メタリルクロライドのラット及びマウスを用いた
吸 入 に よ る が ん 原 性 予 備 試 験 報 告 書

試験番号
2 週間試験：ラット/0195；マウス/0196

APPENDIX

APPENDIXES

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIX A 1-1

CLINICAL OBSERVATION (TWO-WEEK STUDY: SUMMARY)

RAT : MALE

STUDY NO. : 0195
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 0-0 1	1-1 1	1-2 1	1-3 1	1-4 1	1-5 1	1-6 1	1-7 1	2-1 1	2-2 1	2-3 1	2-4 1	2-5 1	2-6 1
LOCOMOTOR MOVEMENT DECR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	90 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	270 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	810 ppm	0	0	7	0	0	0	0	0	0	-	-	-	-	-
TREMOR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	90 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	270 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	810 ppm	0	0	0	1	0	0	0	0	0	-	-	-	-	-
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	90 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	270 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	810 ppm	0	0	0	1	1	0	0	0	0	-	-	-	-	-
EYE OPACITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	90 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	270 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	810 ppm	0	0	0	0	3	0	0	0	0	-	-	-	-	-
CORNEAL OPACITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	90 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	270 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	810 ppm	0	0	0	0	3	0	0	0	0	-	-	-	-	-

Clinical sign	Group Name	Administration Week-day 2-7 1
LOCOMOTOR MOVEMENT DECR	Control	0
	10 ppm	0
	30 ppm	0
	90 ppm	0
	270 ppm	0
	810 ppm	-
TREMOR	Control	0
	10 ppm	0
	30 ppm	0
	90 ppm	0
	270 ppm	0
	810 ppm	-
PILOERECTION	Control	0
	10 ppm	0
	30 ppm	0
	90 ppm	0
	270 ppm	0
	810 ppm	-
EYE OPACITY	Control	0
	10 ppm	0
	30 ppm	0
	90 ppm	0
	270 ppm	0
	810 ppm	-
CORNEAL OPACITY	Control	0
	10 ppm	0
	30 ppm	0
	90 ppm	0
	270 ppm	0
	810 ppm	-

STUDY NO. : 0195
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 0-0 1	1-1 1	1-2 1	1-3 1	1-4 1	1-5 1	1-6 1	1-7 1	2-1 1	2-2 1	2-3 1	2-4 1	2-5 1	2-6 1
IRREGULAR BREATHING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	90 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	270 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	810 ppm	0	0	0	0	1	0	0	0	0	-	-	-	-	-
ABNORMAL RESPIRATION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	90 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	270 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	810 ppm	0	0	0	0	1	0	0	0	0	-	-	-	-	-

STUDY NO. : 0195
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 2-7 1
IRREGULAR BREATHING	Control	0
	10 ppm	0
	30 ppm	0
	90 ppm	0
	270 ppm	0
	810 ppm	-
ABNORMAL RESPIRATION	Control	0
	10 ppm	0
	30 ppm	0
	90 ppm	0
	270 ppm	0
	810 ppm	-

APPENDIX A 1-2

CLINICAL OBSERVATION (TWO-WEEK STUDY: SUMMARY)

RAT : FEMALE

STUDY NO. : 0195
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

Clinical sign	Group Name	Administration Week-day 0-0 1	1-1 1	1-2 1	1-3 1	1-4 1	1-5 1	1-6 1	1-7 1	2-1 1	2-2 1	2-3 1	2-4 1	2-5 1	2-6 1
LOCOMOTOR MOVEMENT DECR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	90 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	270 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	810 ppm	0	0	7	0	-	-	-	-	-	-	-	-	-	-
PRONE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	90 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	270 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	810 ppm	0	0	2	0	-	-	-	-	-	-	-	-	-	-
IRREGULAR BREATHING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	90 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	270 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	810 ppm	0	0	2	0	-	-	-	-	-	-	-	-	-	-
ABNORMAL RESPIRATION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	90 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	270 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	810 ppm	0	0	2	0	-	-	-	-	-	-	-	-	-	-
SUBNORMAL TEMP	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	90 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	270 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	810 ppm	0	0	1	0	-	-	-	-	-	-	-	-	-	-

Clinical sign	Group Name	Administration Week-day 2-7 1
LOCOMOTOR MOVEMENT DECR	Control	0
	10 ppm	0
	30 ppm	0
	90 ppm	0
	270 ppm	0
	810 ppm	-
PRONE	Control	0
	10 ppm	0
	30 ppm	0
	90 ppm	0
	270 ppm	0
	810 ppm	-
IRREGULAR BREATHING	Control	0
	10 ppm	0
	30 ppm	0
	90 ppm	0
	270 ppm	0
	810 ppm	-
ABNORMAL RESPIRATION	Control	0
	10 ppm	0
	30 ppm	0
	90 ppm	0
	270 ppm	0
	810 ppm	-
SUBNORMAL TEMP	Control	0
	10 ppm	0
	30 ppm	0
	90 ppm	0
	270 ppm	0
	810 ppm	-

APPENDIX A 1-3

CLINICAL OBSERVATION (TWO-WEEK STUDY: SUMMARY)

MOSUE : MALE

STUDY NO. : 0196
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day													
		0-0	1-1	1-2	1-3	1-4	1-5	1-6	1-7	2-1	2-2	2-3	2-4	2-5	2-6
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	1	1	1	1	1	1	1
	90 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	270 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	810 ppm	0	0	-	-	-	-	-	-	-	-	-	-	-	-

STUDY NO. : 0196
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 2-7 1
PILOERECTION	Control	0
	10 ppm	0
	30 ppm	1
	90 ppm	0
	270 ppm	0
	810 ppm	-

APPENDIX A 1-4

CLINICAL OBSERVATION (TWO-WEEK STUDY: SUMMARY)

MOSUE: FEMALE

Clinical sign	Group Name	Administration Week-day													
		0-0	1-1	1-2	1-3	1-4	1-5	1-6	1-7	2-1	2-2	2-3	2-4	2-5	2-6
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
LOCOMOTOR MOVEMENT DECR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	90 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	270 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	810 ppm	0	6	4	1	0	0	0	0	0	0	0	0	0	0
PRONE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	90 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	270 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	810 ppm	0	0	2	0	0	0	0	0	0	0	0	0	0	0
IRREGULAR BREATHING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	90 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	270 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	810 ppm	0	0	4	1	0	0	0	0	0	0	0	0	0	0
ABNORMAL RESPIRATION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	90 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	270 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	810 ppm	0	0	4	1	0	0	0	0	0	0	0	0	0	0
BRADYPNEA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	90 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	270 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	810 ppm	0	0	3	0	0	0	0	0	0	0	0	0	0	0

Clinical sign	Group Name	Administration Week-day 2-7 1
LOCOMOTOR MOVEMENT DECR	Control	0
	10 ppm	0
	30 ppm	0
	90 ppm	0
	270 ppm	0
	810 ppm	0
PRONE	Control	0
	10 ppm	0
	30 ppm	0
	90 ppm	0
	270 ppm	0
	810 ppm	0
IRREGULAR BREATHING	Control	0
	10 ppm	0
	30 ppm	0
	90 ppm	0
	270 ppm	0
	810 ppm	0
ABNORMAL RESPIRATION	Control	0
	10 ppm	0
	30 ppm	0
	90 ppm	0
	270 ppm	0
	810 ppm	0
BRADYPNEA	Control	0
	10 ppm	0
	30 ppm	0
	90 ppm	0
	270 ppm	0
	810 ppm	0

STUDY NO. : 0196
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

Clinical sign	Group Name	Administration Week-day													
		0-0	1-1	1-2	1-3	1-4	1-5	1-6	1-7	2-1	2-2	2-3	2-4	2-5	2-6
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
SUBNORMAL TEMP	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	30 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	90 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	270 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	810 ppm	0	0	4	0	0	0	0	0	0	0	0	0	0	0

STUDY NO. : 0196
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

Clinical sign	Group Name	Administration Week-day 2-7 1
SUBNORMAL TEMP	Control	0
	10 ppm	0
	30 ppm	0
	90 ppm	0
	270 ppm	0
	810 ppm	0

APPENDIX A 2-1

BODY WEIGHT CHANGES (TWO-WEEK STUDY: SUMMARY)

RAT : MALE

STUDY NO. : 0195
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-1	1-7	2-7
Control	126± 4	128± 4	142± 4	163± 6
10 ppm	125± 5	128± 5	143± 8	163± 10
30 ppm	126± 5	129± 4	144± 6	164± 7
90 ppm	127± 5	129± 5	146± 7	169± 9
270 ppm	126± 4	122± 4*	138± 5	156± 8
810 ppm	126± 5	106± 5**	109± 9 ?	-

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 A 2-2

BODY WEIGHT CHANGES (TWO-WEEK STUDY: SUMMARY)

RAT : FEMALE

STUDY NO. : 0195
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-1	1-7	2-7
Control	100± 3	102± 3	110± 3	122± 3
10 ppm	102± 3	103± 3	111± 3	125± 4
30 ppm	101± 4	103± 3	111± 4	124± 5
90 ppm	102± 4	102± 4	113± 6	128± 7
270 ppm	101± 4	99± 3	110± 4	122± 5
810 ppm	101± 3	90± 3**	-	-

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

APPENDIX A 2-3

BODY WEIGHT CHANGES (TWO-WEEK STUDY: SUMMARY)

MOSUE : MALE

STUDY NO. : 0196
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-1	1-7	2-7
Control	23.0± 0.7	23.4± 0.7	24.6± 0.7	25.4± 1.1
10 ppm	23.2± 0.8	23.0± 0.9	23.5± 1.2	24.6± 0.7
30 ppm	22.9± 0.8	23.0± 0.9	24.1± 0.4	25.2± 0.3
90 ppm	22.9± 0.7	23.0± 0.9	23.8± 1.1	25.1± 1.2
270 ppm	23.2± 0.8	23.1± 0.7	23.7± 1.0	24.4± 0.8
810 ppm	22.7± 0.8	-	-	-

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

APPENDIX A 2-4

BODY WEIGHT CHANGES (TWO-WEEK STUDY: SUMMARY)

MOSUE: FEMALE

STUDY NO. : 0196
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-1	1-7	2-7
Control	19.0± 0.6	18.6± 0.7	20.2± 0.7	21.1± 0.7
10 ppm	18.9± 0.7	18.6± 0.8	19.7± 0.8	20.9± 1.2
30 ppm	19.1± 0.6	19.0± 0.7	20.3± 0.9	21.3± 0.6
90 ppm	19.1± 0.9	18.8± 0.9	20.3± 0.9	20.7± 0.8
270 ppm	19.0± 0.7	18.8± 0.8	19.4± 0.9	20.6± 0.7
810 ppm	18.9± 0.5	17.0± 0.7**	17.3± 1.3**	18.3± 0.8**

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

APPENDIX A 3-1

FOOD CONSUMPTION CHANGES: SUMMARY, RAT: MALE

(TWO-WEEK STUDY)

STUDY NO. : 0195
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration 1-7(7)	week-day(effective) 2-7(7)
Control	15.8± 1.6	16.0± 2.4
10 ppm	15.6± 1.3	15.8± 1.4
30 ppm	15.4± 1.0	15.6± 1.0
90 ppm	15.2± 0.9	16.1± 1.0
270 ppm	13.7± 0.8**	15.1± 1.4
810 ppm	6.9± 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.

APPENDIX A 3-2

FOOD CONSUMPTION CHANGES: SUMMARY, RAT: FEMALE

(TWO-WEEK STUDY)

STUDY NO. : 0195
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration 1-7(7)	week-day(effective) 2-7(7)
Control	12.1± 0.7	12.2± 0.5
10 ppm	12.3± 0.6	12.8± 0.8
30 ppm	12.1± 0.5	12.1± 0.6
90 ppm	12.2± 0.6	12.9± 1.0
270 ppm	12.2± 0.8	12.6± 0.8
810 ppm	-	-

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

APPENDIX A 3-3

FOOD CONSUMPTION CHANGES: SUMMARY, MOUSE: MALE

(TWO-WEEK STUDY)

STUDY NO. : 0196
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(7)	2-7(7)
Control	3.7± 0.2	3.9± 0.2
10 ppm	3.7± 0.2	3.9± 0.3
30 ppm	3.8± 0.2	4.1± 0.2
90 ppm	3.6± 0.2	4.0± 0.2
270 ppm	3.5± 0.2	3.8± 0.2
810 ppm	2.4± 0.8*	3.8± 0.1

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

APPENDIX A 3-4

FOOD CONSUMPTION CHANGES: SUMMARY, MOUSE: FEMALE

(TWO-WEEK STUDY)

STUDY NO. : 0196
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(7)	2-7(7)
Control	4.5± 0.2	4.4± 0.3
10 ppm	4.1± 0.3*	4.5± 0.3
30 ppm	4.5± 0.3	4.5± 0.2
90 ppm	4.0± 0.4**	4.5± 0.2
270 ppm	3.9± 0.2**	4.2± 0.2
810 ppm	-	-

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

APPENDIX A 4-1

HEMATOLOGY (TWO-WEEK STUDY : SUMMARY)

RAT : MALE

STUDY NO. : 0195
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HEMATOLOGY(1) (SUMMARY)
SURVIVAL ANIMALS (2)

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 $10^3/\mu\ell$
Control	10	8.50± 0.30	16.0± 0.5	45.3± 1.7	53.3± 0.4	18.8± 0.3	35.2± 0.8	863± 44
10 ppm	10	8.53± 0.21	15.9± 0.3	45.1± 0.9	52.9± 0.5	18.7± 0.3	35.3± 0.6	898± 48
30 ppm	10	8.48± 0.14	15.9± 0.4	44.9± 0.6	53.0± 0.5	18.8± 0.2	35.5± 0.4	879± 40
90 ppm	10	8.34± 0.24	15.7± 0.3	44.2± 1.3	53.0± 0.5	18.8± 0.3	35.5± 0.6	874± 57
270 ppm	10	8.63± 0.12	16.1± 0.3	45.9± 0.5	53.2± 0.5	18.7± 0.2	35.1± 0.6	852± 71
810 ppm	0	-	-	-	-	-	-	-

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

STUDY NO. : 0195
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HEMATOLOGY(2) (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHERS
Control	10	3.91± 1.19	1± 1	18± 4	1± 1	0± 0	4± 1	77± 5	0± 0
10 ppm	10	3.24± 0.55	0± 0	17± 5	1± 1	0± 0	3± 1	79± 5	0± 0
30 ppm	10	3.78± 0.65	0± 0	18± 4	1± 1	0± 0	3± 1	78± 4	0± 0
90 ppm	10	3.48± 0.57	0± 1	19± 2	0± 1	0± 0	4± 1	77± 2	0± 0
270 ppm	10	4.09± 1.00	0± 0	18± 4	1± 1	0± 0	3± 1	77± 4	0± 0
810 ppm	0	-	-	-	-	-	-	-	-

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

APPENDIX A 4-2

HEMATOLOGY (TWO-WEEK STUDY : SUMMARY)

RAT : FEMALE

STUDY NO. : 0195
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HEMATOLOGY(1) (SUMMARY)
SURVIVAL ANIMALS (2)

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 $10^3/\mu\ell$
Control	10	8.63± 0.29	16.3± 0.4	45.8± 1.4	53.1± 0.3	18.9± 0.3	35.6± 0.4	815± 53
10 ppm	10	8.54± 0.22	16.3± 0.4	45.6± 0.9	53.4± 0.6	19.0± 0.3	35.7± 0.5	821± 50
30 ppm	10	8.55± 0.24	16.3± 0.3	45.4± 1.2	53.1± 0.7	19.1± 0.3	36.0± 0.6	812± 76
90 ppm	10	8.63± 0.24	16.4± 0.3	46.0± 1.1	53.3± 0.6	19.0± 0.3	35.7± 0.5	861± 55
270 ppm	10	8.59± 0.22	16.3± 0.3	45.5± 1.1	53.0± 0.5	19.0± 0.2	35.9± 0.6	844± 53
810 ppm	0	-	-	-	-	-	-	-

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

STUDY NO. : 0195
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HEMATOLOGY(2) (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHERS
Control	10	3.29± 0.58	0± 1	19± 6	1± 1	0± 0	3± 1	76± 6	0± 0
10 ppm	10	3.88± 2.60	0± 0	21± 7	1± 1	0± 0	3± 1	75± 7	0± 0
30 ppm	10	2.76± 0.82	0± 0	18± 3	1± 1	0± 0	4± 1	77± 3	0± 0
90 ppm	10	4.58± 3.03	0± 0	18± 6	1± 0	0± 0	4± 1	78± 5	0± 0
270 ppm	10	4.03± 1.86	0± 1	20± 5	1± 1	0± 0	3± 1	75± 5	0± 0
810 ppm	0	-	-	-	-	-	-	-	-

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

APPENDIX A 4-3

HEMATOLOGY (TWO-WEEK STUDY : SUMMARY)

MOUSE: MALE

STUDY NO. : 0196
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HEMATOLOGY(1) (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV fℓ	MCH pg	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	10	10.75± 0.31	16.3± 0.3	49.3± 2.3	45.8± 1.5	15.2± 0.4	33.1± 1.2	1082± 79
10 ppm	10	10.51± 0.40	16.0± 0.6	47.6± 2.5	45.3± 1.1	15.2± 0.3	33.6± 0.8	1120± 68
30 ppm	10	10.73± 0.55	16.3± 0.6	49.0± 3.5	45.6± 1.3	15.1± 0.4	33.2± 1.3	1128± 97
90 ppm	10	10.53± 0.39	16.0± 0.5	47.9± 2.3	45.5± 0.9	15.2± 0.3	33.3± 1.2	1183± 47*
270 ppm	10	10.81± 0.47	16.4± 0.7	49.2± 3.2	45.5± 1.4	15.2± 0.3	33.4± 1.1	1192± 134
810 ppm	0	-	-	-	-	-	-	-

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

STUDY NO. : 0196
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HEMATOLOGY(2) (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHERS
Control	10	3.20± 1.74	0± 1	12± 3	2± 1	0± 0	2± 1	84± 4	0± 0
10 ppm	10	3.12± 1.41	1± 1	11± 2	2± 1	0± 0	2± 0	84± 3	0± 0
30 ppm	10	2.78± 1.27	1± 1	12± 2	2± 1	0± 0	3± 1	83± 3	0± 0
90 ppm	10	3.03± 1.14	1± 1	13± 3	2± 1	0± 0	3± 1	82± 4	0± 0
270 ppm	10	2.44± 1.61	1± 1	16± 4*	1± 1	0± 0	3± 1	80± 4*	0± 0
810 ppm	0	-	-	-	-	-	-	-	-

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

(HCL071)

APPENDIX A 4-4

HEMATOLOGY (TWO-WEEK STUDY : SUMMARY)

MOUSE: FEMALE

STUDY NO. : 0196
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

HEMATOLOGY(1) (SUMMARY)
SURVIVAL ANIMALS (2)

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 $10^3/\mu\ell$
Control	10	10.21± 0.51	15.6± 0.8	46.1± 3.1	45.1± 1.2	15.2± 0.4	33.8± 1.1	1028± 133
10 ppm	8	10.30± 0.35	15.8± 0.6	46.6± 2.2	45.2± 1.4	15.3± 0.3	33.8± 0.7	918± 203
30 ppm	10	10.24± 0.32	15.6± 0.4	45.9± 1.9	44.8± 1.2	15.2± 0.3	33.9± 1.0	1024± 65
90 ppm	9	10.31± 0.49	15.8± 0.6	46.4± 2.3	45.0± 1.0	15.4± 0.4	34.1± 0.9	1026± 77
270 ppm	10	10.32± 0.47	15.6± 0.6	46.3± 2.5	44.8± 0.8	15.1± 0.3	33.8± 0.9	1068± 90
810 ppm	3	7.36± 0.14**	11.1± 0.3**	33.4± 1.1**	45.5± 1.2	15.0± 0.3	33.0± 0.3	1501± 120

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

STUDY NO. : 0196
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

HEMATOLOGY(2) (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHERS
Control	10	2.20± 0.92	1± 1	12± 3	2± 1	0± 0	2± 1	83± 2	0± 0
10 ppm	8	2.47± 1.02	1± 1	12± 1	2± 1	0± 0	3± 1	83± 1	0± 0
30 ppm	10	2.77± 1.20	0± 0	11± 3	3± 1	0± 0	3± 1	83± 4	0± 0
90 ppm	9	2.95± 1.75	0± 1	11± 2	2± 1	0± 0	3± 1	83± 2	0± 0
270 ppm	10	1.86± 0.73	1± 1	12± 4	3± 1*	0± 0	3± 1	81± 4	0± 0
810 ppm	3	2.30± 0.89	1± 1	12± 2	1± 1	0± 0	2± 0	84± 3	0± 0

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

APPENDIX A 5-1

BIOCHEMISTRY (TWO-WEEK STUDY : SUMMARY)

RAT : MALE

STUDY NO. : 0195
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

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	GOT IU/ℓ
Control	10	6.0± 0.2	3.5± 0.1	1.4± 0.0	0.30± 0.06	202± 14	59± 4	59± 2
10 ppm	10	6.0± 0.1	3.5± 0.1	1.4± 0.1	0.27± 0.06	200± 8	56± 3*	60± 4
30 ppm	10	6.0± 0.1	3.5± 0.1	1.4± 0.1	0.24± 0.08	201± 13	57± 3	59± 2
90 ppm	10	6.0± 0.1	3.5± 0.1	1.4± 0.0	0.24± 0.05	197± 11	60± 3	57± 3
270 ppm	10	6.1± 0.1	3.5± 0.1	1.4± 0.1	0.27± 0.04	191± 10	61± 2	57± 5
810 ppm	0	-	-	-	-	-	-	-

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

STUDY NO. : 0195
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	GPT IU/ℓ		LDH IU/ℓ		CPK IU/ℓ		UREA NITROGEN mg/dℓ		SODIUM mEq/ℓ		POTASSIUM mEq/ℓ		CHLORIDE mEq/ℓ	
Control	10	18±	1	212±	56	144±	43	15.7±	1.9	142±	1	3.9±	0.3	106±	2
10 ppm	10	19±	2	227±	73	139±	27	15.5±	2.4	142±	1	3.9±	0.3	106±	1
30 ppm	10	18±	1	194±	47	141±	13	14.8±	2.1	142±	1	3.8±	0.3	106±	1
90 ppm	10	18±	2	190±	42	126±	18	15.8±	2.3	142±	1	3.9±	0.3	105±	1
270 ppm	10	18±	2	225±	50	126±	29	14.6±	2.7	142±	1	4.1±	0.3	106±	1
810 ppm	0	-		-		-		-		-		-		-	

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

STUDY NO. : 0195
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	CALCIUM mg/dℓ	INORGANIC PHOSPHORUS mg/dℓ
Control	10	11.6± 0.7	8.4± 1.1
10 ppm	10	11.2± 0.6	8.0± 1.1
30 ppm	10	11.2± 0.6	8.4± 1.1
90 ppm	10	11.3± 0.7	8.1± 1.0
270 ppm	10	10.9± 0.2	7.2± 0.9
810 ppm	0	-	-

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

APPENDIX A 5-2

BIOCHEMISTRY (TWO-WEEK STUDY : SUMMARY)

RAT : FEMALE

STUDY NO. : 0195
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

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	GOT IU/ℓ
Control	10	5.7± 0.2	3.4± 0.1	1.4± 0.0	0.31± 0.07	196± 10	72± 7	59± 4
10 ppm	10	5.8± 0.2	3.4± 0.1	1.4± 0.0	0.29± 0.08	197± 10	71± 5	59± 4
30 ppm	10	5.7± 0.1	3.4± 0.1	1.4± 0.1	0.33± 0.12	196± 11	71± 3	63± 9
90 ppm	10	5.8± 0.1	3.4± 0.1	1.5± 0.1	0.31± 0.10	196± 9	75± 8	57± 5
270 ppm	10	5.9± 0.2	3.4± 0.1	1.4± 0.0	0.27± 0.10	194± 10	72± 5	62± 9
810 ppm	0	-	-	-	-	-	-	-

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

STUDY NO. : 0195
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	GPT IU/ℓ		LDH IU/ℓ		CPK IU/ℓ		UREA NITROGEN mg/dℓ		SODIUM mEq/ℓ		POTASSIUM mEq/ℓ		CHLORIDE mEq/ℓ	
Control	10	17±	1	255±	48	138±	11	16.0±	2.2	143±	1	3.6±	0.3	108±	1
10 ppm	10	17±	2	265±	74	148±	22	17.0±	2.1	143±	1	3.7±	0.3	109±	2
30 ppm	10	18±	1	276±	75	154±	28	17.2±	1.7	142±	1	3.7±	0.3	108±	1
90 ppm	10	17±	2	244±	52	140±	18	17.0±	2.4	143±	2	3.8±	0.4	108±	2
270 ppm	10	18±	2	252±	63	126±	17	14.8±	1.7	143±	1	3.7±	0.3	108±	1
810 ppm	0	-		-		-		-		-		-		-	

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

STUDY NO. : 0195
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	CALCIUM mg/dℓ		INORGANIC PHOSPHORUS mg/dℓ	
Control	10	10.6±	0.2	7.1±	0.9
10 ppm	10	10.7±	0.2	7.6±	0.7
30 ppm	10	10.5±	0.3	7.4±	0.9
90 ppm	10	10.8±	0.3	7.3±	1.1
270 ppm	10	10.6±	0.3	6.7±	1.3
810 ppm	0	-		-	

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

APPENDIX A 5-3

BIOCHEMISTRY (TWO-WEEK STUDY : SUMMARY)

MOUSE: MALE

STUDY NO. : 0196
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

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	GOT IU/ℓ
Control	8	5.4± 0.2	2.9± 0.1	1.1± 0.1	0.51± 0.14	315± 28	89± 6	40± 12
10 ppm	8	5.3± 0.3	2.8± 0.1	1.2± 0.1	0.48± 0.18	322± 25	88± 6	37± 7
30 ppm	9	5.4± 0.4	2.9± 0.2	1.1± 0.1	0.42± 0.11	315± 27	91± 10	39± 5
90 ppm	10	5.5± 0.3	2.9± 0.1	1.2± 0.1	0.47± 0.22	315± 19	95± 8	35± 5
270 ppm	9	6.0± 0.3**	3.2± 0.1**	1.1± 0.1	0.58± 0.15	310± 30	134± 18**	33± 4
810 ppm	0	-	-	-	-	-	-	-

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

STUDY NO. : 0196
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	GPT IU/ℓ		LDH IU/ℓ		CPK IU/ℓ		UREA NITROGEN mg/dℓ		SODIUM mEq/ℓ		POTASSIUM mEq/ℓ		CHLORIDE mEq/ℓ	
Control	8	15±	4	238±	42	65±	29	22.5±	6.1	149±	2	5.0±	0.3	120±	2
10 ppm	8	15±	4	241±	55	66±	37	23.5±	7.7	148±	2	5.0±	0.7	120±	2
30 ppm	9	17±	4	254±	69	68±	48	22.5±	6.0	150±	3	4.9±	0.7	120±	1
90 ppm	10	16±	3	254±	59	64±	32	19.2±	2.4	149±	2	4.9±	0.5	120±	2
270 ppm	9	16±	2	241±	66	51±	22	17.0±	2.7*	149±	2	5.1±	0.5	117±	1*
810 ppm	0	-		-		-		-		-		-		-	

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

STUDY NO. : 0196
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	CALCIUM mg/dℓ	INORGANIC PHOSPHORUS mg/dℓ
Control	8	9.4± 0.3	8.5± 1.2
10 ppm	8	9.0± 0.4	8.3± 1.6
30 ppm	9	9.4± 0.4	8.7± 1.7
90 ppm	10	9.3± 0.3	8.6± 1.6
270 ppm	9	9.8± 0.4	7.8± 1.4
810 ppm	0	-	-

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

APPENDIX A 5-4

BIOCHEMISTRY (TWO-WEEK STUDY : SUMMARY)

MOUSE: FEMALE

STUDY NO. : 0196
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

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	GOT IU/ℓ
Control	9	5.3± 0.3	3.0± 0.2	1.3± 0.1	0.53± 0.23	295± 36	80± 9	41± 5
10 ppm	7	5.4± 0.3	3.1± 0.2	1.4± 0.1	0.55± 0.16	279± 32	81± 3	44± 6
30 ppm	9	5.4± 0.3	3.1± 0.2	1.4± 0.1	0.45± 0.11	297± 20	80± 6	41± 4
90 ppm	9	5.6± 0.3	3.2± 0.2	1.3± 0.0	0.57± 0.14	284± 31	90± 5	39± 3
270 ppm	10	5.8± 0.3**	3.4± 0.2**	1.4± 0.1	0.59± 0.19	287± 16	112± 7**	35± 6*
810 ppm	3	5.9± 0.5*	3.4± 0.4*	1.4± 0.1	0.45± 0.19	194± 19**	192± 36**	38± 4

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

STUDY NO. : 0196
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	GPT IU/ℓ		LDH IU/ℓ		CPK IU/ℓ		UREA NITROGEN mg/dℓ		SODIUM mEq/ℓ		POTASSIUM mEq/ℓ		CHLORIDE mEq/ℓ	
Control	9	15±	2	254±	36	79±	37	18.9±	2.9	149±	3	4.6±	0.5	120±	2
10 ppm	7	16±	4	275±	69	79±	30	19.5±	1.8	149±	3	5.0±	0.7	120±	2
30 ppm	9	16±	5	265±	57	66±	25	21.2±	2.6	150±	2	4.7±	0.7	119±	1
90 ppm	9	12±	3	248±	46	61±	25	18.4±	2.5	149±	2	4.7±	0.7	121±	2
270 ppm	10	13±	3	248±	38	63±	38	14.3±	1.7**	151±	3	5.3±	0.5*	119±	3
810 ppm	3	29±	4**	203±	35	26±	7	10.1±	2.3**	154±	2	4.2±	0.2	121±	2

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

STUDY NO. : 0196
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	CALCIUM mg/dℓ	INORGANIC PHOSPHORUS mg/dℓ
Control	9	9.2± 0.2	7.4± 1.0
10 ppm	7	9.4± 0.4	8.6± 1.0
30 ppm	9	9.3± 0.2	8.3± 1.2
90 ppm	9	9.4± 0.3	8.4± 1.2
270 ppm	10	9.5± 0.3	7.1± 0.8
810 ppm	3	9.1± 0.1	10.1± 1.5**

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

APPENDIX A 6-1

GROSS FINDINGS (TWO-WEEK STUDY : SUMMARY)

RAT : MALE : SACRIFICED ANIMALS

STUDY NO. : 0195
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	10 ppm 10 (%)	30 ppm 10 (%)	90 ppm 10 (%)
thymus	red zone		1 (10)	0 (0)	0 (0)	0 (0)
liver	herniation		0 (0)	0 (0)	0 (0)	0 (0)

STUDY NO. : 0195
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name NO. of Animals	270 ppm 10 (%)	810 ppm 0 (%)
thymus	red zone		0 (0)	- (-)
liver	herniation		1 (10)	- (-)

APPENDIX A 6-2

GROSS FINDINGS (TWO-WEEK STUDY : SUMMARY)

RAT : MALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0195
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name NO. of Animals	Control 0 (%)	10 ppm 0 (%)	30 ppm 0 (%)	90 ppm 0 (%)
lung	red		- (-)	- (-)	- (-)	- (-)
	voluminus		- (-)	- (-)	- (-)	- (-)
thymus	red zone		- (-)	- (-)	- (-)	- (-)
kidney	swollen		- (-)	- (-)	- (-)	- (-)
urin bladd	red		- (-)	- (-)	- (-)	- (-)

STUDY NO. : 0195
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name NO. of Animals	270 ppm 0 (%)	810 ppm 10 (%)
lung	red		- (-)	3 (30)
	voluminus		- (-)	2 (20)
thymus	red zone		- (-)	3 (30)
kidney	swollen		- (-)	1 (10)
urin bladd	red		- (-)	1 (10)

APPENDIX A 6-3

GROSS FINDINGS (TWO-WEEK STUDY : SUMMARY)

RAT : FEMALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0195
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name NO. of Animals	Control 0 (%)	10 ppm 0 (%)	30 ppm 0 (%)	90 ppm 0 (%)
lung	red		- (-)	- (-)	- (-)	- (-)
	red zone		- (-)	- (-)	- (-)	- (-)
thymus	red zone		- (-)	- (-)	- (-)	- (-)
gl stomach	red patch/zone		- (-)	- (-)	- (-)	- (-)
	red zone		- (-)	- (-)	- (-)	- (-)
thoracic ca	pleural fluid		- (-)	- (-)	- (-)	- (-)

STUDY NO. : 0195
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name NO. of Animals	270 ppm 0 (%)	810 ppm 10 (%)
lung	red		- (-)	1 (10)
	red zone		- (-)	3 (30)
thymus	red zone		- (-)	3 (30)
gl stomach	red patch/zone		- (-)	1 (10)
	red zone		- (-)	2 (20)
thoracic ca	pleural fluid		- (-)	6 (60)

APPENDIX A 6-4

GROSS FINDINGS (TWO-WEEK STUDY : SUMMARY)

MOUSE : MALE: SACRIFICED ANIMALS

STUDY NO. : 0196
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	10 ppm 10 (%)	30 ppm 10 (%)	90 ppm 10 (%)
spleen	black zone		2 (20)	0 (0)	0 (0)	0 (0)

STUDY NO. : 0196
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name	270 ppm	810 ppm
		NO. of Animals	10 (%)	0 (%)
spleen	black zone		0 (0)	- (-)

APPENDIX A 6-5

GROSS FINDINGS (TWO-WEEK STUDY : SUMMARY)

MOUSE : FEMALE: SACRIFICED ANIMALS

STUDY NO. : 0196
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	10 ppm 10 (%)	30 ppm 10 (%)	90 ppm 10 (%)
spleen	black zone		0 (0)	1 (10)	0 (0)	1 (10)

STUDY NO. : 0196
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name	270 ppm	810 ppm
		NO. of Animals	10 (%)	3 (%)
spleen	black zone		0 (0)	0 (0)

APPENDIX A 6-6

GROSS FINDINGS (TWO-WEEK STUDY : SUMMARY),

MOUSE : MALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0196
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name NO. of Animals	Control 0 (%)	10 ppm 0 (%)	30 ppm 0 (%)	90 ppm 0 (%)
lung	red		- (-)	- (-)	- (-)	- (-)
	red zone		- (-)	- (-)	- (-)	- (-)
spleen	black zone		- (-)	- (-)	- (-)	- (-)

STUDY NO. : 0196
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name NO. of Animals	270 ppm 0 (%)	810 ppm 10 (%)
lung	red		- (-)	1 (10)
	red zone		- (-)	2 (20)
spleen	black zone		- (-)	1 (10)

APPENDIX A 6-7

GROSS FINDINGS (TWO-WEEK STUDY : SUMMARY)

MOUSE : FEMALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0196
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name NO. of Animals	Control 0 (%)	10 ppm 0 (%)	30 ppm 0 (%)	90 ppm 0 (%)
spleen	black zone		- (-)	- (-)	- (-)	- (-)

STUDY NO. : 0196
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name	270 ppm	810 ppm
		NO. of Animals	0 (%)	7 (%)
spleen	black zone		- (-)	1 (14)

APPENDIX A 7-1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

RAT : MALE : SACRIFICED ANIMALS

STUDY NO. : 0195
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name	Control				10 ppm				30 ppm				90 ppm			
		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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[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)
[Reproductive system]																		
prostate			< 2>				< 2>				< 2>				< 2>			
	lymphocytic infiltration		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	270 ppm				810 ppm			
		No. of Animals on Study	2				0			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]										
liver			< 2>				< 0>			
	herniation		1	0	0	0	-	-	-	-
			(50)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
[Reproductive system]										
prostate			< 2>				< 0>			
	lymphocytic infiltration		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 A 7-2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

RAT : FEMALE : SACRIFICED ANIMALS

STUDY NO. : 0195
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name	Control				10 ppm				30 ppm				90 ppm			
		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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																		
kidney			< 2>				< 2>				< 2>				< 2>			
	mineralization:cortico-medullary junction		0	0	0	0	2	0	0	0	2	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(50)	(0)	(0)	(0)

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

Organ	Findings	Group Name	270 ppm				810 ppm			
		No. of Animals on Study	2				0			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Urinary system]										
kidney			< 2>				< 0>			
	mineralization:cortico-medullary junction		2 (100)	0 (0)	0 (0)	0 (0)	- (-)	- (-)	- (-)	- (-)

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

APPENDIX A 7-3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

RAT : MALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0195
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name	Control				10 ppm				30 ppm				90 ppm			
		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		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
lung			< 0>				< 0>				< 0>				< 0>			
	hemorrhage		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Hematopoietic system]																		
thymus			< 0>				< 0>				< 0>				< 0>			
	hemorrhage		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Digestive system]																		
liver			< 0>				< 0>				< 0>				< 0>			
	necrosis:central		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Urinary system]																		
kidney			< 0>				< 0>				< 0>				< 0>			
	tubular 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	270 ppm				810 ppm			
		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	0	0	0
			(-)	(-)	(-)	(-)	(33)	(0)	(0)	(0)
lung			< 0>				< 3>			
	hemorrhage		-	-	-	-	2	0	0	0
			(-)	(-)	(-)	(-)	(67)	(0)	(0)	(0)
[Hematopoietic system]										
thymus			< 0>				< 3>			
	hemorrhage		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(33)	(0)	(0)	(0)
[Digestive system]										
liver			< 0>				< 3>			
	necrosis:central		-	-	-	-	0	2	0	0
			(-)	(-)	(-)	(-)	(0)	(67)	(0)	(0)
[Urinary system]										
kidney			< 0>				< 3>			
	tubular necrosis		-	-	-	-	3	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	Control				10 ppm				30 ppm				90 ppm			
		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 (%)
[Urinary system]																		
kidney	mineralization:tubule		< 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	270 ppm				810 ppm			
		No. of Animals on Study	0				3			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Urinary system]										
kidney			< 0>				< 3>			
	mineralization:tubule		- (-)	- (-)	- (-)	- (-)	3 (100)	0 (0)	0 (0)	0 (0)

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

APPENDIX A 7-4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

RAT : FEMALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0195
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 0 1 (%)	Control 0 2 (%)	Control 0 3 (%)	Control 0 4 (%)	10 ppm 0 1 (%)	10 ppm 0 2 (%)	10 ppm 0 3 (%)	10 ppm 0 4 (%)	30 ppm 0 1 (%)	30 ppm 0 2 (%)	30 ppm 0 3 (%)	30 ppm 0 4 (%)	90 ppm 0 1 (%)	90 ppm 0 2 (%)	90 ppm 0 3 (%)	90 ppm 0 4 (%)
[Respiratory system]																		
lung		< 0>		< 0>				< 0>				< 0>				< 0>		
	hemorrhage		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
[Digestive system]																		
stomach		< 0>		< 0>				< 0>				< 0>				< 0>		
	erosion:glandular stomach		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
liver		< 0>		< 0>				< 0>				< 0>				< 0>		
	necrosis:central		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
[Urinary system]																		
kidney		< 0>		< 0>				< 0>				< 0>				< 0>		
	tubular necrosis		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
	mineralization: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	270 ppm				810 ppm			
		No. of Animals on Study	0				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
lung			< 0>				< 2>			
	hemorrhage		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(50)	(0)	(0)	(0)
[Digestive system]										
stomach			< 0>				< 2>			
	erosion:glandular stomach		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(50)	(0)	(0)	(0)
liver			< 0>				< 2>			
	necrosis:central		-	-	-	-	2	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
[Urinary system]										
kidney			< 0>				< 2>			
	tubular necrosis		-	-	-	-	2	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
	mineralization:tubule		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(50)	(0)	(0)	(0)

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

APPENDIX A 7-5

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

MOUSE: MALE : SACRIFICED ANIMALS

STUDY NO. : 0196
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name	Control				10 ppm				30 ppm				90 ppm			
		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>			
	desquamation: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)
[Endocrine system]																		
pituitary			< 2>				< 2>				< 2>				< 2>			
	cyst		0 (0)	0 (0)	0 (0)	0 (0)	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	270 ppm				810 ppm			
		No. of Animals on Study	2				0			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
nasal cavit			< 2>				< 0>			
	desquamation:olfactory epithelium		1	0	0	0	-	-	-	-
			(50)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
	atrophy:olfactory epithelium		2	0	0	0	-	-	-	-
			(100)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
[Endocrine system]										
pituitary			< 2>				< 0>			
	cyst		1	0	0	0	-	-	-	-
			(50)	(0)	(0)	(0)	(-)	(-)	(-)	(-)

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

APPENDIX A 7-6

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

MOUSE: FEMALE : SACRIFICED ANIMALS

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 2				10 ppm 2				30 ppm 2				90 ppm 2			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]																		
nasal cavit			< 2>				< 2>				< 2>				< 2>			
	desquamation: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)
[Hematopoietic system]																		
spleen			< 2>				< 2>				< 2>				< 2>			
	deposit of hemosiderin		0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
[Digestive system]																		
liver			< 2>				< 2>				< 2>				< 2>			
	nuclear size increased central		0	0	0	0	0	0	0	0	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>			
	basophilic 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)

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	270 ppm				810 ppm			
		No. of Animals on Study	2				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
nasal cavit			< 2>				< 2>			
	desquamation:olfactory epithelium		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
	atrophy:olfactory epithelium		1	0	0	0	2	0	0	0
			(50)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
[Hematopoietic system]										
spleen			< 2>				< 2>			
	deposit of hemosiderin		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]										
liver			< 2>				< 2>			
	nuclear size increased central		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
[Urinary system]										
kidney			< 2>				< 2>			
	basophilic change		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)

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

STUDY NO. : 0196
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name	Control				10 ppm				30 ppm				90 ppm			
		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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]																		
adrenal			< 2>				< 2>				< 2>				< 2>			
	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)
[Nervous system]																		
brain			< 2>				< 2>				< 2>				< 2>			
	epidermal cyst		0	0	0	0	0	0	0	0	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	270 ppm				810 ppm			
		No. of Animals on Study	2				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Endocrine system]										
adrenal			< 2>				< 2>			
	necrosis		0	0	0	0	0	0	1	0
			(0)	(0)	(0)	(0)	(0)	(0)	(50)	(0)
[Nervous system]										
brain			< 2>				< 2>			
	epidermal cyst		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)

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

APPENDIX A 7-7

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

MOUSE: MALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0196
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name	Control				10 ppm				30 ppm				90 ppm			
		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 melanin		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Urinary system]																		
kidney			< 0>				< 0>				< 0>				< 0>			
	cloudy swelling:straight distal 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	270 ppm				810 ppm			
		No. of Animals on Study	0				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]										
spleen			< 0>				< 2>			
	deposit of melanin		-	-	-	-	2	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
[Urinary system]										
kidney			< 0>				< 2>			
	cloudy swelling:straight distal tubule		-	-	-	-	2	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

APPENDIX A 7-8

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

MOUSE: FEMALE : DEAD AND MORIBUND ANIMALS

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 0 1 (%)	Control 0 2 (%)	Control 0 3 (%)	Control 0 4 (%)	10 ppm 0 1 (%)	10 ppm 0 2 (%)	10 ppm 0 3 (%)	10 ppm 0 4 (%)	30 ppm 0 1 (%)	30 ppm 0 2 (%)	30 ppm 0 3 (%)	30 ppm 0 4 (%)	90 ppm 0 1 (%)	90 ppm 0 2 (%)	90 ppm 0 3 (%)	90 ppm 0 4 (%)
[Respiratory system]																		
nasal cavit		< 0>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	desquamation:olfactory epithelium	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
lung		< 0>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	congestion	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Hematopoietic system]																		
spleen		< 0>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	deposit of melanin	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Circulatory system]																		
heart		< 0>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	necrosis	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Digestive system]																		
liver		< 0>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	nuclear size increased central	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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	270 ppm				810 ppm			
		No. of Animals on Study	0				2			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Respiratory system]										
nasal cavit			< 0>				< 2>			
	desquamation:olfactory epithelium		- (-)	- (-)	- (-)	- (-)	1 (50)	0 (0)	0 (0)	0 (0)
lung			< 0>				< 2>			
	congestion		- (-)	- (-)	- (-)	- (-)	1 (50)	0 (0)	0 (0)	0 (0)
[Hematopoietic system]										
spleen			< 0>				< 2>			
	deposit of melanin		- (-)	- (-)	- (-)	- (-)	1 (50)	0 (0)	0 (0)	0 (0)
[Circulatory system]										
heart			< 0>				< 2>			
	necrosis		- (-)	- (-)	- (-)	- (-)	1 (50)	0 (0)	0 (0)	0 (0)
[Digestive system]										
liver			< 0>				< 2>			
	nuclear size increased central		- (-)	- (-)	- (-)	- (-)	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

STUDY NO. : 0196
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 0				10 ppm 0				30 ppm 0				90 ppm 0			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Endocrine system]																		
pituitary			< 0>				< 0>				< 0>				< 0>			
	cyst		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
adrenal			< 0>				< 0>				< 0>				< 0>			
	hemorrhage		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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	270 ppm				810 ppm			
		No. of Animals on Study	0				2			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Endocrine system]										
pituitary			< 0>				< 2>			
	cyst		- (-)	- (-)	- (-)	- (-)	1 (50)	0 (0)	0 (0)	0 (0)
adrenal			< 0>				< 2>			
	hemorrhage		- (-)	- (-)	- (-)	- (-)	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 A 8-1

IDENTITY AND PURITY OF MEHALLYL CHLORIDE

(TWO-WEEK STUDIES)

IDENTITY OF METHALLYLCHLORIDE(TWO-WEEK STUDIES)

Test Substance Lot No.: LKG5978

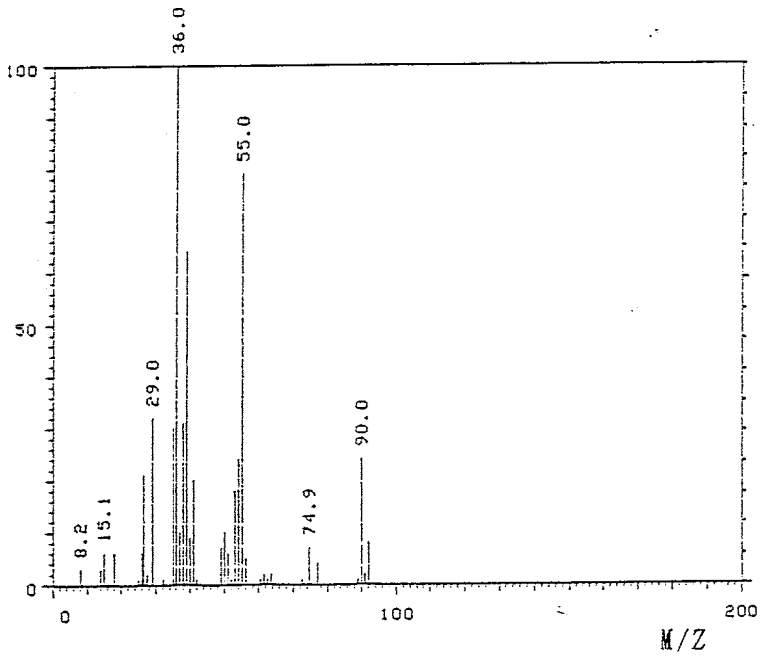
1. Spectral data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI(Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Results: Determined Fragment Peak(M/Z)	Literature Value* Fragment Peak(M/Z)
36.0	36
39.0	39
55.0	55
90.0	90

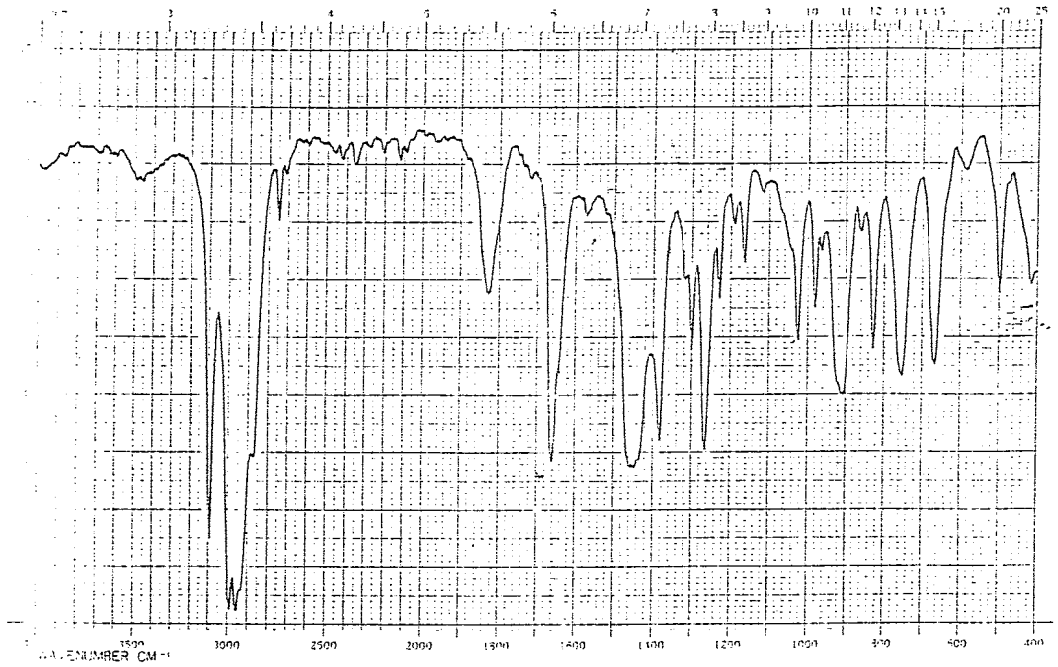
(*EPA/NIH Mass Spectral Data Base (1978) V. 1, p. 53.)

Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium



Infrared Spectrum of Test Substance

Results:

Determined Value Wave Number(cm^{-1})	Literature Value* Wave Number(cm^{-1})
480～ 520	
640～ 690	640～ 670
720～ 780	720～ 770
800～ 840	800～ 830
880～ 940	880～ 940
970～ 990	960～ 990
1000～1040	1000～1040
1150～1180	1140～1170
1220～1240	1210～1230
1240～1280	1230～1280
1290～1310	1280～1300
1360～1400	1360～1390
1410～1480	1410～1480
1620～1680	1620～1680
1780～1860	1780～1860
2800～3030	2800～3000
3050～3130	3050～3130

(*Performed by the WAKO PURE CHEMICAL INDUSTRIES, LTD.)

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

APPENDIX A 8-2

STABILITY OF METHALLYL CHLORIDE

(TWO-WEEK STUDIES)

STABILITY OF METHALLYLCHLORIDE(TWO-WEEK STUDIES)

Test Substance Lot No.: LKG5978

1. Sample: This lot was used from 1992.3.12 to 1992.3.26. Test substance was stored at room temperature .

2. Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium

Results: Infrared spectrum of the test substance agreed with before use and after use.

1992.02.20(date analyzed) Wave Number(cm^{-1})	1992.03.30(date analyzed) Wave Number(cm^{-1})
480～ 520	480～ 520
640～ 690	640～ 690
720～ 780	720～ 780
800～ 840	800～ 840
880～ 940	880～ 940
970～ 990	970～ 990
1000～1040	1000～1040
1150～1180	1150～1180
1220～1240	1220～1240
1240～1280	1240～1280
1290～1310	1290～1310
1360～1400	1360～1400
1410～1480	1410～1480
1620～1680	1620～1680
1780～1860	1780～1860
2800～3030	2800～3030
3050～3130	3050～3130

3. Gas Chromatography

Instrument: Hewlett Packard 5890A

Column: Carbowax 20M(0.2mmϕ × 50m)

Column Temperature: 80°C

Flow Rate: 0.9 ml/min

Detector: FID(Flame Ionization Detector)

Injection Volume: 1 μl

Results: Gas chromatography indicated one major peak(peak No.2) and two impurities(peak No.1,3 < 2% of total area) analyzed at 1992.2.20 and one major peak(peak No.2) and two impurities(peak No.1,3 < 2% of total area) analyzed at 1992.3.30. It was identified only by comparing its gas chromatograph with that of the 1-Chloro-2-methyl-1-propene(peak No.1) and 1,2-Dichloroisobutane (peak No.3) in the Methallylchloride, the amount in the test substance were 1.42% and 0.15% at 1992.2.20. The new treace impurity peak in the test substance analyzed at 1992.3.30 was not detected.

Date	Peak No.	Retention Time(min)	AREA COUNT
1992.02.20	1	4.14	2730
(date analyzed)	2	4.443	170592
	3	5.86	231
1992.03.30	1	4.138	2812
(date analyzed)	2	4.442	175796
	3	5.86	239

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

APPENDIX A 9-1

CONCENTRATION OF METHALLYL CHLORIDE IN INHALATION CHAMBER

(TWO-WEEK STUDIES)

ENVIRONMENT OF INHALATION CHAMBER (RAT : TWO-WEEK STUDY)

Group Name	Temperature(℃) Mean ± S.D.	Humidity(%) Mean ± S.D.	Ventilation Rate(L/min) Mean ± S.D.	Room Air Change(time/h) Mean
Control	22.1 ± 0.3	53.9 ± 0.7	211.2 ± 1.3	12.0
10ppm	22.1 ± 0.2	56.0 ± 1.0	209.9 ± 1.4	11.9
30ppm	22.6 ± 0.2	55.5 ± 0.4	209.3 ± 2.4	11.8
90ppm	22.3 ± 0.2	54.8 ± 0.7	210.4 ± 2.0	11.9
270ppm	22.9 ± 0.2	56.4 ± 0.7	210.2 ± 3.1	11.9
810ppm	22.1 ± 0.4	56.5 ± 0.8	212.4 ± 0.6	12.0

ENVIRONMENT OF INHALATION CHAMBER (MOUSE : TWO-WEEK STUDY)

Group Name	Temperature(℃) Mean ± S.D.	Humidity(%) Mean ± S.D.	Ventilation Rate(L/min) Mean ± S.D.	Room Air Change(time/h) Mean
Control	21.5 ± 0.2	58.2 ± 0.9	103.3 ± 0.9	11.9
10ppm	21.5 ± 0.2	57.3 ± 1.2	103.5 ± 0.5	11.9
30ppm	21.4 ± 0.2	57.2 ± 1.1	103.4 ± 0.7	11.9
90ppm	21.6 ± 0.2	55.3 ± 0.9	103.7 ± 0.8	12.0
270ppm	22.2 ± 0.2	57.5 ± 0.9	103.4 ± 1.0	11.9
810ppm	21.2 ± 0.2	57.6 ± 1.0	103.9 ± 0.8	12.0

APPENDIX A 9-2

ENVIRONMENT OF INHALATION CHAMBER

(TWO-WEEK STUDIES)

CONCENTRATION OF METHALLYL CHLORIDE
IN INHALTION CHAMBER
(RAT : TWO-WEEK STUDY)

Group Name	Concentration (ppm) Mean ± S.D.
Control	0.0 ± 0.0
10ppm	10.0 ± 0.3
30ppm	29.9 ± 0.7
90ppm	89.6 ± 0.9
270ppm	267.2 ± 5.0
810ppm	805.5 ± 9.7

CONCENTRATION OF METHALLYL CHLORIDE
IN INHALTION CHAMBER
(MOUSE : TWO-WEEK STUDY)

Group Name	Concentration (ppm) Mean ± S.D.
Control	0.0 ± 0.0
10ppm	10.2 ± 0.2
30ppm	30.1 ± 0.3
90ppm	90.3 ± 0.4
270ppm	270.4 ± 1.9
810ppm	811.3 ± 3.2