グリシドールのラットを用いた
吸入による 13 週間毒性試験報告書

試験番号：０３１６

APPENDIX

APPENDIXES

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, RAT : MALE

(13 - WEEK STUDY)

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7
		1	1	1	1	1	1	1	1	1	1	1	1	1
DEATH	0ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	10ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	40ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	80ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	160ppm	1	3	3	4	4	4	4	5	5	5	5	5	5
HUNCHBACK POSITION	0ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	10ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	40ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	80ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	160ppm	0	0	0	0	0	0	1	0	0	0	0	0	0
PILOERECTION	0ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	10ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	40ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	80ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	160ppm	0	0	0	0	0	0	1	0	0	0	0	0	0

APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

Clinical sign	Group Name	Administration Week-day 1-7 1	2-7 1	3-7 1	4-7 1	5-7 1	6-7 1	7-7 1	8-7 1	9-7 1	10-7 1	11-7 1	12-7 1	13-7 1
DEATH	0ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	10ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	40ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	80ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	160ppm	0	1	3	4	5	5	7	8	8	8	8	8	8
HUNCHBACK POSITION	0ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	10ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	40ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	80ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	160ppm	0	0	4	3	2	2	1	0	0	0	0	0	0
PILOERECTION	0ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	10ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	40ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	80ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	160ppm	0	0	0	1	0	0	1	2	2	0	0	0	0
EXOPHTHALMOS	0ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	10ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	40ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	80ppm	0	1	1	0	0	0	0	0	0	0	0	0	0
	160ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
EYE OPACITY	0ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	10ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20ppm	0	0	0	0	0	0	0	0	0	0	0	0	1
	40ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	80ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	160ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
CATARACT	0ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	10ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20ppm	0	0	0	0	0	0	0	0	0	0	0	0	1
	40ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	80ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	160ppm	0	0	0	0	0	0	0	0	0	0	0	0	0

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

Clinical sign	Group Name	Administration Week-day 1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7
		1	1	1	1	1	1	1	1	1	1	1	1	1
ABNORMAL RESPIRA.SOUND	0ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	10ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	40ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	80ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	160ppm	1	0	0	0	0	0	0	0	0	0	0	0	0

APPENDIX B 1

BODY WEIGHT CHANGES :SUMMARY, RAT : MALE

(13 - WEEK STUDY)

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7
0ppm	107± 4	135± 7	163± 8	183± 9	202± 9	219± 10	231± 11
10ppm	107± 4	134± 6	162± 7	182± 8	199± 9	215± 8	226± 8
20ppm	107± 4	133± 5	161± 8	180± 10	197± 12	211± 12	222± 12
40ppm	107± 4	130± 6	158± 8	178± 9	195± 10	210± 11	220± 12
80ppm	107± 4	125± 5**	150± 7**	170± 10*	187± 12**	201± 13**	213± 14**
160ppm	107± 4	100± 7**	99± 12**	106± 8**	113± 10**	114± 14**	122± 18**

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

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 7-7	8-7	9-7	10-7	11-7	12-7	13-7
0ppm	243± 13	255± 14	266± 14	274± 17	281± 17	289± 17	294± 18
10ppm	236± 8	247± 8	257± 8	264± 8	271± 10	276± 10	280± 12
20ppm	231± 14	240± 14	251± 14	260± 15	265± 15*	270± 16*	274± 16*
40ppm	229± 12	240± 12	249± 14*	255± 13*	262± 14*	267± 15**	274± 16*
80ppm	219± 13**	227± 15**	235± 13**	242± 14**	246± 13**	251± 13**	255± 12**
160ppm	122± 25**	134± 13**	137± 11**	141± 14**	141± 13**	142± 16**	142± 17**

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

APPENDIX B 2

BODY WEIGHT CHANGES : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7
0ppm	94± 3	112± 3	126± 4	135± 3	142± 5	149± 5	153± 5
10ppm	94± 3	110± 3	123± 4	130± 6	138± 7	143± 6	147± 7
20ppm	95± 3	108± 3	121± 4	128± 4	133± 6*	139± 6**	142± 6**
40ppm	95± 2	109± 4	122± 4	128± 5	134± 5	137± 6**	139± 6**
80ppm	95± 3	104± 3**	116± 4**	124± 4**	129± 4**	134± 6**	138± 6**
160ppm	95± 3	83± 6**	78± 9**	81± 11**	83± 15**	88± 8**	88± 14**

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

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 7-7	8-7	9-7	10-7	11-7	12-7	13-7
0ppm	156± 6	162± 6	164± 7	169± 7	173± 8	175± 8	179± 8
10ppm	150± 7	153± 8*	156± 9	160± 10	162± 9*	165± 9*	166± 10*
20ppm	147± 6*	150± 6**	152± 8**	155± 7**	157± 8**	159± 7**	162± 9**
40ppm	143± 7**	145± 6**	149± 7**	152± 7**	153± 8**	155± 8**	156± 8**
80ppm	141± 7**	142± 7**	148± 9**	148± 8**	152± 7**	152± 8**	153± 9**
160ppm	91± 18**	99± 1 ?	101± 3 ?	105± 1 ?	99± 0 ?	104± 1 ?	100± 1 ?

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, RAT : MALE

(13 - WEEK STUDY)

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(6)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
0ppm	13.2± 1.1	14.3± 0.9	15.4± 1.2	16.2± 1.4	15.8± 0.9	15.6± 1.2	16.0± 1.2
10ppm	13.0± 0.6	14.0± 0.7	15.3± 0.5	15.4± 0.7	15.0± 0.8	14.7± 0.7	15.3± 1.3
20ppm	13.2± 1.0	14.3± 1.2	15.8± 1.7	16.0± 1.5	15.1± 1.3	15.0± 1.4	15.3± 1.7
40ppm	12.1± 0.8*	13.6± 0.9	14.7± 1.2	15.5± 1.3	14.9± 0.9	14.8± 1.1	14.7± 1.2
80ppm	11.2± 0.9**	13.0± 0.7*	14.7± 1.3	15.0± 1.0	14.6± 0.7*	15.3± 1.5	14.2± 1.0*
160ppm	6.3± 1.0**	7.4± 1.6**	8.4± 0.5**	9.6± 1.6**	8.6± 1.4**	9.0± 1.3**	8.6± 1.8**

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

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)
0ppm	15.3± 0.9	15.5± 1.1	16.0± 1.0	15.3± 0.8	15.5± 0.9	15.2± 1.1
10ppm	14.4± 0.4	14.5± 0.6	14.4± 0.7**	14.6± 0.6	14.2± 0.6*	14.1± 0.8
20ppm	14.5± 0.8	14.4± 0.9	14.3± 1.0**	14.5± 0.7	14.2± 0.9*	14.1± 1.2
40ppm	14.6± 0.9	14.6± 1.4	14.2± 1.0**	14.2± 1.2*	14.1± 1.0**	14.5± 1.1
80ppm	14.6± 1.1	14.2± 0.7*	14.1± 1.1**	13.8± 1.2**	13.9± 0.8**	13.6± 0.8**
160ppm	9.2± 0.7**	9.0± 0.3**	9.8± 1.2**	9.3± 0.5**	9.7± 1.2**	9.3± 1.1**

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

APPENDIX C 2

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(6)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
0ppm	11.3± 0.4	11.4± 0.7	11.4± 0.5	11.5± 0.7	11.2± 0.6	10.9± 0.8	10.8± 0.7
10ppm	10.3± 0.5	10.8± 0.8	10.9± 0.9	11.1± 0.7	10.5± 0.8	10.1± 0.7	10.0± 0.9
20ppm	10.9± 0.8	11.0± 0.5	10.9± 0.7	10.8± 0.6	10.3± 0.5*	10.2± 0.7	10.2± 0.6
40ppm	10.3± 0.7	10.8± 0.4	10.7± 0.6	10.9± 1.0	10.2± 1.0**	9.8± 0.7**	9.9± 0.3*
80ppm	9.0± 1.0**	10.3± 0.5*	10.7± 0.4	10.7± 0.5	10.2± 0.6*	10.2± 0.7	9.6± 0.6**
160ppm	4.8± 1.4**	5.8± 1.4**	6.6± 1.5**	7.1± 1.6**	6.7± 0.5**	7.0± 0.8**	6.3± 1.9**

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

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)
0ppm	10.6± 0.8	10.9± 0.8	10.6± 0.7	11.0± 0.8	10.8± 0.7	11.3± 0.8
10ppm	9.7± 0.9*	10.1± 0.9	9.6± 1.0*	9.9± 0.7**	10.2± 0.5	9.8± 0.7**
20ppm	9.9± 0.8	9.9± 1.2	9.4± 0.5**	9.4± 0.4**	9.8± 0.5**	9.9± 0.9**
40ppm	9.4± 0.7**	9.8± 0.8	9.4± 0.6**	9.1± 0.7**	9.5± 0.8**	9.4± 0.7**
80ppm	9.7± 0.8*	9.9± 0.9	9.3± 0.7**	9.4± 0.9**	9.4± 0.7**	9.5± 1.1**
160ppm	6.6± 0.6 ?	6.7± 0.4 ?	7.5± 0.3 ?	6.7± 0.0 ?	7.6± 0.4 ?	6.6± 0.1 ?

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, RAT : MALE

(13 - WEEK STUDY)

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV fℓ	MCH pg	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
0ppm	10	8.61± 0.28	16.4± 0.2	45.9± 1.5	53.3± 1.0	19.0± 0.6	35.7± 1.0	743± 46
10ppm	10	8.51± 0.27	16.2± 0.2	45.0± 1.5	52.9± 0.7	19.1± 0.6	36.1± 1.1	758± 46
20ppm	10	8.61± 0.26	16.2± 0.4	45.8± 1.5	53.1± 0.6	18.8± 0.2	35.4± 0.5	774± 37
40ppm	10	8.27± 0.46	15.8± 0.2**	43.9± 2.3	53.1± 0.9	19.2± 1.4	36.1± 2.4	773± 58
80ppm	10	7.76± 0.43**	15.1± 0.4**	42.1± 2.4**	54.2± 1.0	19.5± 1.1	35.9± 2.1	794± 79
160ppm	2	7.83± 0.47 ?	14.7± 1.1 ?	43.2± 3.7 ?	55.2± 1.3 ?	18.8± 0.3 ?	34.1± 0.3 ?	771± 42 ?

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. : 0316
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RETICULOCYTE ‰	PROTHROMBIN TIME sec	APTT sec
0ppm	10	21± 7	11.5± 0.5	18.2± 1.7
10ppm	10	23± 3	11.9± 0.5	18.4± 0.7
20ppm	10	27± 4*	11.7± 0.5	18.4± 0.6
40ppm	10	24± 4	11.6± 0.4	18.3± 0.7
80ppm	10	29± 5**	11.7± 0.4	18.4± 0.6
160ppm	2	24± 2 ?	12.1± 0.0 ?	19.1± 1.3 ?

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. : 0316
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHERS
0ppm	10	3.31± 1.22	0± 0	22± 6	2± 1	0± 0	4± 2	72± 6	0± 0
10ppm	10	3.75± 1.39	0± 0	22± 6	1± 1	0± 0	4± 2	72± 5	0± 0
20ppm	10	4.09± 1.76	0± 0	24± 8	1± 1	0± 0	4± 2	71± 7	0± 0
40ppm	10	3.14± 0.43	0± 0	25± 5	1± 1	0± 0	3± 1	71± 5	0± 0
80ppm	10	3.55± 0.53	0± 0	26± 6	1± 1	0± 0	4± 1	69± 5	0± 0
160ppm	2	4.20± 0.73 ?	0± 0 ?	43± 23 ?	1± 1 ?	0± 0 ?	2± 1 ?	55± 23 ?	0± 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, RAT : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV f ℓ	MCH p g	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
0ppm	10	9.32± 0.36	16.4± 0.3	46.8± 2.0	50.2± 0.5	17.6± 0.7	35.2± 1.7	711± 42
10ppm	10	9.21± 0.40	16.3± 0.3	46.1± 2.0	50.0± 0.7	17.8± 0.9	35.6± 1.6	697± 50
20ppm	10	9.34± 0.26	16.3± 0.2	47.0± 1.6	50.3± 0.7	17.5± 0.5	34.7± 1.2	708± 45
40ppm	10	9.38± 0.28	16.1± 0.2	47.1± 1.6	50.2± 0.8	17.2± 0.5	34.3± 0.9	710± 46
80ppm	10	8.89± 0.34*	15.6± 0.3**	44.8± 1.7	50.4± 0.9	17.6± 0.8	34.9± 1.3	769± 41
160ppm	5	8.08± 0.52**	14.6± 0.7**	43.2± 3.6**	53.5± 1.3**	18.0± 0.3	33.8± 1.3	712± 86

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

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RETICULOCYTE ‰		PROTHROMBIN TIME sec		APTT sec	
0ppm	10	27±	5	14.8±	3.1	23.9±	2.4
10ppm	10	23±	5	14.9±	2.2	24.9±	2.1
20ppm	10	23±	3	14.4±	2.6	23.5±	3.0
40ppm	10	28±	9	15.1±	3.1	24.5±	1.5
80ppm	10	27±	6	12.9±	1.2	23.2±	0.8
160ppm	5	30±	3	13.2±	2.6	22.8±	3.5

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

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHERS
0ppm	10	6.35± 0.91	0± 0	25± 4	1± 1	0± 0	3± 1	71± 4	0± 0
10ppm	10	6.49± 1.20	0± 0	24± 5	2± 1	0± 0	3± 1	71± 7	0± 0
20ppm	10	6.84± 1.21	0± 0	25± 6	1± 1	0± 0	3± 1	71± 7	0± 0
40ppm	10	6.15± 1.07	0± 0	27± 6	1± 1	0± 0	3± 1	69± 6	0± 0
80ppm	10	7.37± 2.04	0± 0	30± 8	1± 1	0± 0	4± 2	65± 7	0± 0
160ppm	5	4.10± 1.99*	0± 0	39± 10**	1± 1	0± 0	4± 2	56± 9**	0± 0

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

(HCL070)

APPENDIX E 1

BIOCHEMISTRY : SUMMARY, RAT : MALE

(13 - WEEK STUDY)

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	TOTAL PROTEIN g/dl		ALBUMIN g/dl		A/G RATIO		T-BILIRUBIN mg/dl		GLUCOSE mg/dl		T-CHOLESTEROL mg/dl		TRIGLYCERIDE mg/dl	
0ppm	10	6.3±	0.1	3.9±	0.1	1.7±	0.1	0.13±	0.01	183±	11	57±	7	62±	13
10ppm	10	6.3±	0.1	4.0±	0.1	1.7±	0.1	0.14±	0.01	182±	17	62±	6	52±	11
20ppm	10	6.3±	0.1	4.0±	0.1	1.8±	0.1	0.13±	0.01	178±	8	59±	7	51±	19
40ppm	10	6.3±	0.1	4.0±	0.1	1.8±	0.1	0.13±	0.01	181±	7	64±	6	56±	15
80ppm	10	6.4±	0.2	4.1±	0.1*	1.7±	0.1	0.14±	0.01	175±	9	67±	9*	53±	9
160ppm	5	6.3±	0.1	4.1±	0.1**	1.9±	0.1	0.14±	0.01	141±	6**	70±	6**	24±	7**

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

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	PHOSPHOLIPID mg/dℓ		GOT IU/ℓ		GPT IU/ℓ		LDH IU/ℓ		ALP IU/ℓ		G-GTP IU/ℓ		CPK IU/ℓ	
0ppm	10	107±	8	68±	5	43±	3	155±	27	297±	24	2±	1	111±	6
10ppm	10	112±	6	78±	20	45±	8	184±	62	276±	16	3±	1	109±	10
20ppm	10	109±	10	73±	14	42±	7	170±	35	287±	18	2±	1	106±	12
40ppm	10	114±	7	78±	20	44±	10	187±	56	284±	14	2±	1	113±	18
80ppm	10	119±	11*	66±	11	38±	4	172±	33	283±	26	3±	1	100±	6
160ppm	5	123±	13*	68±	9	36±	3	249±	49**	322±	35	2±	1	115±	13

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

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	UREA NITROGEN mg/dℓ	CREATININE mg/dℓ	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dℓ	INORGANIC PHOSPHORUS mg/dℓ
0ppm	10	19.0± 1.3	0.5± 0.0	141± 1	3.5± 0.2	103± 1	10.3± 0.2	5.8± 1.0
10ppm	10	19.0± 2.0	0.5± 0.0	141± 1	3.6± 0.4	103± 1	10.2± 0.2	5.8± 1.0
20ppm	10	18.2± 0.9	0.5± 0.1	141± 1	3.6± 0.2	103± 1	10.3± 0.2	5.9± 0.9
40ppm	10	18.8± 1.2	0.5± 0.1	141± 1	3.5± 0.2	104± 2	10.2± 0.1	5.8± 0.8
80ppm	10	19.1± 1.4	0.5± 0.1	141± 1	3.6± 0.2	104± 1	10.3± 0.2	5.9± 0.7
160ppm	5	19.1± 1.9	0.4± 0.1	140± 1	3.9± 0.2	105± 1	10.0± 0.3**	6.0± 0.9

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

APPENDIX E 2

BIOCHEMISTRY : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	TOTAL PROTEIN g/dℓ	ALBUMIN g/dℓ	A/G RATIO	T-BILIRUBIN mg/dℓ	GLUCOSE mg/dℓ	T-CHOLESTEROL mg/dℓ	TRIGLYCERIDE mg/dℓ
0ppm	10	6.2± 0.2	3.9± 0.1	1.7± 0.1	0.15± 0.01	137± 9	71± 6	14± 2
10ppm	10	6.0± 0.2*	3.8± 0.1	1.7± 0.1	0.15± 0.01	133± 15	71± 8	15± 2
20ppm	10	6.1± 0.1	3.9± 0.1	1.7± 0.1	0.15± 0.01	135± 9	72± 6	16± 3
40ppm	10	6.0± 0.2*	3.9± 0.1	1.8± 0.1	0.15± 0.01	138± 12	71± 11	15± 3
80ppm	10	6.0± 0.1*	3.8± 0.1	1.8± 0.1	0.16± 0.01	133± 11	72± 8	18± 4
160ppm	2	5.9± 0.1 ?	3.7± 0.3 ?	1.8± 0.4 ?	0.16± 0.01 ?	116± 9 ?	96± 13 ?	29± 4 ?

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. : 0316
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	PHOSPHOLIPID mg/dℓ	GOT IU/ℓ	GPT IU/ℓ	LDH IU/ℓ	ALP IU/ℓ	G-GTP IU/ℓ	CPK IU/ℓ
0ppm	10	133± 8	72± 10	39± 11	309± 106	205± 32	3± 1	140± 24
10ppm	10	129± 12	64± 3	32± 4	283± 61	200± 24	2± 1	127± 17
20ppm	10	135± 10	69± 5	36± 4	246± 31	219± 16	3± 1	122± 17
40ppm	10	130± 13	71± 6	37± 5	265± 40	203± 23	3± 1	123± 9
80ppm	10	134± 13	65± 5	32± 5	293± 98	217± 31	3± 1	128± 29
160ppm	2	177± 6 ?	81± 2 ?	39± 1 ?	359± 33 ?	311± 3 ?	6± 1 ?	121± 4 ?

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. : 0316
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	UREA NITROGEN mg/dℓ	CREATININE mg/dℓ	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dℓ	INORGANIC PHOSPHORUS mg/dℓ
0ppm	10	19.2± 2.3	0.6± 0.1	141± 2	3.5± 0.3	106± 2	10.1± 0.2	5.0± 1.5
10ppm	10	17.7± 1.3	0.5± 0.0	140± 2	3.5± 0.2	104± 2	10.0± 0.1	4.9± 1.4
20ppm	10	17.9± 1.6	0.5± 0.0	140± 1	3.5± 0.2	104± 2	10.0± 0.2	5.0± 1.2
40ppm	10	17.9± 1.2	0.5± 0.0*	141± 1	3.3± 0.3	105± 1	9.9± 0.1	5.1± 0.8
80ppm	10	17.0± 2.3	0.5± 0.0**	141± 1	3.5± 0.2	106± 2	9.9± 0.2	5.7± 1.1
160ppm	2	15.6± 0.4 ?	0.4± 0.0 ?	138± 1 ?	4.0± 0.3 ?	102± 3 ?	9.7± 0.2 ?	5.5± 0.8 ?

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

URINALYSIS : SUMMARY, RAT: MALE

(13 - WEEK STUDY)

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	±	+	2+	3+	4+	CHI	Bilirubin −	+	2+	3+	CHI
0ppm	10	0	1	1	3	2	2	1		0	5	3	2	0	0		10	0	0	0	0	0		9	1	0	0	0	0		10	0	0	0	
10ppm	10	0	1	0	3	2	4	0		1	5	3	1	0	0		10	0	0	0	0	0		7	2	1	0	0	0		10	0	0	0	
20ppm	10	0	0	0	3	3	3	1		0	1	9	0	0	0	*	10	0	0	0	0	0		7	3	0	0	0	0		10	0	0	0	
40ppm	10	0	0	0	1	3	5	1		0	7	3	0	0	0		10	0	0	0	0	0		8	2	0	0	0	0		10	0	0	0	
80ppm	10	0	0	0	0	2	5	3		0	3	5	2	0	0		10	0	0	0	0	0		4	5	1	0	0	0		10	0	0	0	
160ppm	5	0	0	0	0	0	2	3		0	0	0	5	0	0	*	5	0	0	0	0	0		0	2	2	1	0	0	**	5	0	0	0	

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

STUDY NO. : 0316 URINALYSIS
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

Group Name	NO. of Animals	Occult blood −	±	+	2+	3+	CHI	Urobilinogen ±	+	2+	3+	4+	CHI
0ppm	10	10	0	0	0	0		10	0	0	0	0	
10ppm	10	10	0	0	0	0		10	0	0	0	0	
20ppm	10	9	0	1	0	0		10	0	0	0	0	
40ppm	10	10	0	0	0	0		10	0	0	0	0	
80ppm	10	8	1	0	0	1		10	0	0	0	0	
160ppm	5	5	0	0	0	0		5	0	0	0	0	

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

APPENDIX F 2

URINALYSIS : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0316 URINALYSIS
ANIMAL : RAT F344/DuCrj
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	Bilirubin −	+	2+	3+	CHI
0ppm	10	0	0	1	0	2	6	1		4	4	2	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
10ppm	10	0	1	0	0	1	6	2		3	4	3	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
20ppm	10	0	0	0	0	5	3	2		2	7	1	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
40ppm	10	0	0	0	6	2	2	0	*	1	7	2	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
80ppm	10	0	0	0	2	1	4	3		3	6	1	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
160ppm	2	0	1	1	0	0	0	0	?	0	0	2	0	0	0	?	2	0	0	0	0	0	?	1	0	0	1	0	0	?	2	0	0	0	?

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

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

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	Occult blood −	±	+	2+	3+	CHI	Urobilinogen ±	+	2+	3+	4+	CHI
0ppm	10	10	0	0	0	0		10	0	0	0	0	
10ppm	10	10	0	0	0	0		10	0	0	0	0	
20ppm	10	10	0	0	0	0		10	0	0	0	0	
40ppm	10	10	0	0	0	0		10	0	0	0	0	
80ppm	10	10	0	0	0	0		10	0	0	0	0	
160ppm	2	2	0	0	0	0	?	2	0	0	0	0	?

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

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

APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, RAT : MALE

(13 - WEEK STUDY)

APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

APPENDIX B 1

BODY WEIGHT CHANGES :SUMMARY, RAT : MALE

(13 - WEEK STUDY)

APPENDIX B 2

BODY WEIGHT CHANGES : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

APPENDIX C 1

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : MALE

(13 - WEEK STUDY)

APPENDIX C 2

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

APPENDIX D 1

HEMATOLOGY : SUMMARY, RAT : MALE

(13 - WEEK STUDY)

APPENDIX D 2

HEMATOLOGY : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

APPENDIX E 1

BIOCHEMISTRY : SUMMARY, RAT : MALE

(13 - WEEK STUDY)

APPENDIX E 2

BIOCHEMISTRY : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

APPENDIX F 1

URINALYSIS : SUMMARY, RAT : MALE

(13 - WEEK STUDY)

APPENDIX F 2

URINALYSIS : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

APPENDIX G 1

GROSS FINDINGS : SUMMARY, RAT : MALE

DEAD AND MORIBUND ANIMALS

(13 - WEEK STUDY)

APPENDIX G 2

GROSS FINDINGS : SUMMARY, RAT : MALE : SACRIFICED ANIMALS

(13 - WEEK STUDY)

APPENDIX G 3

GROSS FINDINGS : SUMMARY, RAT : FEMALE

DEAD AND MORIBUND ANIMALS

(13 - WEEK STUDY)

APPENDIX G 4

GROSS FINDINGS : SUMMARY, RAT : FEMALE : SACRIFICED ANIMALS

(13 - WEEK STUDY)

APPENDIX H 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : MALE

(13 - WEEK STUDY)

APPENDIX H 2

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

APPENDIX I 1

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : MALE

(13 - WEEK STUDY)

APPENDIX I 2

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

APPENDIX J 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : DEAD AND MORIBUND ANIMALS

(13 - WEEK STUDY)

APPENDIX J 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE: SACRIFICED ANIMALS

(13 - WEEK STUDY)

APPENDIX J 3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : DEAD AND MORIBUND ANIMALS

(13 - WEEK STUDY)

APPENDIX J 4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : SACRIFICED ANIMALS

(13 - WEEK STUDY)

APPENDIX K 1

IDENTITY OF GLYCIDOL IN THE 13 - WEEK INHALATION STUDY

APPENDIX K 2

STABILITY OF GLYCIDOL IN THE 13 - WEEK INHALATION STUDY

APPENDIX L 1

CONCENTRATION OF GLYCIDL IN THE INHALATION CHAMBER OF THE 13-WEEK INHALATION STUDY

APPENDIX L 2

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 13 - WEEK INHALATION STUDY OF GLYCIDOL

APPENDIX M 1

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS

IN THE 13 - WEEK INHALATION STUDY OF GLYCIDOL

APPENDIX M 2

UNITS AND DECIMARL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13 - WEEK INHALATION STUDY OF GLYCIDOL

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 14W)

Organ	Findings	Group Name	0ppm	10ppm	20ppm	40ppm
		NO. of Animals	0 (%)	0 (%)	0 (%)	0 (%)
thymus	atrophic		- (-)	- (-)	- (-)	- (-)

Organ	Findings	Group Name	80ppm	160ppm
		NO. of Animals	0 (%)	5 (%)
thymus	atrophic		- (-)	1 (20)

APPENDIX G 2

GROSS FINDINGS : SUMMARY, RAT : MALE : SACRIFICED ANIMALS

(13 - WEEK STUDY)

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name	0ppm	10ppm	20ppm	40ppm
		NO. of Animals	10 (%)	10 (%)	10 (%)	10 (%)
lymph node	enlarged		0 (0)	0 (0)	0 (0)	0 (0)
liver	herniation		0 (0)	1 (10)	0 (0)	0 (0)

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name	80ppm	160ppm
		NO. of Animals	10 (%)	5 (%)
lymph node	enlarged		1 (10)	0 (0)
liver	herniation		0 (0)	0 (0)

APPENDIX G 3

GROSS FINDINGS : SUMMARY, RAT : FEMALE

DEAD AND MORIBUND ANIMALS

(13 - WEEK STUDY)

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 14W)

Organ	Findings	Group Name	0ppm	10ppm	20ppm	40ppm
		NO. of Animals	0 (%)	0 (%)	0 (%)	0 (%)
thymus	atrophic		- (-)	- (-)	- (-)	- (-)
urin bladd	urine:marked retention		- (-)	- (-)	- (-)	- (-)

Organ	Findings	Group Name / NO. of Animals	80ppm 0 (%)	160ppm 8 (%)
thymus	atrophic		- (-)	3 (38)
urin bladd	urine:marked retention		- (-)	1 (13)

APPENDIX G 4

GROSS FINDINGS : SUMMARY, RAT : FEMALE : SACRIFICED ANIMALS

(13 - WEEK STUDY)

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name / NO. of Animals	0ppm 10 (%)	10ppm 10 (%)	20ppm 10 (%)	40ppm 10 (%)
liver	herniation		0 (0)	1 (10)	1 (10)	0 (0)
uterus	nodule		0 (0)	0 (0)	1 (10)	0 (0)
eye	white		0 (0)	0 (0)	1 (10)	0 (0)

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name	80ppm	160ppm
		NO. of Animals	10 (%)	2 (%)
liver	herniation		3 (30)	0 (0)
uterus	nodule		0 (0)	0 (0)
eye	white		0 (0)	0 (0)

APPENDIX H 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : MALE

(13 - WEEK STUDY)

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
0ppm	10	273± 18	0.219± 0.029	0.050± 0.006	2.908± 0.113	0.900± 0.073	0.940± 0.069
10ppm	10	260± 9	0.212± 0.022	0.050± 0.007	2.806± 0.099	0.853± 0.033	0.895± 0.038
20ppm	10	254± 15*	0.205± 0.030	0.051± 0.006	2.844± 0.092	0.897± 0.069	0.916± 0.039
40ppm	10	251± 14**	0.193± 0.026	0.051± 0.004	2.850± 0.150	0.863± 0.064	0.915± 0.047
80ppm	10	233± 11**	0.175± 0.024**	0.052± 0.004	2.654± 0.496	0.870± 0.028	0.937± 0.056
160ppm	5	128± 15**	0.085± 0.027**	0.040± 0.002**	0.890± 0.058**	0.593± 0.047**	0.719± 0.072**

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

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
0ppm	10	1.683± 0.086	0.495± 0.046	6.773± 0.446	1.847± 0.040
10ppm	10	1.657± 0.056	0.479± 0.023	6.512± 0.348	1.853± 0.046
20ppm	10	1.682± 0.096	0.484± 0.041	6.443± 0.488	1.826± 0.051
40ppm	10	1.684± 0.092	0.493± 0.040	6.561± 0.313	1.820± 0.054
80ppm	10	1.777± 0.115	0.496± 0.026	6.432± 0.449	1.794± 0.039
160ppm	5	1.409± 0.087**	0.281± 0.058**	4.047± 0.478**	1.566± 0.064**

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

APPENDIX H 2

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
0ppm	10	163± 8	0.181± 0.013	0.058± 0.011	0.106± 0.018	0.602± 0.032	0.731± 0.046
10ppm	10	153± 9*	0.172± 0.012	0.054± 0.006	0.095± 0.010	0.595± 0.036	0.716± 0.052
20ppm	10	148± 8**	0.164± 0.021	0.051± 0.008	0.097± 0.014	0.605± 0.062	0.676± 0.029**
40ppm	10	142± 8**	0.154± 0.021**	0.054± 0.007	0.094± 0.015	0.569± 0.039	0.697± 0.032
80ppm	10	140± 7**	0.148± 0.034**	0.049± 0.008	0.099± 0.019	0.572± 0.031	0.699± 0.030
160ppm	2	91± 1 ?	0.080± 0.012 ?	0.043± 0.001 ?	0.045± 0.001 ?	0.502± 0.049 ?	0.583± 0.046 ?

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. : 0316
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
0ppm	10	1.057± 0.047	0.359± 0.015	3.849± 0.265	1.698± 0.135
10ppm	10	1.085± 0.068	0.353± 0.021	3.631± 0.246	1.734± 0.038
20ppm	10	1.086± 0.042	0.342± 0.030	3.605± 0.217	1.699± 0.033
40ppm	10	1.119± 0.043	0.335± 0.023	3.467± 0.148**	1.692± 0.017*
80ppm	10	1.207± 0.077**	0.347± 0.026	3.649± 0.286	1.687± 0.030**
160ppm	2	1.246± 0.047 ?	0.222± 0.010 ?	2.855± 0.054 ?	1.469± 0.030 ?

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

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : MALE

(13 - WEEK STUDY)

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
0ppm	10	273± 18	0.081± 0.009	0.018± 0.003	1.070± 0.066	0.330± 0.012	0.345± 0.015
10ppm	10	260± 9	0.082± 0.009	0.019± 0.003	1.079± 0.030	0.328± 0.010	0.345± 0.015
20ppm	10	254± 15*	0.081± 0.011	0.020± 0.003	1.125± 0.074	0.354± 0.022	0.362± 0.015
40ppm	10	251± 14**	0.077± 0.008	0.020± 0.002	1.137± 0.056	0.344± 0.016	0.365± 0.011
80ppm	10	233± 11**	0.075± 0.009	0.023± 0.002**	1.140± 0.217*	0.374± 0.013**	0.402± 0.021**
160ppm	5	128± 15**	0.066± 0.014	0.032± 0.003**	0.704± 0.088	0.467± 0.043**	0.565± 0.029**

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

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
0ppm	10	0.618± 0.023	0.181± 0.007	2.486± 0.046	0.680± 0.037
10ppm	10	0.637± 0.015	0.184± 0.004	2.503± 0.079	0.713± 0.019
20ppm	10	0.664± 0.022*	0.191± 0.009	2.538± 0.072	0.721± 0.036
40ppm	10	0.672± 0.015**	0.197± 0.013*	2.616± 0.054**	0.727± 0.034
80ppm	10	0.762± 0.027**	0.213± 0.007**	2.758± 0.114**	0.771± 0.032**
160ppm	5	1.111± 0.089**	0.218± 0.022**	3.173± 0.099**	1.235± 0.090**

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

APPENDIX I 2

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
0ppm	10	163± 8	0.111± 0.007	0.035± 0.006	0.065± 0.010	0.369± 0.021	0.448± 0.025
10ppm	10	153± 9*	0.113± 0.010	0.035± 0.004	0.062± 0.007	0.390± 0.024	0.469± 0.023
20ppm	10	148± 8**	0.110± 0.013	0.035± 0.005	0.065± 0.009	0.408± 0.023**	0.458± 0.022
40ppm	10	142± 8**	0.109± 0.015	0.038± 0.005	0.066± 0.010	0.402± 0.015**	0.493± 0.028**
80ppm	10	140± 7**	0.106± 0.025	0.035± 0.005	0.071± 0.015	0.410± 0.020**	0.501± 0.018**
160ppm	2	91± 1 ?	0.088± 0.012 ?	0.047± 0.001 ?	0.049± 0.001 ?	0.551± 0.045 ?	0.641± 0.060 ?

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. : 0316
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
0ppm	10	0.648± 0.031	0.220± 0.014	2.358± 0.103	1.042± 0.094
10ppm	10	0.711± 0.029**	0.231± 0.015	2.376± 0.061	1.138± 0.066**
20ppm	10	0.735± 0.028**	0.231± 0.023	2.436± 0.042	1.151± 0.062**
40ppm	10	0.792± 0.034**	0.237± 0.012	2.453± 0.091	1.199± 0.058**
80ppm	10	0.865± 0.027**	0.249± 0.014**	2.614± 0.116**	1.211± 0.044**
160ppm	2	1.369± 0.030 ?	0.244± 0.014 ?	3.137± 0.011 ?	1.615± 0.008 ?

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 J 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : DEAD AND MORIBUND ANIMALS

(13 - WEEK STUDY)

Organ	Findings	Group Name	0ppm				10ppm				20ppm				40ppm			
		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>			
	adhesion		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	inflammatory infiltration		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	respiratory metaplasia:olfactory epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	squamous cell metaplasia:respiratory epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	atrophy:turbinate		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	ulcer:respiratory epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	atrophy:olfactory epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	erosion:respiratory 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	80ppm				160ppm			
		No. of Animals on Study	0				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
nasal cavit			< 0>				< 5>			
	adhesion		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(20)	(0)	(0)	(0)
	inflammatory infiltration		-	-	-	-	3	2	0	0
			(-)	(-)	(-)	(-)	(60)	(40)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(20)	(0)	(0)
	squamous cell metaplasia:respiratory epithelium		-	-	-	-	0	5	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
	atrophy:turbinate		-	-	-	-	1	3	0	0
			(-)	(-)	(-)	(-)	(20)	(60)	(0)	(0)
	ulcer:respiratory epithelium		-	-	-	-	0	2	0	0
			(-)	(-)	(-)	(-)	(0)	(40)	(0)	(0)
	atrophy:olfactory epithelium		-	-	-	-	0	5	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
	erosion:respiratory epithelium		-	-	-	-	2	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

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 14W)

Organ	Findings	Group Name / No. of Animals on Study / Grade	0ppm				10ppm				20ppm				40ppm			
			0				0				0				0			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
nasal cavit			< 0>				< 0>				< 0>				< 0>			
	necrosis:respiratory epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
lung			< 0>				< 0>				< 0>				< 0>			
	congestion		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	edema		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Hematopoietic system]																		
thymus			< 0>				< 0>				< 0>				< 0>			
	atrophy		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
spleen			< 0>				< 0>				< 0>				< 0>			
	deposit of hemosiderin		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Endocrine system]																		
adrenal			< 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	80ppm				160ppm			
		No. of Animals on Study	0				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
nasal cavit			< 0>				< 5>			
	necrosis:respiratory epithelium		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(20)	(0)	(0)
lung			< 0>				< 5>			
	congestion		-	-	-	-	5	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
	edema		-	-	-	-	4	0	0	0
			(-)	(-)	(-)	(-)	(80)	(0)	(0)	(0)
[Hematopoietic system]										
thymus			< 0>				< 4>			
	atrophy		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(25)	(0)	(0)
spleen			< 0>				< 5>			
	deposit of hemosiderin		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(20)	(0)	(0)	(0)
[Endocrine system]										
adrenal			< 0>				< 5>			
	congestion		-	-	-	-	5	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				10ppm				20ppm				40ppm			
		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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Reproductive system]																		
testis			< 0>				< 0>				< 0>				< 0>			
	germ cell necrosis		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
epididymis			< 0>				< 0>				< 0>				< 0>			
	decreased:sperma		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	debris of spermatic elements		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Nervous system]																		
brain			< 0>				< 0>				< 0>				< 0>			
	degeneration:granular cell		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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	80ppm				160ppm			
		No. of Animals on Study	0				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Reproductive system]										
testis			< 0>				< 5>			
	germ cell necrosis		-	-	-	-	4	0	0	0
			(-)	(-)	(-)	(-)	(80)	(0)	(0)	(0)
epididymis			< 0>				< 5>			
	decreased:sperma		-	-	-	-	2	1	2	0
			(-)	(-)	(-)	(-)	(40)	(20)	(40)	(0)
	debris of spermatic elements		-	-	-	-	2	3	0	0
			(-)	(-)	(-)	(-)	(40)	(60)	(0)	(0)
[Nervous system]										
brain			< 0>				< 5>			
	degeneration:granular cell		-	-	-	-	0	3	0	0
			(-)	(-)	(-)	(-)	(0)	(60)	(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 J 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE: SACRIFICED ANIMALS

(13 - WEEK STUDY)

STUDY NO. : 0316
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	0ppm 10				10ppm 10				20ppm 10				40ppm 10			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
nasal cavit			<10>				<10>				<10>				<10>			
	inflammatory 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)
	erosion: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)	0 (0)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:olfactory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	squamous cell metaplasia:respiratory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4 (40)	0 (0)	0 (0)	0 (0)	9 (90)	1 (10)	0 (0)	0 (0) **
	atrophy:turbinate		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	ulcer: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)
	atrophy:olfactory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	erosion: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)

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	80ppm				160ppm			
		No. of Animals on Study	10				5			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]										
nasal cavit			<10>				< 5>			
	inflammatory infiltration		5 (50)	5 (50)	0 (0)	0 (0) **	2 (40)	3 (60)	0 (0)	0 (0) **
	erosion:squamous epithelium		0 (0)	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:olfactory epithelium		0 (0)	1 (10)	0 (0)	0 (0)	1 (20)	2 (40)	0 (0)	0 (0) *
	squamous cell metaplasia:respiratory epithelium		0 (0)	10 (100)	0 (0)	0 (0) **	0 (0)	5 (100)	0 (0)	0 (0) **
	atrophy:turbinate		10 (100)	0 (0)	0 (0)	0 (0) **	3 (60)	2 (40)	0 (0)	0 (0) **
	ulcer:olfactory epithelium		2 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	atrophy:olfactory epithelium		0 (0)	10 (100)	0 (0)	0 (0) **	2 (40)	3 (60)	0 (0)	0 (0) **
	erosion:respiratory epithelium		4 (40)	0 (0)	0 (0)	0 (0)	1 (20)	1 (20)	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	0ppm				10ppm				20ppm				40ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
lung			<10>				<10>				<10>				<10>			
	edema		0	0	0	0	0	0	0	0	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]																		
spleen			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	extramedullary hematopoiesis		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]																		
liver			<10>				<10>				<10>				<10>			
	herniation		0	0	0	0	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)
[Urinary system]																		
kidney			<10>				<10>				<10>				<10>			
	eosinophilic body		10	0	0	0	10	0	0	0	10	0	0	0	10	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(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
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	0ppm				10ppm				20ppm				40ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
lung			<10>				<10>				<10>				<10>			
	edema		0	0	0	0	0	0	0	0	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]																		
spleen			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	extramedullary hematopoiesis		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]																		
liver			<10>				<10>				<10>				<10>			
	herniation		0	0	0	0	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)
[Urinary system]																		
kidney			<10>				<10>				<10>				<10>			
	eosinophilic body		10	0	0	0	10	0	0	0	10	0	0	0	10	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(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
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	80ppm				160ppm			
		No. of Animals on Study	10				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
lung			<10>				< 5>			
	edema		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
[Hematopoietic system]										
spleen			<10>				< 5>			
	deposit of hemosiderin		0	0	0	0	3	0	0	0 *
			(0)	(0)	(0)	(0)	(60)	(0)	(0)	(0)
	extramedullary hematopoiesis		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(40)	(0)	(0)	(0)
[Digestive system]										
liver			<10>				< 5>			
	herniation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Urinary system]										
kidney			<10>				< 5>			
	eosinophilic body		10	0	0	0	3	0	0	0
			(100)	(0)	(0)	(0)	(60)	(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	0ppm				10ppm				20ppm				40ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]																		
adrenal			<10>				<10>				<10>				<10>			
	micro vesicular fatty change		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Reproductive system]																		
testis			<10>				<10>				<10>				<10>			
	germ cell necrosis		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
epididymis			<10>				<10>				<10>				<10>			
	decreased:sperma		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	debris of spermatic elements		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Nervous system]																		
brain			<10>				<10>				<10>				<10>			
	degeneration:granular cell		0	0	0	0	0	0	0	0	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	80ppm				160ppm			
		No. of Animals on Study	10				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]										
adrenal			<10>				< 5>			
	micro vesicular fatty change		0	0	0	0	5	0	0	0 **
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
[Reproductive system]										
testis			<10>				< 5>			
	germ cell necrosis		0	1	0	0	0	3	2	0 **
			(0)	(10)	(0)	(0)	(0)	(60)	(40)	(0)
epididymis			<10>				< 5>			
	decreased:sperma		1	0	0	0	0	2	3	0 **
			(10)	(0)	(0)	(0)	(0)	(40)	(60)	(0)
	debris of spermatic elements		0	1	0	0	2	3	0	0 **
			(0)	(10)	(0)	(0)	(40)	(60)	(0)	(0)
[Nervous system]										
brain			<10>				< 5>			
	degeneration:granular cell		0	0	0	0	1	3	0	0 **
			(0)	(0)	(0)	(0)	(20)	(60)	(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	0ppm				10ppm				20ppm				40ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Special sense organs/appandage]																		
Harder gl			<10>				<10>				<10>				<10>			
	granulation		0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Body cavities]																		
mesenterium			<10>				<10>				<10>				<10>			
	foreign body granuloma		0	0	0	0	0	0	0	0	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	80ppm				160ppm			
		No. of Animals on Study	10				5			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Special sense organs/appandage]										
Harder gl			<10>				< 5>			
	granulation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Body cavities]										
mesenterium			<10>				< 5>			
	foreign body granuloma		1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

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

APPENDIX J 3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : DEAD AND MORIBUND ANIMALS

(13 - WEEK STUDY)

Organ	Findings	Group Name	0ppm				10ppm				20ppm				40ppm			
		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>			
	adhesion		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	inflammatory infiltration		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	respiratory metaplasia:olfactory epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	squamous cell metaplasia:respiratory epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	atrophy:turbinate		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	ulcer:respiratory epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	atrophy:olfactory epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	erosion:respiratory 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	80ppm				160ppm			
		No. of Animals on Study	0				8			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
nasal cavit			< 0>				< 8>			
	adhesion		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(13)	(0)	(0)
	inflammatory infiltration		-	-	-	-	2	4	0	0
			(-)	(-)	(-)	(-)	(25)	(50)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(13)	(0)	(0)	(0)
	squamous cell metaplasia:respiratory epithelium		-	-	-	-	0	8	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
	atrophy:turbinate		-	-	-	-	0	7	1	0
			(-)	(-)	(-)	(-)	(0)	(88)	(13)	(0)
	ulcer:respiratory epithelium		-	-	-	-	0	1	1	0
			(-)	(-)	(-)	(-)	(0)	(13)	(13)	(0)
	atrophy:olfactory epithelium		-	-	-	-	0	8	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
	erosion:respiratory epithelium		-	-	-	-	3	0	0	0
			(-)	(-)	(-)	(-)	(38)	(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				10ppm				20ppm				40ppm			
		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>			
	necrosis:respiratory epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
lung			< 0>				< 0>				< 0>				< 0>			
	congestion		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	edema		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	deposit of hemosiderin		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Homatopoietic system]																		
thymus			< 0>				< 0>				< 0>				< 0>			
	atrophy		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
spleen			< 0>				< 0>				< 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

Organ	Findings	Group Name	80ppm				160ppm			
		No. of Animals on Study	0				8			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
nasal cavit			< 0>				< 8>			
	necrosis:respiratory epithelium		-	-	-	-	1	2	1	0
			(-)	(-)	(-)	(-)	(13)	(25)	(13)	(0)
lung			< 0>				< 8>			
	congestion		-	-	-	-	7	0	0	0
			(-)	(-)	(-)	(-)	(88)	(0)	(0)	(0)
	edema		-	-	-	-	4	0	0	0
			(-)	(-)	(-)	(-)	(50)	(0)	(0)	(0)
	deposit of hemosiderin		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(13)	(0)	(0)	(0)
[Hematopoietic system]										
thymus			< 0>				< 6>			
	atrophy		-	-	-	-	0	5	0	0
			(-)	(-)	(-)	(-)	(0)	(83)	(0)	(0)
spleen			< 0>				< 8>			
	atrophy		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(13)	(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				10ppm				20ppm				40ppm			
		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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
spleen				< 0>				< 0>				< 0>				< 0>		
	deposit of hemosiderin		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Urinary system]																		
urin bladd				< 0>				< 0>				< 0>				< 0>		
	dilatation		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Nervous system]																		
brain				< 0>				< 0>				< 0>				< 0>		
	degeneration:granular cell		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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	80ppm				160ppm			
		No. of Animals on Study	0				8			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]										
spleen			< 0>				< 8>			
	deposit of hemosiderin		-	-	-	-	3	0	0	0
			(-)	(-)	(-)	(-)	(38)	(0)	(0)	(0)
[Urinary system]										
urin bladd			< 0>				< 8>			
	dilatation		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(13)	(0)	(0)	(0)
[Nervous system]										
brain			< 0>				< 8>			
	degeneration:granular cell		-	-	-	-	0	5	3	0
			(-)	(-)	(-)	(-)	(0)	(63)	(38)	(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 J 4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : SACRIFICED ANIMALS

(13 - WEEK STUDY)

Organ	Findings	Group Name	0ppm				10ppm				20ppm				40ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
nasal cavit			<10>				<10>				<10>				<10>			
	inflammatory 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)
	squamous cell metaplasia: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)
	squamous cell metaplasia:olfactory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	atrophy:turbinate		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	atrophy:olfactory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	erosion: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)
[Hematopoietic system]																		
bone marrow			<10>				<10>				<10>				<10>			
	granulation		3	0	0	0	2	0	0	0	1	0	0	0	2	0	0	0
			(30)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)

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

Organ	Findings	Group Name	80ppm				160ppm				
		No. of Animals on Study	10				2				
		Grade	1	2	3	4	1	2	3	4	
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	
[Respiratory system]											
nasal cavit			<10>				< 2>				
	inflammatory infiltration		8	2	0	0 **	0	2	0	0	?
			(80)	(20)	(0)	(0)	(0)	(100)	(0)	(0)	
	squamous cell metaplasia:respiratory epithelium		0	10	0	0 **	0	2	0	0	?
			(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	
	squamous cell metaplasia:olfactory epithelium		1	0	0	0	0	0	0	0	?
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	
	atrophy:turbinate		10	0	0	0 **	0	2	0	0	?
			(100)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	
	atrophy:olfactory epithelium		1	2	0	0	0	2	0	0	?
			(10)	(20)	(0)	(0)	(0)	(100)	(0)	(0)	
	erosion:respiratory epithelium		0	0	0	0	1	0	0	0	?
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)	
[Hematopoiotic system]											
bone marrow			<10>				< 2>				
	granulation		0	0	0	0	0	0	0	0	?
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square
? : Significant test is not applied,because No. of data in this group is less than 3.

Organ	Findings	Group Name	0ppm				10ppm				20ppm				40ppm			
		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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
spleen			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	extramedullary hematopoiesis		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]																		
liver			<10>				<10>				<10>				<10>			
	herniation		0	0	0	0	1	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	epidermal cyst		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
[Urinary system]																		
kidney			<10>				<10>				<10>				<10>			
	mineralization:cortex		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	80ppm				160ppm				
		No. of Animals on Study	10				2				
		Grade	1	2	3	4	1	2	3	4	
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	
[Hematopoietic system]											
spleen			<10>				< 2>				
	deposit of hemosiderin		0	0	0	0	1	0	0	0	?
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)	
	extramedullary hematopoiesis		1	0	0	0	0	0	0	0	?
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	
[Digestive system]											
liver			<10>				< 2>				
	herniation		3	0	0	0	0	0	0	0	?
			(30)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	
	epidermal cyst		0	0	0	0	0	0	0	0	?
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	
[Urinary system]											
kidney			<10>				< 2>				
	mineralization:cortex		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
? : Significant test is not applied,because No. of data in this group is less than 3.

Organ	Findings	Group Name	0ppm				10ppm				20ppm				40ppm			
		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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Reproductive system]																		
uterus			<10>				<10>				<10>				<10>			
	epidermal cyst		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Nervous system]																		
brain			<10>				<10>				<10>				<10>			
	degeneration:granular cell		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Special sense organs/appandage]																		
eye			<10>				<10>				<10>				<10>			
	cataract		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
Harder gl			<10>				<10>				<10>				<10>			
	granulation		0	0	0	0	0	0	0	0	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	80ppm				160ppm			
		No. of Animals on Study	10				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Reproductive system]										
uterus			<10>				< 2>			
	epidermal cyst		0	0	0	0	0	0	0	0 ?
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Nervous system]										
brain			<10>				< 2>			
	degeneration:granular cell		0	0	0	0	0	0	2	0 ?
			(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)
[Special sense organs/appandage]										
eye			<10>				< 2>			
	cataract		0	0	0	0	0	0	0	0 ?
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
Harder gl			<10>				< 2>			
	granulation		1	0	0	0	0	0	0	0 ?
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square
? : Significant test is not applied,because No. of data in this group is less than 3.

APPENDIX K 1

IDENTITY OF GLYCIDOL IN THE 13 - WEEK INHALATION STUDY

IDENTITY OF GLYCIDOL IN THE 13-WEEK INHALATION STUDY

A. Test Substance Lot No.: LER5803

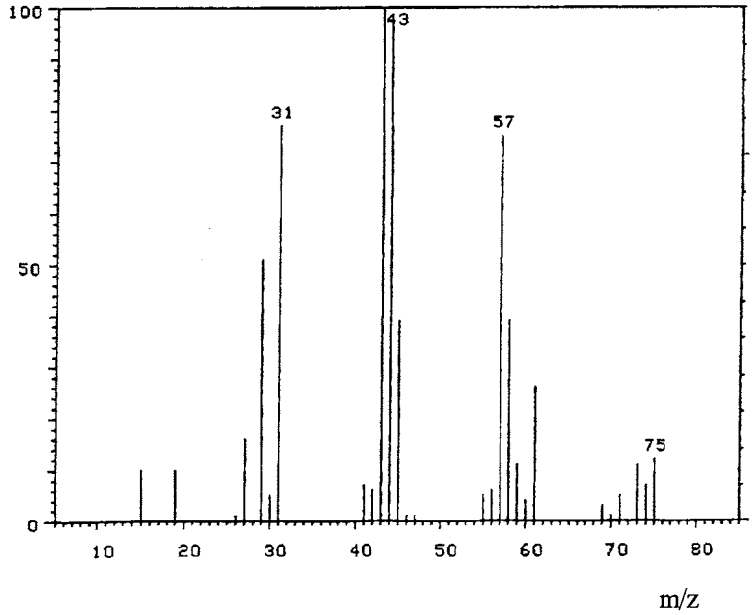
1. Spectral data

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.

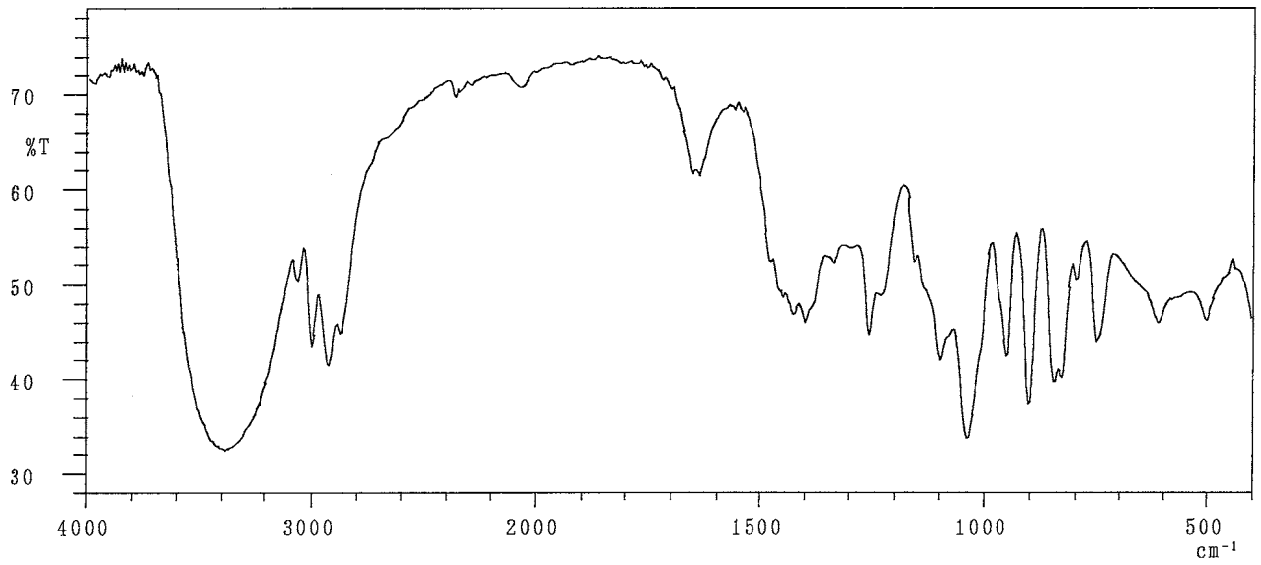
(*Fred W. McLafferty (1994) Wiley Registry of Mass Spectral Data, 6th edition. John Wiley and Sons, Inc. (U.S.), Entry Number 1733)

Infrared Spectrometry

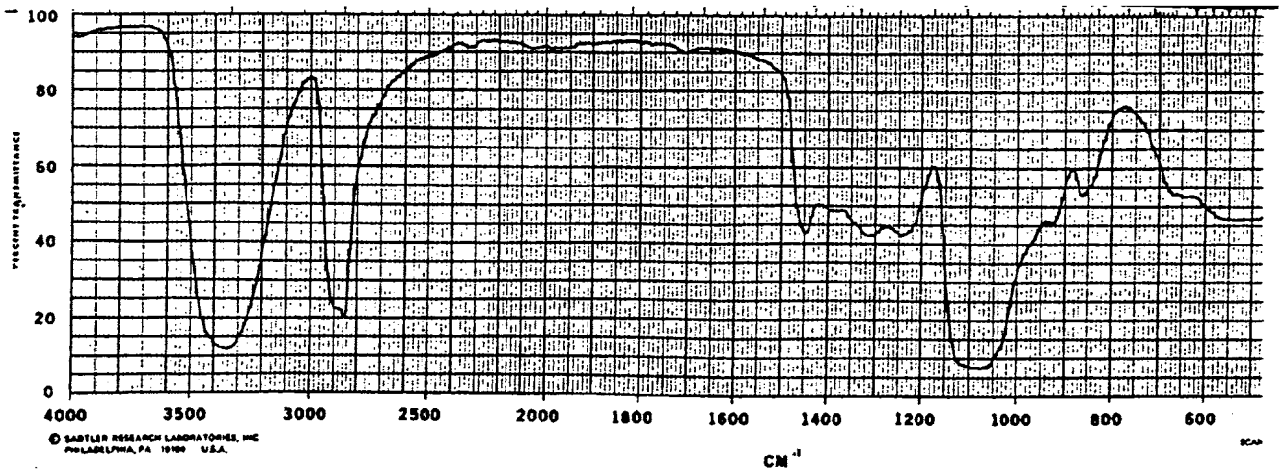
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

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.

B. Test Substance Lot No.: LEQ5980

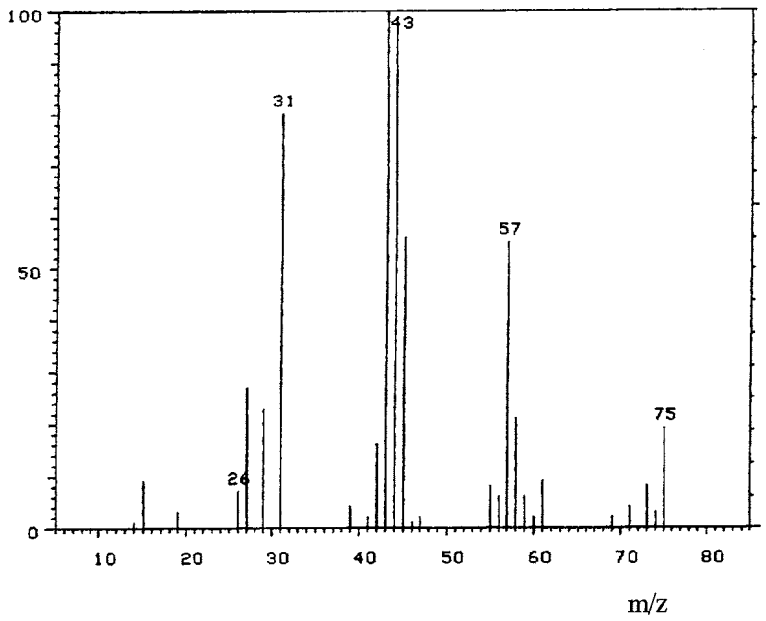
1. Spectral data

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.

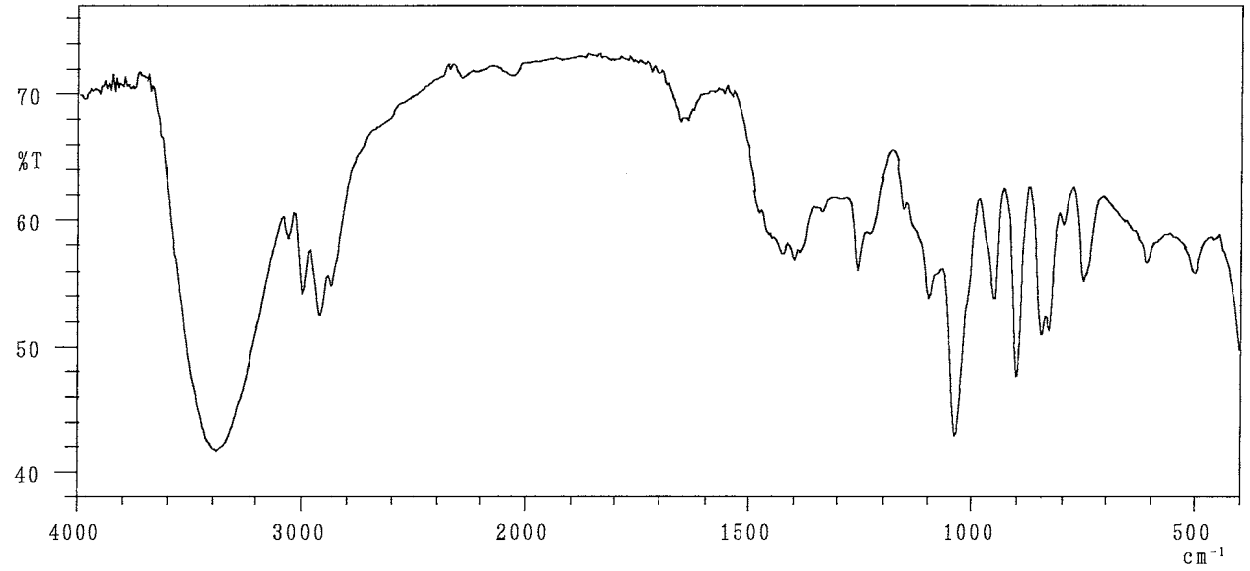
(*Fred W. McLafferty (1994) Wiley Registry of Mass Spectral Data, 6th edition. John Wiley and Sons, Inc. (U.S.), Entry Number 1733)

Infrared Spectrometry

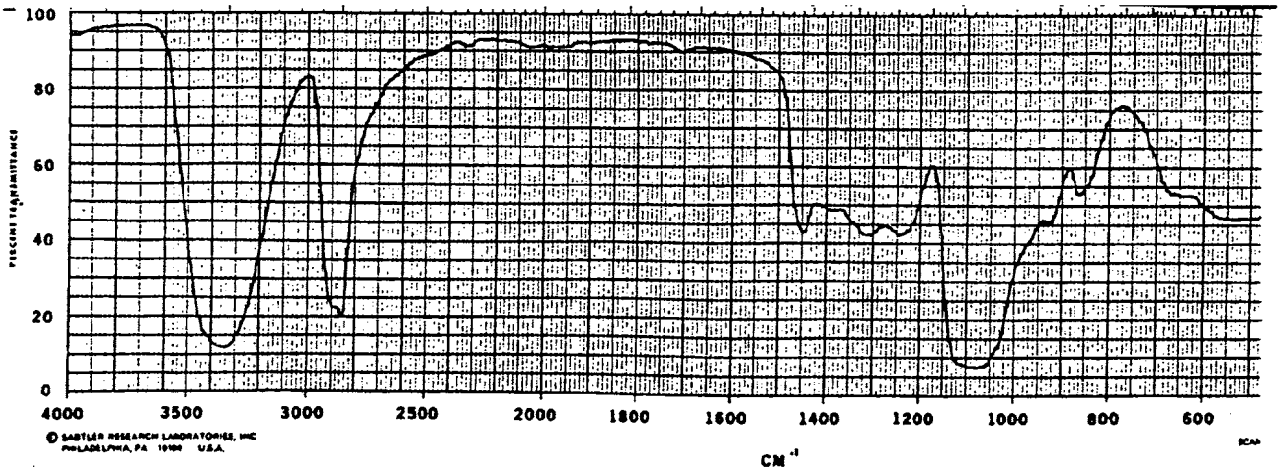
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

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 K 2

STABILITY OF GLYCIDOL IN THE 13 - WEEK INHALATION STUDY

STABILITY OF GLYCIDOL IN THE 13-WEEK INHALATION STUDY

A. Test Substance Lot No.: LER5803

1.Sample: This lot was used from 1996.9.3 to 1996.10.14. 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 1996.8.30 and one major peak (peak No.3) and two impurities (peak No.1,2 < 1% of total area) analyzed at 1996.10.15. No new trace impurity peak in the test substance analyzed at 1996.10.15 was detected.

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
1996.08.30	1	1.89	0.15
	2	2.12	0.23
	3	2.52	99.62
1996.10.15	1	1.90	0.14
	2	2.13	0.23
	3	2.52	99.63

4. Conclusions: The results indicated that the test substance did not change when stored at room temperature during this period (for about 2 months).

B. Test Substance Lot No.: LEQ5980

1.Sample: This lot was used from 1996.10.15 to 1996.12.2. 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 1996.10.11 and one major peak (peak No.3) and two impurities (peak No.1,2 < 1% of total area) analyzed at 1996.12.11. No new trace impurity peak in the test substance analyzed at 1996.12.11 was detected.

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
1996.10.11	1	1.82	0.14
	2	2.12	0.23
	3	2.52	99.63
1996.12.11	1	1.89	0.14
	2	2.12	0.23
	3	2.52	99.63

4. Conclusions: The results indicated that the test substance did not change when stored at room temperature during this period (for about 2 months).

APPENDIX L 1

CONCENTRATION OF GLYCIDL IN THE INHALATION CHAMBER OF THE 13-WEEK INHALATION STUDY

CONCENTRATION OF GLYCIDOL IN THE INHALATION CHAMBER OF THE 13-WEEK INHALATION STUDY

Group Name	Concentration(ppm) Mean ± S.D.
Control	0.0 ± 0.0
10.0ppm	10.1 ± 0.1
20.0ppm	19.8 ± 0.3
40.0ppm	39.6 ± 0.6
80.0ppm	79.8 ± 1.2
160.0ppm	159.6 ± 2.4

APPENDIX L 2

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE

13 - WEEK INHALATION STUDY OF GLYCIDOL

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 13-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	22.6 ± 0.1	55.5 ± 0.6	212.4 ± 1.1	12.0
25ppm	22.5 ± 0.1	56.6 ± 1.3	212.1 ± 1.1	12.0
50ppm	22.6 ± 0.1	55.6 ± 1.5	211.5 ± 1.3	12.0
100ppm	22.6 ± 0.1	54.5 ± 2.0	212.0 ± 1.1	12.0
200ppm	22.6 ± 0.2	54.5 ± 2.9	211.7 ± 1.1	12.0
400ppm	21.8 ± 0.2	53.3 ± 3.3	211.9 ± 1.1	12.0

APPENDIX M 1

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS

IN THE 13 - WEEK INHALATION STUDY OF GLYCIDOL

METHODS FOR HEMATOLOGY,BIOCHEMISTRY AND URINALYSIS IN THE 13-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]
Urinalysis	
pH,Protein,Glucose,Ketone body,Bilirubin,Occult Blood, Urobilinogen	Urinalysis reagent paper method [5]

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

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

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

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

5) Ames reagent strips for urinalysis (Multistix : Bayer-Sankyo Co.,Ltd.,Japan)

APPENDIX M 2

UNITS AND DECIMARL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13 - WEEK INHALATION STUDY OF GLYCIDOL

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-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 transaminase (GOT)	IU/L	0
Glutamic pyruvic transaminase (GPT)	IU/L	0
Lactate dehydrogenase (LDH)	IU/L	0
Alkaline phosphatase (ALP)	IU/L	0
γ-Glutamyl transpeptidase (γ-GTP)	IU/L	0
Creatine phosphokinase (CPK)	IU/L	0
Urea nitrogen	mg/dL	1
Creatinine	mg/dL	1
Sodium	mEq/L	0
Potassium	mEq/L	1
Chloride	mEq/L	0
Calcium	mg/dL	1
Inorganic phosphorus	mg/dL	1