グリシドールのマウスを用いた
吸入による 2 週間毒性試験報告書

試験番号：０３０８

APPENDIX

APPENDIXES

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 1-2 1	1-4 1	1-7 1	2-3 1	2-7 1
DEATH	0ppm	0	0	0	0	0
	37.5ppm	0	0	0	0	0
	75.0ppm	0	0	0	0	0
	150.0ppm	0	3	4	7	8
	300.0ppm	3	-	-	-	-
	600.0ppm	10	-	-	-	-
LOCOMOTOR MOVEMENT DECR	0ppm	0	0	0	0	0
	37.5ppm	0	0	0	0	0
	75.0ppm	0	0	0	0	0
	150.0ppm	0	1	0	1	0
	300.0ppm	7	-	-	-	-
	600.0ppm	0	-	-	-	-
PILOERECTION	0ppm	0	0	0	0	0
	37.5ppm	0	0	0	0	0
	75.0ppm	0	0	0	0	0
	150.0ppm	0	0	0	1	0
	300.0ppm	0	-	-	-	-
	600.0ppm	0	-	-	-	-
FROG BELLY	0ppm	0	0	0	0	0
	37.5ppm	0	0	0	0	0
	75.0ppm	0	0	0	0	0
	150.0ppm	0	1	0	0	0
	300.0ppm	9	-	-	-	-
	600.0ppm	10	-	-	-	-
GASPING	0ppm	0	0	0	0	0
	37.5ppm	0	0	0	0	0
	75.0ppm	0	0	0	0	0
	150.0ppm	0	0	0	0	0
	300.0ppm	7	-	-	-	-
	600.0ppm	0	-	-	-	-
ABNORMAL RESPIRATION	0ppm	0	0	0	0	0
	37.5ppm	0	0	0	0	0
	75.0ppm	0	0	0	0	0
	150.0ppm	0	1	0	0	0
	300.0ppm	7	-	-	-	-
	600.0ppm	0	-	-	-	-

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 1-2 1	1-4 1	1-7 1	2-3 1	2-7 1
BRADYPNEA	0ppm	0	0	0	0	0
	37.5ppm	0	0	0	0	0
	75.0ppm	0	0	0	0	0
	150.0ppm	0	0	0	0	0
	300.0ppm	4	-	-	-	-
	600.0ppm	0	-	-	-	-
DEEP BREATHING	0ppm	0	0	0	0	0
	37.5ppm	0	0	0	0	0
	75.0ppm	0	0	0	0	0
	150.0ppm	0	1	0	0	0
	300.0ppm	3	-	-	-	-
	600.0ppm	0	-	-	-	-
ABNORMAL RESPIRA.SOUND	0ppm	0	0	0	0	0
	37.5ppm	0	0	0	0	0
	75.0ppm	0	0	0	0	0
	150.0ppm	2	3	0	0	0
	300.0ppm	7	-	-	-	-
	600.0ppm	0	-	-	-	-
SUBNORMAL TEMP	0ppm	0	0	0	0	0
	37.5ppm	0	0	0	0	0
	75.0ppm	0	0	0	0	0
	150.0ppm	0	1	0	0	0
	300.0ppm	7	-	-	-	-
	600.0ppm	0	-	-	-	-

APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

Clinical sign	Group Name	Administration Week-day 1-2 1	1-4 1	1-7 1	2-3 1	2-7 1
DEATH	0ppm	0	0	0	0	0
	37.5ppm	0	0	0	0	0
	75.0ppm	0	0	0	0	0
	150.0ppm	0	3	3	8	9
	300.0ppm	6	-	-	-	-
	600.0ppm	10	-	-	-	-
LOCOMOTOR MOVEMENT DECR	0ppm	0	0	0	0	0
	37.5ppm	0	0	0	0	0
	75.0ppm	0	0	0	0	0
	150.0ppm	0	0	0	0	0
	300.0ppm	3	-	-	-	-
	600.0ppm	0	-	-	-	-
FROG BELLY	0ppm	0	0	0	0	0
	37.5ppm	0	0	0	0	0
	75.0ppm	0	0	0	0	0
	150.0ppm	0	0	0	0	0
	300.0ppm	9	-	-	-	-
	600.0ppm	10	-	-	-	-
GASPING	0ppm	0	0	0	0	0
	37.5ppm	0	0	0	0	0
	75.0ppm	0	0	0	0	0
	150.0ppm	0	0	0	0	0
	300.0ppm	3	-	-	-	-
	600.0ppm	0	-	-	-	-
IRREGULAR BREATHING	0ppm	0	0	0	0	0
	37.5ppm	0	0	0	0	0
	75.0ppm	0	0	0	0	0
	150.0ppm	0	0	0	0	0
	300.0ppm	1	-	-	-	-
	600.0ppm	0	-	-	-	-
ABNORMAL RESPIRATION	0ppm	0	0	0	0	0
	37.5ppm	0	0	0	0	0
	75.0ppm	0	0	0	0	0
	150.0ppm	0	0	0	0	0
	300.0ppm	4	-	-	-	-
	600.0ppm	0	-	-	-	-

Clinical sign	Group Name	Administration Week-day 1-2	1-4	1-7	2-3	2-7
		1	1	1	1	1
BRADYPNEA	0ppm	0	0	0	0	0
	37.5ppm	0	0	0	0	0
	75.0ppm	0	0	0	0	0
	150.0ppm	0	0	0	0	0
	300.0ppm	3	-	-	-	-
	600.0ppm	0	-	-	-	-
ABNORMAL RESPIRA.SOUND	0ppm	0	0	0	0	0
	37.5ppm	0	0	0	0	0
	75.0ppm	0	0	0	0	0
	150.0ppm	1	0	0	0	0
	300.0ppm	3	-	-	-	-
	600.0ppm	0	-	-	-	-
SUBNORMAL TEMP	0ppm	0	0	0	0	0
	37.5ppm	0	0	0	0	0
	75.0ppm	0	0	0	0	0
	150.0ppm	0	0	0	0	0
	300.0ppm	3	-	-	-	-
	600.0ppm	0	-	-	-	-

APPENDIX B 1

BODY WEIGHT CHANGES :SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-2	1-4	1-7	2-3	2-7
0ppm	23.8± 0.8	25.0± 1.0	25.1± 1.0	25.3± 0.9	25.6± 1.0	26.4± 1.1
37.5ppm	23.8± 0.8	24.4± 1.0	24.4± 0.8	24.7± 1.0	24.9± 0.8	25.2± 1.0*
75.0ppm	23.9± 0.7	24.0± 0.8	23.8± 0.8*	24.2± 0.8	24.4± 0.9	25.0± 1.0*
150.0ppm	23.8± 0.8	21.6± 1.3**	19.4± 1.6**	20.6± 1.6**	20.3± 3.1**	23.0± 0.5 ?
300.0ppm	23.9± 0.7	21.8± 0.4**	-	-	-	-
600.0ppm	23.8± 0.8	-	-	-	-	-

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

? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX B 2

BODY WEIGHT CHANGES : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-2	1-4	1-7	2-3	2-7
0ppm	19.3± 0.7	20.3± 0.7	20.6± 0.5	20.7± 0.8	21.2± 0.8	21.6± 0.8
37.5ppm	19.3± 0.6	19.4± 1.2	20.3± 0.5	20.6± 0.5	20.5± 0.6	20.6± 0.7**
75.0ppm	19.3± 0.6	19.0± 0.7**	19.7± 0.6*	20.3± 0.5	20.3± 0.8*	20.8± 0.7*
150.0ppm	19.3± 0.7	17.1± 0.9**	15.5± 1.7**	16.7± 1.2**	15.5± 3.6 ?	18.3± 0.0 ?
300.0ppm	19.3± 0.6	17.3± 0.4**	-	-	-	-
600.0ppm	19.3± 0.6	-	-	-	-	-

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

? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX C 1

FOOD CONSUMPTION CHANGES : SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(6)	2-7(7)
0ppm	3.8± 0.3	3.7± 0.2
37.5ppm	3.8± 0.3	3.4± 0.2**
75.0ppm	3.7± 0.4	3.5± 0.2*
150.0ppm	2.4± 0.6**	3.4± 0.0 ?
300.0ppm	-	-
600.0ppm	-	-

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

? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX C 2

FOOD CONSUMPTION CHANGES : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(6)	2-7(7)
0ppm	4.3± 0.2	4.2± 0.2
37.5ppm	4.1± 0.2	4.1± 0.3
75.0ppm	3.9± 0.3**	3.9± 0.2
150.0ppm	2.4± 0.5**	3.9± 0.2 ?
300.0ppm	-	-
600.0ppm	-	-

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

? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX D 1

HEMATOLOGY : SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (3W)

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 $10^3/\mu\ell$
0ppm	5	10.99± 0.17	16.8± 0.3	51.8± 1.6	47.0± 0.8	15.3± 0.2	32.6± 0.6	1251± 103
37.5ppm	5	10.99± 0.17	16.5± 0.2	51.5± 0.5	46.8± 0.5	15.0± 0.3	32.0± 0.6	1255± 57
75.0ppm	5	11.04± 0.39	16.6± 0.9	51.3± 1.9	46.5± 0.4	15.0± 0.3	32.3± 0.6	1265± 51
150.0ppm	2	10.56± 0.62 ?	15.5± 0.9 ?	48.7± 2.3 ?	46.1± 0.6 ?	14.6± 0.0 ?	31.7± 0.4 ?	1282± 147 ?
300.0ppm	0	-	-	-	-	-	-	-
600.0ppm	0	-	-	-	-	-	-	-

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

? : Significant test is not applied,because No. of data in this group is less than 3.

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (3W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHERS
0ppm	5	0.73± 0.37	0± 0	14± 5	1± 1	0± 0	3± 2	82± 6	0± 0
37.5ppm	5	0.97± 0.09	0± 0	8± 2*	0± 1	0± 0	2± 2	89± 4*	0± 0
75.0ppm	5	0.96± 0.38	0± 0	9± 2*	0± 0	0± 0	2± 1	89± 3*	0± 0
150.0ppm	2	0.68± 0.18 ?	0± 0 ?	11± 2 ?	2± 0 ?	0± 0 ?	2± 0 ?	86± 2 ?	0± 0 ?
300.0ppm	0	-	-	-	-	-	-	-	-
600.0ppm	0	-	-	-	-	-	-	-	-

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

? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX D 2

HEMATOLOGY : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (3W)

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 $10^3/\mu\ell$
0ppm	5	10.65± 0.25	15.9± 0.6	50.0± 1.3	46.9± 0.5	14.9± 0.4	31.8± 1.0	1103± 34
37.5ppm	5	10.53± 0.33	15.9± 0.6	49.5± 1.5	46.9± 0.3	15.1± 0.4	32.1± 0.8	1077± 124
75.0ppm	5	10.64± 0.29	15.9± 0.2	50.2± 1.1	47.2± 1.1	15.0± 0.5	31.6± 0.6	1064± 114
150.0ppm	1	10.04± 0.00 ?	14.7± 0.0 ?	45.7± 0.0 ?	45.5± 0.0 ?	14.6± 0.0 ?	32.2± 0.0 ?	1390± 0 ?
300.0ppm	0	-	-	-	-	-	-	-
600.0ppm	0	-	-	-	-	-	-	-

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

? : Significant test is not applied,because No. of data in this group is less than 3.

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (3W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHERS
0ppm	5	0.81± 0.36	0± 0	12± 3	0± 1	0± 0	2± 1	85± 4	0± 0
37.5ppm	5	0.62± 0.21	0± 1	13± 3	0± 0	0± 0	3± 2	84± 4	0± 0
75.0ppm	5	0.81± 0.32	0± 0	11± 2	1± 1	0± 0	2± 1	86± 3	0± 0
150.0ppm	1	0.95± 0.00 ?	0± 0 ?	19± 0 ?	0± 0 ?	0± 0 ?	2± 0 ?	79± 0 ?	0± 0 ?
300.0ppm	0	-	-	-	-	-	-	-	-
600.0ppm	0	-	-	-	-	-	-	-	-

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

? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX E 1

BIOCHEMISTRY : SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (3W)

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
0ppm	5	5.3± 0.2	3.1± 0.1	1.4± 0.1	0.20± 0.05	237± 26	90± 5	24± 4
37.5ppm	5	5.1± 0.1*	3.0± 0.1	1.4± 0.1	0.17± 0.02	226± 9	79± 4**	19± 4
75.0ppm	5	5.1± 0.1	3.0± 0.1	1.4± 0.1	0.18± 0.05	234± 25	89± 5	22± 4
150.0ppm	2	5.0± 0.1 ?	2.9± 0.1 ?	1.4± 0.1 ?	0.18± 0.05 ?	224± 16 ?	94± 2 ?	17± 2 ?
300.0ppm	0	-	-	-	-	-	-	-
600.0ppm	0	-	-	-	-	-	-	-

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

? : Significant test is not applied,because No. of data in this group is less than 3.

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (3W)

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
0ppm	5	178± 12	46± 7	23± 8	388± 149	285± 24	1± 1	96± 44
37.5ppm	5	153± 8**	42± 3	16± 2	291± 44	301± 6	2± 1	92± 32
75.0ppm	5	167± 11	41± 2	15± 2	252± 43	288± 10	1± 1	72± 44
150.0ppm	2	154± 1 ?	37± 0 ?	17± 2 ?	249± 119 ?	296± 28 ?	1± 1 ?	43± 4 ?
300.0ppm	0	-	-	-	-	-	-	-
600.0ppm	0	-	-	-	-	-	-	-

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

? : Significant test is not applied,because No. of data in this group is less than 3.

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (3W)

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
0ppm	5	26.8± 2.3	150± 1	4.6± 0.6	122± 3	9.0± 0.2	8.3± 0.9
37.5ppm	5	24.6± 2.6	150± 1	4.3± 0.8	121± 1	8.8± 0.2	8.4± 0.4
75.0ppm	5	22.2± 3.1	150± 1	4.7± 0.5	120± 1	8.8± 0.2	8.1± 0.8
150.0ppm	2	16.6± 2.4 ?	149± 0 ?	4.4± 0.4 ?	120± 1 ?	8.8± 0.3 ?	8.2± 0.2 ?
300.0ppm	0	-	-	-	-	-	-
600.0ppm	0	-	-	-	-	-	-

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

? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX E 2

BIOCHEMISTRY : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (3W)

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
0ppm	5	5.2± 0.3	3.3± 0.1	1.7± 0.1	0.17± 0.04	213± 35	72± 5	17± 4
37.5ppm	5	5.4± 0.2	3.3± 0.0	1.6± 0.1	0.18± 0.06	197± 10	77± 5	18± 2
75.0ppm	5	5.3± 0.2	3.3± 0.2	1.7± 0.1	0.18± 0.05	198± 32	83± 7*	19± 4
150.0ppm	1	5.5± 0.0 ?	3.4± 0.0 ?	1.6± 0.0 ?	0.14± 0.00 ?	190± 0 ?	115± 0 ?	22± 0 ?
300.0ppm	0	-	-	-	-	-	-	-
600.0ppm	0	-	-	-	-	-	-	-

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

? : Significant test is not applied,because No. of data in this group is less than 3.

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (3W)

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
0ppm	5	143± 10	57± 19	20± 8	323± 182	420± 26	1± 1	113± 101
37.5ppm	5	145± 9	54± 9	20± 6	312± 74	456± 20*	1± 1	104± 23
75.0ppm	5	149± 10	56± 14	22± 12	400± 294	420± 20	1± 1	128± 132
150.0ppm	1	190± 0 ?	56± 0 ?	20± 0 ?	285± 0 ?	346± 0 ?	3± 0 ?	37± 0 ?
300.0ppm	0	-	-	-	-	-	-	-
600.0ppm	0	-	-	-	-	-	-	-

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

? : Significant test is not applied,because No. of data in this group is less than 3.

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (3W)

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
0ppm	5	25.0± 4.6	149± 2	4.2± 0.4	120± 1	9.0± 0.2	6.8± 1.2
37.5ppm	5	23.2± 2.0	150± 1	4.3± 0.5	119± 3	9.0± 0.2	8.1± 0.9
75.0ppm	5	19.7± 2.6	149± 2	4.6± 0.5	119± 2	9.1± 0.3	7.8± 1.2
150.0ppm	1	18.4± 0.0 ?	149± 0 ?	4.1± 0.0 ?	116± 0 ?	9.1± 0.0 ?	10.2± 0.0 ?
300.0ppm	0	-	-	-	-	-	-
600.0ppm	0	-	-	-	-	-	-

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

? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX F 1

GROSS FINDINGS : SUMMARY, MOUSE : MALE

DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 3W)

Organ	Findings	Group Name / NO. of Animals	0ppm 0 (%)	37.5ppm 0 (%)	75.0ppm 0 (%)	150.0ppm 8 (%)
thymus	atrophic		- (-)	- (-)	- (-)	4 (50)
spleen	black zone		- (-)	- (-)	- (-)	0 (0)
stomach	gas		- (-)	- (-)	- (-)	4 (50)
small intes	gas		- (-)	- (-)	- (-)	3 (38)
large intes	gas		- (-)	- (-)	- (-)	2 (25)

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 3W)

Organ	Findings	Group Name / NO. of Animals	300.0ppm 10 (%)	600.0ppm 10 (%)
thymus	atrophic		0 (0)	0 (0)
spleen	black zone		0 (0)	1 (10)
stomach	gas		10 (100)	10 (100)
small intes	gas		10 (100)	10 (100)
large intes	gas		9 (90)	10 (100)

APPENDIX F 2

GROSS FINDINGS : SUMMARY, MOUSE : MALE : SACRIFICED ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (3W)

Organ	Findings	Group Name	0ppm	37.5ppm	75.0ppm	150.0ppm
		NO. of Animals	10 (%)	10 (%)	10 (%)	2 (%)
spleen	black zone		1 (10)	0 (0)	0 (0)	0 (0)

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (3W)

Organ	Findings	Group Name	300.0ppm	600.0ppm
		NO. of Animals	0 (%)	0 (%)
spleen	black zone		- (-)	- (-)

APPENDIX F 3

GROSS FINDINGS : SUMMARY, MOUSE : FEMALE

DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 3W)

Organ	Findings	Group Name / NO. of Animals	0ppm 0 (%)	37.5ppm 0 (%)	75.0ppm 0 (%)	150.0ppm 9 (%)
thymus	atrophic		- (-)	- (-)	- (-)	6 (67)
stomach	gas		- (-)	- (-)	- (-)	1 (11)
small intes	gas		- (-)	- (-)	- (-)	0 (0)
large intes	gas		- (-)	- (-)	- (-)	0 (0)

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 3W)

Organ	Findings	Group Name	300.0ppm	600.0ppm
		NO. of Animals	10 (%)	10 (%)
thymus	atrophic		0 (0)	0 (0)
stomach	gas		10 (100)	10 (100)
small intes	gas		10 (100)	10 (100)
large intes	gas		8 (80)	9 (90)

APPENDIX F 4

GROSS FINDINGS : SUMMARY, MOUSE : FEMALE : SACRIFICED ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (3W)

Organ	Findings	Group Name	0ppm	37.5ppm	75.0ppm	150.0ppm
		NO. of Animals	10 (%)	10 (%)	10 (%)	1 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	1 (100)
spleen	black zone		0 (0)	1 (10)	3 (30)	0 (0)

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (3W)

Organ	Findings	Group Name	300.0ppm	600.0ppm
		NO. of Animals	0 (%)	0 (%)
thymus	atrophic		- (-)	- (-)
spleen	black zone		- (-)	- (-)

APPENDIX G 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (3W)

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
0ppm	5	22.1± 0.6	0.048± 0.004	0.013± 0.002	0.195± 0.010	0.126± 0.009	0.152± 0.013
37.5ppm	5	21.5± 0.9	0.048± 0.012	0.012± 0.002	0.202± 0.028	0.124± 0.012	0.152± 0.012
75.0ppm	5	21.6± 0.8	0.051± 0.007	0.011± 0.002	0.187± 0.014	0.117± 0.004	0.157± 0.004
150.0ppm	2	19.8± 0.4 ?	0.038± 0.006 ?	0.012± 0.002 ?	0.195± 0.008 ?	0.114± 0.004 ?	0.158± 0.010 ?
300.0ppm	0	-	-	-	-	-	-
600.0ppm	0	-	-	-	-	-	-

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

? : Significant test is not applied,because No. of data in this group is less than 3.

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (3W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
0ppm	5	0.358± 0.023	0.041± 0.006	0.991± 0.075	0.448± 0.023
37.5ppm	5	0.356± 0.019	0.041± 0.005	0.901± 0.032*	0.439± 0.017
75.0ppm	5	0.373± 0.021	0.043± 0.002	0.961± 0.036	0.438± 0.016
150.0ppm	2	0.348± 0.017 ?	0.033± 0.000 ?	0.880± 0.035 ?	0.429± 0.016 ?
300.0ppm	0	-	-	-	-
600.0ppm	0	-	-	-	-

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

? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX G 2

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (3W)

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
0ppm	5	17.7± 0.8	0.066± 0.005	0.012± 0.003	0.017± 0.003	0.109± 0.003	0.146± 0.004
37.5ppm	5	17.3± 0.5	0.061± 0.006	0.012± 0.001	0.014± 0.004	0.109± 0.005	0.146± 0.006
75.0ppm	5	17.6± 0.7	0.062± 0.006	0.011± 0.001	0.019± 0.004	0.106± 0.003	0.148± 0.008
150.0ppm	1	15.7± 0.0 ?	0.013± 0.000 ?	0.010± 0.000 ?	0.014± 0.000 ?	0.099± 0.000 ?	0.143± 0.000 ?
300.0ppm	0	-	-	-	-	-	-
600.0ppm	0	-	-	-	-	-	-

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

? : Significant test is not applied,because No. of data in this group is less than 3.

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (3W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
0ppm	5	0.271± 0.016	0.047± 0.006	0.808± 0.026	0.448± 0.018
37.5ppm	5	0.271± 0.016	0.042± 0.004	0.782± 0.024	0.454± 0.005
75.0ppm	5	0.268± 0.013	0.044± 0.004	0.777± 0.035	0.441± 0.015
150.0ppm	1	0.259± 0.000 ?	0.026± 0.000 ?	0.744± 0.000 ?	0.433± 0.000 ?
300.0ppm	0	-	-	-	-
600.0ppm	0	-	-	-	-

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

? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX H 1

ORGAN WEIGHT, RELATIVE : SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (3W)

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
0ppm	5	22.1± 0.6	0.216± 0.018	0.058± 0.009	0.882± 0.045	0.572± 0.046	0.685± 0.053
37.5ppm	5	21.5± 0.9	0.221± 0.052	0.055± 0.010	0.939± 0.108	0.579± 0.049	0.705± 0.038
75.0ppm	5	21.6± 0.8	0.239± 0.035	0.053± 0.007	0.868± 0.076	0.542± 0.011	0.730± 0.030
150.0ppm	2	19.8± 0.4 ?	0.189± 0.028 ?	0.059± 0.012 ?	0.983± 0.061 ?	0.574± 0.030 ?	0.798± 0.033 ?
300.0ppm	0	-	-	-	-	-	-
600.0ppm	0	-	-	-	-	-	-

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

? : Significant test is not applied,because No. of data in this group is less than 3.

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (3W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
0ppm	5	1.617± 0.111	0.187± 0.025	4.476± 0.257	2.027± 0.088
37.5ppm	5	1.660± 0.105	0.193± 0.019	4.195± 0.128	2.047± 0.136
75.0ppm	5	1.730± 0.094	0.199± 0.013	4.452± 0.051	2.034± 0.140
150.0ppm	2	1.757± 0.048 ?	0.167± 0.004 ?	4.442± 0.080 ?	2.167± 0.032 ?
300.0ppm	0	-	-	-	-
600.0ppm	0	-	-	-	-

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

? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX H 2

ORGAN WEIGHT, RELATIVE : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (3W)

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
0ppm	5	17.7± 0.8	0.372± 0.028	0.068± 0.017	0.098± 0.012	0.617± 0.026	0.826± 0.046
37.5ppm	5	17.3± 0.5	0.354± 0.031	0.067± 0.007	0.083± 0.023	0.629± 0.042	0.843± 0.029
75.0ppm	5	17.6± 0.7	0.350± 0.032	0.065± 0.007	0.107± 0.026	0.600± 0.015	0.841± 0.068
150.0ppm	1	15.7± 0.0 ?	0.083± 0.000 ?	0.064± 0.000 ?	0.089± 0.000 ?	0.631± 0.000 ?	0.911± 0.000 ?
300.0ppm	0	-	-	-	-	-	-
600.0ppm	0	-	-	-	-	-	-

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

? : Significant test is not applied,because No. of data in this group is less than 3.

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (3W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
0ppm	5	1.527± 0.078	0.263± 0.035	4.560± 0.085	2.526± 0.087
37.5ppm	5	1.562± 0.108	0.244± 0.020	4.509± 0.078	2.618± 0.090
75.0ppm	5	1.520± 0.066	0.247± 0.013	4.412± 0.164	2.508± 0.169
150.0ppm	1	1.650± 0.000 ?	0.166± 0.000 ?	4.739± 0.000 ?	2.758± 0.000 ?
300.0ppm	0	-	-	-	-
600.0ppm	0	-	-	-	-

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

? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX I 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : MALE : DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 3W)

Organ	Findings	Group Name	0ppm				37.5ppm				75.0ppm				150.0ppm			
		No. of Animals on Study	0				0				0				1			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
nasal cavit			< 0>				< 0>				< 0>				< 1>			
	ulcer		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	0 (0)	0 (0)	1 (100)	0 (0)
	inflammatory infiltration		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	0 (0)	1 (100)	0 (0)	0 (0)
	necrosis:olfactory epithelium		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	0 (0)	0 (0)	1 (100)	0 (0)
	necrosis:respiratory epithelium		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	0 (0)	0 (0)	1 (100)	0 (0)
	necrosis:squamous epithelium		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	0 (0)	0 (0)	0 (0)	0 (0)
trachea			< 0>				< 0>				< 0>				< 1>			
	inflammatory infiltration		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	1 (100)	0 (0)	0 (0)	0 (0)
	necrosis:epithelium		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	0 (0)	1 (100)	0 (0)	0 (0)
lung			< 0>				< 0>				< 0>				< 1>			
	congestion		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	1 (100)	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

Organ	Findings	Group Name	300.0ppm				600.0ppm			
		No. of Animals on Study	2				2			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]										
nasal cavit			< 2>				< 2>			
	ulcer		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	inflammatory infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	necrosis:olfactory epithelium		0 (0)	0 (0)	2 (100)	0 (0)	0 (0)	0 (0)	2 (100)	0 (0)
	necrosis:respiratory epithelium		0 (0)	0 (0)	2 (100)	0 (0)	0 (0)	0 (0)	2 (100)	0 (0)
	necrosis:squamous epithelium		1 (50)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
trachea			< 2>				< 2>			
	inflammatory infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	necrosis:epithelium		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
lung			< 2>				< 2>			
	congestion		2 (100)	0 (0)	0 (0)	0 (0)	2 (100)	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

Organ	Findings	Group Name	0ppm				37.5ppm				75.0ppm				150.0ppm			
		No. of Animals on Study	0				0				0				1			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
thymus			<0>				<0>				<0>				<1>			
	karyorrhexis		-	-	-	-	-	-	-	-	-	-	-	-	0	0	1	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(0)	(0)	(100)	(0)
spleen			<0>				<0>				<0>				<1>			
	deposit of melanin		-	-	-	-	-	-	-	-	-	-	-	-	0	0	0	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(0)	(0)	(0)	(0)
[Urinary system]																		
kidney			<0>				<0>				<0>				<1>			
	tubular necrosis		-	-	-	-	-	-	-	-	-	-	-	-	0	0	0	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(0)	(0)	(0)	(0)
[Special sense organs/appandage]																		
eye			<0>				<0>				<0>				<1>			
	keratitis		-	-	-	-	-	-	-	-	-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)

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

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 3W)

Organ	Findings	Group Name	300.0ppm				600.0ppm			
		No. of Animals on Study	2				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]										
thymus			< 2>				< 2>			
	karyorrhexis		0	0	1	0	0	0	0	0
			(0)	(0)	(50)	(0)	(0)	(0)	(0)	(0)
spleen			< 2>				< 2>			
	deposit of melanin		1	0	0	0	1	0	0	0
			(50)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
[Urinary system]										
kidney			< 2>				< 2>			
	tubular necrosis		0	1	0	0	0	0	0	0
			(0)	(50)	(0)	(0)	(0)	(0)	(0)	(0)
[Special sense organs/appandage]										
eye			< 2>				< 2>			
	keratitis		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

APPENDIX I 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : MALE: SACRIFICED ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (3W)

Organ	Findings	Group Name / No. of Animals on Study / Grade	0ppm 2				37.5ppm 2				75.0ppm 2				150.0ppm 2			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
nasal cavit			< 2>				< 2>				< 2>				< 2>			
	inflammatory infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (50)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	inflammatory polyp		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (50)	0 (0)	0 (0)	0 (0)	1 (50)	1 (50)	0 (0)	0 (0)
	respiratory metaplasia:olfactory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	1 (50)	0 (0)	0 (0)	0 (0)	0 (0)	2 (100)	0 (0)	0 (0)	1 (50)	1 (50)	0 (0)	0 (0)
	atrophy:olfactory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	1 (50)	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)	2 (100)	0 (0)	0 (0)	0 (0)	2 (100)	0 (0)	0 (0)	0 (0)	2 (100)	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)	1 (50)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	necrosis:squamous 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)	2 (100)	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

Organ	Findings	Group Name	300.0ppm				600.0ppm			
		No. of Animals on Study	0				0			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
nasal cavit			< 0>				< 0>			
	inflammatory infiltration		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	inflammatory polyp		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	respiratory metaplasia:olfactory epithelium		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	atrophy:olfactory epithelium		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	necrosis:olfactory epithelium		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	necrosis:respiratory epithelium		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	necrosis:squamous epithelium		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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

APPENDIX I 3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : FEMALE : DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

Organ	Findings	Group Name	0ppm				37.5ppm				75.0ppm				150.0ppm			
		No. of Animals on Study	0				0				0				2			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
nasal cavit			< 0>				< 0>				< 0>				< 2>			
	ulcer		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	1 (50)	0 (0)	1 (50)	0 (0)
	inflammatory infiltration		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	1 (50)	1 (50)	0 (0)	0 (0)
	inflammatory polyp		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	1 (50)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:olfactory epithelium		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	1 (50)	0 (0)	0 (0)	0 (0)
	atrophy:olfactory epithelium		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	0 (0)	1 (50)	0 (0)	0 (0)
	necrosis:olfactory epithelium		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	0 (0)	1 (50)	1 (50)	0 (0)
	necrosis:respiratory epithelium		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	1 (50)	0 (0)	1 (50)	0 (0)
lung			< 0>				< 0>				< 0>				< 2>			
	congestion		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	0 (0)	2 (100)	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

Organ	Findings	Group Name	300.0ppm				600.0ppm			
		No. of Animals on Study	2				2			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]										
nasal cavit			< 2>				< 2>			
	ulcer		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	inflammatory infiltration		0 (0)	2 (100)	0 (0)	0 (0)	1 (50)	0 (0)	0 (0)	0 (0)
	inflammatory polyp		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)
	atrophy:olfactory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	necrosis:olfactory epithelium		0 (0)	0 (0)	2 (100)	0 (0)	0 (0)	0 (0)	2 (100)	0 (0)
	necrosis:respiratory epithelium		0 (0)	0 (0)	2 (100)	0 (0)	0 (0)	0 (0)	2 (100)	0 (0)
lung			< 2>				< 2>			
	congestion		2 (100)	0 (0)	0 (0)	0 (0)	0 (0)	2 (100)	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

STUDY NO. : 0308
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 3W)

Organ	Findings	Group Name	0ppm				37.5ppm				75.0ppm				150.0ppm			
		No. of Animals on Study	0				0				0				2			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Hematopoietic system]																		
thymus			< 0>				< 0>				< 0>				< 2>			
	atrophy		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	0 (0)	0 (0)	1 (50)	0 (0)
	karyorrhexis		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	0 (0)	0 (0)	0 (0)	0 (0)
[Digestive system]																		
liver			< 0>				< 0>				< 0>				< 2>			
	fatty change		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	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

Organ	Findings	Group Name	300.0ppm				600.0ppm			
		No. of Animals on Study	2				2			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Hematopoietic system]										
thymus			< 2>				< 2>			
	atrophy		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	karyorrhexis		0 (0)	0 (0)	1 (50)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Digestive system]										
liver			< 2>				< 2>			
	fatty change		1 (50)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

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

APPENDIX I 4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : FEMALE : SACRIFICED ANIMALS

(2-WEEK STUDY)

Organ	Findings	Group Name / No. of Animals on Study / Grade	0ppm 2				37.5ppm 2				75.0ppm 2				150.0ppm 1			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
nasal cavit			< 2>				< 2>				< 2>				< 1>			
	inflammatory infiltration		0 (0)	0 (0)	0 (0)	0 (0)	1 (50)	0 (0)	0 (0)	0 (0)	2 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	inflammatory polyp		0 (0)	0 (0)	0 (0)	0 (0)	1 (50)	0 (0)	0 (0)	0 (0)	2 (100)	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)	1 (50)	0 (0)	0 (0)	1 (50)	1 (50)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)
	atrophy:olfactory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	1 (50)	0 (0)	0 (0)	0 (0)	2 (100)	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)
	necrosis:olfactory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	2 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)
[Hematopoietic system]																		
thymus			< 2>				< 2>				< 2>				< 1>			
	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)	1 (100)	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

Organ	Findings	Group Name	300.0ppm				600.0ppm			
		No. of Animals on Study	0				0			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]										
nasal cavit			< 0>				< 0>			
	inflammatory infiltration		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
	inflammatory polyp		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
	respiratory metaplasia:olfactory epithelium		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
	atrophy:olfactory epithelium		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
	necrosis:olfactory epithelium		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
[Hematopoietic system]										
thymus			< 0>				< 0>			
	atrophy		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)

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

APPENDIX J 1

IDENTITY OF GLYCIDOL IN THE 2-WEEK INHALATION STUDY

IDENTITY OF GLYCIDOL IN THE 2-WEEK INHALATION STUDY

Test Substance Lot No.: SKG5118

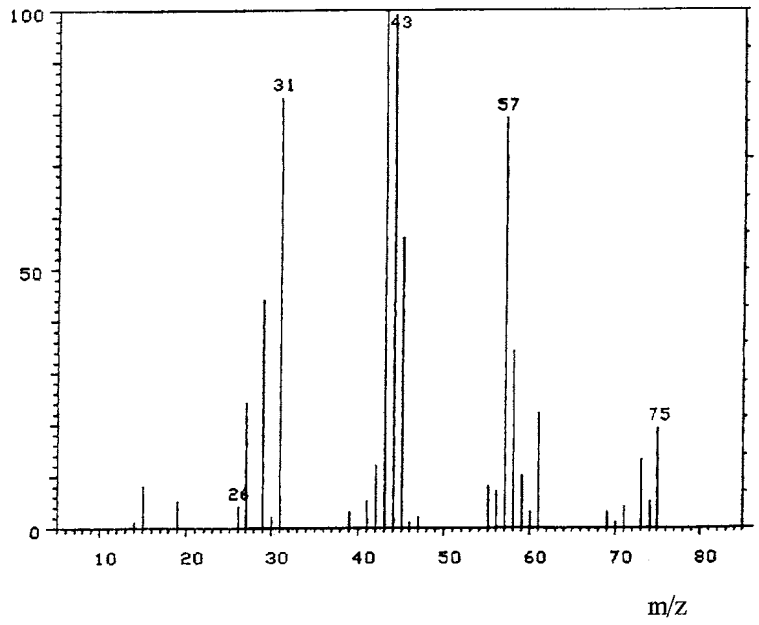
1. Spectral data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Determined Peak(m/z)	Literature Value* Peak(m/z)
31	31
43	43
44	44
57	57
73	73
75	

Results: The mass spectrum was consistent with literature spectrum.

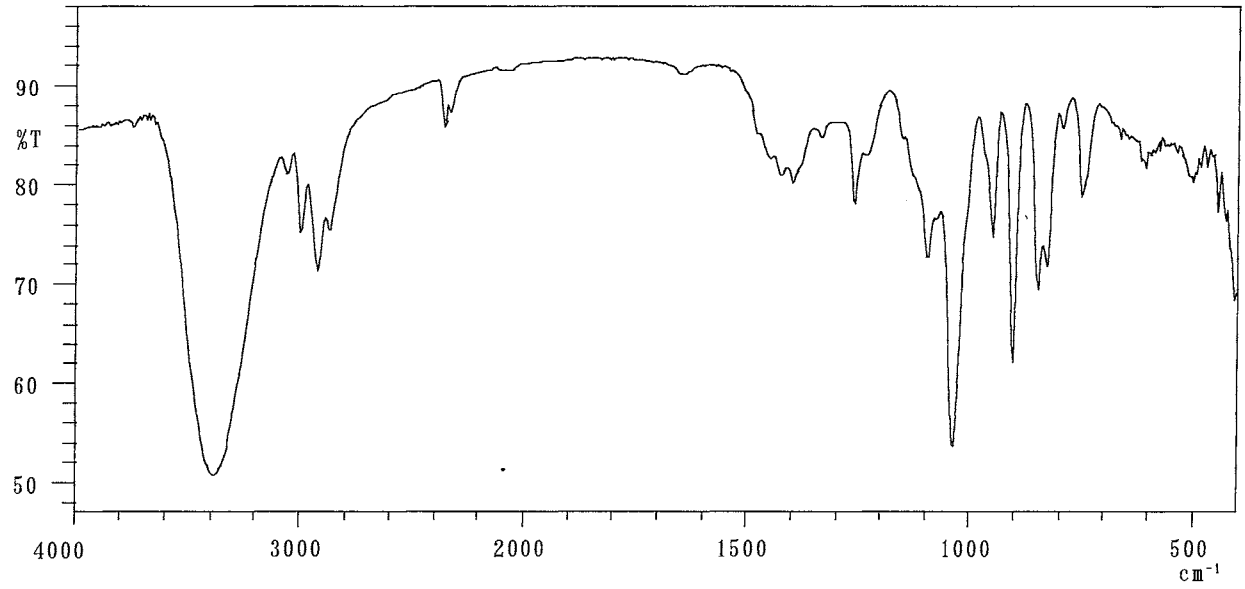
(*Fred W. McLafferty (1994) Wiley Registry of Mass Spectral Data, 6th edition. John Wiley and Sons, Inc. (U.S.), Entry Number 1733)

Infrared Spectrometry

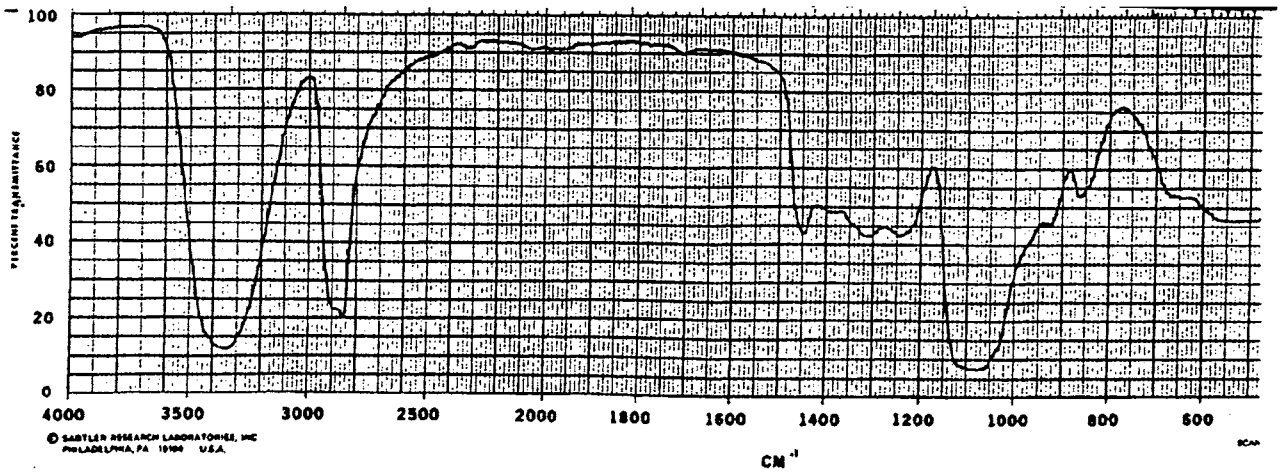
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 4 cm^{-1}



Infrared Spectrum of Test Substance



Infrared Spectrum of Glycidol(literature spectrum*)

Results: The infrared spectrum was consistent with literature spectrum.

(*William W. Simons (1978) The Sadtler Handbook of Infrared Spectra.
Sadtler Research Laboratories, Inc. (U.K.), pp.480)

2. Conclusions: The result of the mass spectrum and the infrared spectrum agreed with the literature values. Consequently, the test substance was identified as glycidol.

APPENDIX J 2

STABILITY OF GLYCIDOL IN THE 2-WEEK INHALATION STUDY

STABILITY OF GLYCIDOL IN THE 2-WEEK INHALATION STUDY

Test Substance Lot No.: SKG5118

1.Sample: This lot was used from 1996.4.3 to 1996.4.16. Test substance was stored at room temperature.

2. Gas Chromatography

Instrument : Hewlett Packard 6890

Column : Methyl Silicone (0.53 mmϕ × 60 m)

Column Temperature : 150°C

Flow Rate : 10 ml/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μL

Results: Gas chromatography indicated one major peak (peak No.3) and two impurities (peak No.1,2 < 1% of total area) analyzed at 1996.3.14 and one major peak (peak No.3) and two impurities (peak No.1,2 < 1% of total area) analyzed at 1996.4.18. No new trace impurity peak in the test substance analyzed at 1996.4.18 was detected.

Date (date analyzed)	Peak No.	Retention Time (min)	Area(%)
1996.03.14	1	1.89	0.15
	2	2.13	0.23
	3	2.52	99.62
1996.04.18	1	1.89	0.15
	2	2.12	0.23
	3	2.52	99.62

4. Conclusions: The results indicated that the test substance did not change when stored at room temperature during this period (for about 1 month).

APPENDIX K 1

CONCENTMOUSEION OF GLYCIDL IN THE INHALATION CHAMBER

CONCENTRATION OF GLYCIDOL IN THE INHALATION CHAMBER OF THE 2-WEEK INHALATION STUDY

Group Name	Concentration(ppm) Mean ± S.D.
Control	0.0 ± 0.0
37.5ppm	36.7 ± 0.9
75.0ppm	73.7 ± 1.4
150.0ppm	148.4 ± 3.4
300.0ppm	304.7 ± 6.2
600.0ppm	597.2 ± 0.0

APPENDIX K 2

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 2-WEEK INHALATION STUDY OF GLYCIDOL

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 2-WEEK INHALATION STUDY OF GLYCIDOL

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	52.6 ± 0.2	103.4 ± 1.1 (55.2 ± 2.5)	11.9 (6.4)
62.5ppm	21.8 ± 0.1	50.1 ± 1.8	104.7 ± 1.4 (54.5 ± 2.9)	12.1 (6.3)
125.0ppm	21.9 ± 0.1	50.7 ± 2.1	103.9 ± 1.5 (55.6 ± 2.7)	12.0 (6.4)
250.0ppm	21.6 ± 0.2	49.0 ± 2.9	104.3 ± 1.3 (55.6 ± 2.7)	12.0 (6.4)
500.0ppm	21.7 ± 0.3	49.7 ± 4.8	104.9 ± 1.1 (53.3 ± 1.1)	12.1 (6.2)
1000.0ppm	21.6 ± 0.5	52.5 ± 8.0	104.9 ± 0.6 (52.7 ± 0.0)	12.1 (6.1)

( ) : durig exposure

APPENDIX L 1

METHODS FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK INHALATION STUDY OF GLYCIDOL

METHODS FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK INHALATION STUDY OF GLYCIDOL

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] (May-Grunwald-Giemsa staining)
Biochemistry	
Total protein (TP)	Biuret method [3]
Albumin (Alb)	BCG method [3]
A/G ratio	Calculated as Alb/(TP−Alb) [3]
T-bilirubin	Alkaline azobilirubin method [3]
Glucose	Enzymatic method (GLK・G-6-PDH) [3]
T-cholesterol	Enzymatic method (CE・COD・POD) [3]
Triglyceride	Enzymatic method (LPL・GK・GPO・POD) [3]
Phospholipid	Enzymatic method (PLD・COD・POD) [3]
Glutamic oxaloacetic transaminase (GOT)	UV・Rate method [3]
Glutamic pyruvic transaminase (GPT)	UV・Rate method [3]
Lactate dehydrogenase (LDH)	UV・Rate method [3]
Alkaline phosphatase (ALP)	p-Nitrophenylphosphate method [3]
γ-Glutamyl transpeptidase (γ-GTP)	L-γ-Glutamyl-p-nitroanilide method [3]
Creatine phosphokinase (CPK)	UV・Rate method [3]
Urea nitrogen	Enzymatic method (Urease・GLDH) [3]
Sodium	Ion selective electrode method [3]
Potassium	Ion selective electrode method [3]
Chloride	Ion selective electrode method [3]
Calcium	OCPC method [3]
Inorganic phosphorus	Enzymatic method (PNP・XOD・POD) [3]

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

2) Automatic blood cell differential analyzer (Hitachi 8200 : Hitachi,Ltd.,Japan)

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

APPENDIX L 2

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK INHALATION STUDY OF GLYCIDOL

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK INHALATION STUDY OF GLYCIDOL

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 transminase (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