アリルクロリドのラットを用いた
吸入による２週間毒性試験報告書

試験番号：０３３２

APPENDIX

APPENDIXES

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0332
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 1-2	1-4	1-7	2-3	2-7
DEATH	0ppm	0	0	0	0	0
	62.5ppm	0	0	0	0	0
	125.0ppm	0	0	0	0	0
	250.0ppm	0	0	0	0	0
	500.0ppm	0	0	0	0	0
	1000.0ppm	0	0	2	6	-
MORIBUND SACRIFICE	0ppm	0	0	0	0	0
	62.5ppm	0	0	0	0	0
	125.0ppm	0	0	0	0	0
	250.0ppm	0	0	0	0	0
	500.0ppm	0	0	0	0	0
	1000.0ppm	0	0	0	0	-
LOCOMOTOR MOVEMENT DECR	0ppm	0	0	0	0	0
	62.5ppm	0	0	0	0	0
	125.0ppm	0	0	0	0	0
	250.0ppm	0	0	0	0	0
	500.0ppm	0	0	0	0	0
	1000.0ppm	0	1	1	4	-
HUNCHBACK POSITION	0ppm	0	0	0	0	0
	62.5ppm	0	0	0	0	0
	125.0ppm	0	0	0	0	0
	250.0ppm	0	0	0	0	0
	500.0ppm	0	0	0	0	0
	1000.0ppm	0	9	8	4	-
TREMOR	0ppm	0	0	0	0	0
	62.5ppm	0	0	0	0	0
	125.0ppm	0	0	0	0	0
	250.0ppm	0	0	0	0	0
	500.0ppm	0	0	0	0	0
	1000.0ppm	0	1	0	0	-
PILOERECTION	0ppm	0	0	0	0	0
	62.5ppm	0	0	0	0	0
	125.0ppm	0	0	0	0	0
	250.0ppm	0	0	0	0	0
	500.0ppm	0	0	0	0	0
	1000.0ppm	0	10	8	4	-

Clinical sign	Group Name	Administration Week-day 1-2	1-4	1-7	2-3	2-7
SOILED PERI GENITALIA	0ppm	0	0	0	0	0
	62.5ppm	0	0	0	0	0
	125.0ppm	0	0	0	0	0
	250.0ppm	0	0	0	0	0
	500.0ppm	0	0	0	0	0
	1000.0ppm	0	0	1	0	-
IRREGULAR BREATHING	0ppm	0	0	0	0	0
	62.5ppm	0	0	0	0	0
	125.0ppm	0	0	0	0	0
	250.0ppm	0	0	0	0	0
	500.0ppm	0	0	0	0	0
	1000.0ppm	0	1	0	0	-

APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

SEX : FEMALE

Clinical sign	Group Name	Administration Week-day 1-2	1-4	1-7	2-3	2-7
DEATH	0ppm	0	0	0	0	0
	62.5ppm	0	0	0	0	0
	125.0ppm	0	0	0	0	0
	250.0ppm	0	0	0	0	0
	500.0ppm	0	0	0	0	0
	1000.0ppm	0	10	-	-	-

APPENDIX B 1

BODY WEIGHT CHANGES :SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0332
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	116± 4	122± 5	127± 5	136± 6	146± 7	158± 7
62.5ppm	116± 4	122± 5	127± 5	136± 5	145± 6	158± 6
125.0ppm	116± 4	122± 5	128± 6	139± 7	151± 8	168± 9*
250.0ppm	116± 4	121± 4	128± 4	138± 5	148± 6	163± 6
500.0ppm	116± 3	118± 4	120± 4**	132± 4	139± 7	145± 9**
1000.0ppm	116± 4	103± 3**	92± 4**	94± 14**	84± 3**	-

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. : 0332
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	97± 3	100± 4	105± 4	109± 5	114± 6
62.5ppm	93± 3	96± 3	100± 3	106± 3	111± 4	117± 4
125.0ppm	93± 3	95± 2	100± 3	107± 3	112± 3	118± 3
250.0ppm	93± 2	94± 3	99± 3	105± 5	109± 5	116± 6
500.0ppm	93± 3	93± 3*	95± 4**	102± 4	107± 4	111± 4
1000.0ppm	93± 3	85± 3**	76± 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 C 1

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0332
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration 1-7(6) week-day(effective) 2-7(7)	
0ppm	12.7± 0.7	14.1± 1.4
62.5ppm	15.0± 1.6*	14.7± 0.9
125.0ppm	15.0± 1.0*	15.7± 1.0*
250.0ppm	15.9± 0.8**	16.3± 1.1**
500.0ppm	14.8± 0.8*	15.6± 2.2
1000.0ppm	5.0± 2.2	-

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. : 0332
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	12.9± 0.9	10.5± 0.8
62.5ppm	11.6± 0.6**	11.5± 0.7*
125.0ppm	12.0± 0.5*	11.6± 0.7*
250.0ppm	11.8± 0.7**	11.3± 0.8
500.0ppm	11.8± 0.8**	12.3± 1.0**
1000.0ppm	-	-

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

APPENDIX D 1

HEMATOLOGY : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0332
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	8.23± 0.17	15.7± 0.3	45.0± 1.0	54.7± 0.3	19.1± 0.3	34.9± 0.5	912± 40
62.5ppm	5	8.29± 0.12	15.7± 0.3	45.2± 1.4	54.5± 1.0	18.9± 0.1	34.7± 0.5	920± 62
125.0ppm	5	7.97± 0.23	15.1± 0.4	43.7± 1.5	54.7± 0.5	19.0± 0.3	34.6± 0.4	943± 39
250.0ppm	5	7.87± 0.34	14.8± 0.6**	42.8± 1.9	54.4± 0.3	18.8± 0.1	34.6± 0.2	955± 39
500.0ppm	5	7.80± 0.21*	14.7± 0.4**	42.7± 0.6*	54.7± 0.9	18.9± 0.7	34.5± 1.0	1062± 68**
1000.0ppm	0	-	-	-	-	-	-	-

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

STUDY NO. : 0332
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	37± 8	13.0± 0.9	25.3± 4.3
62.5ppm	5	45± 10	12.7± 0.4	22.2± 1.7
125.0ppm	5	43± 8	12.4± 0.5	27.4± 7.3
250.0ppm	5	43± 12	12.4± 0.6	22.0± 2.6
500.0ppm	5	45± 13	12.1± 0.6	22.7± 3.5
1000.0ppm	0	-	-	-

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

STUDY NO. : 0332
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	2.83± 0.93	0± 0	20± 2	0± 1	0± 0	4± 2	76± 3	0± 0
62.5ppm	5	2.89± 0.70	0± 0	20± 3	1± 1	0± 0	4± 2	76± 3	0± 0
125.0ppm	5	3.58± 1.06	0± 0	21± 7	1± 1	0± 0	3± 2	75± 6	0± 0
250.0ppm	5	4.20± 0.97	0± 0	16± 3	0± 1	0± 0	3± 2	80± 4	0± 0
500.0ppm	5	5.20± 0.60**	0± 0	17± 3	1± 1	0± 0	4± 2	79± 4	0± 0
1000.0ppm	0	-	-	-	-	-	-	-	-

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

APPENDIX D 2

HEMATOLOGY : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0332
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	8.61± 0.39	16.5± 0.7	46.1± 2.0	53.6± 0.6	19.2± 0.2	35.8± 0.2	847± 74
62.5ppm	5	8.43± 0.19	16.5± 0.3	45.4± 1.4	53.9± 0.7	19.5± 0.4	36.2± 0.8	814± 65
125.0ppm	5	8.19± 0.24	16.4± 0.2	44.3± 1.0	54.0± 0.5	20.0± 0.7*	37.0± 1.1	865± 39
250.0ppm	5	8.20± 0.23	15.6± 0.3	44.2± 1.4	53.9± 0.5	19.1± 0.3	35.4± 0.7	872± 32
500.0ppm	5	7.99± 0.30**	15.4± 0.2*	43.4± 1.4	54.3± 0.5	19.2± 0.6	35.4± 0.9	979± 37**
1000.0ppm	0	-	-	-	-	-	-	-

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

STUDY NO. : 0332
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	22± 8	12.3± 0.4	20.0± 0.6
62.5ppm	5	25± 4	12.2± 0.5	19.7± 2.2
125.0ppm	5	25± 6	12.6± 0.9	23.3± 5.3
250.0ppm	5	26± 6	12.7± 0.4	26.8± 6.1
500.0ppm	5	29± 4	12.0± 0.4	17.8± 1.6
1000.0ppm	0	-	-	-

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

STUDY NO. : 0332
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	3.95± 1.89	0± 0	19± 3	1± 1	0± 0	4± 2	76± 1	0± 0
62.5ppm	5	2.74± 0.45	0± 0	19± 3	2± 1	0± 0	4± 1	75± 3	0± 0
125.0ppm	5	3.85± 1.29	0± 0	20± 6	1± 1	0± 0	3± 2	76± 7	0± 0
250.0ppm	5	3.62± 0.91	0± 0	17± 1	1± 1	0± 0	5± 2	76± 1	0± 0
500.0ppm	5	5.54± 1.78	0± 0	15± 2	2± 1	0± 0	4± 2	79± 1	0± 0
1000.0ppm	0	-	-	-	-	-	-	-	-

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

APPENDIX E 1

BIOCHEMISTRY : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0332
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	5.7± 0.1	3.8± 0.1	2.0± 0.1	0.14± 0.01	134± 8	51± 3	32± 6
62.5ppm	5	5.8± 0.1	3.9± 0.1	2.0± 0.1	0.14± 0.01	138± 10	52± 4	40± 7
125.0ppm	5	5.7± 0.1	3.8± 0.1	1.9± 0.1	0.13± 0.01	141± 16	53± 1	38± 7
250.0ppm	5	5.6± 0.1	3.7± 0.1	2.0± 0.1	0.14± 0.01	138± 6	49± 5	27± 9
500.0ppm	5	5.9± 0.1**	3.9± 0.2	1.9± 0.2	0.15± 0.01	131± 7	66± 9*	34± 10
1000.0ppm	0	-	-	-	-	-	-	-

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

(HCL074)

STUDY NO. : 0332
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	97± 4	71± 2	34± 1	318± 54	815± 55	1± 1	222± 22
62.5ppm	5	98± 6	74± 8	35± 3	330± 65	803± 66	2± 1	239± 27
125.0ppm	5	97± 4	74± 2	37± 3	278± 61	819± 47	2± 1	239± 26
250.0ppm	5	88± 9	73± 1	37± 2	308± 85	678± 46**	2± 1	207± 35
500.0ppm	5	111± 16	66± 3	36± 3	321± 92	595± 50**	2± 1	188± 40
1000.0ppm	0	-	-	-	-	-	-	-

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

STUDY NO. : 0332
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	16.3± 2.4	0.5± 0.0	142± 1	3.8± 0.2	107± 1	10.1± 0.1	7.9± 0.6
62.5ppm	5	16.1± 1.0	0.5± 0.0	142± 1	3.7± 0.3	106± 0	10.3± 0.2	7.7± 0.5
125.0ppm	5	16.2± 1.6	0.4± 0.0	142± 1	3.7± 0.3	106± 0	10.1± 0.2	8.0± 0.5
250.0ppm	5	13.6± 0.4	0.5± 0.1	142± 2	4.0± 0.7	106± 1	10.0± 0.2	8.0± 0.3
500.0ppm	5	11.7± 1.1*	0.4± 0.0	141± 0	4.1± 0.5	105± 1	10.2± 0.1	8.3± 0.8
1000.0ppm	0	-	-	-	-	-	-	-

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

APPENDIX E 2

BIOCHEMISTRY : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0332
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	5.5±	0.1	3.7±	0.1	2.0±	0.1	0.16±	0.01	127±	13	66±	8	16±	8
62.5ppm	5	5.5±	0.0	3.7±	0.1	2.0±	0.2	0.18±	0.03	123±	13	64±	9	15±	5
125.0ppm	5	5.6±	0.1	3.7±	0.1	2.0±	0.1	0.15±	0.01	127±	11	68±	4	17±	7
250.0ppm	5	5.5±	0.2	3.6±	0.1	1.9±	0.0	0.15±	0.01	119±	9	69±	5	18±	6
500.0ppm	5	5.6±	0.1	3.7±	0.1	1.9±	0.1	0.16±	0.01	113±	7	80±	5**	27±	4*
1000.0ppm	0	-		-		-		-		-		-		-	

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

STUDY NO. : 0332
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	118± 12	75± 4	34± 4	424± 117	646± 19	3± 1	239± 40
62.5ppm	5	113± 10	77± 5	34± 2	553± 153	636± 21	3± 1	259± 51
125.0ppm	5	121± 5	70± 4	34± 1	332± 105	639± 52	2± 0	184± 31
250.0ppm	5	125± 7	70± 2	33± 2	328± 145	550± 31**	2± 1	178± 50
500.0ppm	5	142± 7**	70± 7	34± 3	391± 189	495± 50**	3± 1	163± 38*
1000.0ppm	0	-	-	-	-	-	-	-

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

STUDY NO. : 0332
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	17.6±	1.5	0.5±	0.0	140±	1	3.8±	0.3	108±	1	9.9±	0.1	7.2±	0.5
62.5ppm	5	16.6±	0.7	0.5±	0.0	139±	1	3.9±	0.2	108±	1	9.8±	0.2	7.0±	1.4
125.0ppm	5	16.7±	1.8	0.5±	0.0	140±	2	3.9±	0.3	107±	2	9.9±	0.1	7.1±	1.1
250.0ppm	5	15.1±	1.3*	0.5±	0.0	140±	2	4.0±	0.2	108±	1	9.9±	0.2	7.3±	0.9
500.0ppm	5	12.7±	1.7**	0.4±	0.1	140±	2	4.0±	0.3	107±	1	9.8±	0.2	7.7±	0.7
1000.0ppm	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. : 0332
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 (%)	62.5ppm 0 (%)	125.0ppm 0 (%)	250.0ppm 0 (%)
gl stomach	ulcer		- (-)	- (-)	- (-)	- (-)
urin bladd	urine:marked retention		- (-)	- (-)	- (-)	- (-)

STUDY NO. : 0332
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	500.0ppm	1000.0ppm
		NO. of Animals	0 (%)	10 (%)
gl stomach	ulcer		- (-)	2 (20)
urin bladd	urine:marked retention		- (-)	5 (50)

APPENDIX F 2

GROSS FINDINGS : SUMMARY, RAT : MALE SACRIFICED ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0332
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (3W)

Organ	Findings	Group Name / NO. of Animals	0ppm 10 (%)	62.5ppm 10 (%)	125.0ppm 10 (%)	250.0ppm 10 (%)
lung	red zone		0 (0)	0 (0)	0 (0)	0 (0)
liver	herniation		1 (10)	0 (0)	0 (0)	0 (0)

STUDY NO. : 0332
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (3W)

Organ	Findings	Group Name	500.0ppm	1000.0ppm
		NO. of Animals	10 (%)	0 (%)
lung	red zone		1 (10)	- (-)
liver	herniation		0 (0)	- (-)

APPENDIX F 3

GROSS FINDINGS : SUMMARY, RAT : FEMALE

DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0332
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 (%)	62.5ppm 0 (%)	125.0ppm 0 (%)	250.0ppm 0 (%)
trachea	fluid:foamy		- (-)	- (-)	- (-)	- (-)
lung	red zone		- (-)	- (-)	- (-)	- (-)
thoracic ca	pleural fluid		- (-)	- (-)	- (-)	- (-)

Organ	Findings	Group Name / NO. of Animals	500.0ppm 0 (%)	1000.0ppm 10 (%)
trachea	fluid:foamy		- (-)	2 (20)
lung	red zone		- (-)	1 (10)
thoracic ca	pleural fluid		- (-)	2 (20)

APPENDIX F 4

GROSS FINDINGS : SUMMARY, RAT : FEMALE SACRIFICED ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0332
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (3W)

Organ	Findings	Group Name / NO. of Animals	0ppm 10 (%)	62.5ppm 10 (%)	125.0ppm 10 (%)	250.0ppm 10 (%)
liver	herniation		1 (10)	0 (0)	0 (0)	1 (10)

STUDY NO. : 0332
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (3W)

Organ	Findings	Group Name	500.0ppm	1000.0ppm
		NO. of Animals	10 (%)	0 (%)
liver	herniation		1 (10)	- (-)

APPENDIX G 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0332
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	142± 3	0.274± 0.024	0.044± 0.004	2.301± 0.107	0.606± 0.028	0.715± 0.046
62.5ppm	5	144± 6	0.289± 0.024	0.046± 0.006	2.248± 0.075	0.644± 0.059	0.705± 0.016
125.0ppm	5	149± 9	0.293± 0.022	0.042± 0.004	2.253± 0.097	0.615± 0.048	0.731± 0.049
250.0ppm	5	146± 6	0.308± 0.022	0.043± 0.003	2.198± 0.113	0.639± 0.022	0.739± 0.029
500.0ppm	5	135± 10	0.265± 0.032	0.049± 0.005	2.027± 0.140**	0.622± 0.069	0.805± 0.039**
1000.0ppm	0	-	-	-	-	-	-

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

STUDY NO. : 0332
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	1.194± 0.039	0.363± 0.016	4.319± 0.118	1.679± 0.035
62.5ppm	5	1.313± 0.086	0.371± 0.031	4.565± 0.270	1.723± 0.094
125.0ppm	5	1.390± 0.115*	0.353± 0.030	4.737± 0.446	1.652± 0.042
250.0ppm	5	1.404± 0.128**	0.343± 0.027	4.695± 0.293	1.632± 0.027
500.0ppm	5	1.444± 0.080**	0.343± 0.026	4.936± 0.476	1.546± 0.178
1000.0ppm	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. : 0332
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	101± 4	0.241± 0.021	0.051± 0.004	0.076± 0.003	0.476± 0.052	0.576± 0.020
62.5ppm	5	103± 4	0.237± 0.020	0.048± 0.011	0.081± 0.011	0.468± 0.025	0.593± 0.045
125.0ppm	5	108± 3*	0.244± 0.011	0.050± 0.008	0.080± 0.008	0.486± 0.039	0.617± 0.025
250.0ppm	5	102± 3	0.234± 0.013	0.047± 0.002	0.082± 0.008	0.505± 0.059	0.619± 0.015
500.0ppm	5	102± 2	0.235± 0.018	0.053± 0.003	0.078± 0.007	0.494± 0.049	0.668± 0.021**
1000.0ppm	0	-	-	-	-	-	-

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

STUDY NO. : 0332
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	0.947± 0.064	0.277± 0.026	3.138± 0.129	1.597± 0.042
62.5ppm	5	0.981± 0.029	0.284± 0.016	3.250± 0.257	1.577± 0.036
125.0ppm	5	1.054± 0.040**	0.278± 0.020	3.395± 0.188	1.586± 0.021
250.0ppm	5	1.081± 0.063**	0.266± 0.009	3.401± 0.196	1.551± 0.034
500.0ppm	5	1.123± 0.042**	0.267± 0.016	3.687± 0.192**	1.510± 0.014**
1000.0ppm	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. : 0332
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	142± 3	0.193± 0.016	0.031± 0.003	1.624± 0.086	0.428± 0.018	0.504± 0.032
62.5ppm	5	144± 6	0.200± 0.015	0.032± 0.003	1.558± 0.055	0.446± 0.029	0.489± 0.019
125.0ppm	5	149± 9	0.197± 0.011	0.028± 0.003	1.511± 0.078	0.411± 0.017	0.489± 0.014
250.0ppm	5	146± 6	0.211± 0.021	0.030± 0.002	1.505± 0.073	0.438± 0.018	0.506± 0.022
500.0ppm	5	135± 10	0.195± 0.012	0.036± 0.004	1.506± 0.165	0.460± 0.036	0.597± 0.049**
1000.0ppm	0	-	-	-	-	-	-

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

STUDY NO. : 0332
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	0.842± 0.030	0.256± 0.007	3.046± 0.036	1.184± 0.030
62.5ppm	5	0.910± 0.054	0.257± 0.016	3.160± 0.083	1.194± 0.062
125.0ppm	5	0.930± 0.043*	0.236± 0.009	3.166± 0.113	1.108± 0.050
250.0ppm	5	0.959± 0.054**	0.235± 0.013	3.209± 0.074*	1.117± 0.038
500.0ppm	5	1.069± 0.046**	0.255± 0.028	3.642± 0.089**	1.154± 0.202
1000.0ppm	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. : 0332
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	101± 4	0.240± 0.018	0.051± 0.002	0.076± 0.003	0.474± 0.058	0.574± 0.036
62.5ppm	5	103± 4	0.231± 0.027	0.047± 0.009	0.078± 0.009	0.455± 0.017	0.576± 0.025
125.0ppm	5	108± 3*	0.227± 0.006	0.046± 0.007	0.075± 0.008	0.452± 0.040	0.574± 0.022
250.0ppm	5	102± 3	0.228± 0.007	0.046± 0.002	0.080± 0.008	0.493± 0.048	0.605± 0.014
500.0ppm	5	102± 2	0.231± 0.016	0.053± 0.002	0.077± 0.007	0.486± 0.042	0.658± 0.026**
1000.0ppm	0	-	-	-	-	-	-

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

STUDY NO. : 0332
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	0.941± 0.048	0.276± 0.023	3.120± 0.106	1.589± 0.053
62.5ppm	5	0.955± 0.029	0.276± 0.010	3.159± 0.164	1.536± 0.062
125.0ppm	5	0.980± 0.026	0.259± 0.015	3.154± 0.081	1.475± 0.051**
250.0ppm	5	1.057± 0.081**	0.260± 0.004	3.320± 0.124	1.515± 0.032
500.0ppm	5	1.106± 0.051**	0.262± 0.013	3.628± 0.135**	1.487± 0.027**
1000.0ppm	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. : 0332
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				62.5ppm				125.0ppm				250.0ppm			
		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>			
	atrophy:olfactory epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	necrosis:olfactory epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
trachea			< 0>				< 0>				< 0>				< 0>			
	necrosis:epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
lung			< 0>				< 0>				< 0>				< 0>			
	edema		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Hematopoietic system]																		
thymus			< 0>				< 0>				< 0>				< 0>			
	atrophy		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Digestive system]																		
stomach			< 0>				< 0>				< 0>				< 0>			
	erosion:glandular stomach		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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	500.0ppm				1000.0ppm			
		No. of Animals on Study	0				3			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
nasal cavit			< 0>				< 3>			
	atrophy:olfactory epithelium		-	-	-	-	1	1	1	0
	萎縮		(-)	(-)	(-)	(-)	(33)	(33)	(33)	(0)
	necrosis:olfactory epithelium		-	-	-	-	1	2	0	0
			(-)	(-)	(-)	(-)	(33)	(67)	(0)	(0)
trachea			< 0>				< 3>			
	necrosis:epithelium		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(33)	(0)	(0)	(0)
lung			< 0>				< 3>			
	edema		-	-	-	-	2	0	0	0
	浮腫		(-)	(-)	(-)	(-)	(67)	(0)	(0)	(0)
[Hematopoietic system]										
thymus			< 0>				< 3>			
	atrophy		-	-	-	-	0	0	3	0
			(-)	(-)	(-)	(-)	(0)	(0)	(100)	(0)
[Digestive system]										
stomach			< 0>				< 3>			
	erosion:glandular stomach		-	-	-	-	1	0	0	0
	びらん 腺胃		(-)	(-)	(-)	(-)	(33)	(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				62.5ppm				125.0ppm				250.0ppm			
		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>			
	necrosis:focal		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Urinary system]																		
kidney			< 0>				< 0>				< 0>				< 0>			
	regeneration proximal tubule 再生 近位尿細管		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	tubular necrosis:proximale tubule 尿細管壊死		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	nuclear enlargement:proximal tubule 核増大		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Reproductive system]																		
testis			< 0>				< 0>				< 0>				< 0>			
	germ cell 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	500.0ppm				1000.0ppm			
		No. of Animals on Study	0				3			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]										
liver			< 0>				< 3>			
	necrosis:focal		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(33)	(0)	(0)	(0)
[Urinary system]										
kidney			< 0>				< 3>			
	regeneration proximal tubule		-	-	-	-	1	0	2	0
			(-)	(-)	(-)	(-)	(33)	(0)	(67)	(0)
	tubular necrosis:proximale tubule		-	-	-	-	2	0	1	0
			(-)	(-)	(-)	(-)	(67)	(0)	(33)	(0)
	nuclear enlargement:proximal tubule		-	-	-	-	3	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
[Reproductive system]										
testis			< 0>				< 3>			
	germ cell necrosis		-	-	-	-	2	1	0	0
			(-)	(-)	(-)	(-)	(67)	(33)	(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				62.5ppm				125.0ppm				250.0ppm			
		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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Reproductive system]																		
epididymis 精巣上体	debris of spermatic elements 精上皮系 細胞の残屑		< 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	500.0ppm				1000.0ppm			
		No. of Animals on Study	0				3			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Reproductive system]										
epididymis			< 0>				< 3>			
	debris of spermatic elements		-	-	-	-	0	3	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(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. : 0332
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	0ppm				62.5ppm				125.0ppm				250.0ppm			
		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>			
	inflammation:respiratory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lung			< 2>				< 2>				< 2>				< 2>			
	inflammation		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]																		
stomach			< 2>				< 2>				< 2>				< 2>			
	erosion:forestomach		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
liver			< 2>				< 2>				< 2>				< 2>			
	herniation		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)	(0)
[Urinary system]																		
kidney			< 2>				< 2>				< 2>				< 2>			
	eosinophilic body		0	0	0	0	1	1	0	0	0	2	0	0	1	1	0	0
			(0)	(0)	(0)	(0)	(50)	(50)	(0)	(0)	(0)	(100)	(0)	(0)	(50)	(50)	(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. : 0332
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	500.0ppm				1000.0ppm			
		No. of Animals on Study	2				0			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
nasal cavit			< 2>				< 0>			
	inflammation:respiratory epithelium		0	1	0	0	-	-	-	-
	炎症		(0)	(50)	(0)	(0)	(-)	(-)	(-)	(-)
lung			< 2>				< 0>			
	inflammation		0	1	0	0	-	-	-	-
			(0)	(50)	(0)	(0)	(-)	(-)	(-)	(-)
[Digestive system]										
stomach			< 2>				< 0>			
	erosion:forestomach		1	0	0	0	-	-	-	-
	びらん		(50)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
liver			< 2>				< 0>			
	herniation		0	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
[Urinary system]										
kidney			< 2>				< 0>			
	eosinophilic body		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

STUDY NO. : 0332
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	0ppm				62.5ppm				125.0ppm				250.0ppm			
		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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Reproductive system]																		
epididymis				< 2>				< 2>				< 2>				< 2>		
精巣上体	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)

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	500.0ppm				1000.0ppm			
		No. of Animals on Study	2				0			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Reproductive system]										
epididymis			< 2>				< 0>			
	debris of spermatic elements		1 (50)	0 (0)	0 (0)	0 (0)	- (-)	- (-)	- (-)	- (-)

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

APPENDIX I 3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0332
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

Organ / Findings	Group Name	0ppm				62.5ppm				125.0ppm				250.0ppm			
	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>			
	necrosis:olfactory epithelium	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
lung		< 0>				< 0>				< 0>				< 0>			
	edema	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
	浮腫																
[Hematopoietic system]																	
thymus		< 0>				< 0>				< 0>				< 0>			
	karyorrhexis	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
	核崩壊																
[Digestive system]																	
stomach		< 0>				< 0>				< 0>				< 0>			
	erosion:glandular stomach	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
	びらん																
[Urinary system]																	
kidney		< 0>				< 0>				< 0>				< 0>			
	tubular necrosis:proximale tubule	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)

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	500.0ppm				1000.0ppm			
		No. of Animals on Study	0				3			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
nasal cavit			< 0>				< 3>			
	necrosis:olfactory epithelium		-	-	-	-	0	3	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
lung			< 0>				< 3>			
	edema		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(33)	(0)	(0)	(0)
[Hematopoietic system]										
thymus			< 0>				< 3>			
胸腺	karyorrhexis		-	-	-	-	0	0	3	0
	核崩壊		(-)	(-)	(-)	(-)	(0)	(0)	(100)	(0)
[Digestive system]										
stomach			< 0>				< 3>			
	erosion:glandular stomach		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(33)	(0)	(0)	(0)
[Urinary system]										
kidney			< 0>				< 3>			
	tubular necrosis:proximale tubule		-	-	-	-	0	0	3	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				62.5ppm				125.0ppm				250.0ppm			
		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]																		
lung			< 2>				< 2>				< 2>				< 2>			
	inflammation		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]																		
liver			< 2>				< 2>				< 2>				< 2>			
	herniation		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Urinary system]																		
kidney			< 2>				< 2>				< 2>				< 2>			
	mineralization:cortico-medullary junction		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)	(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	500.0ppm				1000.0ppm			
		No. of Animals on Study	2				0			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
lung			< 2>				< 0>			
	inflammation		0	1	0	0	-	-	-	-
			(0)	(50)	(0)	(0)	(-)	(-)	(-)	(-)
[Digestive system]										
liver			< 2>				< 0>			
	herniation		1	0	0	0	-	-	-	-
			(50)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
[Urinary system]										
kidney			< 2>				< 0>			
	mineralization:cortico-medullary junction		0	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)

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

APPENDIX J 1

IDENTITY OF ALLYL CHLORIDE

IN THE 2-WEEK INHALATION STUDY

IDENTITY OF ALLYL CHLORIDE IN THE 2-WEEK INHALATION STUDY

Test Substance : Allyl chloride(Wako Pure Chemical Industries, LTD.)

Lot No. : SKL4453

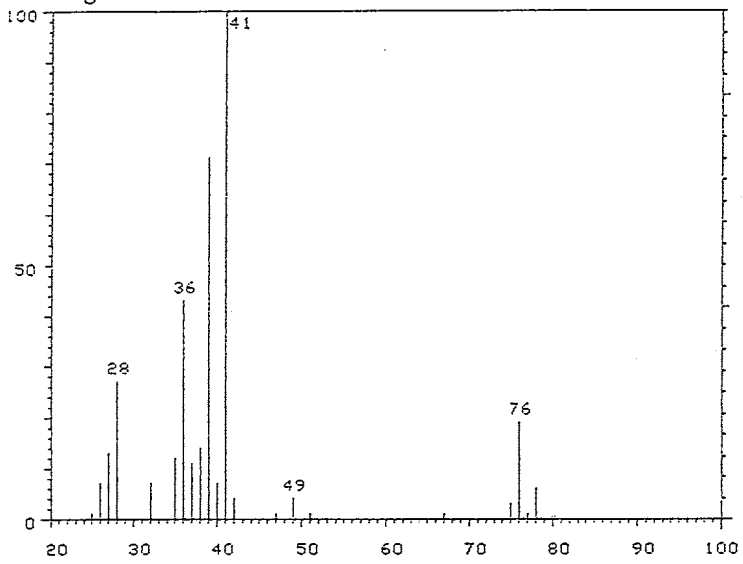
1. Spectral data

Mass Spectrometry

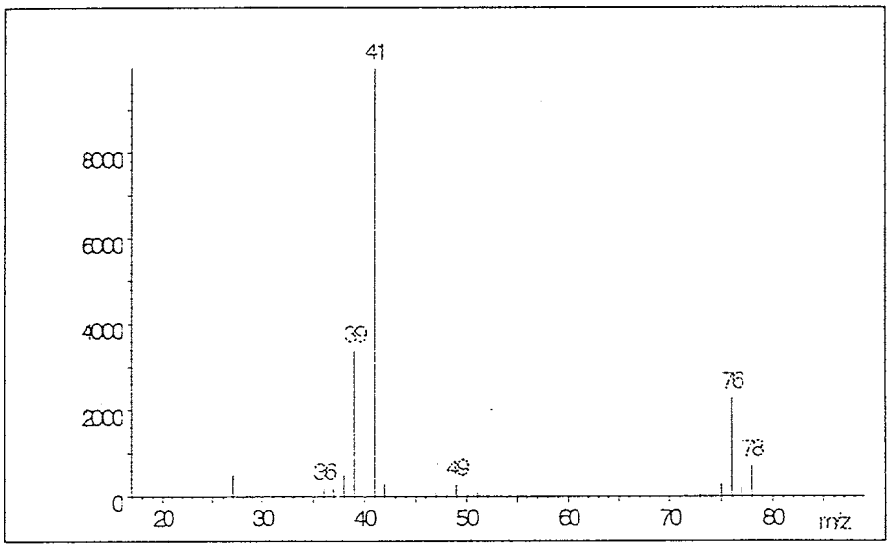
Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI(Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance m/Z



Mass Spectrum of Allyl chloride(Literature data*)

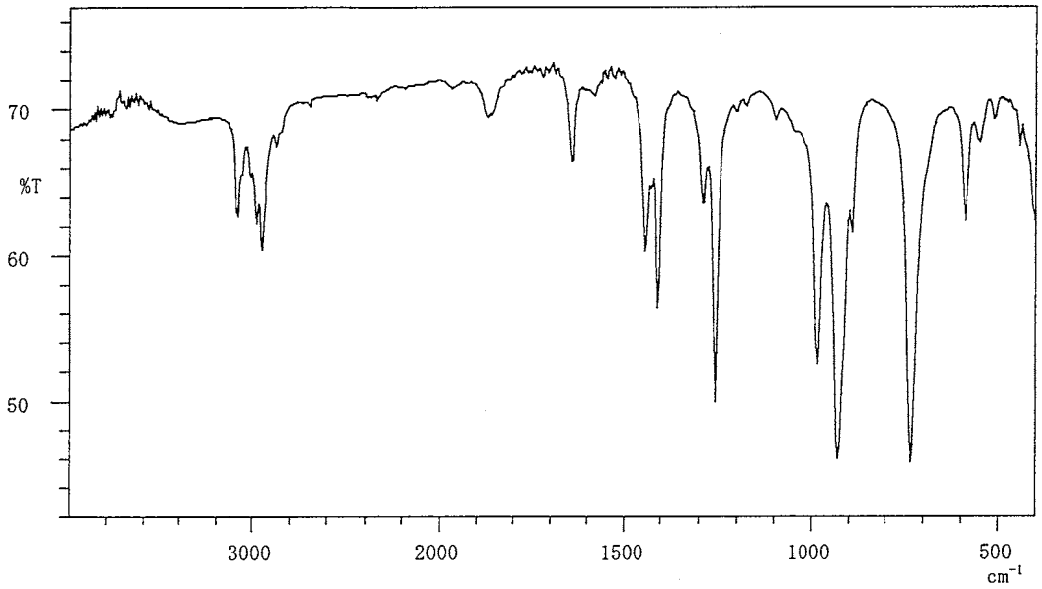
Results: The mass spectrum was consistent with literature spectrum.

*Wiley 138K Mass Spectral Data Base Entry Number 1989(1990)
John Wiley and Sons Inc.,U.K.

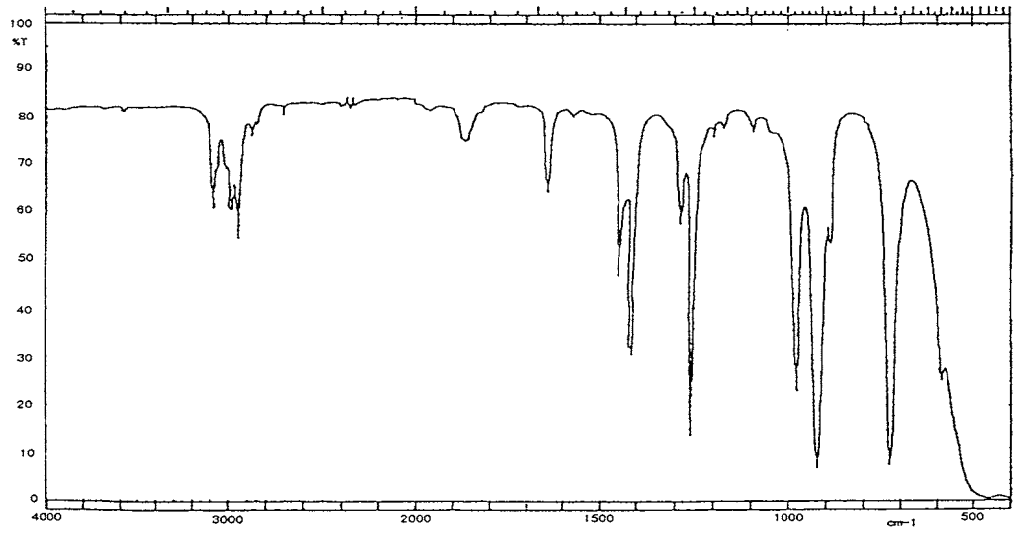
Infrared Spectrometry

Instrument : Shimazdu FT-IR 8200PC Infrared Spectrometer

Cell : KBr



Infrared Spectrum of Test Substance



Infrared Spectrum of Allyl chloride(Literature data*)

*Performed by Wako Pure Chemical Industries, LTD.

Results: The infrared spectrum was consistent with literature spectrum.

2. Conclusions: The test substance was identified as Allyl chloride, by the mass spectrum and the infrared spectrum.

APPENDIX J 2

STABILITY OF ALLYL CHLORIDE

IN THE 2-WEEK INHALATION STUDY

STABILITY OF ALLYL CHLORIDE IN THE 2-WEEK INHALATION STUDY

Test Substance : Allyl chloride(Wako Pure Chemical Industries, LTD.)

Lot No. : SKL4453

1.Sample: This lot was used from 1997.3.25 to 1997.4.7. Test substance was stored at room temperature .

2. Gas Chromatography

Instrument : Hewlett Packard 6890

Column : Hewlett Packard INNOWAX(0.53mmϕ×60m)

Column Temperature : 50°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 three impurities(peak No.1,2,4 < 2% of total area) analyzed at 1997.3.24 and one major peak(peak No.3) and three impurities(peak No.1,2,4 < 2% of total area) analyzed at 1997.4.25. It was identified only by comparing its gas chlomatograph with that of the 1-chloropropene(peak No.1) and 1,5-hexadiene(peak No.2) and 2-propanol(peak No.4) in the allyl chloride, the amount in the test substance were 0.22% and 0.51% and 0.007% at 1997.3.24. No new trace impurity peak in the test substance analyzed at 1997.4.25 was detected.

Date (date analyzed)	Peak No.	Retention Time(min)	AREA(%)
1997.03.24	1	2.540	0.700
	2	2.888	0.919
	3	3.313	98.369
	4	5.482	0.012
1997.04.25	1	2.541	0.695
	2	2.888	0.918
	3	3.315	98.375
	4	5.484	0.012

3. Conclusions: The test substance was stable for about 1 month in the dark at room temperature.

APPENDIX K 1

CONCENTRATION OF ALLYL CHLORIDE IN THE INHALATION CHAMBER OF THE 2-WEEK INHALATION STUDY

CONCENTRATION OF ALLYL CHLORIDE IN THE INHALATION CHAMBER OF THE 2-WEEK INHALATION STUDY

Group Name	Concentration(ppm) Mean ± S.D.
0ppm(Control)	0.0 ± 0.0
62.5ppm	62.5 ± 0.4
125.0ppm	124.8 ± 0.8
250.0ppm	249.3 ± 0.8
500.0ppm	498.5 ± 3.1
1000.0ppm	1004.4 ± 4.4

APPENDIX K 2

ENVORONMENTAL CONDITIONS OF INHALATION CHAMBER

IN THE 2-WEEK INHALATION STUDY OF ALLYL CHLORIDE

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 2-WEEK INHALATION STUDY OF ALLYL CHLORIDE

Group Name	Temperature(℃) Mean ± S.D.	Humidity(%) Mean ± S.D.	Ventilation Rate(L/min) Mean ± S.D.	Air Change(time/h) Mean
0ppm(Control)	22.2 ± 0.2	54.7 ± 0.7	212.0 ± 0.6	12.0
62.5ppm	22.5 ± 0.2	55.9 ± 0.9	210.9 ± 1.2	11.9
125.0ppm	22.1 ± 0.2	54.2 ± 0.5	212.6 ± 0.6	12.0
250.0ppm	22.1 ± 0.2	53.8 ± 0.5	212.1 ± 0.8	12.0
500.0ppm	22.3 ± 0.1	54.2 ± 0.6	211.8 ± 0.9	12.0
1000.0ppm	21.2 ± 0.5	54.9 ± 0.6	212.8 ± 0.9	12.0

APPENDIX L 1

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

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

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 ALLYL CHLORIDE

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

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