アセト酢酸メチルのラットを用いた経口投与による
１３週間毒性試験（混水試験）報告書

試験番号：　０４２６

APPENDIXES

APPENDIXES

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	40000 ppm	5	0	0	0	0	0	0	0	0	0	0	0	0
SMALL STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	40000 ppm	9	3	0	0	0	0	0	0	0	0	0	0	1
OLIGO-STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	40000 ppm	10	1	0	0	0	0	0	0	0	0	0	0	0

APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

Clinical sign	Group Name	Administration Week day 1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7
MORIBUND SACRIFICE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	40000 ppm	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
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	40000 ppm	1	0	0	0	0	0	0	0	0	0	0	0	0
HUNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	40000 ppm	1	0	0	0	0	0	0	0	0	0	0	0	0
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	40000 ppm	5	0	0	0	0	0	0	0	0	0	0	0	0
SOILED PERI GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	1	1	1
	40000 ppm	1	0	0	0	0	0	0	0	1	2	0	2	2
ABNORMAL RESPIRATION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	40000 ppm	1	0	0	0	0	0	0	0	0	0	0	0	0

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

Clinical sign	Group Name	Administration Week-day 1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7
BRADYPNEA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	40000 ppm	1	0	0	0	0	0	0	0	0	0	0	0	0
SMALL STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	40000 ppm	5	1	0	0	0	0	0	0	0	0	0	0	0
OLIGO-STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	40000 ppm	10	0	0	0	0	0	0	0	0	0	0	0	0
SUBNORMAL TEMP	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	40000 ppm	1	0	0	0	0	0	0	0	0	0	0	0	0

APPENDIX B 1

BODY WEIGHT CHANGES : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 0	1	2	3	4	5	6
Control	127± 4	159± 6	190± 9	216± 9	237± 8	251± 8	261± 11
2500 ppm	127± 4	156± 7	185± 11	209± 13	229± 12	244± 12	254± 12
5000 ppm	127± 4	154± 7	183± 8	209± 8	228± 7	242± 8	249± 8
10000 ppm	127± 4	154± 7	185± 8	210± 8	229± 9	242± 9	250± 11
20000 ppm	127± 5	148± 6*	180± 10	204± 13	225± 13*	238± 12*	243± 14**
40000 ppm	127± 4	107± 17**	144± 17**	177± 12**	200± 12**	216± 12**	221± 11**

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

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 7	8	9	10	11	12	13
Control	277± 12	290± 12	300± 13	310± 12	315± 12	323± 12	326± 11
2500 ppm	270± 11	281± 13	288± 14	297± 14	302± 14	308± 15	310± 16
5000 ppm	264± 8	274± 9*	282± 10**	288± 10**	292± 12**	296± 10**	299± 11**
10000 ppm	263± 11*	274± 13*	281± 13**	286± 14**	290± 13**	297± 13**	299± 14**
20000 ppm	258± 13**	267± 13**	273± 13**	280± 16**	281± 16**	285± 16**	287± 15**
40000 ppm	235± 13**	245± 14**	250± 13**	253± 13**	256± 16**	264± 17**	264± 22**

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

APPENDIX B 2

BODY WEIGHT CHANGES : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 0	1	2	3	4	5	6
Control	100± 3	113± 4	123± 5	132± 5	140± 6	147± 6	150± 7
2500 ppm	100± 3	115± 5	126± 5	135± 6	142± 8	149± 8	150± 8
5000 ppm	100± 3	114± 3	126± 5	135± 4	142± 5	147± 5	149± 7
10000 ppm	100± 3	112± 3	124± 5	132± 4	141± 5	147± 7	147± 5
20000 ppm	100± 3	110± 5	121± 5	131± 6	137± 7	141± 6	141± 7*
40000 ppm	100± 3	91± 17**	114± 7**	128± 7	136± 8	139± 11	139± 10**

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

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 7	8	9	10	11	12	13
Control	156± 8	160± 10	162± 10	166± 10	167± 11	166± 13	170± 11
2500 ppm	157± 8	160± 9	163± 9	166± 9	169± 10	170± 10	171± 10
5000 ppm	156± 7	159± 7	162± 8	165± 7	165± 7	168± 7	170± 8
10000 ppm	155± 7	158± 7	162± 7	165± 8	166± 7	170± 8	170± 6
20000 ppm	147± 8	150± 9	153± 10	156± 10	158± 11	160± 12	160± 10
40000 ppm	145± 12*	147± 13*	151± 13	153± 15*	154± 14*	158± 15	160± 13

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

APPENDIX C 1

WATER CONSUMPTION CHANGES : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(4)	2-7(4)	3-7(4)	4-7(4)	5-7(4)	6-7(4)	7-7(4)
Control	17.6± 0.8	18.7± 0.9	19.6± 1.0	19.3± 1.4	18.6± 0.9	17.0± 1.0	18.4± 0.7
2500 ppm	14.5± 1.3	15.4± 1.5**	16.0± 1.5**	15.6± 1.5	15.2± 1.4	14.1± 1.3**	15.5± 1.3**
5000 ppm	13.2± 1.1**	14.7± 1.1**	15.4± 0.9**	14.8± 0.4*	14.1± 0.5	12.3± 0.4**	13.5± 0.7**
10000 ppm	13.4± 0.7**	14.5± 0.7**	14.8± 0.7**	14.2± 0.7**	13.4± 0.5**	11.9± 0.7**	12.8± 0.5**
20000 ppm	13.0± 0.9**	13.7± 1.1**	13.9± 0.9**	13.1± 0.8**	12.6± 0.7**	10.6± 0.8**	11.9± 1.0**
40000 ppm	6.4± 4.3**	11.9± 1.6**	12.6± 0.9**	12.1± 1.1**	11.3± 1.2**	9.5± 0.8**	10.4± 1.0**

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

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(4)	9-7(4)	10-7(4)	11-7(4)	12-7(4)	13-7(4)
Control	18.6± 0.5	18.1± 0.8	17.9± 1.0	17.3± 0.7	16.9± 0.9	18.2± 2.9
2500 ppm	14.9± 1.3**	14.3± 1.1**	14.4± 0.7**	14.7± 1.6**	14.1± 1.2	13.5± 1.3
5000 ppm	13.3± 1.3**	13.6± 1.3**	13.3± 1.2**	12.7± 1.0**	11.9± 0.9**	12.1± 1.0*
10000 ppm	13.0± 1.0**	12.9± 1.0**	12.6± 0.8**	11.4± 0.7**	11.8± 0.4**	11.3± 0.9**
20000 ppm	11.8± 1.2**	11.8± 0.8**	12.0± 1.3**	11.0± 1.1**	10.6± 1.0**	12.8± 4.2**
40000 ppm	10.4± 1.3**	10.1± 1.3**	10.0± 1.7**	9.8± 1.7**	10.1± 1.8**	9.6± 1.6**

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

APPENDIX C 2

WATER CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(4)	2-7(4)	3-7(4)	4-7(4)	5-7(4)	6-7(4)	7-7(4)
Control	16.4± 7.6	15.3± 3.3	15.7± 3.6	17.4± 7.6	15.5± 3.8	15.1± 3.1	15.8± 3.1
2500 ppm	11.7± 0.7	11.5± 1.0	11.5± 0.9	11.2± 0.8	11.2± 1.2	9.9± 1.0	11.3± 1.4
5000 ppm	10.6± 0.6**	10.7± 0.6**	10.6± 1.1**	10.3± 0.5**	9.7± 0.6**	8.9± 0.9*	9.9± 1.6*
10000 ppm	10.4± 0.6**	10.4± 0.5**	10.2± 0.6**	10.3± 0.8**	9.5± 0.8**	7.9± 0.5**	9.0± 0.7**
20000 ppm	9.6± 0.7**	9.8± 0.7**	9.8± 0.6**	9.2± 0.7**	10.8± 4.9**	7.8± 2.3**	8.1± 1.0**
40000 ppm	7.5± 3.4**	10.3± 0.8**	10.7± 2.4**	9.8± 1.9**	8.0± 1.4**	6.8± 1.3**	7.8± 1.6**

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

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(4)	9-7(4)	10-7(4)	11-7(4)	12-7(4)	13-7(4)
Control	16.9± 3.8	19.1± 8.6	14.8± 2.7	21.5± 7.9	17.1± 4.7	23.5± 9.9
2500 ppm	11.7± 2.4	11.0± 1.5	10.8± 1.5	11.5± 2.6	11.0± 1.8	11.8± 4.2
5000 ppm	9.8± 1.8*	10.2± 3.3	9.8± 2.4	9.4± 1.8*	10.0± 2.9*	9.5± 1.5*
10000 ppm	8.8± 0.7**	8.5± 0.7**	8.7± 1.3**	8.6± 2.0**	8.5± 0.5**	8.4± 0.7**
20000 ppm	8.2± 1.4**	7.6± 0.7**	7.9± 0.9**	7.0± 0.9**	7.4± 0.8**	7.0± 0.5**
40000 ppm	7.6± 1.5**	7.2± 1.3**	6.7± 1.2**	6.6± 0.7**	6.8± 1.1**	7.1± 1.4**

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

APPENDIX D 1

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(7)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	14.2± 0.7	15.7± 0.8	15.8± 0.9	16.5± 0.9	15.8± 0.6	15.4± 0.7	15.9± 1.0
2500 ppm	13.4± 0.9	14.9± 1.2	15.3± 1.4	15.7± 1.1	15.2± 0.9	14.5± 1.1	15.4± 1.3
5000 ppm	12.8± 0.8*	14.2± 1.0*	14.8± 0.7	15.2± 0.6**	14.8± 0.7*	14.3± 0.6*	14.7± 0.7*
10000 ppm	12.7± 0.8**	14.4± 0.9*	14.8± 0.8	14.8± 0.8**	14.3± 0.7**	13.9± 0.7**	14.6± 0.8*
20000 ppm	11.5± 0.8**	13.9± 1.1**	14.3± 1.1*	14.7± 0.9**	14.0± 0.9**	13.3± 0.8**	13.9± 0.8**
40000 ppm	5.8± 1.5**	12.0± 1.4**	13.2± 1.0**	13.9± 1.1**	13.6± 0.8**	12.6± 0.7**	12.7± 0.8**

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

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)
Control	15.5± 0.9	15.1± 0.8	15.2± 0.7	15.2± 0.7	15.0± 0.7	15.7± 0.8
2500 ppm	14.8± 1.3	14.6± 1.0	14.5± 0.9	14.3± 0.8	13.7± 1.1*	14.3± 1.2*
5000 ppm	13.9± 0.7**	14.1± 1.0	14.1± 0.7*	13.8± 0.6**	13.1± 0.6**	13.4± 0.9**
10000 ppm	14.0± 0.9**	14.0± 0.9*	13.7± 1.1**	13.5± 0.9**	13.2± 0.7**	13.4± 1.1**
20000 ppm	13.1± 0.8**	13.1± 0.9**	13.1± 1.0**	12.7± 0.8**	12.3± 0.7**	13.0± 0.8**
40000 ppm	12.0± 1.1**	12.2± 0.9**	11.9± 0.7**	12.0± 1.2**	12.1± 1.3**	12.3± 1.3**

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

APPENDIX D 2

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(7)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	10.4± 0.5	10.4± 0.5	10.7± 0.6	10.4± 0.7	10.7± 0.6	10.1± 0.7	10.3± 0.9
2500 ppm	10.5± 0.5	10.5± 0.4	10.6± 0.7	10.2± 0.5	10.4± 0.6	9.7± 0.6	10.0± 0.6
5000 ppm	10.1± 0.5	10.2± 0.6	10.2± 0.6	10.1± 0.6	9.9± 0.4*	9.4± 0.5	9.7± 0.5
10000 ppm	10.1± 0.5	10.2± 0.6	10.1± 0.8	9.9± 0.7	10.0± 0.8*	9.2± 0.6**	9.6± 0.7
20000 ppm	9.2± 0.8*	9.5± 0.5**	9.6± 0.6**	9.5± 0.5**	9.2± 0.6**	9.0± 0.4**	9.0± 0.5**
40000 ppm	5.8± 1.9**	9.6± 0.4**	9.8± 0.9*	9.5± 0.8*	9.0± 1.0**	8.6± 0.7**	8.6± 0.7**

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

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)
Control	9.8± 1.0	9.6± 0.7	9.7± 0.9	9.8± 1.0	9.5± 0.8	9.8± 0.8
2500 ppm	9.5± 0.5	9.2± 0.5	9.4± 0.4	9.4± 0.4	9.3± 0.7	9.5± 0.6
5000 ppm	9.3± 0.6	9.1± 0.5	9.1± 0.6	9.0± 0.6*	9.0± 0.8	9.1± 0.6
10000 ppm	9.1± 0.8	9.0± 0.7	9.1± 0.8	9.0± 0.7*	8.9± 0.5	8.9± 0.7*
20000 ppm	8.7± 0.7**	8.5± 0.8**	8.4± 0.8**	8.7± 0.7**	8.4± 0.7**	8.5± 0.6**
40000 ppm	8.5± 1.0**	8.2± 0.9**	8.0± 0.9**	8.2± 0.9**	8.1± 0.6**	8.2± 0.6**

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

APPENDIX E 1

CHEMICAL INTAKE CHANGES : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
UNIT : g／kg／d a y
REPORT TYPE : A1 13
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2	3	4	5	6	7
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
2500 ppm	0.232± 0.015	0.208± 0.010	0.191± 0.009	0.170± 0.009	0.156± 0.009	0.138± 0.008	0.143± 0.008
5000 ppm	0.429± 0.026	0.400± 0.025	0.368± 0.028	0.325± 0.015	0.290± 0.016	0.248± 0.011	0.256± 0.014
10000 ppm	0.867± 0.027	0.781± 0.022	0.707± 0.029	0.620± 0.034	0.554± 0.016	0.475± 0.014	0.488± 0.028
20000 ppm	1.747± 0.100	1.524± 0.057	1.363± 0.039	1.166± 0.049	1.059± 0.050	0.871± 0.036	0.921± 0.051
40000 ppm	2.200± 1.257	3.294± 0.232	2.851± 0.209	2.422± 0.096	2.090± 0.169	1.718± 0.160	1.775± 0.140

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
UNIT : g／kg／d a y
REPORT TYPE : A1 13
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 8	9	10	11	12	13
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
2500 ppm	0.132± 0.006	0.124± 0.004	0.121± 0.003	0.122± 0.013	0.114± 0.007	0.109± 0.006
5000 ppm	0.243± 0.023	0.241± 0.022	0.230± 0.018	0.217± 0.012	0.200± 0.011	0.202± 0.014
10000 ppm	0.476± 0.032	0.458± 0.027	0.440± 0.025	0.396± 0.026	0.398± 0.015	0.378± 0.026
20000 ppm	0.881± 0.071	0.862± 0.042	0.856± 0.069	0.780± 0.062	0.746± 0.057	0.884± 0.273
40000 ppm	1.703± 0.158	1.619± 0.191	1.583± 0.243	1.529± 0.202	1.526± 0.212	1.438± 0.141

APPENDIX E 2

CHEMICAL INTAKE CHANGES : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
UNIT : g／kg／d a y
REPORT TYPE : A1 13
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2	3	4	5	6	7
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
2500 ppm	0.253± 0.011	0.227± 0.017	0.211± 0.012	0.196± 0.009	0.188± 0.020	0.165± 0.014	0.181± 0.020
5000 ppm	0.463± 0.019	0.425± 0.014	0.395± 0.036	0.363± 0.015	0.329± 0.019	0.297± 0.026	0.317± 0.046
10000 ppm	0.926± 0.066	0.839± 0.052	0.773± 0.049	0.735± 0.049	0.645± 0.045	0.540± 0.028	0.576± 0.038
20000 ppm	1.748± 0.089	1.616± 0.083	1.503± 0.084	1.342± 0.073	1.519± 0.641	1.099± 0.297	1.103± 0.126
40000 ppm	3.115± 1.064	3.616± 0.371	3.343± 0.776	2.882± 0.527	2.307± 0.288	1.937± 0.270	2.154± 0.428

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
UNIT : g／kg／d a y
REPORT TYPE : A1 13
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 8	9	10	11	12	13
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
2500 ppm	0.183± 0.036	0.169± 0.025	0.163± 0.023	0.171± 0.038	0.162± 0.024	0.172± 0.057
5000 ppm	0.308± 0.054	0.314± 0.096	0.297± 0.068	0.283± 0.048	0.296± 0.079	0.281± 0.038
10000 ppm	0.554± 0.038	0.526± 0.038	0.526± 0.073	0.520± 0.106	0.502± 0.029	0.495± 0.042
20000 ppm	1.101± 0.236	0.989± 0.091	1.011± 0.102	0.891± 0.098	0.927± 0.071	0.885± 0.083
40000 ppm	2.054± 0.375	1.918± 0.298	1.732± 0.164	1.733± 0.123	1.721± 0.188	1.782± 0.275

APPENDIX F 1

HEMATOLOGY : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV f ℓ	MCH p g	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	10	9.47± 0.12	16.1± 0.2	47.2± 0.7	49.9± 0.5	17.0± 0.2	34.1± 0.3	715± 55
2500 ppm	10	9.43± 0.26	16.1± 0.4	47.4± 1.3	50.2± 0.5	17.1± 0.2	34.0± 0.4	682± 29
5000 ppm	9	9.21± 0.36	15.8± 0.6	46.6± 1.9	50.6± 0.7*	17.2± 0.2	34.0± 0.4	696± 59
10000 ppm	10	9.27± 0.25	15.9± 0.4	46.8± 1.3	50.4± 0.6	17.1± 0.2	33.9± 0.3	696± 47
20000 ppm	10	9.13± 0.19**	15.6± 0.3**	45.9± 1.0	50.3± 0.3	17.1± 0.2	34.0± 0.4	706± 55
40000 ppm	9	9.15± 0.16**	15.9± 0.3	46.5± 0.7	50.9± 0.4**	17.4± 0.1**	34.2± 0.3	668± 65

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

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RETICULOCYTE %	PROTHROMBIN TIME sec	APTT sec
Control	10	2.0± 0.2	17.2± 2.2	26.5± 2.1
2500 ppm	10	1.9± 0.2	17.6± 2.7	27.5± 2.7
5000 ppm	9	2.0± 0.2	17.3± 1.9	26.5± 3.3
10000 ppm	10	1.8± 0.2	15.0± 0.4**	22.4± 2.0**
20000 ppm	10	2.0± 0.2	15.0± 0.5**	21.3± 2.1**
40000 ppm	9	2.1± 0.2	15.5± 0.5	22.2± 3.0**

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

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$		Differential WBC (%) N-BAND		N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHER	
Control	10	4.72±	1.28	3±	1	21±	4	1±	1	0±	0	2±	1	73±	5	0±	0
2500 ppm	10	4.67±	1.19	2±	1	19±	2	1±	1	0±	0	2±	1	76±	4	0±	0
5000 ppm	9	5.24±	2.21	2±	1	17±	3	2±	1	0±	0	2±	1	78±	4	0±	0
10000 ppm	10	4.53±	1.58	2±	1	21±	5	1±	1	0±	0	2±	1	74±	5	0±	0
20000 ppm	10	3.81±	1.17	2±	1	20±	4	1±	1	0±	0	3±	2	74±	4	0±	0
40000 ppm	9	4.47±	1.03	2±	1	21±	3	1±	1	0±	0	2±	1	73±	4	0±	0

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

APPENDIX F 2

HEMATOLOGY : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV f ℓ	MCH p g	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	10	8.54± 0.28	15.8± 0.4	45.0± 1.5	52.7± 0.5	18.5± 0.2	35.1± 0.6	790± 52
2500 ppm	10	8.50± 0.18	15.6± 0.3	44.6± 0.8	52.5± 0.5	18.4± 0.2	35.0± 0.5	756± 78
5000 ppm	10	8.42± 0.18	15.6± 0.4	44.5± 1.0	52.8± 0.4	18.5± 0.2	35.0± 0.4	755± 61
10000 ppm	10	8.46± 0.11	15.7± 0.2	44.7± 0.6	52.8± 0.3	18.5± 0.1	35.0± 0.4	753± 65
20000 ppm	10	8.37± 0.28	15.4± 0.6	44.2± 1.3	52.8± 0.5	18.4± 0.2	34.9± 0.5	710± 70
40000 ppm	9	8.42± 0.19	15.5± 0.3	44.3± 0.9	52.6± 1.0	18.5± 0.3	35.1± 0.5	730± 67

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

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RETICULOCYTE %	PROTHROMBIN TIME sec	APTT sec
Control	10	2.1± 0.2	15.0± 0.6	18.4± 1.3
2500 ppm	10	2.0± 0.2	14.3± 0.7*	17.1± 2.1
5000 ppm	10	2.0± 0.2	15.5± 0.6	17.6± 1.6
10000 ppm	10	2.1± 0.2	14.9± 0.8	16.4± 2.7
20000 ppm	10	2.0± 0.2	15.1± 0.5	16.3± 1.6
40000 ppm	9	2.2± 0.4	15.3± 0.4	17.6± 2.5

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

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$		Differential WBC (%) N-BAND		N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHER	
Control	10	3.38±	1.43	1±	1	20±	5	1±	0	0±	0	2±	1	76±	5	0±	0
2500 ppm	10	2.39±	0.88	2±	1	19±	4	1±	1	0±	0	3±	2	75±	4	0±	0
5000 ppm	10	2.71±	1.05	2±	1	19±	6	1±	1	0±	0	3±	1	76±	6	0±	0
10000 ppm	10	2.67±	0.88	2±	1	19±	6	1±	1	0±	0	2±	2	76±	7	0±	0
20000 ppm	10	3.03±	0.81	2±	1	19±	6	1±	1	0±	0	2±	1	76±	7	0±	0
40000 ppm	9	2.83±	0.90	2±	1	18±	5	1±	1	0±	0	2±	1	76±	6	0±	0

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

APPENDIX G 1

BIOCHEMISTRY : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	TOTAL PROTEIN g/dl	ALBUMIN g/dl	A/G RATIO	T-BILIRUBIN mg/dl	GLUCOSE mg/dl	T-CHOLESTEROL mg/dl	TRIGLYCERIDE mg/dl
Control	10	6.4± 0.1	4.0± 0.1	1.7± 0.1	0.13± 0.01	208± 18	68± 5	52± 23
2500 ppm	10	6.2± 0.2	3.9± 0.1	1.7± 0.1	0.13± 0.01	215± 20	62± 4*	58± 31
5000 ppm	9	6.2± 0.3	3.9± 0.2	1.6± 0.1	0.14± 0.01	223± 26	64± 6	53± 23
10000 ppm	10	6.2± 0.2	3.9± 0.1	1.7± 0.1	0.13± 0.01	210± 17	63± 4	51± 25
20000 ppm	10	6.1± 0.1**	3.8± 0.1*	1.7± 0.1	0.13± 0.01	199± 14	64± 4	49± 18
40000 ppm	9	6.0± 0.1**	3.7± 0.1**	1.7± 0.1	0.14± 0.02	194± 19	60± 5**	52± 10

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

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	PHOSPHOLIPID mg/dℓ		GOT IU/ℓ		GPT IU/ℓ		LDH IU/ℓ		ALP IU/ℓ		G-GTP IU/ℓ		CPK IU/ℓ	
Control	10	125±	10	81±	17	51±	8	249±	101	237±	16	1±	1	112±	19
2500 ppm	10	119±	11	77±	21	51±	10	249±	84	242±	13	2±	1	116±	21
5000 ppm	9	124±	14	75±	24	48±	9	260±	59	229±	20	2±	1	116±	22
10000 ppm	10	118±	7	64±	14	44±	6	229±	41	238±	16	2±	1	107±	11
20000 ppm	10	118±	6	60±	18	41±	10*	221±	66	221±	15	1±	1	101±	18
40000 ppm	9	115±	6	54±	12**	40±	4*	189±	33	255±	29	2±	1	107±	15

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

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	UREA NITROGEN mg/dℓ	CREATININE mg/dℓ	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dℓ	INORGANIC PHOSPHORUS mg/dℓ
Control	10	17.7± 1.6	0.6± 0.1	142± 1	3.3± 0.3	105± 1	10.4± 0.2	5.6± 0.6
2500 ppm	10	19.4± 2.1	0.6± 0.1	141± 1	3.3± 0.3	105± 1	10.3± 0.2	5.3± 0.6
5000 ppm	9	20.1± 1.1**	0.6± 0.1	140± 2	3.4± 0.4	105± 1	10.3± 0.3	5.6± 0.9
10000 ppm	10	20.5± 0.9**	0.6± 0.1	141± 1	3.4± 0.1	105± 1	10.2± 0.2	5.2± 0.6
20000 ppm	10	20.4± 1.6**	0.5± 0.0	141± 1	3.4± 0.2	105± 1	10.1± 0.2	5.3± 0.6
40000 ppm	9	21.2± 1.8**	0.5± 0.1	140± 1	3.5± 0.2	106± 1	10.1± 0.3	5.3± 0.7

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

APPENDIX G 2

BIOCHEMISTRY : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	TOTAL PROTEIN g/dl	ALBUMIN g/dl	A/G RATIO	T-BILIRUBIN mg/dl	GLUCOSE mg/dl	T-CHOLESTEROL mg/dl	TRIGLYCERIDE mg/dl
Control	10	6.1± 0.3	3.8± 0.2	1.6± 0.1	0.16± 0.02	147± 15	69± 11	16± 3
2500 ppm	10	6.0± 0.1	3.7± 0.1	1.6± 0.1	0.16± 0.01	157± 17	71± 5	16± 4
5000 ppm	10	5.9± 0.2	3.6± 0.1*	1.6± 0.1	0.16± 0.01	162± 21	68± 5	16± 5
10000 ppm	10	5.8± 0.3**	3.6± 0.2**	1.6± 0.1	0.15± 0.01	170± 24	70± 8	17± 5
20000 ppm	10	5.7± 0.2**	3.5± 0.1**	1.6± 0.1	0.16± 0.01	161± 28	66± 6	18± 4
40000 ppm	9	5.6± 0.2**	3.5± 0.1**	1.6± 0.1	0.15± 0.02	160± 22	66± 6	18± 6

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

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	PHOSPHOLIPID mg/dℓ	GOT IU/ℓ	GPT IU/ℓ	LDH IU/ℓ	ALP IU/ℓ	G-GTP IU/ℓ	CPK IU/ℓ
Control	10	141± 14	74± 22	46± 32	294± 87	169± 18	3± 1	119± 22
2500 ppm	10	141± 9	78± 22	41± 16	366± 133	164± 18	2± 1	166± 85
5000 ppm	10	136± 8	64± 6	33± 5	354± 152	167± 13	2± 1	147± 45
10000 ppm	10	139± 13	63± 7	31± 3	316± 147	170± 16	2± 1	134± 44
20000 ppm	10	133± 7	62± 7	32± 4	318± 134	173± 13	2± 1	139± 46
40000 ppm	9	134± 13	61± 9	34± 8	336± 201	203± 15**	3± 1	141± 45

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

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	UREA NITROGEN mg/dℓ	CREATININE mg/dℓ	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dℓ	INORGANIC PHOSPHORUS mg/dℓ
Control	10	20.0± 1.8	0.6± 0.1	139± 1	3.6± 0.3	108± 2	9.9± 0.2	5.2± 0.8
2500 ppm	10	20.2± 1.4	0.6± 0.1	139± 2	3.6± 0.1	107± 1	9.9± 0.3	4.9± 1.0
5000 ppm	10	22.1± 1.3*	0.6± 0.1	139± 1	3.6± 0.2	107± 1	9.7± 0.4	4.9± 1.2
10000 ppm	10	21.6± 1.5	0.6± 0.1	139± 1	3.5± 0.3	107± 1	9.7± 0.3	5.0± 0.5
20000 ppm	10	22.1± 2.3*	0.6± 0.1	139± 1	3.6± 0.4	107± 1	9.7± 0.3	5.1± 0.5
40000 ppm	9	22.3± 1.5*	0.6± 0.1	139± 1	3.6± 0.3	106± 1	9.7± 0.2	5.5± 0.6

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

APPENDIX H 1

URINALYSIS : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	±	+	2+	3+	4+	CHI	Bilirubin −	+	2+	3+	CHI
Control	10	0	0	0	0	0	5	5		0	0	9	1	0	0		10	0	0	0	0	0		6	2	1	1	0	0		10	0	0	0	
2500 ppm	10	0	0	0	1	0	5	4		0	0	6	4	0	0		10	0	0	0	0	0		1	7	2	0	0	0		10	0	0	0	
5000 ppm	10	0	0	0	0	1	6	3		0	0	6	4	0	0		10	0	0	0	0	0		0	3	6	1	0	0	*	10	0	0	0	
10000 ppm	10	0	0	0	0	5	3	2	*	0	0	1	9	0	0	**	10	0	0	0	0	0		0	5	3	2	0	0	*	10	0	0	0	
20000 ppm	10	0	0	0	0	4	4	2		0	0	2	8	0	0	**	10	0	0	0	0	0		0	4	3	3	0	0	*	10	0	0	0	
40000 ppm	10	0	0	0	2	5	0	3	**	0	0	3	7	0	0	**	10	0	0	0	0	0		1	4	3	1	1	0		10	0	0	0	

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

STUDY NO. : 0426 URINALYSIS
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

Group Name	NO. of Animals	Occult blood −	±	+	2+	3+	CHI	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0		10	0	0	0	0	
2500 ppm	10	10	0	0	0	0		10	0	0	0	0	
5000 ppm	10	9	1	0	0	0		10	0	0	0	0	
10000 ppm	10	10	0	0	0	0		10	0	0	0	0	
20000 ppm	10	10	0	0	0	0		10	0	0	0	0	
40000 ppm	10	10	0	0	0	0		10	0	0	0	0	

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of CHI SQUARE

APPENDIX H 2

URINALYSIS : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0426 URINALYSIS
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	±	+	2+	3+	4+	CHI	Bilirubin −	+	2+	3+	CHI
Control	10	0	0	0	0	0	6	4		0	3	7	0	0	0		10	0	0	0	0	0		4	6	0	0	0	0		10	0	0	0	
2500 ppm	10	0	0	0	0	0	8	2		0	0	10	0	0	0		10	0	0	0	0	0		3	7	0	0	0	0		10	0	0	0	
5000 ppm	10	0	0	0	0	2	4	4		0	0	6	4	0	0	*	10	0	0	0	0	0		0	10	0	0	0	0	*	10	0	0	0	
10000 ppm	10	0	0	1	0	1	5	3		0	0	4	6	0	0	**	10	0	0	0	0	0		0	10	0	0	0	0	*	10	0	0	0	
20000 ppm	10	0	0	0	0	4	4	2		0	0	4	6	0	0	**	10	0	0	0	0	0		0	9	1	0	0	0		10	0	0	0	
40000 ppm	9	0	0	0	1	1	6	1		0	0	2	7	0	0	**	9	0	0	0	0	0		0	6	3	0	0	0	*	9	0	0	0	

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

STUDY NO. : 0426 URINALYSIS
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

Group Name	NO. of Animals	Occult blood −	±	+	2+	3+	CHI	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0		10	0	0	0	0	
2500 ppm	10	10	0	0	0	0		10	0	0	0	0	
5000 ppm	10	10	0	0	0	0		10	0	0	0	0	
10000 ppm	10	10	0	0	0	0		10	0	0	0	0	
20000 ppm	10	10	0	0	0	0		10	0	0	0	0	
40000 ppm	9	9	0	0	0	0		9	0	0	0	0	

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

APPENDIX I 1

GROSS FINDINGS : SUMMARY, RAT : MALE : ALL ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
ALL ANIMALS (0- 14W)

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	2500 ppm 10 (%)	5000 ppm 10 (%)	10000 ppm 10 (%)
liver	herniation		0 (0)	1 (10)	2 (20)	0 (0)

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
ALL ANIMALS (0- 14W)

Organ	Findings	Group Name	20000 ppm	40000 ppm
		NO. of Animals	10 (%)	10 (%)
liver	herniation		0 (0)	0 (0)

APPENDIX I 2

GROSS FINDINGS : SUMMARY, RAT : FEMALE : ALL ANIMALS

(13-WEEK STUDY)

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	2500 ppm 10 (%)	5000 ppm 10 (%)	10000 ppm 10 (%)
liver	herniation		1 (10)	0 (0)	3 (30)	2 (20)
ovary	cyst		0 (0)	1 (10)	0 (0)	0 (0)

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
ALL ANIMALS (0- 14W)

Organ	Findings	Group Name / NO. of Animals	20000 ppm 10 (%)	40000 ppm 10 (%)
liver	herniation		2 (20)	4 (40)
ovary	cyst		0 (0)	0 (0)

APPENDIX I 3

GROSS FINDINGS : SUMMARY, RAT : FEMALE : SACRIFICED ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	2500 ppm 10 (%)	5000 ppm 10 (%)	10000 ppm 10 (%)
liver	herniation		1 (10)	0 (0)	3 (30)	2 (20)
ovary	cyst		0 (0)	1 (10)	0 (0)	0 (0)

Organ	Findings	Group Name NO. of Animals	20000 ppm 10 (%)	40000 ppm 9 (%)
liver	herniation		2 (20)	3 (33)
ovary	cyst		0 (0)	0 (0)

APPENDIX I 4

GROSS FINDINGS : SUMMARY, RAT : FEMALE : DEAD AND MORIBUND ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name NO. of Animals	20000 ppm 0 (%)	40000 ppm 1 (%)
liver	herniation		- (-)	1 (100)

APPENDIX J 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	308± 11	0.226± 0.036	0.047± 0.004	3.043± 0.175	0.949± 0.064	1.061± 0.053
2500 ppm	10	294± 14	0.220± 0.031	0.050± 0.010	3.087± 0.146	0.929± 0.060	1.006± 0.047
5000 ppm	10	285± 11**	0.210± 0.022	0.048± 0.004	3.029± 0.094	0.885± 0.036*	1.000± 0.044
10000 ppm	10	284± 14**	0.210± 0.032	0.047± 0.004	3.030± 0.088	0.875± 0.046*	0.990± 0.048*
20000 ppm	10	274± 14**	0.189± 0.019*	0.046± 0.003	2.975± 0.158	0.864± 0.051**	0.979± 0.076**
40000 ppm	10	256± 19**	0.174± 0.028**	0.044± 0.003	2.919± 0.107	0.799± 0.057**	0.936± 0.063**

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

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.834± 0.064	0.572± 0.029	7.632± 0.219	1.920± 0.037
2500 ppm	10	1.817± 0.111	0.540± 0.041	7.276± 0.430	1.920± 0.044
5000 ppm	10	1.803± 0.084	0.530± 0.034	7.141± 0.383	1.901± 0.043
10000 ppm	10	1.837± 0.116	0.523± 0.032*	6.918± 0.375**	1.908± 0.038
20000 ppm	10	1.820± 0.127	0.522± 0.031*	6.794± 0.497**	1.899± 0.037
40000 ppm	10	1.709± 0.142	0.498± 0.052**	6.158± 0.688**	1.858± 0.058*

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

APPENDIX J 2

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	157± 12	0.168± 0.028	0.055± 0.005	0.109± 0.016	0.596± 0.041	0.753± 0.046
2500 ppm	10	160± 10	0.177± 0.023	0.052± 0.005	0.110± 0.019	0.593± 0.033	0.753± 0.044
5000 ppm	10	161± 10	0.162± 0.018	0.052± 0.004	0.105± 0.010	0.576± 0.031	0.734± 0.037
10000 ppm	10	160± 7	0.166± 0.008	0.049± 0.004**	0.096± 0.012	0.582± 0.032	0.744± 0.036
20000 ppm	10	153± 11	0.160± 0.018	0.050± 0.004*	0.098± 0.010	0.574± 0.040	0.720± 0.028
40000 ppm	9	153± 12	0.151± 0.016	0.047± 0.006**	0.094± 0.016	0.561± 0.042	0.715± 0.041

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

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.087± 0.069	0.371± 0.044	3.883± 0.343	1.747± 0.054
2500 ppm	10	1.160± 0.048	0.396± 0.052	3.844± 0.285	1.746± 0.031
5000 ppm	10	1.147± 0.076	0.373± 0.025	3.737± 0.194	1.754± 0.047
10000 ppm	10	1.199± 0.056**	0.376± 0.012	3.778± 0.221	1.786± 0.049
20000 ppm	10	1.168± 0.035*	0.365± 0.030	3.652± 0.269	1.751± 0.038
40000 ppm	9	1.175± 0.083*	0.348± 0.028	3.553± 0.270	1.753± 0.060

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

APPENDIX K 1

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	308± 11	0.073± 0.011	0.015± 0.001	0.990± 0.054	0.308± 0.012	0.345± 0.011
2500 ppm	10	294± 14	0.075± 0.008	0.017± 0.004	1.050± 0.032	0.316± 0.016	0.342± 0.011
5000 ppm	10	285± 11**	0.074± 0.006	0.017± 0.001*	1.063± 0.028*	0.311± 0.015	0.351± 0.014
10000 ppm	10	284± 14**	0.074± 0.009	0.016± 0.002	1.067± 0.030*	0.308± 0.013	0.348± 0.009
20000 ppm	10	274± 14**	0.069± 0.006	0.017± 0.001*	1.087± 0.056**	0.316± 0.012	0.357± 0.016
40000 ppm	10	256± 19**	0.068± 0.007	0.017± 0.002**	1.147± 0.081**	0.313± 0.009	0.367± 0.012**

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

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.596± 0.013	0.186± 0.005	2.482± 0.069	0.624± 0.019
2500 ppm	10	0.618± 0.021	0.183± 0.006	2.474± 0.090	0.654± 0.034
5000 ppm	10	0.633± 0.024**	0.186± 0.009	2.506± 0.103	0.668± 0.020*
10000 ppm	10	0.646± 0.028**	0.184± 0.004	2.433± 0.032	0.673± 0.034**
20000 ppm	10	0.664± 0.024**	0.191± 0.006	2.479± 0.088	0.695± 0.026**
40000 ppm	10	0.669± 0.026**	0.195± 0.009*	2.405± 0.139	0.730± 0.045**

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

APPENDIX K 2

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	157± 12	0.107± 0.013	0.035± 0.003	0.069± 0.007	0.380± 0.021	0.481± 0.025
2500 ppm	10	160± 10	0.111± 0.012	0.032± 0.004	0.069± 0.014	0.370± 0.013	0.470± 0.016
5000 ppm	10	161± 10	0.100± 0.007	0.032± 0.002	0.065± 0.007	0.358± 0.015**	0.456± 0.018
10000 ppm	10	160± 7	0.103± 0.006	0.030± 0.003**	0.060± 0.008	0.363± 0.013	0.464± 0.018
20000 ppm	10	153± 11	0.104± 0.010	0.033± 0.004	0.064± 0.006	0.375± 0.014	0.471± 0.027
40000 ppm	9	153± 12	0.099± 0.009	0.031± 0.005*	0.061± 0.008	0.368± 0.018	0.470± 0.028

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

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.695± 0.036	0.237± 0.020	2.475± 0.094	1.118± 0.070
2500 ppm	10	0.725± 0.037	0.247± 0.025	2.398± 0.097	1.093± 0.058
5000 ppm	10	0.712± 0.031	0.231± 0.012	2.319± 0.076**	1.090± 0.052
10000 ppm	10	0.748± 0.023*	0.235± 0.010	2.356± 0.112*	1.114± 0.043
20000 ppm	10	0.764± 0.055**	0.238± 0.013	2.380± 0.058	1.146± 0.073
40000 ppm	9	0.771± 0.043**	0.229± 0.017	2.328± 0.046**	1.152± 0.067

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

APPENDIX L 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : ALL ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
ALL ANIMALS (0- 14W)

Organ	Findings	Group Name	Control				2500 ppm				5000 ppm				10000 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}																		
nasal cavit			<10>				<10>				<10>				<10>			
	mineralization		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}																		
spleen			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		10	0	0	0	10	0	0	0	10	0	0	0	10	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Circulatory system}																		
heart			<10>				<10>				<10>				<10>			
	granulation		0	0	0	0	2	0	0	0	2	0	0	0	4	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(40)	(0)	(0)	(0)
{Digestive system}																		
liver			<10>				<10>				<10>				<10>			
	herniation		0	0	0	0	1	0	0	0	2	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	20000 ppm				40000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			<10>				<10>			
	mineralization		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}										
spleen			<10>				<10>			
	deposit of hemosiderin		10	0	0	0	10	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Circulatory system}										
heart			<10>				<10>			
	granulation		3	0	0	0	1	0	0	0
			(30)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Digestive system}										
liver			<10>				<10>			
	herniation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				2500 ppm				5000 ppm				10000 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
liver			<10>				<10>				<10>				<10>			
	granulation		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	basophilic change		0	0	0	0	3	0	0	0	3	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(30)	(0)	(0)	(0)
	eosinophilic body		10	0	0	0	10	0	0	0	10	0	0	0	10	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	hyaline cast		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	papillary necrosis		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:papilla		1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Endocrine system}																		
pituitary			<10>				<10>				<10>				<10>			
	Rathke pouch		1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	20000 ppm				40000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
liver			<10>				<10>			
	granulation		1	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Urinary system}										
kidney			<10>				<10>			
	basophilic change		2	0	0	0	4	0	0	0
			(20)	(0)	(0)	(0)	(40)	(0)	(0)	(0)
	eosinophilic body		10	0	0	0	10	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	hyaline cast		2	0	0	0	1	0	0	0
			(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	papillary necrosis		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	mineralization:papilla		1	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Endocrine system}										
pituitary			<10>				<10>			
	Rathke pouch		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				2500 ppm				5000 ppm				10000 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Endocrine system}																		
thyroid			<10>				<10>				<10>				<10>			
	ultimobranchial body remanet		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Reproductive system}																		
testis			<10>				<10>				<10>				<10>			
	atrophy		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
prostate			<10>				<10>				<10>				<10>			
	inflammation		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Special sense organs/appendage}																		
Harder gl			<10>				<10>				<10>				<10>			
	lymphocytic infiltration		2	0	0	0	2	0	0	0	1	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	20000 ppm				40000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Endocrine system}										
thyroid			<10>				<10>			
	ultimobranchial body remanet		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Reproductive system}										
testis			<10>				<10>			
	atrophy		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
prostate			<10>				<10>			
	inflammation		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Special sense organs/appendage}										
Harder gl			<10>				<10>			
	lymphocytic infiltration		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)

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

APPENDIX L 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : ALL ANIMALS

(13-WEEK STUDY)

Organ	Findings	Group Name	Control				2500 ppm				5000 ppm				10000 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}																		
lung			<10>				<10>				<10>				<10>			
	osseous metaplasia		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}																		
bone marrow			<10>				<10>				<10>				<10>			
	granulation		3	0	0	0	2	0	0	0	1	0	0	0	0	0	0	0
			(30)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lymph node			<10>				<10>				<10>				<10>			
	lymphadenitis		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		10	0	0	0	10	0	0	0	10	0	0	0	10	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Circulatory system}																		
heart			<10>				<10>				<10>				<10>			
	granulation		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	20000 ppm				40000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
lung			<10>				<10>			
	osseous metaplasia		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}										
bone marrow			<10>				<10>			
	granulation		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
lymph node			<10>				<10>			
	lymphadenitis		1	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
spleen			<10>				<10>			
	deposit of hemosiderin		10	0	0	0	9	0	0	0
			(100)	(0)	(0)	(0)	(90)	(0)	(0)	(0)
{Circulatory system}										
heart			<10>				<10>			
	granulation		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				2500 ppm				5000 ppm				10000 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
liver			<10>				<10>				<10>				<10>			
	herniation		1	0	0	0	0	0	0	0	3	0	0	0	2	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	granulation		1	0	0	0	2	0	0	0	1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	infarct		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	basophilic change		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyaline cast		0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	papillary 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)
	mineralization:cortico-medullary junction		5	0	0	0	4	0	0	0	0	0	0	0 *	3	0	0	0
			(50)	(0)	(0)	(0)	(40)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(30)	(0)	(0)	(0)

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

Organ	Findings	Group Name	20000 ppm				40000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
liver			<10>				<10>			
	herniation		2	0	0	0	4	0	0	0
			(20)	(0)	(0)	(0)	(40)	(0)	(0)	(0)
	granulation		0	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(30)	(0)	(0)	(0)
{Urinary system}										
kidney			<10>				<10>			
	infarct		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	basophilic change		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyaline cast		3	0	0	0	1	0	0	0
			(30)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	papillary necrosis		2	0	0	0	5	0	0	0 *
			(20)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
	mineralization:cortico-medullary junction		2	0	0	0	4	0	0	0
			(20)	(0)	(0)	(0)	(40)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				2500 ppm				5000 ppm				10000 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	mineralization:papilla		1	0	0	0	2	0	0	0	2	0	0	0	2	1	0	0
			(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(20)	(10)	(0)	(0)
{Reproductive system}																		
ovary			<10>				<10>				<10>				<10>			
	cyst		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Special sense organs/appendage}																		
Harder gl			<10>				<10>				<10>				<10>			
	lymphocytic infiltration		1	0	0	0	1	1	0	0	1	0	0	0	2	0	0	0
			(10)	(0)	(0)	(0)	(10)	(10)	(0)	(0)	(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)

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

Organ	Findings	Group Name	20000 ppm				40000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}										
kidney			<10>				<10>			
	mineralization:papilla		4	0	0	0	1	0	0	0
			(40)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Reproductive system}										
ovary			<10>				<10>			
	cyst		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Special sense organs/appendage}										
Harder gl			<10>				<10>			
	lymphocytic infiltration		1	0	0	0	2	0	0	0
			(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)

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

APPENDIX L 3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : SACRIFICED ANIMALS

(13-WEEK STUDY)

Organ	Findings	Group Name	Control				2500 ppm				5000 ppm				10000 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}																		
lung			<10>				<10>				<10>				<10>			
	osseous metaplasia		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}																		
bone marrow			<10>				<10>				<10>				<10>			
	granulation		3	0	0	0	2	0	0	0	1	0	0	0	0	0	0	0
			(30)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lymph node			<10>				<10>				<10>				<10>			
	lymphadenitis		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		10	0	0	0	10	0	0	0	10	0	0	0	10	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Circulatory system}																		
heart			<10>				<10>				<10>				<10>			
	granulation		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	20000 ppm				40000 ppm			
		No. of Animals on Study	10				9			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
lung			<10>				< 9>			
	osseous metaplasia		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}										
bone marrow			<10>				< 9>			
	granulation		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(22)	(0)	(0)	(0)
lymph node			<10>				< 9>			
	lymphadenitis		1	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(11)	(0)	(0)	(0)
spleen			<10>				< 9>			
	deposit of hemosiderin		10	0	0	0	9	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Circulatory system}										
heart			<10>				< 9>			
	granulation		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(11)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				2500 ppm				5000 ppm				10000 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
liver			<10>				<10>				<10>				<10>			
	herniation		1	0	0	0	0	0	0	0	3	0	0	0	2	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	granulation		1	0	0	0	2	0	0	0	1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	infarct		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	basophilic change		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyaline cast		0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	papillary 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)
	mineralization:cortico-medullary junction		5	0	0	0	4	0	0	0	0	0	0	0 *	3	0	0	0
			(50)	(0)	(0)	(0)	(40)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(30)	(0)	(0)	(0)

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

Organ	Findings	Group Name	20000 ppm				40000 ppm			
		No. of Animals on Study	10				9			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
liver			<10>				< 9>			
	herniation		2	0	0	0	3	0	0	0
			(20)	(0)	(0)	(0)	(33)	(0)	(0)	(0)
	granulation		0	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(33)	(0)	(0)	(0)
{Urinary system}										
kidney			<10>				< 9>			
	infarct		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	basophilic change		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyaline cast		3	0	0	0	1	0	0	0
			(30)	(0)	(0)	(0)	(11)	(0)	(0)	(0)
	papillary necrosis		2	0	0	0	5	0	0	0 *
			(20)	(0)	(0)	(0)	(56)	(0)	(0)	(0)
	mineralization:cortico-medullary junction		2	0	0	0	4	0	0	0
			(20)	(0)	(0)	(0)	(44)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				2500 ppm				5000 ppm				10000 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	mineralization:papilla		1	0	0	0	2	0	0	0	2	0	0	0	2	1	0	0
			(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(20)	(10)	(0)	(0)
{Reproductive system}																		
ovary			<10>				<10>				<10>				<10>			
	cyst		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Special sense organs/appendage}																		
Harder gl			<10>				<10>				<10>				<10>			
	lymphocytic infiltration		1	0	0	0	1	1	0	0	1	0	0	0	2	0	0	0
			(10)	(0)	(0)	(0)	(10)	(10)	(0)	(0)	(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)

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

Organ	Findings	Group Name	20000 ppm				40000 ppm			
		No. of Animals on Study	10				9			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}										
kidney			<10>				< 9>			
	mineralization:papilla		4	0	0	0	1	0	0	0
			(40)	(0)	(0)	(0)	(11)	(0)	(0)	(0)
{Reproductive system}										
ovary			<10>				< 9>			
	cyst		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Special sense organs/appendage}										
Harder gl			<10>				< 9>			
	lymphocytic infiltration		1	0	0	0	2	0	0	0
			(10)	(0)	(0)	(0)	(22)	(0)	(0)	(0)

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

APPENDIX L 4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : DEAD AND MORIBUND ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0426
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name	Control				2500 ppm				5000 ppm				10000 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
liver			< 0>				< 0>				< 0>				< 0>			
	herniation		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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

Organ	Findings	Group Name	20000 ppm				40000 ppm			
		No. of Animals on Study	0				1			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
liver			< 0>				< 1>			
	herniation		-	-	-	-	1	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 M 1

IDENTITY OF METHYL ACETOACETATE

IN THE 13-WEEK DRINKING WATER STUDY

IDENTITY OF METHYL ACETOACETATE IN THE 13-WEEK DRINKING WATER STUDY

Test Substance : Methyl Acetoacetate (Tokyo Kasei Kogyo Co., Ltd.)

Lot No. : GK01

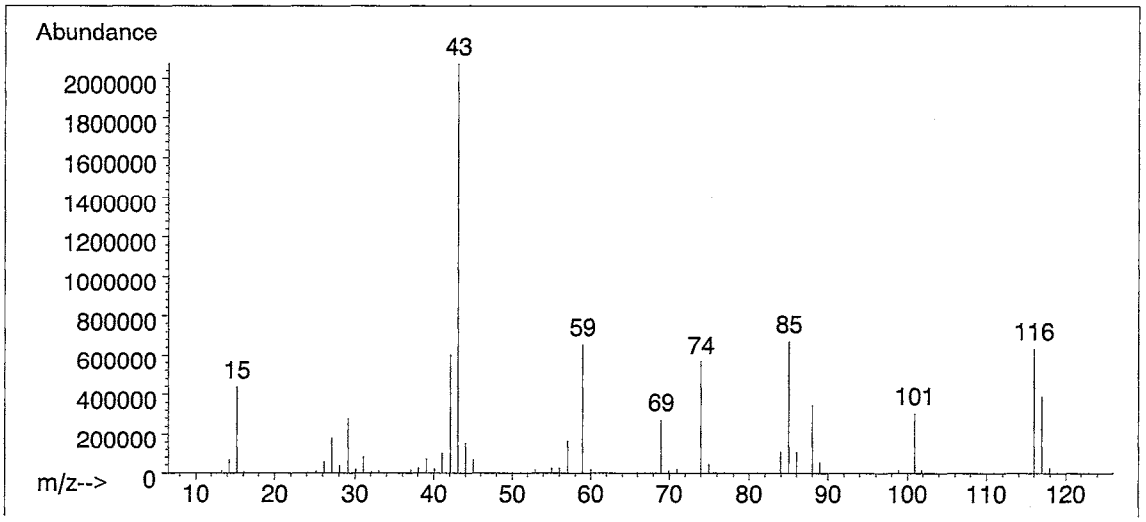
1. Spectral Data

Mass Spectrometry

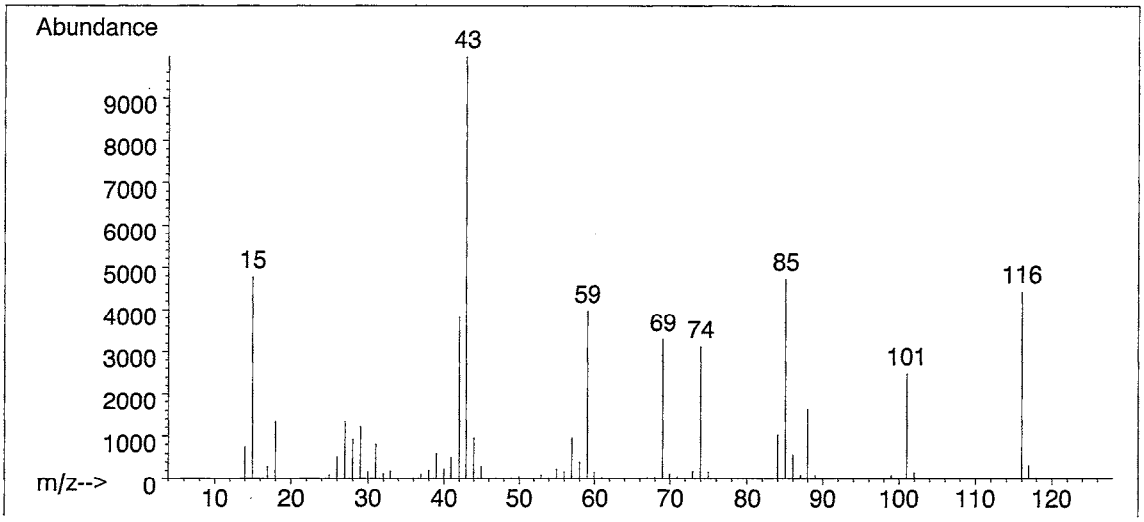
Instrument : Hewlett Packard 5989B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance



Mass Spectrum of Literature Data*

Results: The mass spectrum was consistent with literature spectrum.

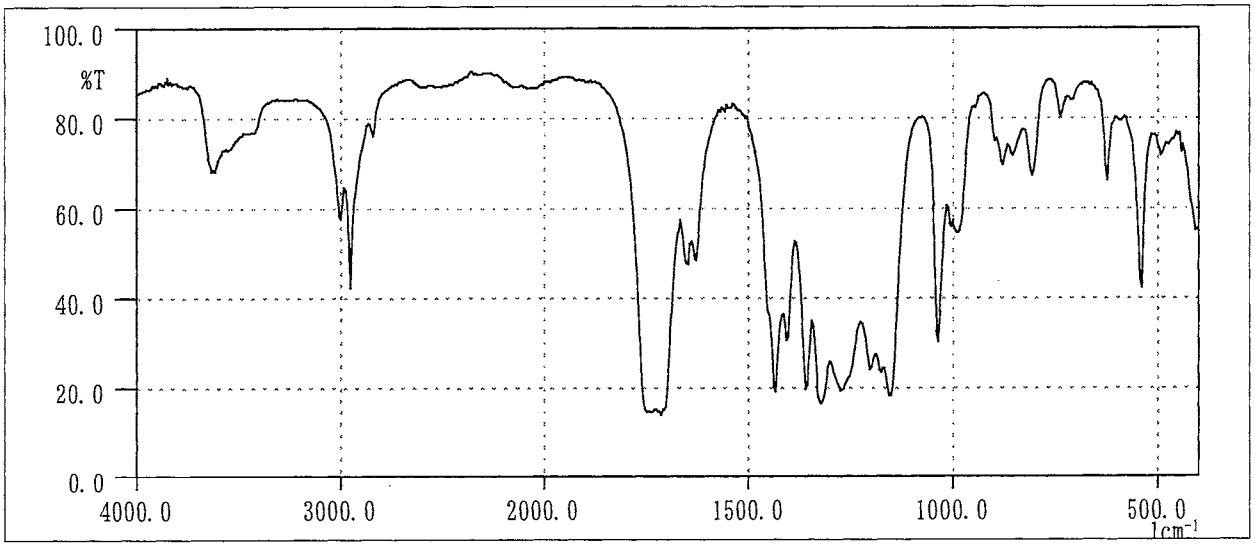
(*Fred W. McLafferty (1994) Wiley Registry of Mass Spectral Data, 6th edition. John Wiley and Sons, Inc. (U.S.), Entry Number 12752)

Infrared Spectrometry

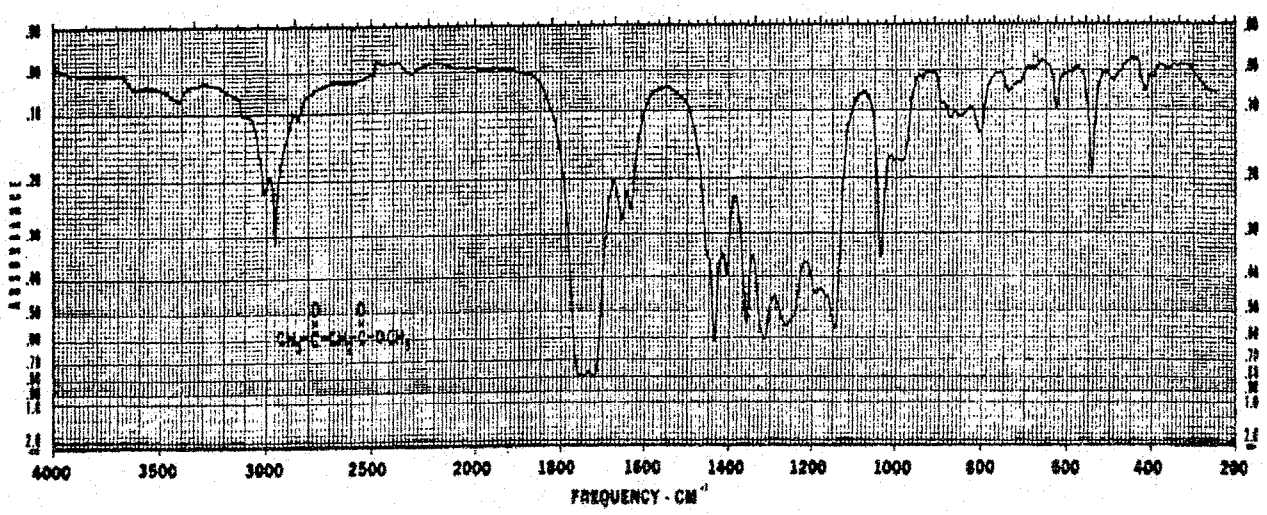
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 2 cm^{-1}



Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data*

Results: The infrared spectrum was consistent with literature spectrum.
(*William W. Simons (1978) The Sadtler Handbook of Infrared Spectra. Sadtler Research Laboratories, Inc. (U.K.), p.766)

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

APPENDIX M 2

STABILITY OF METHYL ACETOACETATE

IN THE 13-WEEK DRINKING WATER STUDY

STABILITY OF METHYL ACETOACETATE IN THE 13-WEEK DRINKING WATER STUDY

Test Substance : Methyl Acetoacetate (Tokyo Kasei Kogyo Co., Ltd.)

Lot No. : GK01

1. Sample : This lot was used from 2001.4.6 to 2000.7.10. Test substance was stored in a dark place at room temperature.

2. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : INNOWAX (0.2 mmϕ × 50 m)

Column Temperature : 100 °C (1 min) → (10 ℃/min) → 190 °C

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μL

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
2001.03.21	1	6.815	100
2001.07.24	1	6.811	100

Results: Gas chromatography indicated one major peak (peak No.1) analyzed at 2001.03.21 and one major peak (peak No.1) analyzed at 2001.07.24. No new trace impurity peak in the test substance analyzed at 2001.07.24 was detected.

3. Conclusions: The test substance was stable for about 4 months in a dark place at room temperature.

APPENDIX M 3

CONCENTRATION OF METHYL ACETOACETATE IN FORMULATED WATER IN THE 13-WEEK DRINKING WATER STUDY

CONCENTRATION OF METHYL ACETOACETATE IN FORMULATED WATER IN THE 13-WEEK DRINKING WATER STUDY

	Target Concentration				
Date Analyzed	2500[a]	5000	10000	20000	40000
2001.04.06	2490 (99.6)[b]	5010 (100)	9970 (99.7)	19800 (99.0)	37400 (93.5)

[a] ppm
[b] %

Analytical Method : The samples were analyzed by gas chromatography.

Instrument : Hewlett Packard 5890A Gas Chromatograph
Column : INNOWAX (0.2 mmϕ × 50 m)
Column Temperature : 100 °C (1 min) → (10 ℃/min) → 190 °C
Flow Rate : 1 mL/min
Detector : FID (Flame Ionization Detector)
Injection Volume : 1 µL

APPENDIX M 4

STABILITY OF METHYL ACETOACETATE IN FORMULATED WATER IN THE 13-WEEK DRINKING WATER STUDY

STABILITY OF METHYL ACETOACETATE IN FORMULATED WATER IN THE 13-WEEK DRINKING WATER STUDY

		Target Concentration	
Date Prepared	Date Analyzed	2500[a]	40000
2000.10.02	2000.10.02	2590 (100)[b]	39000 (100)
	2000.10.06[c]	2510 (96.9)	41200 (106)
	2000.10.12[c]	2540 (98.1)	40300 (103)

[a] ppm
[b] % (Percentage was based on the concentration on date of preparation.)
[c] Animal room samples

Analytical Method : The samples were analyzed by gas chromatography.

Instrument : Hewlett Packard 5890A Gas Chromatograph
Column : INNOWAX (0.2 mmϕ × 50 m)
Column Temperature : 100 °C (1 min) → (10 ℃/min) → 190 °C
Flow Rate : 1 mL/min
Detector : FID (Flame Ionization Detector)
Injection Volume : 1 μL

APPENDIX N 1

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS IN THE 13-WEEK DRINKING WATER STUDY OF METHYL ACETOACETATE

METHODS FOR HEMATOLOGY,BIOCHEMISTRY AND URINALYSIS IN THE 13-WEEK DRINKING WATER STUDY OF METHYL ACETOACETATE

Item	Method
Hematology	
Red blood cell (RBC)	Light scattering method [1]
Hemoglobin (Hgb)	Cyanmethemoglobin method [1]
Hematocrit (Hct)	Calculated as RBC×MCV/10 [1]
Mean corpuscular volume (MCV)	Light scattering method [1]
Mean corpuscular hemoglobin (MCH)	Calculated as Hgb/RBC×10 [1]
Mean corpuscular hemoglobin concentration (MCHC)	Calculated as Hgb/Hct×100 [1]
Platelet	Light scattering method [1]
Reticulocyte	Light scattering method [1]
Prothrombin time	Quick one stage method [2]
Activated partial thromboplastin time (APTT)	Ellagic acid activaterd method [2]
White blood cell (WBC)	Light scattering method [1]
Differential WBC	Pattern recognition method [3] (Wright staining)
Biochemistry	
Total protein (TP)	Biuret method [4]
Albumin (Alb)	BCG method [4]
A/G ratio	Calculated as Alb/(TP−Alb) [4]
T-bilirubin	Alkaline azobilirubin method [4]
Glucose	GlcK・G-6-PDH method [4]
T-cholesterol	CE・COD・POD method [4]
Triglyceride	LPL・GK・GPO・POD method [4]
Phospholipid	PLD・ChOD・POD method [4]
Glutamic oxaloacetic transaminase (GOT)	JSCC method [4]
Glutamic pyruvic transaminase (GPT)	JSCC method [4]
Lactate dehydrogenase (LDH)	SFBC method [4]
Alkaline phosphatase (ALP)	GSCC method [4]
γ-Glutamyl transpeptidase (γ-GTP)	L-γ-Glutamyl-p-nitroanilide method [4]
Creatine phosphokinase (CPK)	JSCC method [4]
Urea nitrogen	Urease・GLDH method [4]
Creatinine	Jaffe method [4]
Sodium	Ion selective electrode method [4]
Potassium	Ion selective electrode method [4]
Chloride	Ion selective electrode method [4]
Calcium	OCPC method [4]
Inorganic phosphorus	PNP・XOD・POD method [4]
Urinalysis	
pH,Protein,Glucose,Ketone body,Bilirubin,Occult Blood, Urobilinogen	Urinalysis reagent paper method [5]

1) Automatic blood cell analyzer (ADVIA120 : Bayer Corporation)

2) Automatic coagulometer (Sysmex CA-5000 : Sysmex Corporation)

3) Automatic blood cell differential analyzer (MICROX HEG-120NA : OMRON Corporation)

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

5) Ames reagent strips for urinalysis (Multistix : Bayer Corporation)

APPENDIX O 1

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK DRINKING WATER STUDY OF METHYL ACETOACETATE

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK DRINKING WATER STUDY OF METHYL ACETOACETATE

Item	Unit	Decimal place
Hematology		
Red blood cell (RBC)	$\times 10^6/\mu L$	2
Hemoglobin	g/dL	1
Hematocrit	%	1
Mean corpuscular volume (MCV)	fL	1
Mean corpuscular hemoglobin (MCH)	pg	1
Mean corpuscular hemoglobin concentration (MCHC)	g/dL	1
Platelet	$\times 10^3/\mu L$	0
Reticulocyte	%	1
Prothrombin time	sec	1
Activated partial thromboplastin time (APTT)	sec	1
White blood cell (WBC)	$\times 10^3/\mu L$	2
Differential WBC	%	0
Biochemistry		
Total protein	g/dL	1
Albumin	g/dL	1
A/G ratio	–	1
T-bilirubin	mg/dL	2
Glucose	mg/dL	0
T-cholesterol	mg/dL	0
Triglyceride	mg/dL	0
Phospholipid	mg/dL	0
Glutamic oxaloacetic transminase (GOT)	IU/L	0
Glutamic pyruvic transaminase (GPT)	IU/L	0
Lactate dehydrogenase (LDH)	IU/L	0
Alkaline phosphatase (ALP)	IU/L	0
γ-Glutamyl transpeptidase (γ-GTP)	IU/L	0
Creatine phosphokinase (CPK)	IU/L	0
Urea nitrogen	mg/dL	1
Creatinine	mg/dL	1
Sodium	mEq/L	0
Potassium	mEq/L	1
Chloride	mEq/L	0
Calcium	mg/dL	1
Inorganic phosphorus	mg/dL	1