/dL	2
Glucose	mg/dL	0
T-cholesterol	mg/dL	0
Triglyceride	mg/dL	0
Phospholipid	mg/dL	0
Glutamic oxaloacetic transaminase (GOT)	IU/L	0
Glutamic pyruvic transaminase (GPT)	IU/L	0
Lactate dehydrogenase (LDH)	IU/L	0
Alkaline phosphatase (ALP)	IU/L	0
γ-Glutamyl transpeptidase (γ-GTP)	IU/L	0
Creatine phosphokinase (CPK)	IU/L	0
Urea nitrogen	mg/dL	1
Sodium	mEq/L	0
Potassium	mEq/L	1
Chloride	mEq/L	0
Calcium	mg/dL	1
Inorganic phosphorus	mg/dL	1