グリシドールのラットを用いた
吸入による 2 週間毒性試験報告書

試験番号：０３０７

APPENDIX

APPENDIXES

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
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	0	0	0	0
	300.0ppm	0	10	-	-	-
	600.0ppm	2(10)	-	-	-	-
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	0	0
	300.0ppm	0	0	-	-	-
	600.0ppm	8	-	-	-	-
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	0	0	-	-	-
	600.0ppm	8	-	-	-	-
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	0	0	-	-	-
	600.0ppm	8	-	-	-	-
RESPIRATORY SOUND ABNORMAL	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	0	0	-	-	-
	600.0ppm	3	-	-	-	-

( ):after exposure

APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
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
NOSE HEMORRHAGIC DISCHAGE	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	0	0	-	-	-
	600.0ppm	8	-	-	-	-

APPENDIX B 1

BODY WEIGHT CHANGES :SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
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	115± 3	124± 4	129± 5	138± 6	150± 7	166± 8
37.5ppm	115± 3	123± 3	126± 4	136± 5	145± 7	159± 9
75.0ppm	115± 3	121± 5	122± 5**	133± 7	140± 8*	154± 10**
150.0ppm	115± 3	114± 4**	109± 4**	120± 4**	117± 5**	129± 6**
300.0ppm	115± 4	106± 3**	-	-	-	-
600.0ppm	115± 3	99± 4**	-	-	-	-

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

APPENDIX B 2

BODY WEIGHT CHANGES : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
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	93± 3	98± 3	100± 4	104± 4	108± 5	116± 6
37.5ppm	93± 3	97± 3	99± 3	104± 4	108± 4	114± 5
75.0ppm	93± 3	96± 3	96± 4*	101± 4	103± 4*	110± 3*
150.0ppm	93± 3	92± 3**	87± 4**	95± 4**	93± 5**	102± 5**
300.0ppm	93± 3	86± 5**	-	-	-	-
600.0ppm	93± 3	-	-	-	-	-

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

APPENDIX C 1

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
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	15.2± 0.8	15.2± 0.9
37.5ppm	14.4± 0.5*	14.3± 0.8
75.0ppm	13.0± 0.8**	14.0± 1.3
150.0ppm	9.9± 0.8**	10.7± 0.4**
300.0ppm	-	-
600.0ppm	-	-

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

APPENDIX C 2

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration 1-7(6)	week-day(effective) 2-7(7)
0ppm	11.5± 0.6	10.9± 0.7
37.5ppm	11.3± 0.8	10.7± 0.6
75.0ppm	11.0± 0.7	10.3± 0.5
150.0ppm	8.2± 0.7**	9.3± 0.6**
300.0ppm	-	-
600.0ppm	-	-

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

APPENDIX D 1

HEMATOLOGY : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
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	8.17± 0.41	15.5± 0.8	44.0± 2.2	53.9± 0.3	19.0± 1.8	35.2± 3.4	907± 45
37.5ppm	5	8.54± 0.18	15.7± 0.6	45.6± 1.2	53.4± 0.6	18.4± 0.4	34.4± 0.8	879± 55
75.0ppm	5	8.52± 0.11	15.7± 0.4	45.7± 0.6	53.6± 0.3	18.4± 0.5	34.4± 0.9	894± 59
150.0ppm	5	8.25± 0.14	15.3± 0.3	44.0± 1.0	53.4± 0.6	18.6± 0.5	34.7± 1.2	776± 79**
300.0ppm	0	-	-	-	-	-	-	-
600.0ppm	0	-	-	-	-	-	-	-

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

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (3W)

Group Name	NO. of Animals	RETICULOCYTE ‰		PROTHROMBIN TIME sec		APTT sec	
0ppm	5	43±	7	12.5±	1.2	22.2±	7.6
37.5ppm	5	41±	9	12.3±	0.6	21.8±	1.8
75.0ppm	5	40±	7	12.6±	0.8	20.2±	4.8
150.0ppm	5	20±	4**	12.1±	0.9	22.5±	4.1
300.0ppm	0	-		-		-	
600.0ppm	0	-		-		-	

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

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
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	4.61± 0.93	0± 0	19± 3	1± 0	0± 0	4± 2	76± 4	-
37.5ppm	5	5.81± 1.80	0± 0	14± 2	1± 1	0± 0	3± 1	81± 3	-
75.0ppm	5	4.87± 0.73	0± 0	19± 4	1± 1	0± 0	4± 2	76± 5	-
150.0ppm	5	5.60± 0.27	0± 0	20± 6	0± 1	0± 0	5± 2	75± 7	-
300.0ppm	0	-	-	-	-	-	-	-	-
600.0ppm	0	-	-	-	-	-	-	-	-

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

APPENDIX D 2

HEMATOLOGY : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
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	8.95± 0.19	16.7± 0.7	47.0± 1.1	52.5± 0.3	18.6± 0.5	35.5± 0.8	804± 32
37.5ppm	5	9.07± 0.35	17.1± 0.5	47.9± 1.8	52.8± 0.3	18.8± 0.4	35.6± 0.8	810± 48
75.0ppm	5	8.73± 0.56	16.9± 0.6	45.9± 3.0	52.6± 0.3	19.4± 1.5	36.9± 2.9	716± 85*
150.0ppm	5	8.93± 0.20	16.2± 0.2	46.9± 1.2	52.5± 0.5	18.2± 0.3	34.6± 0.8	747± 26
300.0ppm	0	-	-	-	-	-	-	-
600.0ppm	0	-	-	-	-	-	-	-

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

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (3W)

Group Name	NO. of Animals	RETICULOCYTE ‰	PROTHROMBIN TIME sec	APTT sec
0ppm	5	23± 3	11.6± 0.5	18.6± 5.5
37.5ppm	5	22± 4	11.1± 0.6	19.0± 4.9
75.0ppm	5	20± 4	11.5± 0.3	17.0± 3.9
150.0ppm	5	19± 2	11.6± 0.4	17.2± 3.3
300.0ppm	0	-	-	-
600.0ppm	0	-	-	-

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

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
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	4.07±	1.96	0±	0	19±	3	1±	1	0±	0	4±	1	76±	4	-
37.5ppm	5	3.59±	1.34	0±	0	18±	7	1±	1	0±	0	4±	2	77±	8	-
75.0ppm	5	3.21±	0.59	0±	0	18±	7	1±	1	0±	0	4±	2	77±	6	-
150.0ppm	5	4.78±	1.37	0±	0	18±	4	1±	1	0±	0	4±	2	77±	4	-
300.0ppm	0	-		-		-		-		-		-		-		-
600.0ppm	0	-		-		-		-		-		-		-		-

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

APPENDIX E 1

BIOCHEMISTRY : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
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	5.6±	0.0	3.8±	0.1	2.0±	0.1	0.14±	0.01	158±	12	49±	4	32±	3
37.5ppm	5	5.6±	0.1	3.7±	0.1	2.0±	0.1	0.13±	0.01	141±	8	49±	4	26±	6
75.0ppm	5	5.6±	0.1	3.7±	0.0	2.0±	0.1	0.13±	0.00	136±	10*	49±	3	25±	4*
150.0ppm	5	5.6±	0.1	3.7±	0.1	2.0±	0.1	0.14±	0.01	133±	11**	53±	3	21±	3**
300.0ppm	0	-		-		-		-		-		-		-	
600.0ppm	0	-		-		-		-		-		-		-	

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

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
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	88±	4	70±	2	33±	1	231±	77	831±	38	1±	1	228±	24
37.5ppm	5	88±	4	73±	4	35±	3	217±	53	806±	34	1±	1	199±	23
75.0ppm	5	88±	4	70±	3	34±	1	206±	28	812±	81	1±	1	203±	33
150.0ppm	5	92±	3	64±	1*	31±	2	184±	15	747±	43	2±	1	161±	20**
300.0ppm	0	-		-		-		-		-		-		-	
600.0ppm	0	-		-		-		-		-		-		-	

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

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (3W)

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
0ppm	5	16.9± 1.1	0.4± 0.1	140± 2	4.1± 0.2	104± 0	10.2± 0.1	8.7± 0.2
37.5ppm	5	16.0± 0.9	0.4± 0.0	140± 1	4.4± 0.3	104± 1	10.2± 0.1	9.0± 0.3
75.0ppm	5	16.0± 0.5	0.4± 0.0	140± 1	4.2± 0.2	104± 1	10.2± 0.1	8.7± 0.4
150.0ppm	5	14.4± 1.7**	0.4± 0.0	140± 2	4.2± 0.2	104± 1	10.2± 0.2	8.8± 0.3
300.0ppm	0	-	-	-	-	-	-	-
600.0ppm	0	-	-	-	-	-	-	-

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

APPENDIX E 2

BIOCHEMISTRY : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
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	5.6± 0.2	3.7± 0.1	2.0± 0.1	0.18± 0.04	128± 13	67± 5	16± 3
37.5ppm	5	5.6± 0.1	3.7± 0.1	2.0± 0.1	0.15± 0.01	115± 6	64± 5	16± 2
75.0ppm	5	5.6± 0.1	3.7± 0.1	1.9± 0.0	0.17± 0.02	116± 10	70± 5	17± 4
150.0ppm	5	5.4± 0.2	3.5± 0.1	1.9± 0.1	0.17± 0.02	120± 13	74± 5	21± 3
300.0ppm	0	-	-	-	-	-	-	-
600.0ppm	0	-	-	-	-	-	-	-

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

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
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	115±	5	74±	5	31±	2	539±	334	601±	30	2±	1	268±	114
37.5ppm	5	112±	4	76±	6	34±	5	380±	72	618±	37	2±	2	217±	25
75.0ppm	5	122±	9	75±	3	33±	2	376±	83	663±	30	2±	1	214±	24
150.0ppm	5	138±	8**	72±	6	32±	4	498±	144	676±	59*	3±	1	196±	47
300.0ppm	0	-		-		-		-		-		-		-	
600.0ppm	0	-		-		-		-		-		-		-	

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

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (3W)

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
0ppm	5	16.9± 1.0	0.4± 0.1	139± 1	4.0± 0.1	107± 1	9.8± 0.2	7.9± 0.6
37.5ppm	5	15.6± 1.8	0.4± 0.1	140± 1	3.8± 0.2	106± 1	10.0± 0.1	7.9± 0.4
75.0ppm	5	16.8± 0.8	0.4± 0.1	139± 1	3.7± 0.2	106± 1	10.0± 0.1	7.5± 0.5
150.0ppm	5	14.5± 2.2	0.4± 0.1	137± 1*	4.0± 0.4	105± 1*	9.9± 0.2	8.0± 0.6
300.0ppm	0	-	-	-	-	-	-	-
600.0ppm	0	-	-	-	-	-	-	-

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

APPENDIX F 1

GROSS FINDINGS : SUMMARY, RAT : MALE

DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
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 0 (%)
stomach	gas		- (-)	- (-)	- (-)	- (-)
small intes	gas		- (-)	- (-)	- (-)	- (-)
large intes	gas		- (-)	- (-)	- (-)	- (-)
thoracic ca	pleural fluid		- (-)	- (-)	- (-)	- (-)

Organ	Findings	Group Name	300.0ppm		600.0ppm	
		NO. of Animals	10	(%)	10	(%)
stomach	gas		10	(100)	10	(100)
small intes	gas		10	(100)	2	(20)
large intes	gas		10	(100)	2	(20)
thoracic ca	pleural fluid		0	(0)	2	(20)

APPENDIX F 2

GROSS FINDINGS : SUMMARY, RAT : MALE : SACRIFICED ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
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 (%)	10 (%)
liver	herniation		1 (10)	0 (0)	1 (10)	0 (0)

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (3W)

Organ	Findings	Group Name	300.0ppm	600.0ppm
		NO. of Animals	0 (%)	0 (%)
liver	herniation		- (-)	- (-)

APPENDIX F 3

GROSS FINDINGS : SUMMARY, RAT : FEMALE

DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
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 0 (%)
stomach	gas		- (-)	- (-)	- (-)	- (-)
small intes	gas		- (-)	- (-)	- (-)	- (-)
large intes	gas		- (-)	- (-)	- (-)	- (-)
thoracic ca	pleural fluid		- (-)	- (-)	- (-)	- (-)

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
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	(%)
stomach	gas		10	(100)	8	(80)
small intes	gas		9	(90)	9	(90)
large intes	gas		10	(100)	8	(80)
thoracic ca	pleural fluid		0	(0)	1	(10)

APPENDIX F 4

GROSS FINDINGS : SUMMARY, RAT : FEMALE : SACRIFICED ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
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 (%)	10 (%)
liver	herniation		2 (20)	0 (0)	1 (10)	1 (10)

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (3W)

Organ	Findings	Group Name	300.0ppm	600.0ppm
		NO. of Animals	0 (%)	0 (%)
liver	herniation		- (-)	- (-)

APPENDIX G 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
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	151± 6	0.283± 0.015	0.056± 0.008	2.347± 0.078	0.619± 0.041	0.726± 0.045
37.5ppm	5	140± 6**	0.288± 0.039	0.061± 0.015	2.235± 0.160	0.611± 0.038	0.726± 0.041
75.0ppm	5	143± 5*	0.290± 0.035	0.055± 0.010	2.348± 0.113	0.638± 0.062	0.747± 0.010
150.0ppm	5	115± 3**	0.224± 0.021*	0.055± 0.016	2.097± 0.094**	0.529± 0.015*	0.680± 0.037
300.0ppm	0	-	-	-	-	-	-
600.0ppm	0	-	-	-	-	-	-

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

(HCL040)

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
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	1.228± 0.040	0.370± 0.015	4.709± 0.158	1.656± 0.026
37.5ppm	5	1.228± 0.052	0.359± 0.038	4.319± 0.227**	1.621± 0.036
75.0ppm	5	1.272± 0.018	0.353± 0.016	4.423± 0.188	1.653± 0.031
150.0ppm	5	1.201± 0.024	0.298± 0.013**	3.822± 0.125**	1.562± 0.034**
300.0ppm	0	-	-	-	-
600.0ppm	0	-	-	-	-

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

APPENDIX G 2

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
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	104± 6	0.233± 0.009	0.064± 0.014	0.076± 0.012	0.471± 0.029	0.590± 0.041
37.5ppm	5	101± 3	0.219± 0.016	0.052± 0.007	0.068± 0.004	0.440± 0.024	0.557± 0.019
75.0ppm	5	98± 2	0.235± 0.021	0.062± 0.007	0.072± 0.009	0.465± 0.027	0.578± 0.012
150.0ppm	5	90± 5**	0.199± 0.029*	0.058± 0.009	0.064± 0.005	0.448± 0.020	0.585± 0.035
300.0ppm	0	-	-	-	-	-	-
600.0ppm	0	-	-	-	-	-	-

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

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
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	0.913± 0.039	0.274± 0.017	3.139± 0.225	1.548± 0.036
37.5ppm	5	0.925± 0.049	0.257± 0.013	3.117± 0.099	1.495± 0.061
75.0ppm	5	0.912± 0.013	0.268± 0.020	3.039± 0.126	1.539± 0.021
150.0ppm	5	0.990± 0.066	0.239± 0.025*	3.007± 0.097	1.488± 0.050
300.0ppm	0	-	-	-	-
600.0ppm	0	-	-	-	-

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

APPENDIX H 1

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
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	151± 6	0.187± 0.008	0.037± 0.006	1.555± 0.093	0.410± 0.026	0.480± 0.025
37.5ppm	5	140± 6**	0.206± 0.023	0.044± 0.012	1.600± 0.087	0.438± 0.020	0.520± 0.018*
75.0ppm	5	143± 5*	0.203± 0.019	0.038± 0.006	1.644± 0.052	0.447± 0.033	0.524± 0.023*
150.0ppm	5	115± 3**	0.195± 0.022	0.047± 0.013	1.828± 0.091**	0.461± 0.012**	0.592± 0.018**
300.0ppm	0	-	-	-	-	-	-
600.0ppm	0	-	-	-	-	-	-

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

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
0ppm	5	0.813± 0.024	0.245± 0.008	3.115± 0.058	1.096± 0.035
37.5ppm	5	0.880± 0.019**	0.257± 0.020	3.093± 0.079	1.163± 0.052*
75.0ppm	5	0.892± 0.032**	0.247± 0.011	3.097± 0.071	1.159± 0.042
150.0ppm	5	1.047± 0.017**	0.259± 0.009	3.329± 0.038**	1.361± 0.023**
300.0ppm	0	-	-	-	-
600.0ppm	0	-	-	-	-

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

APPENDIX H 2

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
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	104± 6	0.226± 0.017	0.061± 0.013	0.073± 0.009	0.454± 0.017	0.569± 0.016
37.5ppm	5	101± 3	0.218± 0.018	0.051± 0.007	0.067± 0.004	0.437± 0.016	0.553± 0.014
75.0ppm	5	98± 2	0.241± 0.019	0.064± 0.007	0.074± 0.009	0.477± 0.030	0.592± 0.025
150.0ppm	5	90± 5**	0.222± 0.028	0.064± 0.011	0.072± 0.005	0.499± 0.016**	0.652± 0.037**
300.0ppm	0	-	-	-	-	-	-
600.0ppm	0	-	-	-	-	-	-

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

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
0ppm	5	0.881± 0.019	0.265± 0.010	3.024± 0.098	1.495± 0.082
37.5ppm	5	0.917± 0.030	0.255± 0.006	3.092± 0.030	1.486± 0.106
75.0ppm	5	0.935± 0.026*	0.275± 0.020	3.113± 0.055	1.578± 0.054
150.0ppm	5	1.102± 0.041**	0.265± 0.020	3.353± 0.137**	1.659± 0.075*
300.0ppm	0	-	-	-	-
600.0ppm	0	-	-	-	-

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

APPENDIX I 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
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				0			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
nasal cavit			< 0>				< 0>				< 0>				< 0>			
	ulcer		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	inflammatory infiltration		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	necrosis:olfactory epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	necrosis:respiratory epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
nasopharynx			< 0>				< 0>				< 0>				< 0>			
	necrosis:epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
larynx			< 0>				< 0>				< 0>				< 0>			
	inflammatory infiltration		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	necrosis: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

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)	2 (100)	0 (0)	0 (0)	0 (0)	1 (50)	0 (0)
	inflammatory infiltration		0 (0)	0 (0)	2 (100)	0 (0)	0 (0)	0 (0)	2 (100)	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)
nasopharynx			< 2>				< 2>			
	necrosis:epithelium		0 (0)	2 (100)	0 (0)	0 (0)	0 (0)	1 (50)	0 (0)	0 (0)
larynx			< 2>				< 2>			
	inflammatory infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (50)	0 (0)	0 (0)
	necrosis:epithelium		0 (0)	0 (0)	0 (0)	0 (0)	1 (50)	1 (50)	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				0			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
trachea			< 0>				< 0>				< 0>				< 0>			
	necrosis:epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
lung			< 0>				< 0>				< 0>				< 0>			
	congestion		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	edema		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Hematopoietic system]																		
thymus			< 0>				< 0>				< 0>				< 0>			
	karyorrhexis		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Digestive system]																		
liver			< 0>				< 0>				< 0>				< 0>			
	congestion		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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]										
trachea			< 2>				< 2>			
	necrosis:epithelium		1	1	0	0	0	0	2	0
			(50)	(50)	(0)	(0)	(0)	(0)	(100)	(0)
lung			< 2>				< 2>			
	congestion		1	1	0	0	1	1	0	0
			(50)	(50)	(0)	(0)	(50)	(50)	(0)	(0)
	edema		1	0	0	0	1	0	0	0
			(50)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
[Hematopoietic system]										
thymus			< 2>				< 2>			
	karyorrhexis		0	0	2	0	1	0	1	0
			(0)	(0)	(100)	(0)	(50)	(0)	(50)	(0)
[Digestive system]										
liver			< 2>				< 2>			
	congestion		0	0	0	0	2	0	0	0
			(0)	(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

Organ	Findings	Group Name	0ppm				37.5ppm				75.0ppm				150.0ppm			
		No. of Animals on Study	0				0				0				0			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]																		
adrenal			< 0>				< 0>				< 0>				< 0>			
	necrosis		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Special sense organs/appandage]																		
eye			< 0>				< 0>				< 0>				< 0>			
	keratitis		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]										
adrenal			< 2>				< 2>			
	necrosis		0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(50)	(0)	(0)
[Special sense organs/appandage]										
eye			< 2>				< 2>			
	keratitis		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(50)	(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

RAT : MALE: SACRIFICED ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0307
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

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

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>			
	ulcer		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
	inflammatory infiltration		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
	squamous cell metaplasia:respiratory epithelium		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
	atrophy:olfactory epithelium		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
	necrosis:olfactory epithelium		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
	necrosis:squamous epithelium		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
[Reproductive system]										
prostate			< 0>				< 0>			
	inflammation		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)

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

RAT : 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				0			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
nasal cavit			< 0>				< 0>				< 0>				< 0>			
	ulcer		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	inflammatory infiltration		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	necrosis:olfactory epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	necrosis:respiratory epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
nasopharynx			< 0>				< 0>				< 0>				< 0>			
	necrosis:epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
larynx			< 0>				< 0>				< 0>				< 0>			
	inflammatory infiltration		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	necrosis: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

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	1	1	0	0	1	0	0
			(0)	(50)	(50)	(0)	(0)	(50)	(0)	(0)
	inflammatory infiltration		0	2	0	0	0	1	1	0
			(0)	(100)	(0)	(0)	(0)	(50)	(50)	(0)
	necrosis:olfactory epithelium		0	0	2	0	0	0	2	0
			(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)
	necrosis:respiratory epithelium		0	0	2	0	0	0	2	0
			(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)
nasopharynx			< 2>				< 2>			
	necrosis:epithelium		1	1	0	0	0	1	0	0
			(50)	(50)	(0)	(0)	(0)	(50)	(0)	(0)
larynx			< 2>				< 2>			
	inflammatory infiltration		1	0	0	0	0	0	0	0
			(50)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:epithelium		0	1	0	0	0	1	1	0
			(0)	(50)	(0)	(0)	(0)	(50)	(50)	(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				0			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
trachea			< 0>				< 0>				< 0>				< 0>			
	necrosis:epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
lung			< 0>				< 0>				< 0>				< 0>			
	congestion		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	edema		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Hematopoietic system]																		
thymus			< 0>				< 0>				< 0>				< 0>			
	karyorrhexis		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Digestive system]																		
stomach			< 0>				< 0>				< 0>				< 0>			
	erosion:forestomach		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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]										
trachea			< 2>				< 2>			
	necrosis:epithelium		0	1	1	0	0	0	2	0
			(0)	(50)	(50)	(0)	(0)	(0)	(100)	(0)
lung			< 2>				< 2>			
	congestion		1	1	0	0	1	1	0	0
			(50)	(50)	(0)	(0)	(50)	(50)	(0)	(0)
	edema		1	0	0	0	2	0	0	0
			(50)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
[Hematopoietic system]										
thymus			< 2>				< 2>			
	karyorrhexis		0	0	2	0	2	0	0	0
			(0)	(0)	(100)	(0)	(100)	(0)	(0)	(0)
[Digestive system]										
stomach			< 2>				< 2>			
	erosion:forestomach		1	0	0	0	0	0	0	0
			(50)	(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	0ppm				37.5ppm				75.0ppm				150.0ppm			
		No. of Animals on Study	0				0				0				0			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																		
liver			< 0>				< 0>				< 0>				< 0>			
	congestion		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Endocrine system]																		
adrenal			< 0>				< 0>				< 0>				< 0>			
	necrosis		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]										
liver			< 2>				< 2>			
	congestion		0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(50)	(0)	(0)
[Endocrine system]										
adrenal			< 2>				< 2>			
	necrosis		0	0	0	0	0	0	2	0
			(0)	(0)	(0)	(0)	(0)	(0)	(100)	(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

RAT : FEMALE : SACRIFICED ANIMALS

(2-WEEK STUDY)

Organ	Findings	Group Name	0ppm				37.5ppm				75.0ppm				150.0ppm			
		No. of Animals on Study	2				2				2				2			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
[Respiratory system]																		
nasal cavit			< 2>				< 2>				< 2>				< 2>			
	ulcer		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)	(50)	(0)	(0)	(0)
	atrophy:olfactory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(50)	(50)	(0)	(0)
	necrosis:olfactory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(50)	(50)	(0)	(0)
	necrosis:respiratory epithelium		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)	(50)	(0)	(0)	(0)
	necrosis:squamous epithelium		0	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)	(50)	(0)	(0)
[Digestive system]																		
liver			< 2>				< 2>				< 2>				< 2>			
	herniation		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)	(50)	(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	Grade	Group Name	300.0ppm				600.0ppm			
			No. of Animals on Study	0				0			
				1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]											
nasal cavit				< 0>				< 0>			
	ulcer			- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
	atrophy:olfactory epithelium			- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
	necrosis:olfactory epithelium			- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
	necrosis:respiratory epithelium			- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
	necrosis:squamous epithelium			- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
[Digestive system]											
liver				< 0>				< 0>			
	herniation			- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)

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

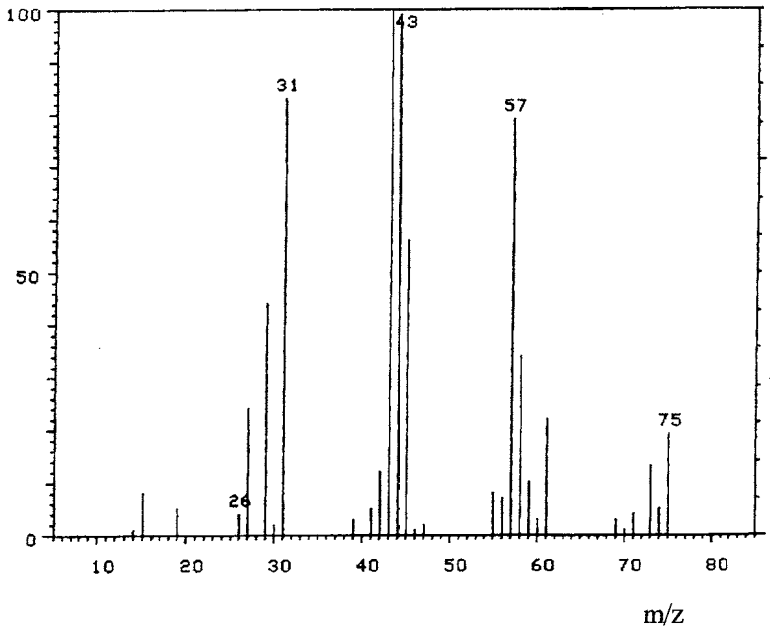
1. Spectral data

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.

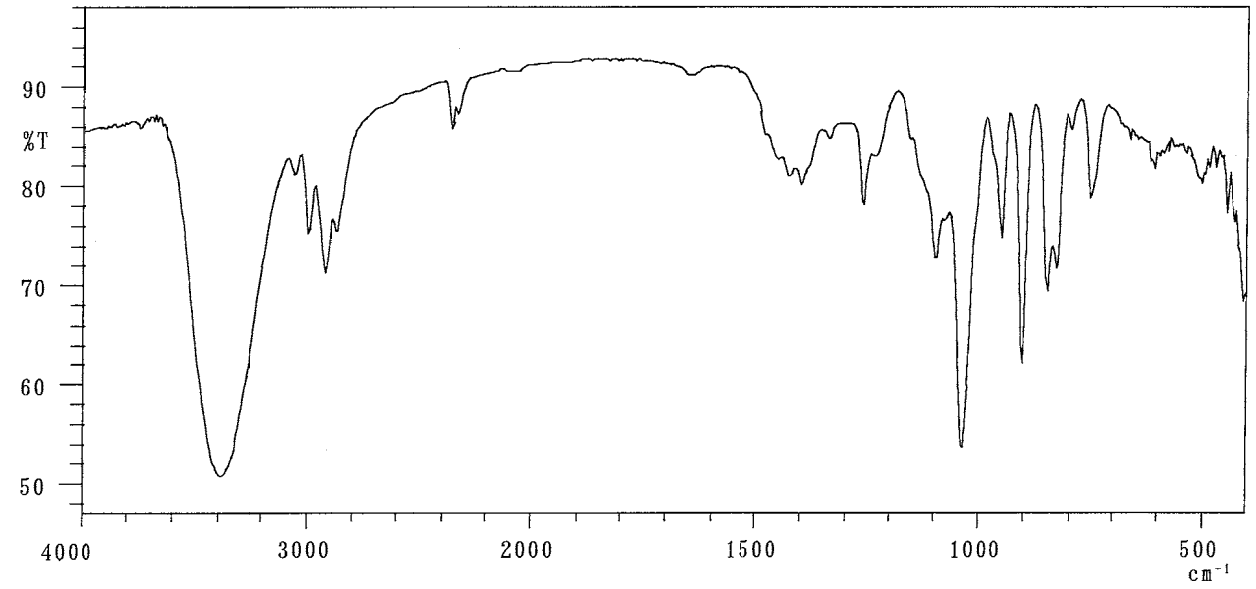
(*Fred W. McLafferty (1994) Wiley Registry of Mass Spectral Data, 6th edition. John Wiley and Sons, Inc. (U.S.), Entry Number 1733)

Infrared Spectrometry

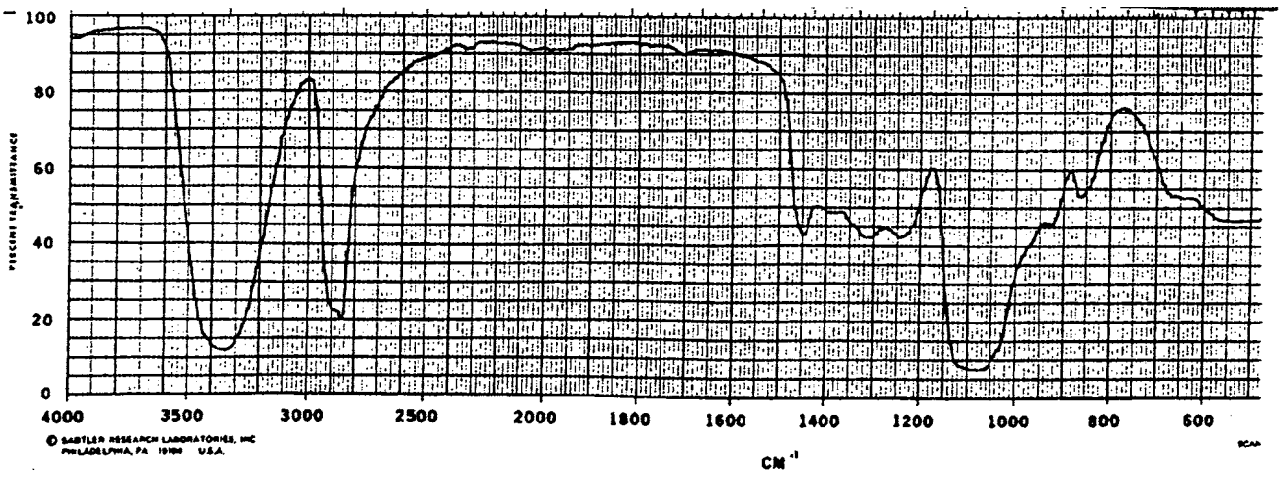
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

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 1996.3.19 to 1996.4.1. 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

CONCENTRATION 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	37.7 ± 0.7
75.0ppm	75.2 ± 1.3
150.0ppm	149.7 ± 2.0
300.0ppm	301.4 ± 1.4
600.0ppm	613.2 ± 3.6

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	22.2 ± 0.1	54.2 ± 0.3	212.2 ± 2.2 (113.0 ± 6.1)	12.0 (6.4)
37.5ppm	22.4 ± 0.1	53.3 ± 1.6	211.2 ± 2.3 (114.1 ± 5.9)	12.0 (6.5)
75.0ppm	22.3 ± 0.1	52.8 ± 2.0	209.8 ± 2.1 (112.5 ± 5.9)	11.9 (6.4)
150.0ppm	22.4 ± 0.1	52.3 ± 2.4	211.7 ± 2.2 (112.8 ± 5.8)	12.0 (6.4)
300.0ppm	22.3 ± 0.6	49.1 ± 3.4	209.8 ± 2.2 (112.6 ± 6.5)	11.9 (6.4)
600.0ppm	22.2 ± 0.5	48.3 ± 1.5	210.8 ± 0.3 (108.0 ± 2.7)	11.9 (6.1)

( ) : during 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]
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] (May-Grunwald-Giemsa staining)
Biochemistry	
Total protein (TP)	Biuret method [4]
Albumin (Alb)	BCG method [4]
A/G ratio	Calculated as Alb/(TP−Alb) [4]
T-bilirubin	Alkaline azobilirubin method [4]
Glucose	Enzymatic method (GLK・G-6-PDH) [4]
T-cholesterol	Enzymatic method (CE・COD・POD) [4]
Triglyceride	Enzymatic method (LPL・GK・GPO・POD) [4]
Phospholipid	Enzymatic method (PLD・COD・POD) [4]
Glutamic oxaloacetic transaminase (GOT)	UV・Rate method [4]
Glutamic pyruvic transaminase (GPT)	UV・Rate method [4]
Lactate dehydrogenase (LDH)	UV・Rate method [4]
Alkaline phosphatase (ALP)	p-Nitrophenylphosphate method [4]
γ-Glutamyl transpeptidase (γ-GTP)	L-γ-Glutamyl-p-nitroanilide method [4]
Creatine phosphokinase (CPK)	UV・Rate method [4]
Urea nitrogen	Enzymatic method (Urease・GLDH) [4]
Creatinine	Jaffe method [4]
Sodium	Ion selective electrode method [4]
Potassium	Ion selective electrode method [4]
Chloride	Ion selective electrode method [4]
Calcium	OCPC method [4]
Inorganic phosphorus	Enzymatic method (PNP・XOD・POD) [4]

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

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

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

4) 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
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 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
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