アセト酢酸メチルのラットを用いた経口投与
による2週間毒性試験（混水試験）報告書

試験番号：　０４１９

APPENDIXES

APPENDIXES

APPENDIXES (CONTINUED)

APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 1-4	1-7	2-4	2-7
PILOERECTION	Control	0	0	0	0
	2500 ppm	0	0	0	0
	5000 ppm	0	0	0	0
	10000 ppm	0	0	0	0
	20000 ppm	0	0	0	0
	40000 ppm	2	2	4	0
SMALL STOOL	Control	0	0	0	0
	2500 ppm	0	0	0	0
	5000 ppm	0	0	0	0
	10000 ppm	0	0	0	0
	20000 ppm	4	0	0	0
	40000 ppm	5	5	5	0
OLIGO-STOOL	Control	0	0	0	0
	2500 ppm	0	0	0	0
	5000 ppm	0	0	0	0
	10000 ppm	0	0	0	0
	20000 ppm	0	0	0	0
	40000 ppm	5	1	0	0

APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

Clinical sign	Group Name	Administration Week-day 1-4	1-7	2-4	2-7
PILOERECTION	Control	0	0	0	0
	2500 ppm	0	0	0	0
	5000 ppm	0	0	0	0
	10000 ppm	0	0	0	0
	20000 ppm	0	0	0	0
	40000 ppm	4	3	3	0
SOILED PERI GENITALIA	Control	0	0	0	0
	2500 ppm	0	0	0	0
	5000 ppm	0	0	0	0
	10000 ppm	0	0	0	0
	20000 ppm	0	0	0	0
	40000 ppm	1	0	0	0
SMALL STOOL	Control	0	0	0	0
	2500 ppm	0	0	1	0
	5000 ppm	0	0	0	0
	10000 ppm	0	0	0	0
	20000 ppm	4	0	2	0
	40000 ppm	5	4	3	2
OLIGO-STOOL	Control	0	0	0	0
	2500 ppm	0	0	0	0
	5000 ppm	0	0	0	0
	10000 ppm	0	0	0	0
	20000 ppm	0	0	0	0
	40000 ppm	5	1	1	0

APPENDIX B 1

BODY WEIGHT CHANGES : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-4	1-7	2-4	2-7
Control	132± 4	152± 7	166± 7	186± 10	196± 10
2500 ppm	131± 5	148± 5	160± 7	178± 8	189± 7
5000 ppm	131± 4	146± 4	159± 6	178± 8	188± 8
10000 ppm	131± 5	146± 6	159± 7	175± 8	186± 8
20000 ppm	131± 5	136± 5**	153± 6*	169± 6*	181± 6*
40000 ppm	132± 4	110± 1**	120± 10**	143± 11**	157± 9**

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

APPENDIX B 2

BODY WEIGHT CHANGES : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-4	1-7	2-4	2-7
Control	99± 3	109± 2	116± 2	123± 2	128± 3
2500 ppm	99± 3	108± 5	113± 6	122± 4	127± 5
5000 ppm	99± 3	107± 4	113± 5	121± 5	126± 6
10000 ppm	99± 3	107± 3	112± 3	122± 3	127± 3
20000 ppm	99± 2	103± 2	109± 4	117± 5	121± 4
40000 ppm	99± 3	83± 7**	95± 10**	109± 6**	117± 8**

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

APPENDIX C 1

WATER CONSUMPTION CHANGES : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-4(4)	1-7(3)	2-4(4)	2-7(3)
Control	18.9± 1.5	19.4± 1.1	20.1± 1.5	19.8± 1.4
2500 ppm	15.6± 1.1**	15.3± 1.6	15.4± 1.4**	15.1± 1.1**
5000 ppm	15.1± 1.1**	15.5± 1.4	15.3± 1.2**	14.4± 0.7**
10000 ppm	13.7± 0.8**	14.2± 0.8*	14.7± 1.0**	14.2± 0.5**
20000 ppm	10.2± 1.4**	13.6± 0.5**	13.0± 0.4**	13.2± 0.4**
40000 ppm	3.1± 1.0**	9.3± 3.2**	12.6± 2.0**	12.6± 0.6**

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

APPENDIX C 2

WATER CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-4(4)	1-7(3)	2-4(4)	2-7(3)
Control	14.9± 0.6	15.9± 1.6	16.9± 1.4	16.7± 1.6
2500 ppm	12.4± 0.6	11.6± 0.9	12.3± 1.3**	12.2± 1.8
5000 ppm	11.5± 1.2	11.2± 1.2	10.6± 0.9**	10.7± 0.6
10000 ppm	10.6± 0.4*	10.5± 0.4*	11.1± 0.8**	10.2± 0.3**
20000 ppm	9.4± 0.4**	10.4± 0.7**	10.3± 0.6**	9.9± 0.9**
40000 ppm	3.6± 1.5**	10.1± 3.3*	11.0± 1.1**	9.7± 1.2**

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

APPENDIX D 1

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-4(4)	1-7(3)	2-4(4)	2-7(3)
Control	14.7± 1.2	15.9± 1.3	16.2± 1.5	16.6± 1.5
2500 ppm	13.9± 0.9	15.0± 1.1	14.8± 1.3	15.2± 0.7
5000 ppm	13.2± 0.8*	14.6± 1.2	14.9± 0.5	14.8± 0.6
10000 ppm	12.7± 0.8**	14.2± 0.6	14.4± 0.4	14.6± 0.4
20000 ppm	11.5± 0.7**	13.3± 0.4**	13.6± 0.8**	14.0± 0.4*
40000 ppm	7.1± 0.6**	7.9± 1.7**	12.5± 1.6**	13.6± 0.4**

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

APPENDIX D 2

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-4(4)	1-7(3)	2-4(4)	2-7(3)
Control	10.9± 0.2	11.5± 0.4	11.1± 0.2	11.5± 0.5
2500 ppm	10.7± 0.7	10.9± 0.7	10.9± 0.7	11.3± 0.7
5000 ppm	10.0± 0.8	10.5± 1.1	10.0± 0.8	10.4± 0.9
10000 ppm	9.9± 0.4	10.3± 0.3	10.5± 0.6	10.2± 0.4
20000 ppm	9.1± 0.2**	10.0± 0.2*	10.1± 0.7	9.8± 0.7*
40000 ppm	5.2± 1.2**	7.9± 2.0**	10.1± 0.9	10.1± 1.2*

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

APPENDIX E 1

CHEMICAL INTAKE CHANGES : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
UNIT : g／kg／d a y
REPORT TYPE : A1 2
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (Week-Day) 1-4	1-7	2-4	2-7
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
2500 ppm	0.263± 0.014	0.238± 0.020	0.217± 0.013	0.200± 0.012
5000 ppm	0.517± 0.029	0.486± 0.029	0.430± 0.019	0.382± 0.026
10000 ppm	0.939± 0.027	0.893± 0.035	0.839± 0.052	0.761± 0.031
20000 ppm	1.491± 0.161	1.779± 0.081	1.540± 0.064	1.454± 0.075
40000 ppm	1.107± 0.364	3.030± 0.818	3.520± 0.341	3.202± 0.199

APPENDIX E 2

CHEMICAL INTAKE CHANGES : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
UNIT : g／kg／d a y
REPORT TYPE : A1 2
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (Week-Day) 1-4	1-7	2-4	2-7
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
2500 ppm	0.288± 0.008	0.256± 0.012	0.252± 0.019	0.239± 0.028
5000 ppm	0.539± 0.040	0.493± 0.036	0.440± 0.024	0.426± 0.013
10000 ppm	0.991± 0.035	0.937± 0.020	0.906± 0.051	0.800± 0.015
20000 ppm	1.827± 0.118	1.913± 0.135	1.759± 0.100	1.635± 0.152
40000 ppm	1.714± 0.601	4.197± 1.176	4.041± 0.479	3.328± 0.294

APPENDIX F 1

HEMATOLOGY : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

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	5	7.97± 0.14	15.2± 0.4	44.1± 1.2	55.3± 0.8	19.0± 0.2	34.3± 0.3	948± 40
2500 ppm	5	7.99± 0.12	15.3± 0.3	43.9± 0.5	55.0± 0.2	19.1± 0.3	34.7± 0.6	907± 32
5000 ppm	5	8.01± 0.29	15.1± 0.3	44.0± 1.1	55.0± 0.8	18.9± 0.3	34.4± 0.3	919± 76
10000 ppm	5	7.99± 0.23	15.2± 0.4	43.9± 0.9	54.9± 0.4	19.1± 0.1	34.7± 0.3	886± 64
20000 ppm	5	7.89± 0.20	14.9± 0.3	43.2± 1.2	54.7± 0.5	18.9± 0.2	34.6± 0.6	876± 50
40000 ppm	5	7.79± 0.26	14.9± 0.4	42.8± 1.2	54.9± 0.3	19.1± 0.2	34.8± 0.3	809± 116

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

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	RETICULOCYTE ‰	PROTHROMBIN TIME sec	APTT sec
Control	5	32± 5	13.9± 0.2	21.4± 1.5
2500 ppm	5	27± 3	13.9± 0.4	21.1± 0.9
5000 ppm	5	35± 12	13.6± 0.1	18.3± 1.6
10000 ppm	5	31± 7	13.7± 0.4	19.5± 2.7
20000 ppm	5	26± 5	13.8± 0.5	19.0± 3.3
40000 ppm	5	37± 9	14.3± 0.4	21.3± 1.2

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

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHER
Control	5	3.36± 0.38	0± 0	18± 2	1± 1	0± 0	3± 1	78± 3	0± 1
2500 ppm	5	3.47± 0.41	0± 1	15± 2	1± 1	0± 0	3± 2	80± 2	0± 0
5000 ppm	5	3.63± 1.40	1± 1	18± 5	1± 1	0± 0	3± 1	77± 6	0± 0
10000 ppm	5	3.64± 0.35	0± 1	18± 2	1± 1	0± 0	3± 1	78± 3	0± 0
20000 ppm	5	3.87± 0.55	0± 0	20± 5	1± 1	0± 0	3± 1	76± 5	0± 0
40000 ppm	5	3.10± 1.11	1± 1	22± 4	1± 1	0± 0	3± 1	73± 5	0± 1

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

APPENDIX F 2

HEMATOLOGY : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

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	5	7.95± 0.50	15.3± 0.8	43.4± 1.6	54.6± 1.4	19.3± 0.3	35.3± 0.4	873± 120
2500 ppm	5	8.06± 0.21	15.7± 0.4	43.9± 1.3	54.5± 0.5	19.4± 0.3	35.7± 0.5	826± 44
5000 ppm	5	8.05± 0.21	15.5± 0.4	43.8± 1.3	54.4± 0.4	19.2± 0.3	35.3± 0.3	746± 84
10000 ppm	5	8.14± 0.27	15.8± 0.5	44.4± 1.4	54.5± 0.3	19.4± 0.3	35.6± 0.5	830± 58
20000 ppm	5	8.18± 0.09	15.7± 0.2	44.2± 0.5	54.1± 0.4	19.1± 0.2	35.4± 0.4	761± 38
40000 ppm	3	8.12± 0.12	15.5± 0.2	43.9± 0.5	54.2± 0.7	19.0± 0.2	35.2± 0.2	693± 105*

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

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	RETICULOCYTE ‰		PROTHROMBIN TIME sec		APTT sec	
Control	5	14±	4	14.0±	0.6	18.3±	2.3
2500 ppm	5	27±	5*	14.4±	0.3	19.4±	2.8
5000 ppm	5	20±	6	14.5±	0.4	19.3±	2.0
10000 ppm	5	23±	3	14.7±	0.2*	19.9±	1.6
20000 ppm	5	15±	6	14.9±	0.1**	20.7±	1.0
40000 ppm	3	21±	7	14.3±	0.3	20.8±	3.6

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

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHER
Control	5	2.75± 1.16	0± 0	20± 5	1± 1	0± 0	3± 2	76± 4	0± 0
2500 ppm	5	3.03± 1.00	1± 1	21± 4	2± 1	0± 0	3± 2	74± 4	0± 0
5000 ppm	5	2.58± 0.61	0± 0	19± 4	1± 0	0± 0	3± 1	78± 4	0± 1
10000 ppm	5	2.56± 0.87	0± 1	17± 3	1± 1	0± 0	4± 1	78± 3	0± 0
20000 ppm	5	3.50± 0.48	0± 1	18± 2	1± 1	0± 0	4± 2	77± 2	0± 0
40000 ppm	3	2.74± 1.37	0± 1	16± 7	1± 1	0± 0	5± 1	76± 5	1± 1

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

APPENDIX G 1

BIOCHEMISTRY : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

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	PHOSPHOLIPID mg/dℓ
Control	5	5.8± 0.2	3.6± 0.1	1.7± 0.1	0.13± 0.01	227± 20	66± 3	145± 6
2500 ppm	5	5.7± 0.1	3.6± 0.1	1.7± 0.1	0.14± 0.03	213± 10	66± 2	145± 9
5000 ppm	5	5.7± 0.1	3.6± 0.1	1.7± 0.1	0.14± 0.02	227± 23	64± 2	138± 7
10000 ppm	5	5.5± 0.2*	3.5± 0.1	1.7± 0.1	0.13± 0.01	216± 6	65± 2	139± 5
20000 ppm	5	5.5± 0.0**	3.4± 0.0**	1.7± 0.1	0.14± 0.02	212± 8	65± 3	142± 7
40000 ppm	5	5.3± 0.1**	3.4± 0.1**	1.7± 0.1	0.15± 0.02	201± 14	78± 6	165± 13**

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

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	GOT IU/ℓ		GPT IU/ℓ		LDH IU/ℓ		G-GTP IU/ℓ		CPK IU/ℓ		UREA NITROGEN mg/dℓ		CREATININE mg/dℓ	
Control	5	60±	9	32±	5	262±	56	1±	1	163±	27	18.3±	4.2	0.4±	0.1
2500 ppm	5	58±	3	30±	2	303±	105	1±	1	185±	40	18.7±	2.8	0.4±	0.1
5000 ppm	5	56±	4	30±	2	290±	76	1±	1	177±	40	18.9±	1.7	0.4±	0.1
10000 ppm	5	54±	3	27±	1	308±	117	1±	1	154±	35	18.6±	2.4	0.4±	0.0
20000 ppm	5	55±	5	28±	2	314±	143	1±	1	164±	70	16.8±	2.9	0.4±	0.1
40000 ppm	5	57±	2	29±	2	281±	73	1±	1	165±	33	17.5±	2.0	0.4±	0.1

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

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	SODIUM mEq／ℓ		POTASSIUM mEq／ℓ		CHLORIDE mEq／ℓ		CALCIUM mg／dℓ		INORGANIC PHOSPHORUS mg／dℓ	
Control	5	139±	1	3.7±	0.3	101±	1	10.6±	0.1	7.9±	0.8
2500 ppm	5	138±	1	3.9±	0.4	101±	2	10.7±	0.2	6.9±	0.9
5000 ppm	5	138±	2	4.0±	0.2	101±	1	10.5±	0.3	7.3±	1.2
10000 ppm	5	138±	1	3.8±	0.4	101±	1	10.6±	0.2	7.1±	1.1
20000 ppm	5	137±	1	4.2±	0.5	102±	1	10.3±	0.3	6.7±	1.2
40000 ppm	5	139±	2	4.5±	0.5*	102±	1	10.8±	0.2	6.5±	1.1

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

APPENDIX G 2

BIOCHEMISTRY : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

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	PHOSPHOLIPID mg/dl
Control	5	5.5± 0.1	3.5± 0.1	1.7± 0.1	0.15± 0.02	216± 8	72± 4	141± 7
2500 ppm	5	5.5± 0.2	3.4± 0.1	1.7± 0.1	0.14± 0.04	204± 14	73± 5	145± 8
5000 ppm	5	5.3± 0.1	3.3± 0.1	1.7± 0.1	0.13± 0.01	208± 9	74± 4	140± 5
10000 ppm	5	5.3± 0.2	3.4± 0.1	1.7± 0.0	0.13± 0.01	204± 8	72± 2	145± 6
20000 ppm	5	5.3± 0.1	3.3± 0.1	1.6± 0.1	0.14± 0.01	200± 3	74± 2	148± 6
40000 ppm	4	5.3± 0.2	3.3± 0.2	1.7± 0.1	0.16± 0.03	206± 4	82± 3**	166± 5**

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

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	GOT IU/ℓ	GPT IU/ℓ	LDH IU/ℓ	G-GTP IU/ℓ	CPK IU/ℓ	UREA NITROGEN mg/dℓ	CREATININE mg/dℓ
Control	5	57± 3	26± 1	410± 125	1± 1	225± 109	17.6± 3.4	0.4± 0.0
2500 ppm	5	65± 12	30± 5	430± 241	2± 1	240± 127	18.8± 0.7	0.4± 0.0
5000 ppm	5	58± 4	27± 2	397± 215	2± 1	178± 54	18.7± 2.0	0.4± 0.0
10000 ppm	5	58± 2	27± 1	336± 87	1± 1	165± 40	19.3± 2.2	0.4± 0.1
20000 ppm	5	61± 3	27± 2	443± 169	1± 1	217± 70	19.2± 1.9	0.4± 0.0
40000 ppm	4	62± 2	30± 2	385± 69	1± 1	197± 25	20.2± 2.0	0.4± 0.1

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

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	SODIUM mEq／ℓ		POTASSIUM mEq／ℓ		CHLORIDE mEq／ℓ		CALCIUM mg／dℓ		INORGANIC PHOSPHORUS mg／dℓ	
Control	5	137±	1	3.7±	0.3	104±	1	10.0±	0.2	6.9±	1.2
2500 ppm	5	136±	2	4.0±	0.4	103±	2	10.0±	0.2	6.4±	1.5
5000 ppm	5	136±	1	4.0±	0.6	104±	1	9.9±	0.3	6.1±	0.7
10000 ppm	5	137±	1	3.9±	0.2	103±	1	10.0±	0.2	6.0±	1.1
20000 ppm	5	137±	1	4.0±	0.4	104±	1	9.9±	0.2	6.1±	1.0
40000 ppm	4	137±	1	3.8±	0.0	103±	1	10.1±	0.2	5.8±	1.4

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

APPENDIX H 1

GROSS FINDINGS : SUMMARY, RAT : MALE : ALL ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
ALL ANIMALS (0- 2W)

Organ	Findings	Group Name NO. of Animals	Control 5 (%)	2500 ppm 5 (%)	5000 ppm 5 (%)	10000 ppm 5 (%)
liver	herniation		0 (0)	0 (0)	0 (0)	1 (20)

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
ALL ANIMALS (0- 2W)

Organ	Findings	Group Name NO. of Animals	20000 ppm 5 (%)	40000 ppm 5 (%)
liver	herniation		1 (20)	1 (20)

APPENDIX H 2

GROSS FINDINGS : SUMMARY, RAT : FEMALE : ALL ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
ALL ANIMALS (0- 2W)

Organ	Findings	Group Name / NO. of Animals	Control 5 (%)	2500 ppm 5 (%)	5000 ppm 5 (%)	10000 ppm 5 (%)
liver	herniation		1 (20)	0 (0)	0 (0)	1 (20)

Organ	Findings	Group Name	20000 ppm	40000 ppm
		NO. of Animals	5 (%)	5 (%)
liver	herniation		0 (0)	0 (0)

APPENDIX I 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	5	196± 10	0.355± 0.038	0.041± 0.002	2.445± 0.149	0.696± 0.066	0.809± 0.050
2500 ppm	5	189± 7	0.340± 0.022	0.042± 0.005	2.329± 0.161	0.657± 0.042	0.801± 0.024
5000 ppm	5	188± 8	0.338± 0.027	0.043± 0.003	2.434± 0.133	0.693± 0.024	0.797± 0.031
10000 ppm	5	186± 8	0.352± 0.036	0.045± 0.002	2.367± 0.131	0.667± 0.057	0.829± 0.081
20000 ppm	5	181± 6*	0.315± 0.030	0.038± 0.003	2.345± 0.143	0.625± 0.019	0.759± 0.028
40000 ppm	5	157± 9**	0.301± 0.051	0.042± 0.004	2.265± 0.068	0.569± 0.052**	0.697± 0.041**

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

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	1.427± 0.095	0.445± 0.020	7.868± 0.472	1.756± 0.022
2500 ppm	5	1.443± 0.074	0.439± 0.020	7.474± 0.369	1.731± 0.025
5000 ppm	5	1.450± 0.083	0.432± 0.025	7.209± 0.331*	1.746± 0.018
10000 ppm	5	1.423± 0.066	0.436± 0.024	7.098± 0.346*	1.717± 0.046
20000 ppm	5	1.411± 0.042	0.424± 0.013	6.722± 0.301**	1.713± 0.047
40000 ppm	5	1.322± 0.084	0.370± 0.021**	6.138± 0.379**	1.677± 0.063

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

APPENDIX I 2

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	5	128± 3	0.292± 0.023	0.047± 0.003	0.089± 0.006	0.492± 0.031	0.646± 0.026
2500 ppm	5	127± 5	0.281± 0.022	0.046± 0.004	0.085± 0.011	0.512± 0.061	0.666± 0.064
5000 ppm	5	126± 6	0.286± 0.027	0.044± 0.004	0.072± 0.008	0.488± 0.028	0.639± 0.028
10000 ppm	5	127± 3	0.292± 0.017	0.045± 0.002	0.073± 0.008	0.484± 0.030	0.633± 0.049
20000 ppm	5	121± 4	0.274± 0.013	0.044± 0.004	0.079± 0.018	0.475± 0.010	0.636± 0.010
40000 ppm	5	117± 8**	0.277± 0.039	0.043± 0.006	0.059± 0.010**	0.453± 0.032	0.579± 0.018

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

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	0.986± 0.053	0.320± 0.010	4.776± 0.231	1.618± 0.048
2500 ppm	5	1.046± 0.057	0.356± 0.057	4.711± 0.331	1.625± 0.026
5000 ppm	5	1.015± 0.050	0.318± 0.026	4.475± 0.261	1.629± 0.031
10000 ppm	5	1.048± 0.017	0.323± 0.019	4.541± 0.281	1.626± 0.046
20000 ppm	5	1.052± 0.035	0.303± 0.013	4.384± 0.228	1.598± 0.021
40000 ppm	5	1.023± 0.020	0.288± 0.022	4.349± 0.327	1.568± 0.046

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

APPENDIX J 1

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	5	196± 10	0.180± 0.010	0.021± 0.002	1.246± 0.075	0.354± 0.025	0.412± 0.022
2500 ppm	5	189± 7	0.180± 0.008	0.022± 0.003	1.234± 0.093	0.348± 0.019	0.424± 0.011
5000 ppm	5	188± 8	0.179± 0.008	0.023± 0.002	1.294± 0.091	0.368± 0.018	0.424± 0.027
10000 ppm	5	186± 8	0.189± 0.013	0.024± 0.001	1.270± 0.056	0.357± 0.019	0.444± 0.030
20000 ppm	5	181± 6*	0.174± 0.014	0.021± 0.002	1.294± 0.051	0.345± 0.010	0.419± 0.009
40000 ppm	5	157± 9**	0.190± 0.023	0.027± 0.003**	1.444± 0.091**	0.362± 0.026	0.444± 0.027

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

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	0.727± 0.021	0.227± 0.006	4.006± 0.109	0.896± 0.047
2500 ppm	5	0.763± 0.017	0.232± 0.009	3.954± 0.104	0.917± 0.031
5000 ppm	5	0.769± 0.020	0.230± 0.007	3.827± 0.088	0.928± 0.039
10000 ppm	5	0.763± 0.022	0.234± 0.006	3.808± 0.111	0.922± 0.017
20000 ppm	5	0.779± 0.026*	0.234± 0.009	3.710± 0.129**	0.946± 0.012*
40000 ppm	5	0.842± 0.043**	0.236± 0.007	3.906± 0.148	1.070± 0.080**

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

APPENDIX J 2

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	5	128± 3	0.228± 0.019	0.037± 0.002	0.069± 0.005	0.384± 0.025	0.504± 0.024
2500 ppm	5	127± 5	0.221± 0.016	0.036± 0.002	0.066± 0.008	0.402± 0.034	0.524± 0.040
5000 ppm	5	126± 6	0.227± 0.015	0.035± 0.003	0.057± 0.005	0.388± 0.018	0.508± 0.015
10000 ppm	5	127± 3	0.230± 0.015	0.035± 0.002	0.058± 0.006	0.381± 0.023	0.498± 0.034
20000 ppm	5	121± 4	0.226± 0.012	0.036± 0.003	0.065± 0.014	0.392± 0.007	0.526± 0.027
40000 ppm	5	117± 8**	0.237± 0.024	0.037± 0.003	0.051± 0.009**	0.388± 0.014	0.498± 0.035

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

STUDY NO. : 0419
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	0.768± 0.036	0.249± 0.008	3.721± 0.188	1.260± 0.043
2500 ppm	5	0.823± 0.025*	0.280± 0.044	3.706± 0.135	1.280± 0.033
5000 ppm	5	0.806± 0.011	0.252± 0.014	3.551± 0.118	1.295± 0.057
10000 ppm	5	0.825± 0.014*	0.255± 0.011	3.574± 0.162	1.281± 0.031
20000 ppm	5	0.869± 0.040**	0.250± 0.008	3.616± 0.090	1.320± 0.065
40000 ppm	5	0.880± 0.057**	0.247± 0.008	3.729± 0.111	1.351± 0.120

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

APPENDIX K 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : ALL ANIMALS

(2-WEEK STUDY)

Organ	Findings	Group Name	Control				2500 ppm				5000 ppm				10000 ppm			
		No. of Animals on Study	5				5				5				5			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
liver			< 5>				< 5>				< 5>				< 5>			
	herniation		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
{Urinary system}																		
kidney			< 5>				< 5>				< 5>				< 5>			
	eosinophilic body		2	0	0	0	2	0	0	0	1	0	0	0	2	0	0	0
			(40)	(0)	(0)	(0)	(40)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(40)	(0)	(0)	(0)
{Endocrine system}																		
pituitary			< 5>				< 5>				< 5>				< 5>			
	Rathke pouch		0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(40)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thyroid			< 5>				< 5>				< 5>				< 5>			
	ultimobranchial body remanet		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
{Reproductive system}																		
prostate			< 5>				< 5>				< 5>				< 5>			
	lymphocytic infiltration		2	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(40)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(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

Organ	Findings	Group Name	20000 ppm				40000 ppm			
		No. of Animals on Study	5				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
liver			< 5>				< 5>			
	herniation		1	0	0	0	1	0	0	0
			(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
{Urinary system}										
kidney			< 5>				< 5>			
	eosinophilic body		1	0	0	0	1	0	0	0
			(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
{Endocrine system}										
pituitary			< 5>				< 5>			
	Rathke pouch		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thyroid			< 5>				< 5>			
	ultimobranchial body remanet		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(40)	(0)	(0)	(0)
{Reproductive system}										
prostate			< 5>				< 5>			
	lymphocytic infiltration		4	0	0	0	2	0	0	0
			(80)	(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

APPENDIX K 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : ALL ANIMALS

(2-WEEK STUDY)

Organ	Findings	Group Name	Control				2500 ppm				5000 ppm				10000 ppm			
		No. of Animals on Study	5				5				5				5			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}																		
lung			< 5>				< 5>				< 5>				< 5>			
	osseous metaplasia		1	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)	(0)	(0)	(0)	(0)
	focal hyperplasia		0	0	0	0	1	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)
{Hematopoietic system}																		
lymph node			< 5>				< 5>				< 5>				< 5>			
	hemorrhage		1	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)	(0)	(0)	(0)	(0)
{Digestive system}																		
liver			< 5>				< 5>				< 5>				< 5>			
	herniation		1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	granulation		0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(20)	(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

Organ	Findings	Group Name	20000 ppm				40000 ppm			
		No. of Animals on Study	5				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
lung			< 5>				< 5>			
	osseous metaplasia		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	focal hyperplasia		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}										
lymph node			< 5>				< 5>			
	hemorrhage		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}										
liver			< 5>				< 5>			
	herniation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	granulation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				2500 ppm				5000 ppm				10000 ppm			
		No. of Animals on Study	5				5				5				5			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}																		
kidney			< 5>				< 5>				< 5>				< 5>			
	mineralization:cortico-medullary junction		2	0	0	0	2	0	0	0	1	0	0	0	1	0	0	0
			(40)	(0)	(0)	(0)	(40)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
{Endocrine system}																		
pituitary			< 5>				< 5>				< 5>				< 5>			
	Rathke pouch		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thyroid			< 5>				< 5>				< 5>				< 5>			
	ultimobranchial body remanet		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(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

Organ	Findings	Group Name	20000 ppm				40000 ppm			
		No. of Animals on Study	5				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}										
kidney			< 5>				< 5>			
	mineralization:cortico-medullary junction		1	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Endocrine system}										
pituitary			< 5>				< 5>			
	Rathke pouch		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thyroid			< 5>				< 5>			
	ultimobranchial body remanet		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

APPENDIX L 1

IDENTITY OF METHYL ACETOACETATE

IN THE 2-WEEK DRINKING WATER STUDY

IDENTITY OF METHYL ACETOACETATE IN THE 2-WEEK DRINKING WATER STUDY

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

Lot No. : GI01

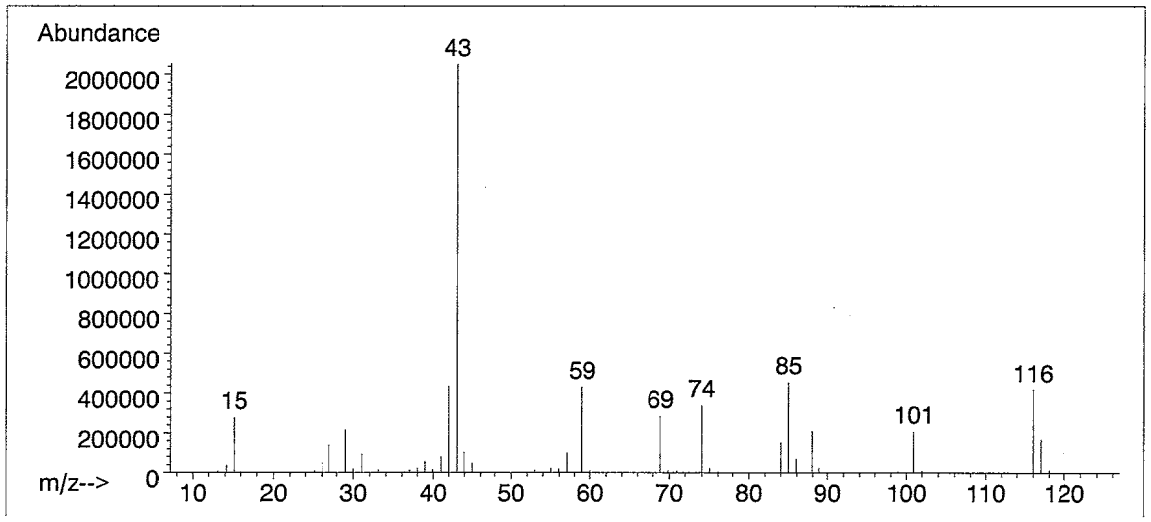
1. Spectral Data

Mass Spectrometry

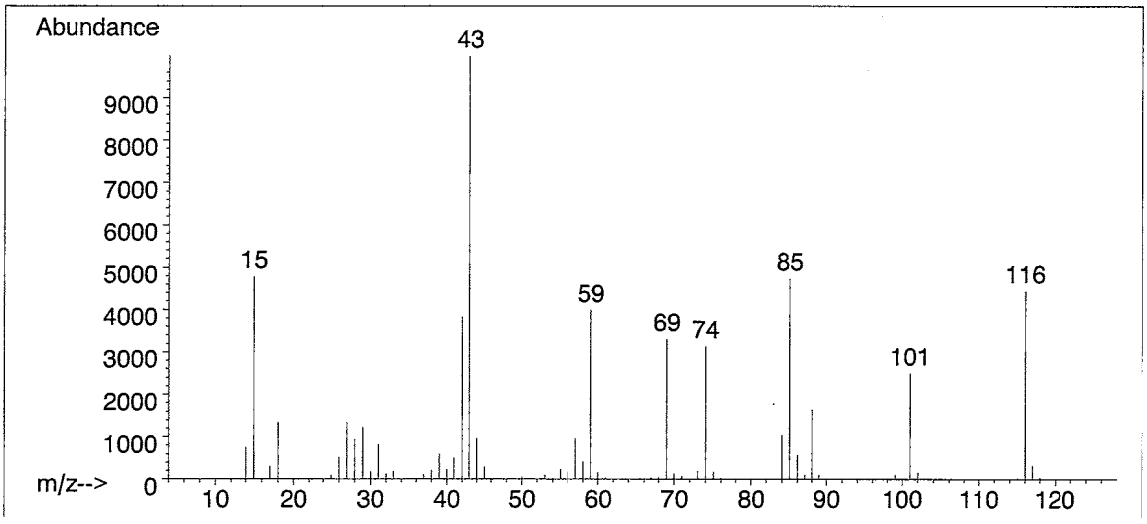
Instrument : Hewlett Packard 5989B Mass Spectrometer

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.

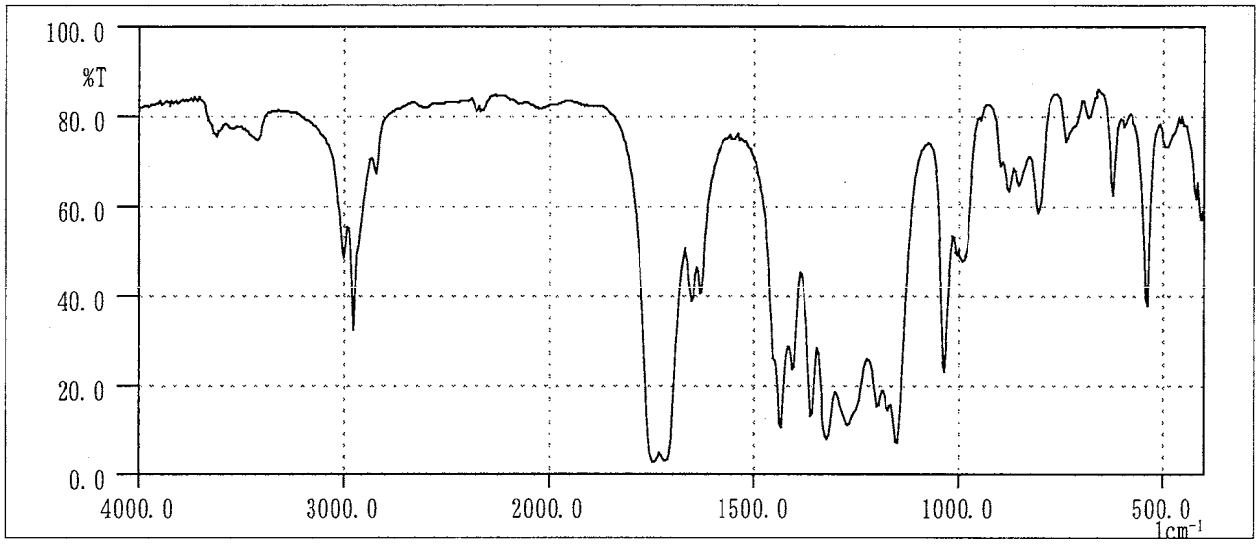
(*Fred W. McLafferty (1994) Wiley Registry of Mass Spectral Data, 6th edition. John Wiley and Sons, Inc. (U.S.), Entry Number 12752)

Infrared Spectrometry

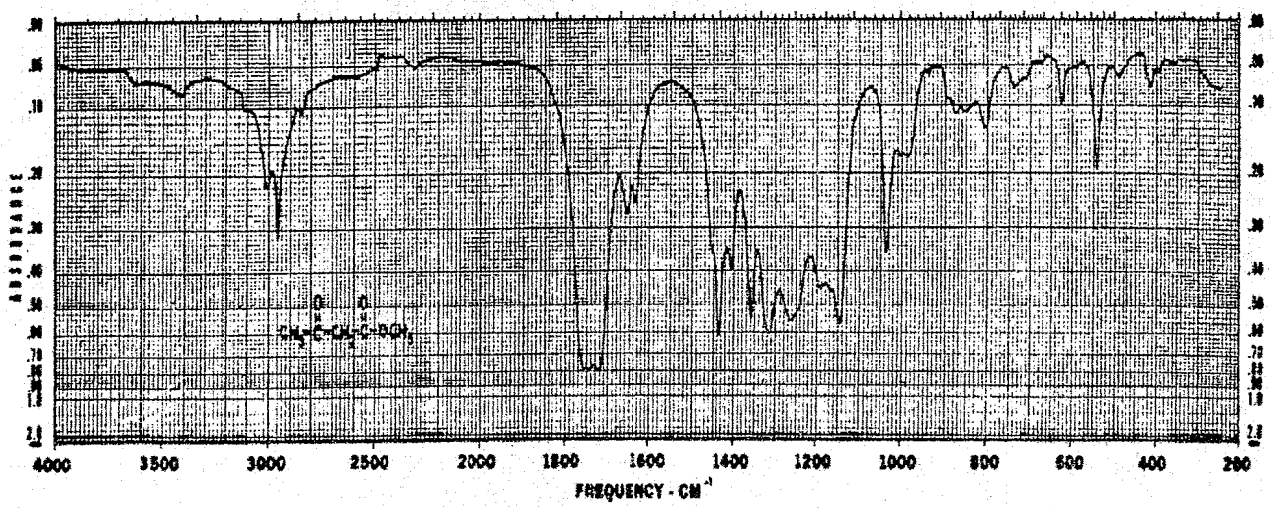
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

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 L 2

STABILITY OF METHYL ACETOACETATE

IN THE 2-WEEK DRINKING WATER STUDY

STABILITY OF METHYL ACETOACETATE IN THE 2-WEEK DRINKING WATER STUDY

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

Lot No. : GI01

1. Sample : This lot was used from 2000.10.27 to 2000.11.10. 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 (%)
2000.10.04	1	6.853	100
2000.11.22	1	6.819	100

Results: Gas chromatography indicated one major peak (peak No.1) analyzed at 2000.10.4 and one major peak (peak No.1) analyzed at 2000.11.22. No new trace impurity peak in the test substance analyzed at 2000.11.22 was detected.

3. Conclusions: The test substance was stable for about 7 weeks in a dark place at room temperature.

APPENDIX L 3

CONCENTRATION OF METHYL ACETOACETATE IN FORMULATED WATER IN THE 2-WEEK DRINKING WATER STUDY

CONCENTRATION OF METHYL ACETOACETATE IN FORMULATED WATER IN THE 2-WEEK DRINKING WATER STUDY

	Target Concentration				
Date Analyzed	2500[a]	5000	10000	20000	40000
2000.10.27	2520 (101)[b]	5050 (101)	10000 (100)	18800 (94.0)	39700 (99.3)

[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 L 4

STABILITY OF METHYL ACETOACETATE IN FORMULATED WATER IN THE 2-WEEK DRINKING WATER STUDY

STABILITY OF METHYL ACETOACETATE IN FORMULATED WATER IN THE 2-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 M 1

METHODS FOR HEMATOLOGY AND BIOCHEMISTRY

IN THE 2-WEEK DRINKING WATER STUDY OF METHYL ACETOACETATE

METHODS FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-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	Pattern recognition method [3] (New methyleneblue staining)
Prothrombin time	Quick one stage method [2]
Activated partial thromboplastin time (APTT)	Ellagic acid activaterd method [2]
White blood cell (WBC)	Light scattering method [1]
Differential WBC	Pattern recognition method [3] (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]
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]
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]

1) Automatic blood cell analyzer (Technicon H·1 : 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.)

APPENDIX N 1

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK DRINKING WATER STUDY OF METHYL ACETOACETATE

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY
IN THE 2-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
Phospholipid	mg/dL	0
Glutamic oxaloacetic transminase (GOT)	IU/L	0
Glutamic pyruvic transaminase (GPT)	IU/L	0
Lactate dehydrogenase (LDH)	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