アセト酢酸メチルのマウス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：　０４２７

APPENDIXES

APPENDIXES

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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
INTERNAL MASS	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	1	1	1	1
	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	0	0	0	0	0	0	0	0	0	0	0	0	0

APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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
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	1
	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	0	0	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	1
	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	0	0	0	0	0	0	0	0	0	0	0	0	0

APPENDIX B 1

BODY WEIGHT CHANGES : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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	22.9± 0.7	24.0± 0.9	25.0± 1.0	25.9± 1.0	27.3± 1.1	27.8± 1.6	28.9± 1.7
2500 ppm	22.9± 0.7	23.9± 0.4	25.1± 0.7	26.1± 0.6	27.3± 0.7	27.3± 1.0	28.6± 0.8
5000 ppm	22.9± 0.7	24.0± 0.8	25.0± 0.9	25.5± 0.9	26.8± 1.3	27.4± 1.4	28.1± 1.7
10000 ppm	22.9± 0.6	24.0± 0.8	24.9± 0.7	25.7± 0.8	26.9± 0.7	27.4± 1.1	28.6± 1.1
20000 ppm	22.9± 0.6	23.4± 0.7	24.7± 0.5	25.7± 0.6	26.9± 0.8	27.4± 1.0	28.6± 1.1
40000 ppm	22.9± 0.7	24.0± 0.8	25.4± 0.8	25.9± 0.7	27.2± 1.0	27.4± 1.1	28.4± 1.5

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

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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	29.4± 1.7	30.7± 2.2	31.5± 2.3	32.3± 2.5	33.1± 2.6	33.8± 2.7	34.1± 2.7
2500 ppm	29.3± 1.1	30.2± 1.5	31.1± 1.6	32.2± 1.7	32.9± 1.8	33.5± 2.0	33.8± 2.1
5000 ppm	29.2± 1.7	30.1± 2.0	30.7± 2.1	31.9± 2.3	32.7± 2.4	33.4± 2.6	33.7± 2.6
10000 ppm	29.2± 1.3	30.4± 1.5	31.2± 1.5	32.5± 1.8	33.2± 1.8	33.8± 2.0	34.1± 2.0
20000 ppm	29.2± 1.3	30.3± 1.6	31.1± 1.7	32.4± 1.8	32.9± 2.1	33.9± 2.2	34.0± 2.1
40000 ppm	29.2± 1.1	30.0± 1.1	30.4± 1.2	31.6± 1.2	32.3± 1.6	33.3± 1.6	33.3± 1.7

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

APPENDIX B 2

BODY WEIGHT CHANGES : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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	18.8± 0.7	19.4± 1.0	19.9± 0.8	20.6± 0.7	20.9± 0.9	21.5± 0.6	21.9± 0.6
2500 ppm	18.8± 0.7	19.3± 0.6	20.3± 0.6	20.5± 0.7	21.0± 0.8	21.7± 0.6	22.3± 0.4
5000 ppm	18.8± 0.7	19.4± 1.2	20.2± 1.2	20.8± 1.3	21.4± 1.1	21.4± 1.3	21.9± 1.3
10000 ppm	18.8± 0.7	18.8± 1.0	19.8± 0.8	20.3± 0.9	20.7± 1.0	21.0± 1.4	21.5± 1.2
20000 ppm	18.8± 0.7	19.2± 1.0	20.2± 1.1	20.2± 1.0	21.3± 1.1	21.4± 1.1	22.3± 1.1
40000 ppm	18.8± 0.7	19.3± 0.9	20.1± 0.9	20.7± 0.8	21.4± 1.0	21.8± 1.2	22.2± 1.3

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

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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	22.5± 0.7	22.9± 0.7	23.5± 1.0	23.8± 1.1	24.0± 1.5	24.5± 1.2	24.8± 1.5
2500 ppm	22.7± 0.6	23.1± 0.8	23.5± 1.0	24.0± 1.0	24.0± 1.2	24.3± 1.6	24.9± 1.4
5000 ppm	22.6± 1.4	22.4± 1.1	23.4± 1.8	23.3± 1.4	24.1± 1.8	24.2± 1.4	24.1± 2.9
10000 ppm	21.7± 1.2	22.3± 1.3	22.7± 1.6	23.2± 1.7	23.4± 1.5	24.0± 2.2	23.5± 1.5
20000 ppm	22.3± 1.4	23.5± 1.4	23.7± 1.2	23.6± 1.2	24.2± 1.3	24.5± 1.4	24.5± 1.7
40000 ppm	22.6± 1.5	23.2± 1.3	23.5± 1.6	24.2± 1.6	23.9± 1.7	24.9± 2.2	24.5± 1.9

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

APPENDIX C 1

WATER CONSUMPTION CHANGES : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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	4.4± 0.7	4.3± 0.7	4.1± 0.6	4.0± 0.6	3.9± 0.4	3.9± 0.4	3.7± 0.4
2500 ppm	5.1± 1.4	4.9± 1.1	4.7± 1.1	4.3± 0.7	4.3± 0.8	4.3± 0.7	4.1± 0.7
5000 ppm	4.6± 0.8	4.7± 1.3	4.4± 1.2	4.1± 0.8	4.1± 0.7	4.0± 0.6	4.2± 1.3
10000 ppm	4.1± 0.4	4.1± 0.4	4.0± 0.7	4.0± 0.8	3.9± 0.7	3.9± 0.5	3.7± 0.5
20000 ppm	5.0± 1.2	4.9± 1.3	4.6± 1.2	4.3± 1.0	4.3± 0.8	4.2± 0.8	3.8± 0.6
40000 ppm	4.4± 0.8	4.7± 0.9	4.6± 0.8	4.6± 1.1	4.4± 0.8	4.3± 0.7	4.1± 0.8

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

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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	3.7± 0.4	3.6± 0.6	3.5± 0.5	3.5± 0.4	3.5± 0.4	3.7± 0.5
2500 ppm	4.2± 0.7	4.1± 0.7	4.0± 0.6	3.8± 0.5	3.8± 0.5	4.0± 0.6
5000 ppm	3.9± 0.6	4.0± 0.7	3.6± 0.4	4.0± 1.1	3.9± 1.1	3.9± 0.5
10000 ppm	3.9± 0.6	3.7± 0.5	3.6± 0.4	3.8± 0.5	3.6± 0.5	3.8± 0.4
20000 ppm	3.8± 0.5	4.0± 1.2	3.8± 1.0	3.8± 1.0	3.8± 1.0	3.9± 0.8
40000 ppm	4.1± 0.7	4.0± 0.7	4.1± 0.8	4.0± 0.7	4.0± 0.7	4.0± 0.7

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

APPENDIX C 2

WATER CONSUMPTION CHANGES : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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	4.5± 0.4	4.8± 0.4	4.4± 0.7	4.2± 0.6	4.0± 0.4	4.1± 0.4	4.0± 0.3
2500 ppm	4.2± 0.2	4.4± 0.3	4.2± 0.3	4.2± 0.3	4.1± 0.2	4.2± 0.4	4.0± 0.2
5000 ppm	4.4± 0.3	4.5± 0.3	4.3± 0.3	4.3± 0.3	4.1± 0.3	4.3± 0.3	4.3± 0.3
10000 ppm	3.9± 0.3**	4.1± 0.4**	3.9± 0.3	4.0± 0.5	4.0± 0.4	4.2± 0.5	4.0± 0.4
20000 ppm	3.7± 0.7**	4.0± 0.7**	3.9± 0.6	4.0± 0.5	4.0± 0.4	4.1± 0.4	4.0± 0.4
40000 ppm	3.8± 0.4**	4.1± 0.5**	4.0± 0.5	3.8± 0.5	3.9± 0.5	3.9± 0.6	3.7± 0.6

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

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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	4.2± 0.3	4.2± 0.3	4.2± 0.4	4.3± 0.3	4.4± 0.5	4.3± 0.4
2500 ppm	4.2± 0.3	4.2± 0.3	4.3± 0.3	4.2± 0.2	4.3± 0.4	4.3± 0.3
5000 ppm	4.4± 0.4	4.5± 0.4	4.2± 0.3	4.5± 0.3	4.3± 0.3	4.0± 1.3
10000 ppm	4.1± 0.4	4.1± 0.3	4.1± 0.3	4.1± 0.3	4.1± 0.3	4.1± 0.4
20000 ppm	4.2± 0.4	4.1± 0.3	4.0± 0.3	4.0± 0.4	3.9± 0.3*	4.0± 0.3
40000 ppm	3.8± 0.6	3.9± 0.6	3.9± 0.5	3.6± 0.5**	3.6± 0.4**	3.9± 0.8

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

APPENDIX D 1

FOOD CONSUMPTION CHANGES : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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	3.9± 0.2	4.0± 0.2	4.0± 0.2	4.0± 0.2	4.0± 0.3	4.0± 0.2	4.0± 0.3
2500 ppm	4.0± 0.2	3.9± 0.4	3.9± 0.2	3.9± 0.2	3.9± 0.2	3.9± 0.2	4.0± 0.3
5000 ppm	3.9± 0.2	3.8± 0.3	3.8± 0.3	4.0± 0.4	3.9± 0.4	3.9± 0.3	4.0± 0.4
10000 ppm	3.8± 0.2	3.8± 0.1	3.8± 0.2	3.9± 0.2	3.9± 0.3	3.9± 0.3	3.9± 0.2
20000 ppm	3.9± 0.2	4.0± 0.2	3.9± 0.2	4.0± 0.2	4.0± 0.2	4.1± 0.3	4.0± 0.2
40000 ppm	3.9± 0.2	3.9± 0.1	3.7± 0.2	3.9± 0.2	3.9± 0.2	4.0± 0.2	3.9± 0.2

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

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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	4.1± 0.4	4.1± 0.3	4.0± 0.4	4.2± 0.3	4.1± 0.3	4.2± 0.3
2500 ppm	4.0± 0.3	4.1± 0.3	4.1± 0.3	4.1± 0.2	4.0± 0.3	4.1± 0.3
5000 ppm	4.0± 0.3	4.0± 0.3	4.0± 0.4	4.1± 0.3	4.0± 0.3	4.0± 0.2
10000 ppm	4.0± 0.1	4.0± 0.1	4.0± 0.2	4.2± 0.1	4.0± 0.1	4.1± 0.1
20000 ppm	4.1± 0.3	4.1± 0.3	4.1± 0.4	4.1± 0.2	5.0± 0.3**	4.1± 0.3
40000 ppm	3.9± 0.2	3.9± 0.2	4.0± 0.2	4.0± 0.2	4.9± 0.2**	3.9± 0.3

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

APPENDIX D 2

FOOD CONSUMPTION CHANGES : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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	3.4± 0.2	3.3± 0.1	3.4± 0.3	3.5± 0.2	3.5± 0.3	3.6± 0.2	3.6± 0.1
2500 ppm	3.4± 0.1	3.5± 0.1	3.5± 0.2	3.5± 0.1	3.7± 0.2	3.7± 0.2	3.7± 0.2
5000 ppm	3.5± 0.3	3.4± 0.3	3.6± 0.2	3.5± 0.2	3.7± 0.2	3.6± 0.3	3.8± 0.2
10000 ppm	3.2± 0.3	3.3± 0.2	3.4± 0.1	3.4± 0.2	3.5± 0.2	3.4± 0.2	3.6± 0.2
20000 ppm	3.2± 0.3	3.3± 0.2	3.3± 0.2	3.5± 0.2	3.5± 0.2	3.6± 0.2	3.6± 0.3
40000 ppm	3.3± 0.1	3.2± 0.2	3.3± 0.1	3.3± 0.2	3.4± 0.2	3.4± 0.2	3.5± 0.2

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

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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	3.6± 0.2	3.7± 0.2	3.6± 0.2	3.7± 0.2	3.7± 0.2	3.7± 0.2
2500 ppm	3.8± 0.2	3.9± 0.2	3.8± 0.2	3.7± 0.2	3.8± 0.2	3.8± 0.2
5000 ppm	3.6± 0.2	3.8± 0.3	3.7± 0.3	3.9± 0.3	3.8± 0.4	3.7± 0.5
10000 ppm	3.6± 0.3	3.5± 0.2	3.7± 0.3	3.7± 0.3	3.7± 0.4	3.5± 0.3
20000 ppm	3.7± 0.3	3.6± 0.3	3.5± 0.3	3.8± 0.3	3.6± 0.2	3.7± 0.3
40000 ppm	3.5± 0.3	3.4± 0.3	3.4± 0.2	3.4± 0.3	3.5± 0.3	3.4± 0.2*

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

APPENDIX E 1

CHEMICAL INTAKE CHANGES : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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	0.534± 0.156	0.487± 0.112	0.447± 0.106	0.398± 0.065	0.396± 0.071	0.379± 0.065	0.348± 0.056
5000 ppm	0.952± 0.150	0.953± 0.251	0.867± 0.216	0.773± 0.138	0.752± 0.108	0.712± 0.087	0.725± 0.213
10000 ppm	1.701± 0.177	1.641± 0.174	1.562± 0.272	1.492± 0.295	1.427± 0.245	1.380± 0.194	1.269± 0.189
20000 ppm	4.314± 1.171	4.016± 1.113	3.576± 0.982	3.217± 0.776	3.129± 0.664	2.968± 0.578	2.631± 0.477
40000 ppm	7.344± 1.385	7.475± 1.391	7.061± 1.301	6.786± 1.829	6.453± 1.298	6.011± 1.063	5.698± 1.246

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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	0.345± 0.065	0.328± 0.062	0.311± 0.054	0.288± 0.039	0.284± 0.042	0.297± 0.051
5000 ppm	0.654± 0.098	0.649± 0.124	0.569± 0.061	0.611± 0.192	0.590± 0.175	0.585± 0.096
10000 ppm	1.272± 0.211	1.178± 0.173	1.119± 0.175	1.137± 0.215	1.081± 0.195	1.125± 0.173
20000 ppm	2.529± 0.437	2.611± 0.796	2.348± 0.668	2.298± 0.618	2.270± 0.624	2.291± 0.533
40000 ppm	5.502± 1.040	5.327± 0.992	5.201± 1.020	4.925± 0.922	4.775± 0.885	4.790± 0.903

APPENDIX E 2

CHEMICAL INTAKE CHANGES : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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	0.537± 0.031	0.542± 0.026	0.510± 0.036	0.506± 0.040	0.469± 0.020	0.471± 0.048	0.443± 0.032
5000 ppm	1.127± 0.087	1.109± 0.088	1.033± 0.080	1.013± 0.090	0.963± 0.088	0.989± 0.090	0.947± 0.084
10000 ppm	2.076± 0.207	2.053± 0.253	1.945± 0.205	1.917± 0.251	1.918± 0.219	1.943± 0.265	1.841± 0.242
20000 ppm	3.808± 0.643	3.970± 0.659	3.804± 0.539	3.746± 0.514	3.710± 0.406	3.703± 0.332	3.573± 0.331
40000 ppm	7.954± 0.841	8.131± 1.062	7.785± 0.973	7.086± 1.115	7.252± 1.061	6.945± 1.028	6.562± 1.067

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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	0.457± 0.033	0.449± 0.032	0.448± 0.036	0.435± 0.031	0.442± 0.043	0.433± 0.045
5000 ppm	0.978± 0.087	0.958± 0.076	0.907± 0.067	0.934± 0.070	0.879± 0.047	0.813± 0.232
10000 ppm	1.852± 0.197	1.822± 0.183	1.775± 0.167	1.759± 0.144	1.710± 0.192	1.733± 0.195
20000 ppm	3.564± 0.278	3.506± 0.311	3.403± 0.239	3.284± 0.377	3.211± 0.365	3.234± 0.301
40000 ppm	6.611± 1.079	6.703± 0.965	6.443± 0.997	6.117± 0.944	5.854± 0.938	6.460± 1.637

APPENDIX F 1

HEMATOLOGY : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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	10.74± 0.23	15.7± 0.4	50.5± 1.2	47.0± 0.7	14.7± 0.3	31.3± 0.6	1479± 91
2500 ppm	10	10.82± 0.30	15.8± 0.3	50.2± 0.8	46.4± 0.7	14.6± 0.2	31.4± 0.4	1447± 79
5000 ppm	10	10.85± 0.24	15.8± 0.3	50.3± 1.0	46.4± 0.5	14.6± 0.2	31.5± 0.4	1514± 90
10000 ppm	10	10.74± 0.18	15.6± 0.5	50.0± 1.4	46.6± 0.8	14.5± 0.4	31.1± 0.8	1486± 71
20000 ppm	10	10.80± 0.18	15.8± 0.4	50.4± 1.2	46.7± 0.7	14.6± 0.2	31.3± 0.2	1429± 103
40000 ppm	10	10.83± 0.22	15.6± 0.3	49.9± 1.1	46.1± 0.3	14.5± 0.2	31.5± 0.4	1403± 204

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

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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	1.12± 0.46	1± 1	16± 4	2± 1	0± 0	2± 1	79± 5	0± 0
2500 ppm	10	1.28± 0.55	2± 1	17± 7	2± 2	0± 0	3± 2	76± 8	0± 0
5000 ppm	10	1.25± 0.77	1± 1	16± 5	2± 3	0± 0	2± 1	79± 6	0± 0
10000 ppm	10	1.22± 0.53	1± 1	14± 3	2± 2	0± 0	3± 1	80± 5	0± 0
20000 ppm	10	1.11± 0.53	1± 1	13± 3	2± 1	0± 0	3± 1	81± 3	0± 0
40000 ppm	10	0.96± 0.45	0± 1	16± 4	2± 1	0± 0	3± 1	79± 4	0± 0

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

APPENDIX F 2

HEMATOLOGY : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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 fℓ	MCH pg	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	9	10.64± 0.36	15.6± 0.6	49.4± 1.8	46.4± 0.6	14.7± 0.1	31.7± 0.3	1326± 107
2500 ppm	10	10.67± 0.33	15.8± 0.5	49.6± 1.3	46.5± 0.5	14.8± 0.2	31.9± 0.5	1335± 80
5000 ppm	10	10.53± 0.26	15.6± 0.4	49.2± 1.5	46.7± 0.8	14.8± 0.1	31.8± 0.5	1303± 68
10000 ppm	10	10.58± 0.22	15.6± 0.4	48.8± 1.0	46.1± 0.2	14.8± 0.2	32.0± 0.4	1347± 71
20000 ppm	10	10.79± 0.35	15.9± 0.5	49.7± 1.4	46.1± 0.6	14.7± 0.2	32.0± 0.3	1360± 86
40000 ppm	8	10.71± 0.40	15.8± 0.5	49.4± 1.6	46.1± 0.3	14.7± 0.2	31.9± 0.4	1253± 197

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

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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	9	1.19±	0.74	1±	2	18±	8	1±	2	0±	0	2±	1	78±	8	0±	0
2500 ppm	10	1.03±	0.49	1±	1	17±	4	1±	1	0±	0	2±	1	79±	5	0±	0
5000 ppm	10	1.23±	1.16	0±	0	15±	4	2±	2	0±	0	2±	1	82±	5	0±	0
10000 ppm	10	1.01±	0.46	1±	1	19±	4	1±	1	0±	0	2±	1	77±	5	0±	1
20000 ppm	10	1.09±	0.41	1±	1	16±	4	2±	1	0±	0	1±	1	80±	4	0±	0
40000 ppm	8	1.22±	0.30	1±	1	16±	5	1±	1	0±	0	2±	1	80±	5	0±	0

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

APPENDIX G 1

BIOCHEMISTRY : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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	5.3± 0.2	3.2± 0.1	1.5± 0.1	0.13± 0.01	227± 28	86± 7	37± 14
2500 ppm	10	5.3± 0.3	3.2± 0.1	1.5± 0.1	0.13± 0.01	219± 34	91± 14	42± 13
5000 ppm	10	5.3± 0.1	3.2± 0.1	1.6± 0.1	0.13± 0.01	217± 21	91± 11	35± 10
10000 ppm	10	5.2± 0.1	3.1± 0.1	1.5± 0.1	0.14± 0.00	224± 25	86± 9	41± 13
20000 ppm	10	5.2± 0.2	3.1± 0.2	1.5± 0.1	0.13± 0.01	220± 34	84± 5	46± 12
40000 ppm	10	5.0± 0.2**	3.0± 0.1**	1.6± 0.1	0.13± 0.01	215± 26	78± 8	39± 10

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

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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	181± 16	39± 4	16± 2	189± 28	138± 10	1± 1	48± 13
2500 ppm	10	191± 25	41± 5	18± 5	189± 23	135± 10	2± 1	41± 9
5000 ppm	10	191± 16	40± 4	18± 4	181± 27	139± 9	2± 1	35± 9
10000 ppm	10	182± 16	36± 3	16± 2	175± 19	136± 4	2± 1	41± 16
20000 ppm	10	181± 11	39± 4	16± 2	187± 24	138± 10	1± 1	43± 13
40000 ppm	10	172± 18	40± 3	16± 1	187± 30	139± 6	2± 1	43± 16

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

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	UREA NITROGEN mg/dℓ	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dℓ	INORGANIC PHOSPHORUS mg/dℓ
Control	10	28.5± 3.4	151± 1	4.7± 0.3	121± 3	9.0± 0.3	7.7± 1.6
2500 ppm	10	28.9± 4.5	151± 1	4.5± 0.4	120± 3	9.1± 0.3	7.1± 0.6
5000 ppm	10	30.1± 7.4	150± 1	4.4± 0.3	119± 2	9.1± 0.2	7.0± 0.7
10000 ppm	10	27.3± 2.3	151± 1	4.4± 0.3	120± 2	9.0± 0.2	7.4± 0.8
20000 ppm	10	27.4± 3.5	151± 1	4.6± 0.4	121± 2	9.1± 0.3	7.5± 1.1
40000 ppm	10	28.4± 4.5	151± 1	4.6± 0.5	120± 2	8.9± 0.2	7.7± 0.9

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

APPENDIX G 2

BIOCHEMISTRY : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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	5.2± 0.2	3.5± 0.1	2.0± 0.3	0.13± 0.01	177± 19	77± 8	20± 12
2500 ppm	10	5.3± 0.1	3.4± 0.1	1.8± 0.1	0.13± 0.02	174± 17	73± 7	20± 11
5000 ppm	10	5.1± 0.2	3.3± 0.2	1.9± 0.4	0.13± 0.01	175± 25	73± 8	20± 4
10000 ppm	10	5.0± 0.1*	3.4± 0.1	2.1± 0.3	0.13± 0.03	179± 34	73± 13	18± 9
20000 ppm	10	5.2± 0.1	3.4± 0.1	2.0± 0.3	0.13± 0.01	183± 24	75± 9	18± 7
40000 ppm	10	5.0± 0.2*	3.3± 0.1*	1.9± 0.2	0.12± 0.02	167± 18	76± 8	27± 10

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

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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	160± 14	49± 7	19± 3	239± 80	218± 26	1± 1	54± 17
2500 ppm	10	155± 17	47± 3	19± 2	218± 36	219± 15	1± 1	45± 12
5000 ppm	10	155± 13	49± 10	21± 9	217± 38	205± 25	1± 1	64± 22
10000 ppm	10	153± 21	47± 7	19± 2	214± 30	221± 13	2± 2	44± 10
20000 ppm	10	156± 22	44± 5	17± 2	204± 35	215± 25	1± 1	54± 16
40000 ppm	10	160± 16	47± 6	20± 2	207± 41	209± 28	1± 1	44± 10

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

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	UREA NITROGEN mg/dℓ	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dℓ	INORGANIC PHOSPHORUS mg/dℓ
Control	10	27.0± 4.6	150± 2	4.4± 0.2	121± 2	9.1± 0.2	7.0± 1.2
2500 ppm	10	23.6± 1.9	150± 2	4.4± 0.3	121± 2	9.0± 0.2	6.3± 1.2
5000 ppm	10	23.1± 2.2	151± 2	4.4± 0.3	122± 2	8.9± 0.2	6.7± 0.8
10000 ppm	10	27.3± 3.2	150± 1	4.5± 0.3	122± 2	8.8± 0.4	6.6± 1.2
20000 ppm	10	24.8± 2.5	151± 2	4.4± 0.3	121± 2	9.0± 0.2	6.6± 1.6
40000 ppm	10	22.3± 1.7**	151± 1	4.4± 0.2	121± 2	8.8± 0.1*	6.4± 1.1

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

APPENDIX H 1

URINALYSIS : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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	Occult blood −	±	+	2+	3+	CHI
Control	10	0	0	0	1	2	5	2		0	0	5	5	0	0		10	0	0	0	0	0		2	2	6	0	0	0		10	0	0	0	0	
2500 ppm	10	0	0	0	2	3	3	2		0	0	3	6	1	0		10	0	0	0	0	0		5	4	1	0	0	0		10	0	0	0	0	
5000 ppm	10	0	0	1	0	1	5	3		0	0	7	3	0	0		10	0	0	0	0	0		4	3	3	0	0	0		10	0	0	0	0	
10000 ppm	10	0	0	0	1	3	6	0		0	0	5	5	0	0		10	0	0	0	0	0		1	8	1	0	0	0	*	10	0	0	0	0	
20000 ppm	10	0	0	0	2	5	3	0		0	0	5	5	0	0		10	0	0	0	0	0		3	2	4	1	0	0		10	0	0	0	0	
40000 ppm	10	0	1	2	0	4	3	0		0	1	2	7	0	0		10	0	0	0	0	0		1	3	5	1	0	0		10	0	0	0	0	

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

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

URINALYSIS

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

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

APPENDIX H 2

URINALYSIS : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0427 URINALYSIS
ANIMAL : MOUSE Crj:BDF1
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	Occult blood −	±	+	2+	3+	CHI
Control	10	0	0	1	2	0	7	0		0	0	7	3	0	0		10	0	0	0	0	0		0	8	2	0	0	0		10	0	0	0	0	
2500 ppm	10	0	0	1	2	3	4	0		0	1	7	2	0	0		10	0	0	0	0	0		0	8	1	1	0	0		10	0	0	0	0	
5000 ppm	10	0	0	2	1	0	7	0		0	0	9	1	0	0		10	0	0	0	0	0		0	8	2	0	0	0		10	0	0	0	0	
10000 ppm	10	0	0	1	3	3	3	0		0	0	8	2	0	0		10	0	0	0	0	0		0	8	2	0	0	0		10	0	0	0	0	
20000 ppm	10	0	0	0	4	4	2	0	*	0	0	5	5	0	0		10	0	0	0	0	0		0	4	5	1	0	0		10	0	0	0	0	
40000 ppm	10	0	0	1	3	1	4	1		0	0	4	4	2	0		10	0	0	0	0	0		0	1	1	5	2	1	**	10	0	0	0	0	

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

STUDY NO. : 0427 URINALYSIS
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

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

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

APPENDIX I 1

GROSS FINDINGS : SUMMARY, MOUSE : MALE : ALL ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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 (%)
spleen	black zone		0 (0)	1 (10)	0 (0)	0 (0)
kidney	hydronephrosis		0 (0)	1 (10)	2 (20)	0 (0)

Organ	Findings	Group Name	20000 ppm	40000 ppm
		NO. of Animals	10 (%)	10 (%)
spleen	black zone		1 (10)	0 (0)
kidney	hydronephrosis		0 (0)	0 (0)

APPENDIX I 2

GROSS FINDINGS : SUMMARY, MOUSE : FEMALE : ALL ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

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 (%)
spleen	black zone		1 (10)	1 (10)	0 (0)	0 (0)
kidney	hydronephrosis		2 (20)	0 (0)	0 (0)	0 (0)

Organ	Findings	Group Name	20000 ppm	40000 ppm
		NO. of Animals	10 (%)	10 (%)
spleen	black zone		0 (0)	1 (10)
kidney	hydronephrosis		1 (10)	0 (0)

APPENDIX J 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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	31.6± 2.9	0.038± 0.008	0.010± 0.002	0.227± 0.021	0.151± 0.010	0.159± 0.026
2500 ppm	10	31.3± 2.3	0.040± 0.008	0.011± 0.001	0.211± 0.042	0.154± 0.010	0.158± 0.016
5000 ppm	10	31.0± 2.7	0.035± 0.006	0.012± 0.003	0.223± 0.026	0.157± 0.015	0.150± 0.007
10000 ppm	10	31.7± 1.8	0.038± 0.009	0.013± 0.003	0.232± 0.027	0.154± 0.013	0.153± 0.011
20000 ppm	10	31.3± 2.1	0.037± 0.007	0.011± 0.003	0.228± 0.035	0.159± 0.010	0.154± 0.012
40000 ppm	10	30.9± 1.6	0.033± 0.005	0.010± 0.002	0.228± 0.023	0.160± 0.011	0.154± 0.006

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

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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	0.421± 0.025	0.047± 0.004	1.136± 0.073	0.444± 0.017
2500 ppm	10	0.488± 0.242	0.049± 0.012	1.138± 0.062	0.449± 0.015
5000 ppm	10	0.733± 0.972	0.049± 0.011	1.154± 0.074	0.442± 0.017
10000 ppm	10	0.434± 0.022	0.050± 0.006	1.161± 0.056	0.450± 0.015
20000 ppm	10	0.446± 0.027	0.049± 0.005	1.189± 0.064	0.448± 0.014
40000 ppm	10	0.456± 0.017	0.050± 0.004	1.164± 0.059	0.450± 0.011

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

APPENDIX J 2

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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	22.1± 1.8	0.041± 0.006	0.012± 0.002	0.025± 0.007	0.122± 0.006	0.143± 0.010
2500 ppm	10	21.7± 1.5	0.039± 0.006	0.012± 0.002	0.025± 0.007	0.129± 0.006	0.148± 0.009
5000 ppm	10	21.9± 1.1	0.039± 0.008	0.012± 0.001	0.028± 0.009	0.124± 0.007	0.150± 0.009
10000 ppm	10	20.8± 1.4	0.038± 0.005	0.013± 0.002	0.027± 0.004	0.122± 0.008	0.148± 0.018
20000 ppm	10	21.8± 1.6	0.040± 0.004	0.014± 0.003	0.028± 0.008	0.129± 0.011	0.147± 0.020
40000 ppm	10	22.1± 2.2	0.044± 0.006	0.013± 0.002	0.026± 0.005	0.123± 0.008	0.139± 0.004

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

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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	0.447± 0.364	0.056± 0.009	0.911± 0.093	0.459± 0.019
2500 ppm	10	0.282± 0.015	0.051± 0.006	0.906± 0.063	0.464± 0.012
5000 ppm	10	0.283± 0.014	0.055± 0.005	0.946± 0.074	0.458± 0.017
10000 ppm	10	0.279± 0.012	0.050± 0.007	0.878± 0.075	0.460± 0.016
20000 ppm	10	0.316± 0.085	0.056± 0.006	0.901± 0.057	0.459± 0.018
40000 ppm	10	0.292± 0.016	0.056± 0.012	0.903± 0.068	0.457± 0.013

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

APPENDIX K 1

ORGAN WEIGHT, RELATIVE : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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	31.6± 2.9	0.121± 0.018	0.032± 0.006	0.723± 0.089	0.480± 0.028	0.504± 0.073
2500 ppm	10	31.3± 2.3	0.129± 0.023	0.036± 0.003	0.679± 0.148	0.496± 0.054	0.509± 0.066
5000 ppm	10	31.0± 2.7	0.114± 0.023	0.039± 0.010	0.726± 0.103	0.509± 0.055	0.486± 0.047
10000 ppm	10	31.7± 1.8	0.119± 0.027	0.040± 0.009	0.735± 0.104	0.488± 0.050	0.484± 0.051
20000 ppm	10	31.3± 2.1	0.118± 0.020	0.034± 0.011	0.732± 0.125	0.510± 0.038	0.493± 0.038
40000 ppm	10	30.9± 1.6	0.107± 0.014	0.033± 0.007	0.739± 0.078	0.518± 0.046	0.499± 0.032

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

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.340± 0.114	0.150± 0.014	3.610± 0.205	1.419± 0.155
2500 ppm	10	1.574± 0.829	0.157± 0.040	3.646± 0.134	1.445± 0.136
5000 ppm	10	2.404± 3.253	0.159± 0.037	3.733± 0.151	1.434± 0.120
10000 ppm	10	1.373± 0.102	0.158± 0.021	3.672± 0.144	1.426± 0.078
20000 ppm	10	1.430± 0.106	0.158± 0.023	3.805± 0.212	1.437± 0.092
40000 ppm	10	1.475± 0.075*	0.161± 0.016	3.764± 0.115	1.458± 0.085

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

APPENDIX K 2

ORGAN WEIGHT, RELATIVE : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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	22.1± 1.8	0.187± 0.025	0.056± 0.007	0.115± 0.031	0.558± 0.055	0.655± 0.080
2500 ppm	10	21.7± 1.5	0.180± 0.022	0.057± 0.007	0.117± 0.036	0.595± 0.044	0.687± 0.063
5000 ppm	10	21.9± 1.1	0.177± 0.032	0.056± 0.005	0.126± 0.040	0.566± 0.030	0.685± 0.049
10000 ppm	10	20.8± 1.4	0.184± 0.027	0.062± 0.009	0.128± 0.020	0.588± 0.038	0.712± 0.070
20000 ppm	10	21.8± 1.6	0.184± 0.018	0.062± 0.011	0.126± 0.029	0.592± 0.047	0.676± 0.098
40000 ppm	10	22.1± 2.2	0.198± 0.020	0.059± 0.012	0.117± 0.020	0.558± 0.042	0.636± 0.067

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

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	2.030± 1.659	0.254± 0.028	4.126± 0.162	2.094± 0.179
2500 ppm	10	1.307± 0.085	0.237± 0.027	4.189± 0.262	2.148± 0.124
5000 ppm	10	1.293± 0.055	0.250± 0.023	4.321± 0.242	2.095± 0.118
10000 ppm	10	1.347± 0.078	0.240± 0.027	4.227± 0.248	2.219± 0.100
20000 ppm	10	1.441± 0.332	0.257± 0.022	4.133± 0.179	2.113± 0.144
40000 ppm	10	1.327± 0.092	0.253± 0.032	4.094± 0.251	2.080± 0.150

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

APPENDIX L 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : MALE : ALL ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0427
ANIMAL : MOUSE Crj:BDF1
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>			
	eosinophilic change:olfactory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lung			<10>				<10>				<10>				<10>			
	hemorrhage		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)	(10)	(0)	(0)	(0)
{Hematopoietic system}																		
lymph node			<10>				<10>				<10>				<10>			
	lymphadenitis		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)
spleen			<10>				<10>				<10>				<10>			
	deposit of melanin		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)
{Digestive system}																		
liver			<10>				<10>				<10>				<10>			
	granulation		2	0	0	0	3	0	0	0	1	0	0	0	3	0	0	0
			(20)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(10)	(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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			<10>				<10>			
	eosinophilic change:olfactory epithelium		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
lung			<10>				<10>			
	hemorrhage		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}										
lymph node			<10>				<10>			
	lymphadenitis		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen			<10>				<10>			
	deposit of melanin		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}										
liver			<10>				<10>			
	granulation		2	0	0	0	2	0	0	0
			(20)	(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	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}																		
pancreas			<10>				<10>				<10>				<10>			
	inflammatory infiltration		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)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	hydronephrosis		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)
	mineralization:papilla		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)
{Musculoskeletal system}																		
muscle			<10>				<10>				<10>				<10>			
	inflammatory infiltration		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)

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}										
pancreas			<10>				<10>			
	inflammatory infiltration		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Urinary system}										
kidney			<10>				<10>			
	hydronephrosis		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:papilla		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Musculoskeletal system}										
muscle			<10>				<10>			
	inflammatory infiltration		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

APPENDIX L 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : 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}																		
nasal cavit			<10>				<10>				<10>				<10>			
	eosinophilic change:olfactory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	atrophy:olfactory epithelium		0	0	0	0	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)
lung			<10>				<10>				<10>				<10>			
	hemorrhage		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)
{Hematopoietic system}																		
spleen			<10>				<10>				<10>				<10>			
	deposit of melanin		1	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}																		
liver			<10>				<10>				<10>				<10>			
	granulation		2	0	0	0	3	0	0	0	1	0	0	0	3	0	0	0
			(20)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(10)	(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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			<10>				<10>			
	eosinophilic change:olfactory epithelium		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	atrophy:olfactory epithelium		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lung			<10>				<10>			
	hemorrhage		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}										
spleen			<10>				<10>			
	deposit of melanin		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Digestive system}										
liver			<10>				<10>			
	granulation		1	0	0	0	1	0	0	0
			(10)	(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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	hydronephrosis		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)	(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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}										
kidney			<10>				<10>			
	hydronephrosis		1	0	0	0	0	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

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

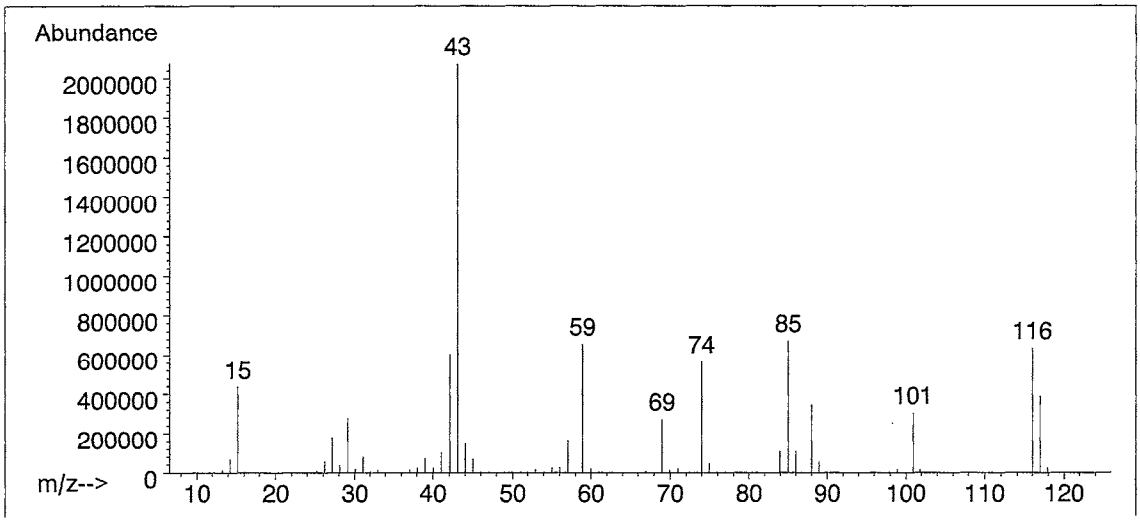
1. Spectral Data

Mass Spectrometry

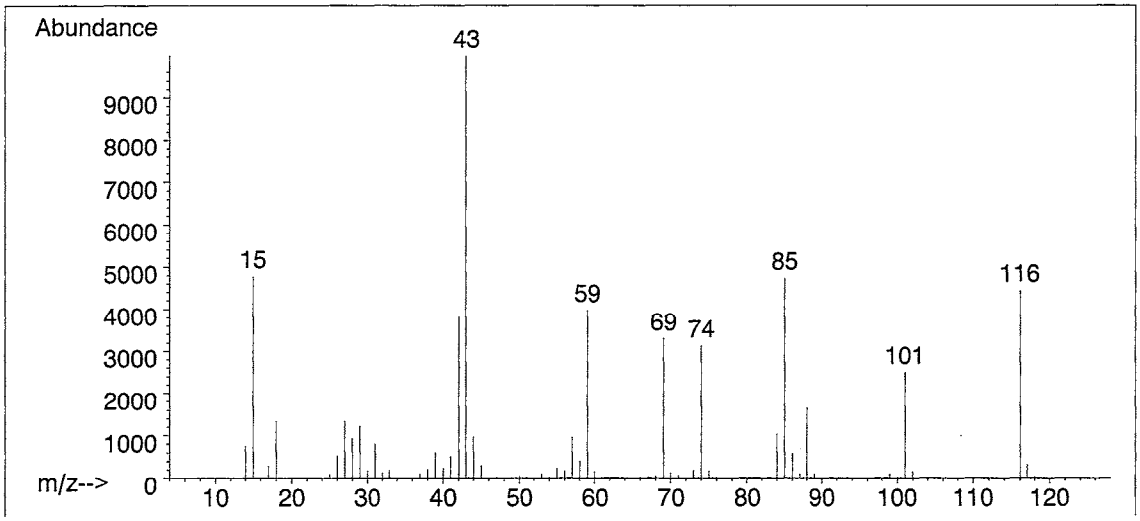
Instrument : Hewlett Packard 5989B Mass Spectrometer

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.

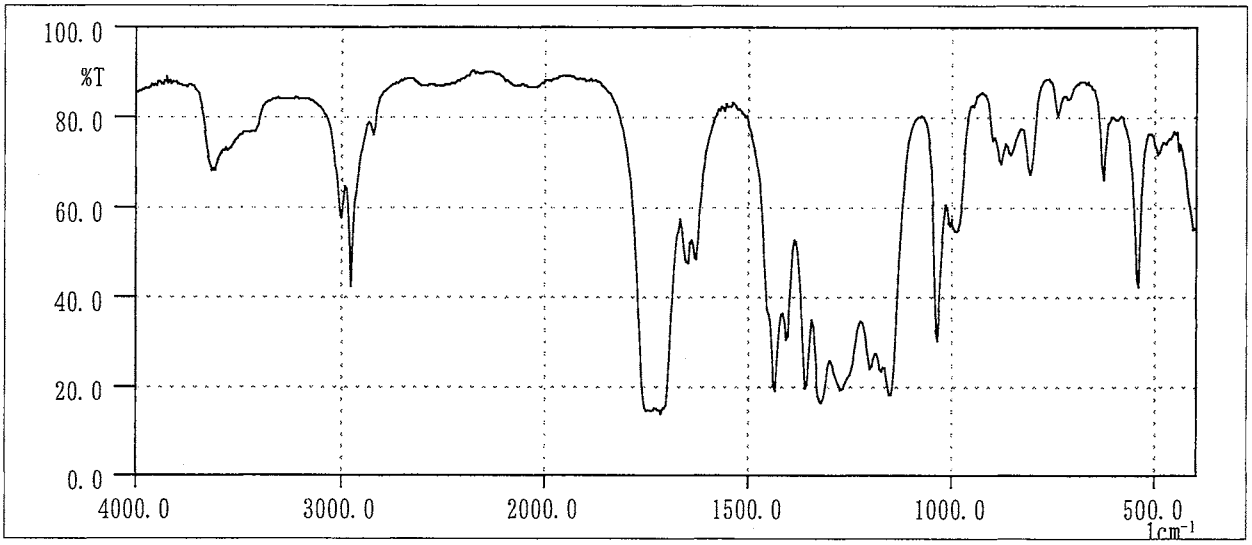
(*Fred W. McLafferty (1994) Wiley Registry of Mass Spectral Data, 6th edition. John Wiley and Sons, Inc. (U.S.), Entry Number 12752)

Infrared Spectrometry

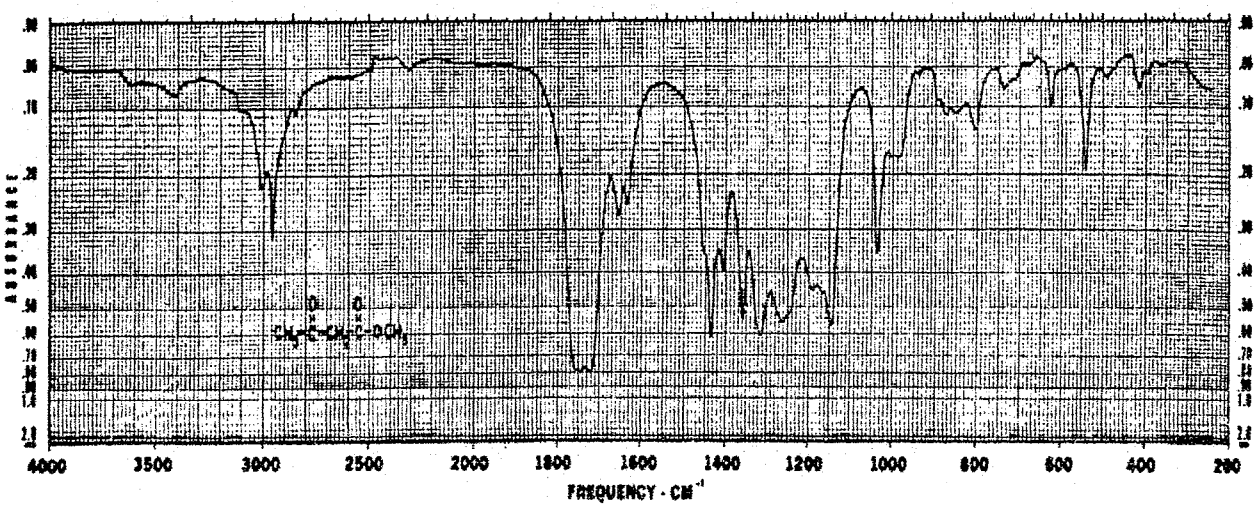
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

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 2001.4.13 to 2000.7.17. 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
2001.04.13	2530 (101)[b]	4850 (97.0)	9590 (95.9)	18900 (94.5)	37200 (93.0)

[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]	2590 (100)	39800 (102)
	2000.10.12[c]	2770 (107)	39300 (101)

[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]
White blood cell (WBC)	Light scattering method [1]
Differential WBC	Pattern recognition method [2] (Wright staining)
Biochemistry	
Total protein (TP)	Biuret method [3]
Albumin (Alb)	BCG method [3]
A/G ratio	Calculated as Alb/(TP−Alb) [3]
T-bilirubin	Alkaline azobilirubin method [3]
Glucose	GlcK・G-6-PDH method [3]
T-cholesterol	CE・COD・POD method [3]
Triglyceride	LPL・GK・GPO・POD method [3]
Phospholipid	PLD・ChOD・POD method [3]
Glutamic oxaloacetic transaminase (GOT)	JSCC method [3]
Glutamic pyruvic transaminase (GPT)	JSCC method [3]
Lactate dehydrogenase (LDH)	SFBC method [3]
Alkaline phosphatase (ALP)	GSCC method [3]
γ-Glutamyl transpeptidase (γ-GTP)	L-γ-Glutamyl-p-nitroanilide method [3]
Creatine phosphokinase (CPK)	JSCC method [3]
Urea nitrogen	Urease・GLDH method [3]
Sodium	Ion selective electrode method [3]
Potassium	Ion selective electrode method [3]
Chloride	Ion selective electrode method [3]
Calcium	OCPC method [3]
Inorganic phosphorus	PNP・XOD・POD method [3]
Urinalysis	
pH,Protein,Glucose,Ketone body,Occult Blood, Urobilinogen	Urinalysis reagent paper method [4]

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

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

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

4) Ames reagent strips for urinalysis (Uro-Labstix : 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
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
Sodium	mEq/L	0
Potassium	mEq/L	1
Chloride	mEq/L	0
Calcium	mg/dL	1
Inorganic phosphorus	mg/dL	1