アリルクロリドのマウスを用いた 吸入による 2 週間毒性試験報告書

試験番号:0333

APPENDIX

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APPENDIX A 1

CLINICAL OBSERVATION: SUMMARY, MOUSE: MALE

STUDY NO. : 0333

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1 2

SEX : MALE

PAGE: 1

Clinical sign	Group Name	Administration Week-day						
	· · · · · · · · · · · · · · · · · · ·	1-2	1-4	1-7	2-3	2-7		
DEATH	mqq0	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	2	7	8	10	-		
	1000.0ppm	10	-	-	-	-		
LOCOMOTOR MOVEMENT DECR	mqq0	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	3	2	1	0	_		
	1000.0ppm	0	-	••		~		
PILOERECTION	maq0	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	2	0	1	0	_		
	1000.0ppm	0	_		-	~		
RED URINE	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	2	0	0	-		
	1000.0ppm	0	_	-	-	~		
SUBNORMAL TEMP	0ppm	0	0	0	0	0		
	62.5ppm	Ö	Ö	ŏ	Ö	Ö		
	125.0ppm	Ö	Ö	ő	Ö	Ŏ		
	250.0ppm	ŏ	Õ	Ö	Ö	Ö		
	500.0ppm	3	Ö	Ö	Ö	_		
	1000.0ppm	Õ	_	_	_	_		
	1000.0bbit	v						

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APPENDIX A 2

CLINICAL OBSERVATION: SUMMARY, MOUSE: FEMALE

STUDY NO.: 0333

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 2

SEX : FEMALE

PAGE: 2

Clinical sign	Group Name	Admini	stration W	eek-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	10	_
	1000.0ppm	6	9	-	-	-
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	Ö	0	Ŏ	Ö	_
	1000.0ppm	0	ī	_		
	1000:0ppm	U	-			
IRREGULAR BREATHING	0ppm	0	0	0	0	0
Innedobni bilbiliino	62.5ppm	0	0	0	0	Ŏ
	125.0ppm	٥	0	0	0	Ŏ
	250.0ppm	٥	0	0	0	0
	500.0ppm	۸	0	0	0	-
		0	1	U	-	-
	1000.0ppm	0	1	-	-	-

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BAIS 3

APPENDIX B 1

BODY WEIGHT CHANGES :SUMMARY, MOUSE : MALE (2-WEEK STUDY)

STUDY NO.: 0333

ANIMAL : MOUSE Crj:BDF1

UNIT : g
REPORT TYPE : A1 2

SEX : MALE

BODY WEIGHT CHANGES ALL ANIMALS

(SUMMARY)

p Name		stratit	n week-day					
	0-0		1-2	1-4	1-7	2-3	2–7	
Oppm	22.6± (0.9	23.2± 1.1	23.9± 1.0	24.5± 0.9	24.7± 1.1	25.2± 1.4	
62.5ppm	22.6± (0.9	22.7± 1.4	23.1± 1.5	23.5± 1.6	23.5± 1.3	23.9± 1.5	
125.0ppm	22.6± (0.9	22.9± 0.7	23.2± 1.0	23.1± 0.9	23.3± 1.2	23.3± 0.9*	
250.0ppm	22.6± (0.9	22.3± 1.0	22.9± 1.2	23.9± 1.5	25.3± 1.8	25.7± 1.6	
500.0ppm	22.5± (0.9	20.2± 1.4**	19.2± 0.6**	17.7± 1.5 ?	-	-	
1000.0ррт	22.6± (0.9	-	-	-	-	-	
Significant difference;	*: P ≤ 0	.05	**: P ≤ 0.01		Test of Dunnett			

APPENDIX B 2

BODY WEIGHT CHANGES: SUMMARY, MOUSE: FEMALE

STUDY NO.: 0333

ANIMAL : MOUSE Crj:BDF1

UNIT : g
REPORT TYPE : A1 2

SEX : FEMALE

BODY WEIGHT CHANGES ALL ANIMALS

(SUMMARY)

up Name	Administratio	n week-day					
	0-0	1-2	1-4	1-7	2-3	2-7	
Mada ()	18.6± 0.6	18.9± 0.9	19.5± 1.1	19.8± 1.1	20.1± 1.1	20.2± 0.9	
62.5ppm	18.6± 0.6	18.1± 0.7	18.9± 0.6	19.6± 0.7	19.9± 1.0	19.9± 0.8	
125.0ppm	18.6± 0.6	18.6± 0.8	19.1± 0.5	19.4± 0.6	19.6± 0.8	20.4± 0.5	•
250.0ppm	18.5± 0.7	18.2± 0.5	19.2± 0.7	20.2± 0.6	21.5± 0.9**	21.0± 0.8*	
500.0ppm	18.5± 0.6	17.6± 0.6**	17.4± 0.8**	17.6± 1.5*	-	-	
1000.0ppm	18.6± 0.6	16.8± 1.1**	15.1± 0.0 ?	-	-	-	
C:::::	*: P ≤ 0.05	** : P ≤ 0.01		Test of Dunnett			

APPENDIX C 1

FOOD CONSUMPTION CHANGES: SUMMARY, MOUSE: MALE

STUDY NO.: 0333

ANIMAL : MOUSE Crj:BDF1

UNIT : g
REPORT TYPE : A1 2
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

up Name	Administration	week-day(effective)		
p numo	1-7(6)	2-7(7)		
Oppm	4.7± 0.3	4.2± 0.4		
62.5ppm	4.3± 0.4	3.9± 0.4		
125.0ppm	4.3± 0.4	4.2± 0.5		
250.0ppm	4.0± 0.4**	4.8± 0.4**		
500.0ppm	1.5± 0.8 ?	-		
1000.0ppm	-	-		
Significant difference	; *:P≦0.05	**: P ≤ 0.01	Test of Dunnett	
Significant difference ?: Significant test i		** : P ≦ 0.01 of data in this group is less		
		d outle outle outle out		BA

APPENDIX C 2

FOOD CONSUMPTION CHANGES: SUMMARY, MOUSE: FEMALE
(2-WEEK STUDY)

STUDY NO. : 0333

ANIMAL : MOUSE Crj:BDF1
UNIT : g

REPORT TYPE : A1 2

SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)

PAGE: 2

ALL ANIMALS

roup Name	Administration	week-day(effective)		
	1-7(6)	2-7(7)		
0ppm	3.8± 0.3	3.6± 0.2		
62,5ppm	3.8± 0.2	3.4± 0.2		
125,0ppm	3.8± 0.3	3.6± 0.2		
250.0ppm	4.0± 0.3	4.2± 0.2**		
500.0ppm	3.0± 0.4**	-		
1000.0ppm	-	-		
Significant differenc	e; *:P≦0.05	**: P ≦ 0.01	Test of Dunnett	
HAN260)				BAIS

APPENDIX D 1

HEMATOLOGY: SUMMARY, MOUSE: MALE

HEMATOLOGY (SUMMARY) ALL ANIMALS (3W)

STUDY NO.: 0333

ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME: 1

SEX : MALE

REPORT TYPE : A1

PLATELET MCHC HEMATOCRIT MCV MCH HEMOGLOBIN RED BLOOD CELL NO. of Group Name 1 03/με g/dl % fΩ рg Animals 106/HR g/dl 87 $31.9\pm$ 0.6 1382± $51.8 \pm$ 2.1 47.0± 2.1 $15.0 \pm$ 0.5 $16.5 \pm$ 0.4 11.02 ± 0.52 5 mqq0 135 $1286 \pm$ 0.3 $32.0 \pm$ 0.5 $47.5 \pm$ 0.9 $15.2 \pm$ $16.7 \pm$ 0.7 $52.0 \pm$ 1.6 10.95± 0.51 5 62.5ppm 1264士 148 15.2± 0.2 $31.9 \pm$ 0.4 47.5± 0.3 50.2± 1.4 $16.0 \pm$ 0.5 5 10.57 ± 0.23 125.0ppm 59 $15.2 \pm$ 0.1 $30.8 \pm$ 0.3** 1491士 $49.3 \pm$ 0.2* 0.6** 46.7士 2.1** 5 9.47± 0.40** $14.4 \pm$ 250.0ppm 0 500.0ppm 0 1000.0ppm Test of Dunnett ** : $P \leq 0.01$ Significant difference; $*: P \leq 0.05$

PAGE: 1

(HCL070) BAIS 3

HEMATOLOGY (SUMMARY) ALL ANIMALS (3W)

STUDY NO.: 0333

ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME: 1

SEX : MALE

REPORT TYPE : A1

Differential WBC (%) WBC NO. of Group Name OTHERS LYMPHO **EOSINO** BASO MONO N-SEG Animals 1 03/με N-BAND $2\pm$ 71士 13 0± 0 1 1± 1 0土 0± 0 26± 12 5 1.13± 0.71 0ppm 0± 0 $2\pm$ 1 65± 16 $32\pm$ 17 0土 1 0± 0 1.10± 0.98 1± 1 62.5ppm 0± 0 0土 0 1± 1 70± 9 0士 1± 1 $27\pm$ 9 125.0ppm 0.70± 0.44 1± $77 \pm$ 6 0± 1 0± 0 3士 2 17± 3 1.12± 0.41 $2\pm$ 1 250.0ppm 500.0ppm 0 1000.0ppm Test of Dunnett Significant difference : $*: P \le 0.05$ ** : $P \le 0.01$

(HCL070)

BAIS 3

APPENDIX D 2

HEMATOLOGY: SUMMARY, MOUSE: FEMALE

HEMATOLOGY (SUMMARY) ALL ANIMALS (3W)

STUDY NO. : 0333

ANIMAL : MOUSE Crj:BDF1

MEASURE, TIME: 1

SEX : FEMALE REPORT TYPE : A1

PLATELET MCH MCHC MCV RED BLOOD CELL HEMOGLOBIN HEMATOCRIT NO. of Group Name 1 03/με g/dl 1 06/με g/dl % f Q рg Animals $32.6 \pm$ 1.0 1178± 37 50.7 ± 2.5 47.0± 0.6 $15.3 \pm$ 0.3 5 10.78± 0.44 $16.5 \pm$ 0.5 0ppm 106 15.2± 0.8 $32.6 \pm$ 1.9 1144土 16.0± 49.1± 1.9 46.7士 0.7 10.53 ± 0.42 0.5 62.5ppm 1120士 90 45.2± 3.3 14.7士 0.5 $32.7 \pm$ 1.5 49.1± 2.5 5 10.87 ± 0.30 $16.0 \pm$ 0.2 125.0ppm $30.6 \pm$ 0.3* 1414土 53** 15.4士 0.1 0.3** 45.9士 0.7** $50.4 \pm$ 0.4* 250.0ppm 5 9.12± 0.18** $14.1 \pm$ 500.0ppm 1000.0ppm Test of Dunnett ** : $P \le 0.01$ Significant difference: $*: P \leq 0.05$

(IICL070)

BAIS 3

HEMATOLOGY (SUMMARY)
ALL ANIMALS (3W)

STUDY NO.: 0333

ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME: 1

SEX : FEMALE

REPORT TYPE : A1

(%) WBC Differential WBC NO. of Group Name LYMPHO OTHERS EOSINO BASO MONO N-BAND N-SEG Animals 1 03/µl 0土 0 0± 0 $3\pm$ 1 79士 1土 1 16士 3 1± 5 0.67± 0.35 0ppm $3\pm$ 2 $78\pm$ 3 0土 0 3 1士 1 0± 0 1± 18士 5 0.76± 0.20 62.5ppm 0土 0士 0 2± 1 ±08 6 0 17± 6 1± 0.75± 0.30 0± 1 125.0ppm 5 3± 84士 3 0土 1 $0\pm$ 0 1 10士 2 $2\pm$ 1 $1\pm$ 1 250.0ppm 5 1.23± 0.70 500.0ppm 1000.0ppm 0 Test of Dunnett $**: P \leq 0.01$ Significant difference: $*: P \le 0.05$

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(IICL070) BAIS 3

APPENDIX E 1

BIOCHEMISTRY: SUMMARY, MOUSE: MALE

STUDY NO.: 0333

ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME: 1

SEX : MALE

REPORT TYPE : A1

T-CHOLESTEROL TRIGLYCERIDE GLUCOSE ALBUMIN A/G RATIO T-BILIRUBIN NO. of TOTAL PROTEIN Group Name mg/dl mg/dl mg/dl g/dl g/dl mg/dl Animals 38 40± 23 1.2± 0.2 0.17± 0.01 219± 42 102± 5.6± 0.5 $3.1\pm$ 0.0 0ppm 5 $193\pm$ 8 82士 21 20± 8 3.0± 0.2 $1.3\pm$ 0.1 0.19± 0.04 5 $5.3 \pm$ 0.4 62.5ppm 33 19± 13 196土 11 $78\pm$ 0.22± 0.05 $2.9 \pm$ 0.1 1.4士 0.3 125.0ppm 5 $5.1\pm$ 0.4 24士 4 99± 6 0.30± 0.02** $225\pm$ 16 $2.8 \pm$ $1.3 \pm$ 0.1 250.0ppm 5 $5.0 \pm$ 0.1 0.1** 500.0ppm 0 1000.0ppm Test of Dunnett **: $P \le 0.01$ Significant defference : $*: P \leq 0.05$

(HCL074)

BAIS 3

STUDY NO. : 0333

ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME: 1

SEX : MALE

REPORT TYPE : A1

G-GTP CPK ALP PHOSPHOLIPID GOT GPT LDH NO. of Group Name IU/Q IU/2 IU/l IU/l IU/Q IU/l Animals mg/dl $273 \pm$ 76 $2\pm$ 1 75± 26 41± 3 $19\pm$ 2 $255\pm$ 53 5 $202 \pm$ 50 0ppm 1± 84士 39 19± 2 317± 98 296士 29 1 43± 6 5 161± 37 62.5ppm $23\pm$ 339± 133 259± 73 $1\pm$ 1 66土 20 5 142± 34 45± 4 125.0ppm 18 1± 38± 7 29 $214\pm$ 29 35± 19 $232\pm$ 60± 250.0ppm 5 175土 10 0 500.0ppm 0 1000.0ppm Test of Dunnett Significant defference : $*: P \leq 0.05$ ** : $P \leq 0.01$

PAGE: 2

(HCL074) BAIS 3

STUDY NO.: 0333

ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME: 1

SEX : MALE

REPORT TYPE : A1

INORGANIC PHOSPHORUS POTASSIUM CHLORIDE CALCIUM UREA NITROGEN SODIUM NO. of Group Name mEq/Qmg/dl mg/dl mg/dl mEq/Q mEq∕ l Animals 9.4± 0.8 $7.0\pm$ 1.3 $152\pm$ $4.2\pm$ 0.2 119± 3 5 31.3± 4.5 0ppm $6.5 \pm$ 1.7 2 4.5± 0.2 120土 3 $9.0 \pm$ 0.7 $151 \pm$ 62.5ppm 5 $30.3 \pm$ 6.4 1 8.9± 0.4 $6.6 \pm$ 1.5 4.4± 121士 28.2± 6.1 152± 1 0.5 125.0ppm 6.5± 1.0 $4.7 \pm$ 120士 1 $9.0 \pm$ 0.1 0.3 250.0ppm 5 $13.5 \pm$ 0.5** 151± 1 500.0ppm 0 1000.0ppm Test of Dunnett $**: P \leq 0.01$ Significant defference: $*: P \leq 0.05$

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(HCL074) BAIS 3

APPENDIX E 2

BIOCHEMISTRY: SUMMARY, MOUSE: FEMALE

STUDY NO.: 0333

ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME: 1

SEX: FEMALE

REPORT TYPE : A1

T-CHOLESTEROL TRIGLYCERIDE ALBUMIN A/G RATIO T-BILIRUBIN GLUCOSE NO. of TOTAL PROTEIN Group Name mg/dl mg/dl mg/dl mg/dl g/dl g/dl Animals 18± 7 175士 23 67± 8 0.17± 0.01 3.5± 0.2 $1.8 \pm$ 0.1 0ppm 5 5.4± 0.2 3 27 71士 9 17± 180± $1.5\pm$ 0.1** 0.21 ± 0.12 62.5ppm 5 $5.2 \pm$ 0.2 $3.1\pm$ 0.1** 3 $17\pm$ 197± 23 74土 3.2± 0.1* 1.6± 0.1* 0.19± 0.01 5 $5.3\pm$ 0.1 125.0ppm $13\pm$ 2 $0.30 \pm$ 0.02** 217± 24 85± 5** $3.1\pm$ 0.1** $1.6 \pm$ 0.1** 5 5.1± 0.2* 250.0ppm 500.0ppm 0 1000.0ppm Test of Dunnett Significant defference; $*: P \leq 0.05$ ** : $P \le 0.01$

(HCL074)

BAIS 3

ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME: 1

SEX : FEMALE

STUDY NO. : 0333

REPORT TYPE : A1

PE: A1 .

PAGE: 5

oup Name	NO. of Animals	PHOSPHOL mg/dl	IPID	GOT IU/l		GPT IU/0		LDH I U/J	Q	ALP IU/0	,	G−GTP IU∕£		CPK IU∕Ω	
0ppm	5	140±	20	55±	3	22±	4	235±	22	490±	57	1±	1	69±	20
62.5ppm	5	142±	12	53士	7	20±	3	325±	182	436±	41	1±	1	94±	25
125.0ppm	5	147±	. 11	50±	5	21±	2	266±	53	418±	20*	0±	1	74±	13
250.0ppm	5	149±	7	46±	4	18±	1	222±	28	324±	16**	2±	2	41±	7
500.0ppm	0	-		-		-		-		-		-		-	
1000.0ppm	0	-		-		-		-		-		-		-	
Significant o	defference ;	*: P ≤ 0.	.05	**: P ≤ 0.01	L			Test of Dur	nett						

(HCL074) BAIS 3

STUDY NO.: 0333

ANIMAL : MOUSE Crj:BDF1

MEASURE, TIME: 1 SEX : FEMALE

REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (3W)

up Name	NO. of Animals	UREA NI mg/dl		SODIUM mEq/l		POTASSI mEq/		CHLORIDE mEq/Q		CALCIUM mg/dl		INORGAN mg/dl	NIC PHOSPHORUS
0ppm	5	26.2±	2.2	153±	1	4.8±	0.5	122±	1	9.1±	0.2	6.9±	1.5
62.5ppm	5	24.0±	3.6	152±	1	4.1±	0.3*	121±	1	9.1±	0.2	6.3±	1.0
125.0ppm	5	26.1±	3.8	152±	2	4.2±	0.1*	120±	1**	9.1±	0.2	6.5±	1.7
250.0ppm	5	13.7±	1.5**	151±	2	4.3±	0.4	120±	1*	9.1±	0.1	6.4±	1.2
500.0ppm	0	-		-		-				-		-	
1000.0ppm	0	-		-		-				-		-	
Significant (defference;	*; P ≦ (0.05	**: P ≤ 0.01				Test of Dunr	ett				
CL074)												-	

APPENDIX F 1

GROSS FINDINGS: SUMMARY, MOUSE: MALE

DEAD AND MORIBUND ANIMALS

STUDY NO. : 0333

ANIMAL : MOUSE Crj:BDF1

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

REPORT TYPE : A1 SEX : MALE

PAGE: 1

Organ	Findings	Group Name NO. of Animals	0ppm 0 (%)	62.5ppm 0 (%)	125.0ppm 0 (%)	250.0ppm 0 (%)
kidney	white zone		- (-)	- (-)	- (-)	- (-)
(107000)						BAIS3

(HPT080)

STUDY NO. : 0333

ANIMAL : MOUSE Crj:BDF1

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

REPORT TYPE : A1

SEX : MALE

Organ	Findings	Group Name 500.0ppm NO. of Animals 10 (%)	1000.0ppm 10 (%)	
kidney	white zone	1 (10)	0 (0)	
(HPT080)				BAIS3

APPENDIX F 2

GROSS FINDINGS: SUMMARY, MOUSE: MALE SACRIFICED ANIMALS

STUDY NO. : 0333

ANIMAL : MOUSE Crj:BDF1

GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (3W)

REPORT TYPE : A1

SEX : MALE

)rgan	Findings	Group Name NO. of Animals	0ppm 10 (%)	62.5ppm 10 (%)	125.0ppm 10 (%)	250.0ppm 10 (%)
spleen	black zone		0 (0)	1 (10)	1 (10)	0 (0)
idney	hydronephrosis		1 (10)	2 (20)	0 (0)	1 (10)

STUDY NO. : 0333

ANIMAL : MOUSE Crj:BDF1

GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (3W)

REPORT TYPE : A1

SEX : MALE

0rgan	Findings	Group Name NO. of Animals	500.0ppm 0 (%)	1000.0ppm 0 (%)	
spleen	black zone		- (-)	- (-)	
kidney	hydronephrosis		- (-)	- (-)	
(HPT080)					BAIS3

APPENDIX F 3

GROSS FINDINGS: SUMMARY, MOUSE: FEMALE

DEAD AND MORIBUND ANIMALS

ANIMAL : MOUSE C-j:BDF1

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

REPORT TYPE : A1

PAGE: 3 SEX : FEMALE

Organ	Findings	Group Name NO, of Animals	0 (%)	62.5ppm 0 (%)	125.0ppm 0 (%)	250.0ppm 0 (%)
lung	red		- (-)	- (-)	- (-)	- (-)
	red zone		- (-)	- (-)	- (-)	- (-)

ANIMAL : MOUSE Crj:BDF1

GROSS FINDINGS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 3W)

REPORT TYPE : A1 : FEMALE SEX

lung

1000.0ppm Group Name 500.0ppm 10 (%) 10 (%) NO. of Animals Findings__

PAGE: 4

BAIS3

0 (0) 1 (10) red

1 (10) 0 (0) red zone

(HPT080)

APPENDIX F 4

GROSS FINDINGS : SUMMARY, MOUSE : FEMALE SACRIFICED ANIMALS (2-WEEK STUDY)

STUDY NO. : 0333 ANIMAL : MOUSE Crj:BDF1

GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (3W)

REPORT TYPE : A1
SEX : FEMALE

Organ	Findings	Group Name Oppn NO. of Animals 10 (%)	n 62.5ppm 10 (%)	125.0ppm 10 (%)	250.0ppm 10 (%)
spleen	black zone	2 (20)	0 (0)	2 (20)	0 (0)
dney	hydronephrasis	0 (0)	1 (10)	0 (0)	0 (0)

ANIMAL : MOUSE Crj:BDF1

GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (3W)

REPORT TYPE : A1

SEX : FEMALE

Organ	Findings	Group Name NO. of Animals	500.0ppm 0 (%)	1000.0ppm 0 (%)	
spleen	black zone		- (-)	- (-)	
kidney	hydronephrosis		- (-)	- (-)	
(HPT080)					BAIS 3

APPENDIX G 1

ORGAN WEIGHT, ABSOLUTE: SUMMARY, MOUSE: MALE

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

STUDY NO.: 0333 ANIMAL: MOUSE Crj:BDF1

1000.0ppm

Significant difference; $*: P \leq 0.05$

 $** : P \leq 0.01$

REPORT TYPE : A1

SEX : MALE UNIT: g

LUNGS HEART THYMUS ADRENALS TESTES Body Weight Group Name NO. of Animals 0.141± 0.010 0.009± 0.001 0.179± 0.006 0.133± 0.009 20.9± 0.9 0.046± 0.006 0ppm 5 0.129± 0.008 0.134± 0.006 0.009± 0.001 0.175± 0.027 0.037± 0.007 5 19.5± 0.7 62.5ppm 0.119± 0.007 0.137± 0.006 0.168± 0.016 0.029± 0.008** 0.008± 0.002 125.0ppm 5 19.4± 1.1* 0.129± 0.014 0.157± 0.015* 0.184± 0.018 5 21.6± 0.7 0.027士 0.004** 0.008± 0.002 250.0ppm 500.0ppm 0

PAGE: 1

(HCL040) BAIS 3

Test of Dunnett

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : MALE UNIT: g

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

PAGE: 2

-oup Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN	
mqq0	5	0.397± 0.081	0.051± 0.015	0.935± 0.053	0.430± 0.018	
62.5ppm	5	0.470± 0.164	0.049± 0.012	0.863± 0.064	0.435± 0.007	
125.0ppm	5	0.422± 0.115	0.039± 0.007	0.859± 0.047	0.438± 0.019	
250.0ppm	5	0.421± 0.020	0.044± 0.003	0.977± 0.106	0.429± 0.010	
500.0ppm	0	-	-	-	-	
1000.0ppm	0	-	-	-	-	
Significant	difference;	*: P ≤ 0.05 *	*: P ≤ 0.01	Te	est of Dunnett	

(HCL040)

BAIS 3

APPENDIX G 2

ORGAN WEIGHT, ABSOLUTE: SUMMARY, MOUSE: FEMALE

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

STUDY NO.: 0333 ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : FEMALE

UNIT: g

oup Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
mad0	5	17.3± 0.9	0.057± 0.009	0.011± 0.002	0.022± 0.002	0.112± 0.009	0.126± 0.005
62.5ppm	5	16.6± 0.6	0.065± 0.011	0.012± 0.002	0.022± 0.007	0.104± 0.008	0.126± 0.007
125.0ppm	5	17.0± 0.5	0.066± 0.008	0.010± 0.002	0.019± 0.004	0.108± 0.009	0.124± 0.008
250.0ppm	5	17.1± 0.5	0.046± 0.008	0.014± 0.003	0.017± 0.001	0.105± 0.007	0.132± 0.009
500.0ppm	0	-	-		-	-	-
1000.0ppm	0	-	-	-	-	-	-
Significant	difference;	*: P ≤ 0.05 **	: P ≤ 0.01	Test	t of Dunnett		
71040)							

(HCL040)

ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1

SEX : FEMALE UNIT: g

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

PAGE: 4

up Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN	
mapp0	5	0.254± 0.012	0.045± 0.004	0.759± 0.048	0.436± 0.015	
62.5ppm	5	0.313± 0.137	0.044± 0.009	0.708± 0.036	0.433± 0.004	
125.0ppm	5	0.260± 0.009	0.047± 0.007	0.771± 0.052	0.436± 0.014	
250.0ppm	5	0.273± 0.012	0.048± 0.001	0.804± 0.026	0.420± 0.018	
500.0ppm	0	-	-	-	-	
1000.0ppm	0	-	-	-	-	
Significant	difference;	*: P ≤ 0.05	** : P ≤ 0.01	Т	est of Dunnett	
L040)						

APPENDIX H 1

ORGAN WEIGHT, RELATIVE: SUMMARY, MOUSE: MALE

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

STUDY NO.: 0333
ANIMAL: MOUSE Crj:BDF1
REPORT TYPE: A1

SEX : MALE UNIT: %

PAGE: 1

p Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
mqq0	5	20.9± 0.9	0.218± 0.024	0.043± 0.005	0.859± 0.058	0.637± 0.027	0.674± 0.053
62.5ppm	5	19.5± 0.7	0.190± 0.034	0.045± 0.007	0.899± 0.163	0.662± 0.032	0.688± 0.041
125.0ppm	5	19.4± 1.1*	0.147± 0.035**	0.043± 0.010	0.867± 0.087	0.615± 0.058	0.710± 0.036
250.0ppm	5	21.6± 0.7	0.127± 0.017**	0.039± 0.007	0.853± 0.068	0.597± 0.048	0.725± 0.059
500.0ppm	0	-	-	-	-	-	-
1000.0ppm	0		-	-		-	-

(HCL042)

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

STUDY NO.: 0333 ANIMAL: MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : MALE

UNIT: %

PAGE: 2

Group Name NO. of KIDNEYS SPLEEN LIVER BRAIN

up Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN	
mqq0	5	1.916± 0.464	0.247± 0.082	4.479± 0.116	2.061± 0.084	
62.5ppm	5	2.436± 0.924	0.254± 0.066	4.424± 0.189	2.237± 0.078	
125.0ppm	5	2.198± 0.675	0.204± 0.036	4.441± 0.249	2.273± 0.197*	
250.0ppm	5	1.947± 0.044	0.205± 0.011	4.519± 0.403	1.985± 0.066	
500.0ppm	0	-	- -	-	-	
1000.0ppm	0	-	<u>-</u>	_	-	

(IICL042) BAIS 3

APPENDIX H 2

ORGAN WEIGHT, RELATIVE: SUMMARY, MOUSE: FEMALE

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

STUDY NO.: 0333 ANIMAL: MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : FEMALE UNIT: %

LUNGS OVARIES HEART THYMUS ADRENALS Group Name NO. of Body Weight (g) Animals 0.128 ± 0.010 0.646 ± 0.044 0.727 ± 0.038 5 17.3 ± 0.9 0.325 ± 0.045 0.063± 0.009 0ppm 0.762 ± 0.042 0.071 ± 0.009 0.133 ± 0.038 0.627 ± 0.044 5 16.6± 0.6 0.394± 0.062 62.5ppm 0.112± 0.023 0.635 ± 0.049 0.728± 0.033 0.056± 0.010 5 17.0± 0.5 0.388 ± 0.036 125.0ppm 0.771 ± 0.052 0.612 ± 0.042 0.269± 0.047 0.079± 0.015 0.101 ± 0.007 5 17.1± 0.5 250.0ppm 500.0ppm 0 1000.0ppm Test of Dunnett Significant difference; $*: P \leq 0.05$ ** : $P \le 0.01$

PAGE: 3

(HCL042) BAIS 3

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

STUDY NO.: 0333 ANIMAL: MOUSE Crj:BDF1

Significant difference; $*: P \leq 0.05$

 $** : P \leq 0.01$

REPORT TYPE: A1
SEX: FEMALE
UNIT: %

BRAIN SPLEEN LIVER KIDNEYS Group Name NO. of Animals 0.258 ± 0.017 4.379 ± 0.203 2.518 ± 0.127 0ppm 5 1.466± 0.028 2.617 ± 0.074 0.265 ± 0.047 4.277 ± 0.161 5 1.885± 0.801* 62.5ppm 2.557 ± 0.052 4.521 ± 0.232 0.276 ± 0.034 5 1.528 ± 0.019 125.0ppm 0.283 ± 0.005 4.705 ± 0.207 2.454± 0.107 1.596士 0.092** 250.0ppm 5 500.0ppm 0 1000.0ppm

PAGE: 4

(HCL042) BAIS 3

Test of Dunnett

APPENDIX I 1

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY

MOUSE: MALE: DEAD AND MORIBUND ANIMALS

STUDY NO. : 0333 ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : MALE HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0- 3W)

Organ	N	Toup Name Oppm o. of Animals on Study 0 rade 1 2 3 4 (%) (%) (%) (%)	62.5ppm 0 1 2 3 4 (%) (%) (%) (%)	125.0ppm 0 1 2 3 4 (%) (%) (%) (%)	250.0ppm 0 1 2 3 4 (%) (%) (%) (%)
[Respiratory	system]	·			
nasal cauit	necrosis:olfactory epithelium	< 0> (-) (-) (-) (-)	< 0> (-) (-) (-) (-)	(-) (-) (-) (-)	< 0> (-) (-) (-) (-)
lung	consestion うっぺっ	(-) (-) (-) (-)	< 0> (-) (-) (-) (-)	< 0> (-) (-) (-) (-)	< 0> (-) (-) (-) (-)
	hemorrhage Knj	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
	edema	(-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
[Hematopoiet	ic system]				
thymus	atrophy	<pre></pre>	(-) (-) (-) (-)	< 0> (-) (-) (-) (-)	(-) (-) (-) (-)
	karyorrhexis	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
Grade <a> b (c)	1: Slight 2: Moderate 3: a: Number of animals examined at the sit b: Number of animals with lesion c: b/a * 100	Marked 4: Severe			**************************************

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

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX

: MALE

Organ		Group Name 500.0ppm No. of Animals on Study 3 Grade 1 2 3 4 (%) (%) (%) (%)	1000.0ppm 2 1 2 3 4 (%) (%) (%) (%)	
[Respiratory	system]			
nasal cavit	necrosis:olfactory epithelium	2 0 0 0 (67) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	
lung	congestion	3> 1 0 0 0 (33) (0) (0) (0)	2 0 0 0 (100) (0) (0) (0)	
	hemorrhage	1 0 0 0 (33) (0) (0) (0)	(50) (0) (0)	
	edema	0 0 0 0 0 (0) (0)	1 0 0 0 (50) (0) (0) (0)	
[Nematopoiet	tic system]			
thymus	atrophy	<pre></pre>	<pre></pre>	
	karyorrhexis	1 0 1 0 (50) (0) (50) (0)	1 0 0 0 (50) (0) (0) (0)	
Grade <a>> b (c)	1: Slight 2: Moderate 3 a: Number of animals examined at the s b: Number of animals with lesion c: b / a * 100	: Marked 4 : Severe ite		
(HPT150)				BAIS3

ANIMAL : MOUSE Crj:BDF1 REPORT TYPE : A1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 3W)

PAGE: 3 : MALE 125.0ppm 250.0ppm Group Name 62.5ppm 0 No. of Animals on Study (%) (%) Findings Organ [[lematopoietic system] < 0> spleen atrophy (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) congestion (-) (-) (-) (-) (-) (-) (-) karyorrhexis (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) extramedullary hematopoiesis (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) [Circulatory system] heart necrosis (-) (-) (-) (-) (-) (-) [Digestive system] < 0> stomach hyperplasia: forestomach (-) (-) (-) (-) (-) (-) (-) (-) 3 : Marked 4 : Severe 1 : Slight 2 : Moderate Grade <a>> a: Number of animals examined at the site b: Number of animals with lesion b c:b/a * 100

BAIS3

(c)

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

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1
SEX : MALE

STUDY NO. : 0333

SEX	:	MALE

(HPT150)

Organ		o Name 500.0ppm of Animals on Study 3 e 1 2 3 4 (%) (%) (%) (%)	1000.0ppm 2 1 2 3 4 (%) (%) (%) (%)	
[Hematopoiet	tic system]			
spleen	atrophy	<pre></pre>	<pre></pre>	
	congestion	1 0 0 0 (33) (0) (0) (0)	2 0 0 0 0 (100) (0) (0) (0)	
	karyorrhexis	1 0 0 0 (33) (0) (0) (0)	2 0 0 0 (100) (0) (0) (0)	
	extramedullary hematopoiesis	0 1 0 0 (0) (33) (0) (0)	0 0 0 0 0 (0) (0)	
[Circulator	y system]			
heart	necrosis	<pre></pre>	<pre></pre>	
[Digestive	system]			
stomach	hyperplasia:forestomach	<pre></pre>	<pre></pre>	
Grade (a > b (c)	1: Slight 2: Moderate 3: Ma a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	arked 4: Severe		

BAIS3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 3W)

: MOUSE Crj:BDF1 REPORT TYPE : A1

: MALE

125.0ppm 250.0ppm Group Name 62.5ppm maa0 No. of Animals on Study Findings_ [Urinary system] kidney tubular necrosis:proximale tubule (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) [Reproductive system] testis germ cell necrosis (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) epididymis debris of spermatic elements (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) 4 : Severe 2 : Moderate 3 : Marked Grade 1 : Slight < a > a: Number of animals examined at the site b: Number of animals with lesion b c:b/a*100(c) BAIS3 (HPT150)

: MOUSE Crj:BDF1

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

REPORT TYPE: A1 : MALE

Group Name 500.0ppm 1000.0ppm No. of Animals on Study 3 2 3 (%) Findings Organ_ [Urinary system] < 3> < 2> kidney 0 0 0 0 0 2 0 0 tubular necrosis:proximale tubule (0)(67)(0)(0) (0)(0)(0)(0) [Reproductive system] < 2> < 3> testis 1 1 0 0 0 0 0 0 germ cell necrosis (33) (33) (0) (0) (0)(0)(0)(0) < 3> epididymis 2 0 0 0 0 0 0 0 debris of spermatic elements (67) (0) (0) (0) (0)(0)(0)(0) 3 : Marked 4 : Severe Grade 1: Slight 2 : Moderate < a > a: Number of animals examined at the site b: Number of animals with lesion b c:b/a*100(c)

(HPT150)

BAIS3

APPENDIX I 2

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY

MOUSE: MALE: SACRIFICED ANIMALS

STUDY NO. : 0333 ANIMAL : MOUSE Crj:BDF1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (3W)

REPORT TYPE : A1

SEX : MALE

Organ	N		0ppm 3 4 1 (%)	62.5ppm 2 2 3 4 (%) (%) (%)	125.0ppm 2 1 2 3 4 (%) (%) (%) (%)	250.0ppm 2 1 2 3 4 (%) (%) (%) (%)
[Hematopoie	tic system]					
spleen	deposit of melanin		0 0 0 0	<pre></pre>	<pre></pre>	<pre></pre>
[Urinary sy	stem]					
kidney	hydronephrosis	<pre></pre>	0 0 0 0	<pre></pre>	<pre></pre>	<pre></pre>
Grade <a> b (c)	1: Slight 2: Moderate 3: a: Number of animals examined at the sinb: Number of animals with lesion c: b/a * 100	Marked 4: Severe te		A		

: MOUSE Crj:BDF1

REPORT TYPE : A1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (3W)

: MALE 1000.0ppm 500.0ppm Group Name 0 No. of Animals on Study Findings_ [Hematopoietic system] < 0> spleen deposit of melanin (-) (-) (-) (-) (-) (-) [Urinary system] kidney hydronephrosis (-) (-) (-) (-) (-) (-) (-) (-) 4 : Severe 2 : Moderate 3 : Marked 1: Slight Grade a: Number of animals examined at the site (a) b: Number of animals with lesion b (c) c:b/a*100 BAIS3 (HPT150)

APPENDIX I 3

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY

MOUSE: FEMALE: DEAD AND MORIBUND ANIMALS

ANIMAL : MOUSE Crj:BDF1

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

REPORT TYPE : A1

: FEMALE

0rgan	No	Oup Name	62.5ppm 0 1 2 3 4 (%) (%) (%) (%)	125.0ppm 0 1 2 3 4 (%) (%) (%) (%)	250.0ppm 0 1 2 3 4 (%) (%) (%) (%)
[Respiratory	system]				
nasal cavit		< 0>	< 0>	< 0>	< 0>
	necrosis:olfactory epithelium	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
lung		< 0>	< 0>	< 0>	< 0>
	congestion	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
	hemorrhage		(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
	edema	(-) (-) (-) (-)	(-) (-) (-)	(-) (-) (-)	(-) (-) (-)
[Hematopoieti	ic system]				
tl.ymus		< 0>	< 0>	< 0>	< 0>
	atrophy	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
	karyorrhexis	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
Grade (a> b (c)	1: Slight 2: Moderate 3: a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	Marked 4: Severe			

STUDY NO. : 0333 REPORT TYPE : A1

ANIMAL

(HPT150)

: FEMALE

: MOUSE Crj:BDF1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

PAGE: 8

BAIS3

DEAD AND MORIBUND ANIMALS (0- 3W)

1000.0ppm 500.0ppm Group Name 3 No. of Animals on Study 3 (%) Findings Organ_ [Respiratory system] < 2> < 3> nasal cavit 3 0 0 0 necrosis:olfactory epithelium 0 0 0 (100) (0) (0) (0) (100) (0) (0) (0) < 2> < 3> lung 1 0 0 0 1 0 0 0 congestion (33) (0) (0) (0) (50) (0) (0) (0) hemorrhage (0)(0)(0)(0) (33) (0) (0) (0) 1 0 0 0 edema (50) (0) (0) (0) (33) (0) (0) (0) [Hematopoietic system] < 3> < 1> tl:ymus 0 0 1 0 0 1 0 atrophy (0) (0) (100) (0) (0)(0)(33)(0) 0 0 0 0 1 1 0 karyorrhexis (0) (0) (0) (0) (0)(33)(33)(0) 3 : Marked 4 : Severe 1 : Slight 2 : Moderate Grade a: Number of animals examined at the site <a>> b: Number of animals with lesion b c:b/a*100(c)

: MOUSE Crj:BDF1

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

ANIMAL REPORT TYPE : A1

: FEMALE

250.0ppm 125.0ppm Group Name maga() 62.5ppm No. of Animals on Study 3 (%) (%) (%) Findings_ [Hematopoietic system] < 0> < 0> < 0> spleen atrophy (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) congestion (-) (-) (-) (-) (-) (-) (-) (-) karyorrhexis (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) extramedullary hematopoiesis (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) [Urinary system] kidney tubular necrosis:proximale tubule (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) 3 : Marked 1: Slight 2 : Moderate 4 : Severe Grade <a>> a: Number of animals examined at the site

(c) (HPT150)

b

b: Number of animals with lesion

c:b/a*100

BAIS3

SEX : FEMALE

STUDY NO. : 0333 ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1

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

0r-gan	No	Toup Name 500.0ppm 5. of Animals on Study 2 Tade 1 2 3 4 (%) (%) (%) (%)	1000.0ppm 3 1 2 3 4 (%) (%) (%) (%)	
[Hematopoie	etic system]			
spleen	atrophy	<pre></pre>	<pre></pre>	
	cangestian	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	1 0 0 0 (33) (0) (0) (0)	
	karyorrhexis	0 0 0 0 0 0 (0) (0)	2 0 0 0 (67) (0) (0) (0)	
	extramedullary hematopoiesis	0 2 0 0 (0) (100) (0) (0)	0 0 0 0 0 (0) (0)	
[Urinary sy	ystem]			
kidney	tubular necrosis:proximale tubule	<pre></pre>	2 0 1 0 (67) (0) (33) (0)	
Grade <a>> b (c)	1: Slight 2: Moderate 3: a: Number of animals examined at the sit b: Number of animals with lesion c: b/a * 100	Marked 4: Severe e		
(HPT150)				Bi

APPENDIX I 4

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY

MOUSE: FEMALE: SACRIFICED ANIMALS

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

PAGE: 3

ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1

SEX : FEMALE

STUDY NO. : 0333

rgan	· ·	Group Name io. of Animals on Study Grade 1 (%)	2 2 2 3 (%) (%)	9m 4 (%)	1 (%)	62.5ppm 2 2 2 (%) (%) (%)	1 (%)	125.0ppm 2 2 3 4 %) (%) (%)	250.0ppm 2 1 2 3 4 (%) (%) (%) (%)
Respirator	y system]								
ung	perivascular inflammation	(0) (< 2> 0 0 0) (0)	0 (0)	0 (0) (<pre></pre>	1 (50) (< 2> 0 0 0 0) (0) (0)	<pre></pre>
llematopoie	tic system]								
pleen	deposit of melanin	0 (0) (< 2> 0 0 0) (0)	0 (0)	(0) (< 2> 0 0 0 0) (0) (0)	1 (50) (< 2> 0 0 0 0) (0) (0)	0 0 0 0 (0) (0) (0) (0)
Digestive	system]								
tomach	erosion:forestomach	(0) (< 2> 0 0 0) (0)	0 (0)	(0) (< 2> 0 0 0 0) (0) (0)	0 (0) (<pre>< 2> 0 0 0 0) (0) (0)</pre>	1 0 0 0 (50) (0) (0) (0)
	hyperplasia:forestomach	0 (0) (0 0 0) (0)	0 (0)	0 (0) (0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	(0) (0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 1 0 0 (0) (50) (0) (0)
irade (a> b	1: Slight 2: Moderate 3 a: Number of animals examined at the si b: Number of animals with lesion c: b / a * 100	: Marked 4 : Severe te	. , ,	• • • • • • • • • • • • • • • • • • • •					

ANIMAL : MOUSE Crj:BDF1

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

REPORT TYPE : A1 PAGE: 4 : FEMALE

Organ	Findings	Group Name 500.0ppm No. of Animals on Study 0 Grade 1 2 3 4 (%) (%) (%) (%)	1000.0ppm 0 1 2 3 4 (%) (%) (%) (%)	
[Respiratory	/system]			
lung:	perivascular inflammation	(-) (-) (-) (-)	(-) (-) (-)	
[Hematopoiet	tic system]			
spleen	deposit of melanin	(-) (-) (-) (-)	(-) (-) (-)	
[Digestive s	system]			
stomach	erosion:forestomach	(-) (-) (-)	< 0> (-) (-) (-) (-)	
	hyperplasia:forestomach	(-) (-) (-) (-)	(-) (-) (-)	

Grade < a > 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

a : Number of animals examined at the site b: Number of animals with lesion b

c:b/a*100 (c)

(HPT150)

BAIS3

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

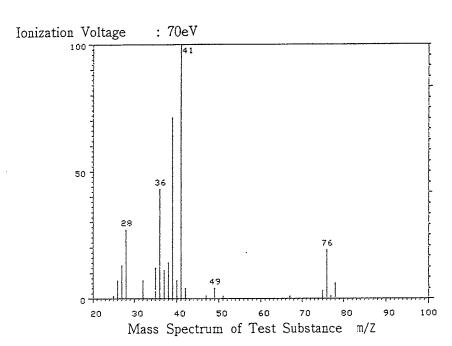
Mass Spectrometry

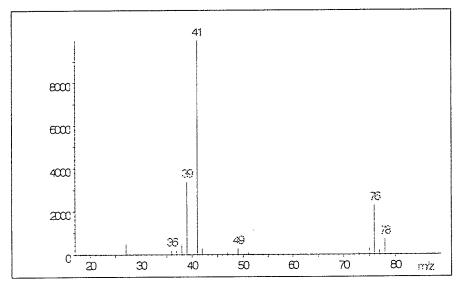
Instrument

: Hitachi M-80B Mass Spectrometer

Ionization

: EI(Electron Ionization)





Mass Spectrum of Allyl chloride(Literature data*)

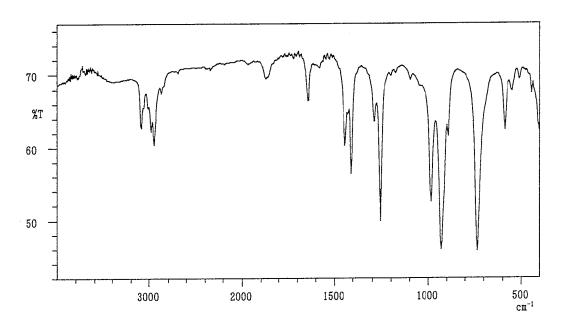
Results: The mass spectrum was consistent with literature spectrum.

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

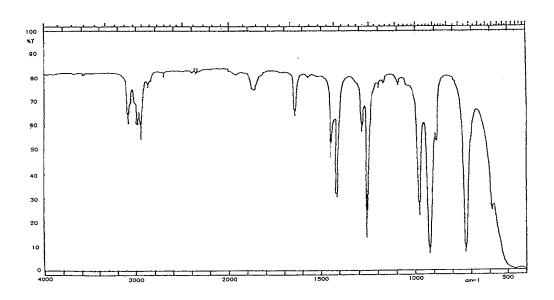
Infrared Spectrometry

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 1997.4.9 to 1997.4.22. Test substance was stored at room temperature.

2. Gas Chromatography

Instrument

: Hewlett Packard 6890

Column

: Hewlett Packard INNOWAX(0.53mm $\phi \times 60$ m)

Column Temperature

: 50°C

Flow Rate

: 10 ml/min

Detector

: FID(Flame Ionization Detector)

Injection Volume

 $: 1 \mu$ l

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

CONCENTMOUSEION 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	62.4 ± 0.3
125.0ppm	125.0 ± 0.7
250.0ppm	248.6 ± 2.0
500.0ppm	498.1 ± 1.8
1000.0ppm	1001.0 ± 5.2

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 (°C) Mean \pm S.D.	Humidity(%) Mean \pm S.D.	Ventilation Rate(L/min) Mean \pm S.D.	Air Change(time/h) Mean
Oppm(Control)	22.1 ± 0.1	51.1 ± 0.5	104.9 ± 0.3	12.1
62.5ppm	22.2 ± 0.1	49.3 ± 0.5	104.6 ± 0.2	12.1
125.0ppm	21.8 ± 0.1	51.9 ± 0.6	105.2 ± 0.2	12.1
250.0ppm	21.7 ± 0.1	51.2 ± 0.5	104.9 ± 0.4	12.1
500.0ppm	21.3 ± 0.3	50.7 ± 0.7	105.5 ± 0.3	12.2
1000.0ppm	21.2 ± 0.3	50.3 ± 0.7	103.7 ± 0.6	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)
White blood cell (WBC)	Light scattering method 1)
Differential WBC	Pattern recognition method 2)
	(May-Grunwald-Giemsa staining)
Biochemistry	
Total protein (TP)	Biuret method 3)
Albumin (Alb)	BCG method 3)
A/G ratio	Calculated as Alb/(TP—Alb) 3)
T-bilirubin	Alkaline azobilirubin method 3)
Glucose	Enzymatic method (GLK·G-6-PDH)
T-cholesterol	Enzymatic method (CE·COD·POD) 3)
Triglyceride	Enzymatic method (LPL·GK·GPO·POD) 3)
Phospholipid	Enzymatic method (PLD·COD·POD) 3)
Glutamic oxaloacetic transaminase (GOT)	UV·Rate method 3)
Glutamic pyruvic transaminase (GPT)	UV·Rate method 3)
Lactate dehydrogenase (LDH)	UV·Rate method 3)
Alkaline phosphatase (ALP)	p-Nitrophenylphosphate method 3)
γ -Glutamyl transpeptidase (γ -GTP)	L-γ-Glutamyl-p-nitroanilide method 3)
Creatine phosphokinase (CPK)	UV·Rate method 3)
Urea nitrogen	Enzymatic method (Urease GLDH)
Sodium	Ion selective electrode method 3)
Potassium	Ion selective electrode method 3)
Chloride	Ion selective electrode method 3)
Calcium	OCPC method 3)
Inorganic phosphorus	Enzymatic method (PNP·XOD·POD) 3)

- 1) Automatic blood cell analyzer (Technicon H·1: Technicon Instruments Corporation, USA)
- 2) Automatic blood cell differential analyzer (Hitachi 8200: Hitachi, Ltd., Japan)
- 3) Automatic analyzer (Hitachi 7070: Hitachi, Ltd., Japan)

APPENDIX L 2

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK INHALATION STUDY OF 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)	×10 ⁸ /µL	2
Hemoglobin	g/dL	1
Hematocrit	%	1
Mean corpuscular volume (MCV)	fL	1
Mean corpuscular hemoglobin (MCH)	pg	1
Mean corpuscular hemoglobin concentration (MCHC)	g/dL	1
Platelet	$\times 10^3/\mu L$	0
White blood cell (WBC)	$\times 10^3/\mu L$	2
Differential WBC	%	0
Biochemistry		
Total protein	g/dL	1
Albumin	g/dL	1
A/G ratio	-	1
T-bilirubin	mg/dL	2
Glucose	mg/dL	0
T-cholesterol	mg/dL	0
Triglyceride	mg/dL	0
Phospholipid	mg/dL	0
Glutamic oxaloacetic transaminase (GOT)	IU/L	0
Glutamic pyruvic transaminase (GPT)	IU/L	0
Lactate dehydrogenase (LDH)	IU/L	0
Alkaline phosphatase (ALP)	IU/L	0
γ -Glutamyl transpeptidase (γ -GTP)	IU/L	0
Creatine phosphokinase (CPK)	IU/L	0
Urea nitrogen	mg/dL	1
Sodium	mEq/L	0
Potassium	mEq/L	1
Chloride	mEq/L	0
Calcium	mg/dL	1
Inorganic phosphorus	mg/dL	1