

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

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## APPENDIXES

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METHYL ACETOACETATE

## 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

PAGE : 1

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

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## 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

PAGE : 2

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
PILOERECTOR	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

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## 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

PAGE : 1

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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

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STUDY NO. : 0427  
 ANIMAL : MOUSE Crj:BDF1  
 UNIT : g  
 REPORT TYPE : A1 13  
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 2

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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

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## 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

PAGE : 3

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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

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STUDY NO. : 0427  
ANIMAL : MOUSE Crj:BDF1  
UNIT : g  
REPORT TYPE : A1 13  
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)  
ALL ANIMALS

PAGE : 4

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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

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## 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

PAGE : 1

Group Name	Administration 1-7(4)	week-day(effective) 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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

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STUDY NO. : 0427  
 ANIMAL : MOUSE Crj:BDF1  
 UNIT : g  
 REPORT TYPE : A1 13  
 SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 2

Group Name	Administration 8-7(4)	week-day(effective) 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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

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## APPENDIX C 2

### WATER CONSUMPTION CHANGES : SUMMARY, MOUSE : FEMALE (13-WEEK STUDY)

STUDY NO. : 0427  
 ANIMAL : MOUSE Crj:BDP1  
 UNIT : g  
 REPORT TYPE : A1 13  
 SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 3

Group Name	Administration 1-7(4)	week-day(effective) 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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

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STUDY NO. : 0427  
ANIMAL : MOUSE Crj:BDF1  
UNIT : g  
REPORT TYPE : A1 13  
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)  
ALL ANIMALS

PAGE : 4

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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

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## 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

PAGE : 1

Group Name	Administration 1-7(7)	week-day(effective) 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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

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STUDY NO. : 0427  
 ANIMAL : MOUSE Crj:BDF1  
 UNIT : g  
 REPORT TYPE : A1 13  
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 2

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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

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## 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

PAGE : 3

Group Name	Administration 1-7(7)	week-day(effective) 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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of Dunnett

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STUDY NO. : 0427  
 ANIMAL : MOUSE Crj:BDF1  
 UNIT : g  
 REPORT TYPE : A1 13  
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 4

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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of Dunnett

(HAN260)

BAIS 3

## APPENDIX E 1

CHEMICAL INTAKE CHANGES : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0427  
 ANIMAL : MOUSE Crj:BDF1  
 UNIT : g/kg/day  
 REPORT TYPE : A1 13  
 SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 1

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	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/day  
 REPORT TYPE : A1 13  
 SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 2

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	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/day  
 REPORT TYPE : A1 13  
 SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 3

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	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/day  
 REPORT TYPE : A1 13  
 SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 4

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	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

HEMATOLOGY (SUMMARY)  
ALL ANIMALS ( 14W)

REPORT TYPE : A1

PAGE : 1

Group Name	NO. of Animals	RED BLOOD CELL 1 0 <sup>6</sup> /μl		HEMOGLOBIN g/dl		HEMATOCRIT %		MCV fl		MCH pg		MCHC g/dl		PLATELET 1 0 <sup>3</sup> /μl	
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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of Dunnett

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

HEMATOLOGY (SUMMARY)  
 ALL ANIMALS ( 14W)

REPORT TYPE : A1

PAGE : 2

Group Name	NO. of Animals	WBC 10 <sup>3</sup> /μℓ		Differential N-BAND		WBC (%) 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 ; \* :  $P \leq 0.05$

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 3

## APPENDIX F 2

HEMATOLOGY : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

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

HEMATOLOGY (SUMMARY)  
ALL ANIMALS ( 14W)

REPORT TYPE : A1

PAGE : 3

Group Name	NO. of Animals	RED BLOOD CELL 10 <sup>6</sup> /μl	HEMOGLOBIN g/dl	HEMATOCRIT %	MCV fl	MCH pg	MCHC g/dl	PLATELET 10 <sup>3</sup> /μl
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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 3

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

HEMATOLOGY (SUMMARY)  
 ALL ANIMALS ( 14W)

REPORT TYPE : A1

PAGE : 4

Group Name	NO. of Animals	WBC 10 <sup>3</sup> /μl		Differential N-BAND		WBC (%) 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 ; \* :  $P \leq 0.05$

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 3

## APPENDIX G 1

BIOCHEMISTRY : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

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

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS ( 14W)

REPORT TYPE : A1

PAGE : 1

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 ; \* :  $P \leq 0.05$       \*\* :  $P \leq 0.01$

Test of Dunnett



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

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS ( 14W)

REPORT TYPE : A1

PAGE : 2

Group Name	NO. of Animals	PHOSPHOLIPID mg/dl		GOT I U / l		GPT I U / l		LDH I U / l		ALP I U / l		G-GTP I U / l		CPK I U / 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 ; \* :  $P \leq 0.05$

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 3

STUDY NO. : 0427  
 ANIMAL : MOUSE Crl:BDF1  
 MEASURE. TIME : 1  
 SEX : MALE

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS ( 14W)

REPORT TYPE : A1

PAGE : 3

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 ; \* :  $P \leq 0.05$       \*\* :  $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 3

## APPENDIX G 2

BIOCHEMISTRY : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

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

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS ( 14W)

REPORT TYPE : A1

PAGE : 4

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 ; \* :  $P \leq 0.05$       \*\* :  $P \leq 0.01$

Test of Dunnett

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

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS ( 14W)

REPORT TYPE : A1

PAGE : 5

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 ; \* :  $P \leq 0.05$       \*\* :  $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 3

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

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS ( 14W)

REPORT TYPE : A1

PAGE : 6

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 ; \* :  $P \leq 0.05$

\*\* :  $P \leq 0.01$

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

URINALYSIS

REPORT TYPE : A1

PAGE : 1

Group Name	NO. of Animals	pH							CHI	Protein					CHI	Glucose					CHI	Ketone body					CHI	Occult blood				CHI				
		5.0	6.0	6.5	7.0	7.5	8.0	8.5		-	±	+	2+	3+		4+	-	±	+	2+		3+	4+	-	±	+		2+	3+	4+	-		±	+	2+	3+
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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of CHI SQUARE

(HCL101)

BAIS 3



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

URINALYSIS

REPORT TYPE : A1

PAGE : 2

Group Name	NO. of Animals	Urobilinogen $\pm$ + 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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of CHI SQUARE

(HCL101)

BAIS 3

## APPENDIX H 2

URINALYSIS : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

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

URINALYSIS

REPORT TYPE : A1

PAGE : 3

Group Name	NO. of Animals	pH								CHI	Protein						CHI	Glucose						CHI	Ketone body						CHI	Occult blood				
		5.0	6.0	6.5	7.0	7.5	8.0	8.5	—		±	+	2+	3+	4+	—		±	+	2+	3+	4+	—		±	+	2+	3+	4+	—		±	+	2+	3+	
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 : \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of CHI SQUARE

(HCL101)

BAIS 3

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

URINALYSIS

REPORT TYPE : A1

PAGE : 4

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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of CHI SQUARE

(HCL101)

BAIS 3

## 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)

PAGE : 1

Organ_____	Findings_____	Group Name	Control	2500 ppm	5000 ppm	10000 ppm
		NO. of Animals	10 (%)	10 (%)	10 (%)	10 (%)
spleen	black zone		0 ( 0)	1 ( 10)	0 ( 0)	0 ( 0)
kidney	hydronephrosis		0 ( 0)	1 ( 10)	2 ( 20)	0 ( 0)

(HPT080)

BAIS 3

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

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

PAGE : 2

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)

(HPT080)

BAIS 3

## 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)

PAGE : 3

Organ	Findings	Group Name NO. of Animals	Control	2500 ppm	5000 ppm	10000 ppm
			10 (%)	10 (%)	10 (%)	10 (%)
spleen	black zone		1 ( 10)	1 ( 10)	0 ( 0)	0 ( 0)
kidney	hydronephrosis		2 ( 20)	0 ( 0)	0 ( 0)	0 ( 0)

(HPT080)

BAIS 3

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

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

PAGE : 4

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)

(HPT080)

BAIS 3

## 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)

PAGE : 1

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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of Dunnett

(HCL040)

BAIS 3

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

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

PAGE : 2

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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of Dunnett

(HCL040)

BAIS 3

## 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)

PAGE : 3

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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of Dunnett

(HCL040)

BAIS 3

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

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

PAGE : 4

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 : \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of Dunnett

(HCL040)

BAIS 3



## 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)

PAGE : 1

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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of Dunnett

(HCL042)

BAIS 3

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

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

PAGE : 2

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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of Dunnett

(HCL042)

BAIS 3

## 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)

PAGE : 3

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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of Dunnett

(HCL042)

BAIS 3

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

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

PAGE : 4

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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$

Test of Dunnett

(HCL042)

BAIS 3

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)

PAGE : 1

Organ	Findings	Group Name No. of Animals on Study Grade	Control 10				2500 ppm 10				5000 ppm 10				10000 ppm 10			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}																		
nasal cavit	eosinophilic change:olfactory epithelium		<10>				<10>				<10>				<10>			
			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	hemorrhage		<10>				<10>				<10>				<10>			
			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	lymphadenitis		<10>				<10>				<10>				<10>			
			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	deposit of melanin		<10>				<10>				<10>				<10>			
			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	granulation		<10>				<10>				<10>				<10>			
			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 : Number of animals with lesion  
( c ) c : b / a \* 100  
Significant difference ; \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square



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

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

PAGE : 2

Organ	Findings	Group Name No. of Animals on Study Grade	20000 ppm				40000 ppm			
			10				10			
			1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit	eosinophilic change:olfactory epithelium		<10>				<10>			
			0	0	0	0	1	0	0	0
			( 0)	( 0)	( 0)	( 0)	( 10)	( 0)	( 0)	( 0)
lung	hemorrhage		<10>				<10>			
			0	0	0	0	0	0	0	0
			( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
{Hematopoietic system}										
lymph node	lymphadenitis		<10>				<10>			
			0	0	0	0	0	0	0	0
			( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
spleen	deposit of melanin		<10>				<10>			
			1	0	0	0	0	0	0	0
			( 10)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
{Digestive system}										
liver	granulation		<10>				<10>			
			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 : \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$  Test of Chi Square

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

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

PAGE : 3

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	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 )
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	hydronephrosis	0	0	0	0	0	1	0	0	0	2	0	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	0
		( 10 )	( 0 )	( 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	0	1	0	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 : Number of animals with lesion  
 ( c ) c : b / a \* 100  
 Significant difference ; \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

(HPT150)

BAIS3

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

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

PAGE : 4

		Group Name	20000 ppm				40000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
Organ_____	Findings_____		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
<hr/>										
{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 : 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)

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

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

PAGE : 5

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 )
			<10>				<10>				<10>				<10>			
	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 : Number of animals with lesion  
 ( c ) c : b / a \* 100  
 Significant difference ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$  Test of Chi Square

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

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

PAGE : 6

Organ	Findings	Group Name No. of Animals on Study Grade	20000 ppm				40000 ppm			
			10				10			
			1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit	eosinophilic change:olfactory epithelium		<10>				<10>			
			0	0	0	0	1	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 10 )	( 0 )	( 0 )	( 0 )
	atrophy:olfactory epithelium		<10>				<10>			
			0	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
{Hematopoietic system}										
lung	hemorrhage		<10>				<10>			
			1	0	0	0	0	0	0	0
			( 10 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
{Digestive system}										
liver	granulation		<10>				<10>			
			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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$  Test of Chi Square

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

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

PAGE : 7

Organ	Findings	Group Name No. of Animals on Study Grade	Control 10				2500 ppm 10				5000 ppm 10				10000 ppm 10			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

{Urinary system}

kidney	hydronephrosis	<10>				<10>				<10>				<10>			
		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 : Number of animals with lesion  
 ( c ) c : b / a \* 100  
 Significant difference : \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$  Test of Chi Square

(HPT150)

BAIS3

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

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

PAGE : 8

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

hydronephrosis

<10>				<10>			
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 : Number of animals with lesion

( c ) c : b / a \* 100

Significant difference : \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$  Test of Chi Square

(HPT150)

BAIS3



## 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

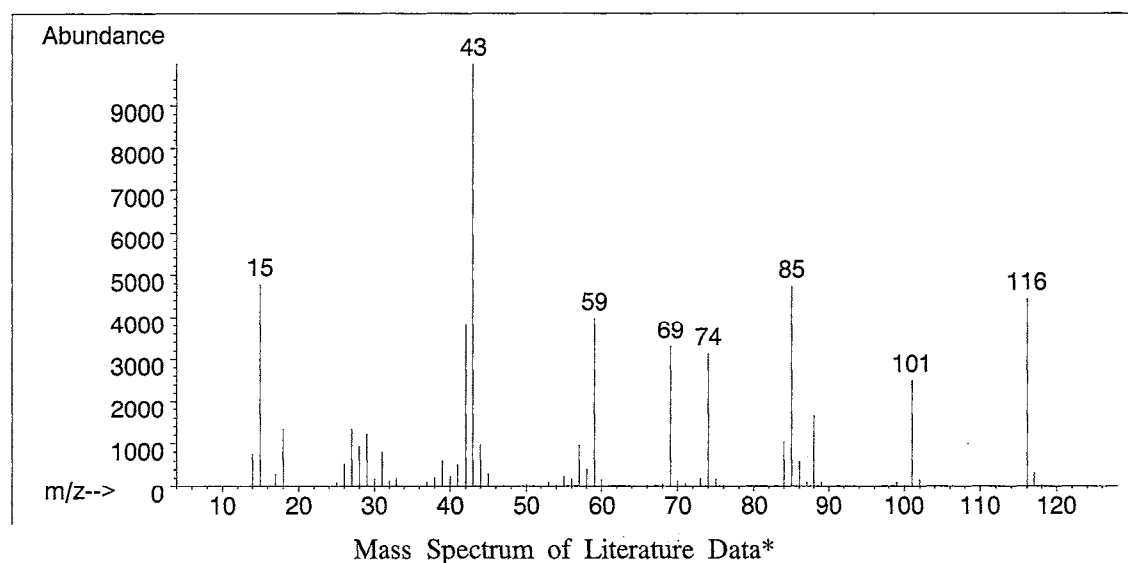
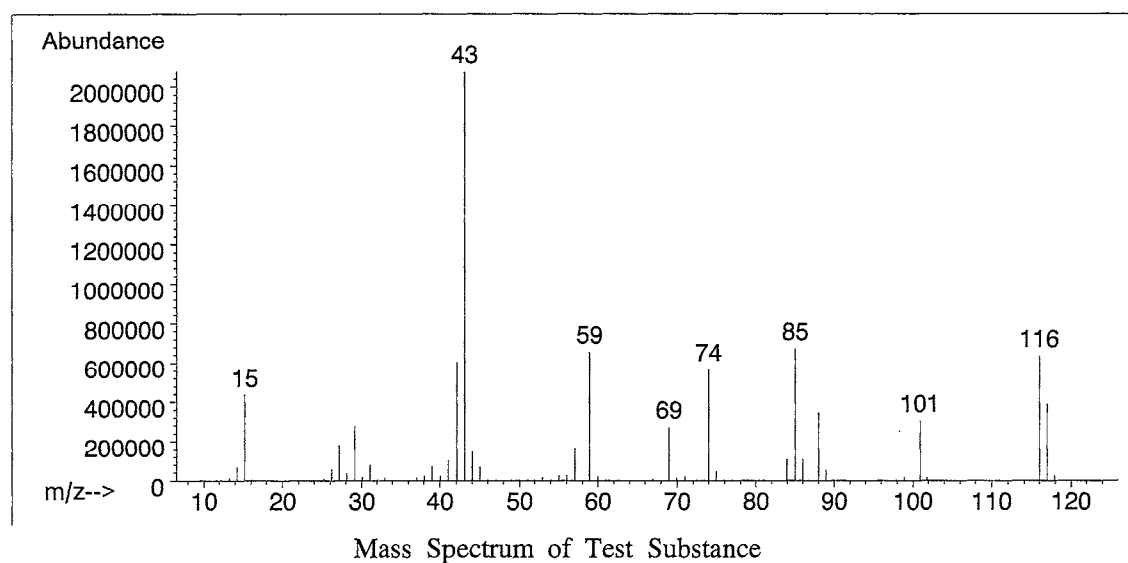
## 1. Spectral Data

Mass Spectrometry

Instrument : Hewlett Packard 5989B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Results: The mass spectrum was consistent with literature spectrum.

(\*Fred W. McLafferty (1994) Wiley Registry of Mass Spectral Data, 6th edition.

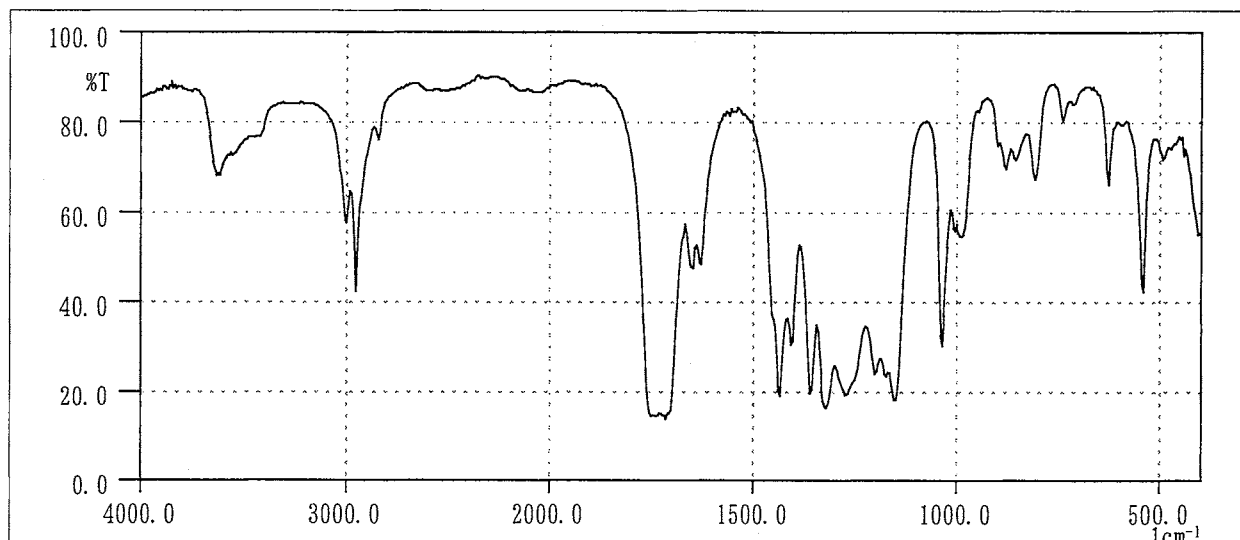
John Wiley and Sons, Inc. (U.S.), Entry Number 12752)

Infrared Spectrometry

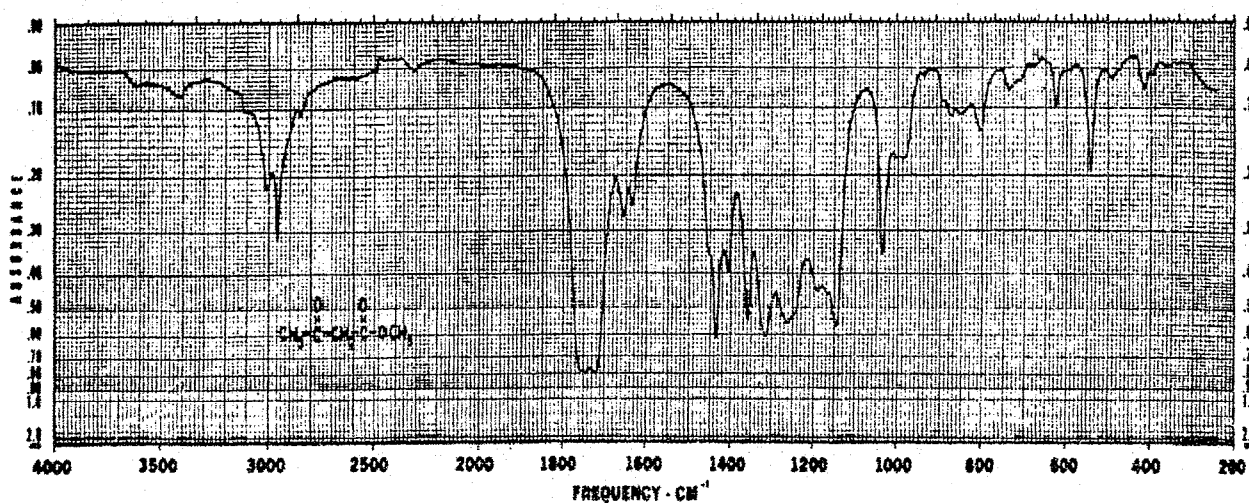
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 2  $\text{cm}^{-1}$



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)

- 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 mm $\phi$   $\times$  50 m)

Column Temperature : 100 °C (1 min)  $\rightarrow$  (10 °C/min)  $\rightarrow$  190 °C

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1  $\mu$ L

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

Date Analyzed	Target Concentration				
	2500 <sup>a</sup>	5000	10000	20000	40000
2001.04.13	2530 (101) <sup>b</sup>	4850 ( 97.0)	9590 ( 95.9)	18900 ( 94.5)	37200 ( 93.0)

<sup>a</sup> ppm

<sup>b</sup> %

Analytical Method : The samples were analyzed by gas chromatography.

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : INNOWAX (0.2 mm  $\phi$   $\times$  50 m)

Column Temperature : 100 °C (1 min)  $\rightarrow$  (10 °C/min)  $\rightarrow$  190 °C

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1  $\mu$ L

## 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

Date Prepared	Date Analyzed	Target Concentration	
		2500 <sup>a</sup>	40000
2000.10.02	2000.10.02	2590 (100) <sup>b</sup>	39000 (100)
	2000.10.06 <sup>c</sup>	2590 (100)	39800 (102)
	2000.10.12 <sup>c</sup>	2770 (107)	39300 (101)

<sup>a</sup> ppm

<sup>b</sup> % (Percentage was based on the concentration on date of preparation.)

<sup>c</sup> Animal room samples

Analytical Method : The samples were analyzed by gas chromatography.

Instrument : Hewlett Packard 5890A Gas Chromatograph  
 Column : INNOWAX (0.2 mm $\phi$   $\times$  50 m)  
 Column Temperature : 100 °C (1 min)  $\rightarrow$  (10 °C/min)  $\rightarrow$  190 °C  
 Flow Rate : 1 mL/min  
 Detector : FID (Flame Ionization Detector)  
 Injection Volume : 1  $\mu$ L

## 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
<b>Hematology</b>	
Red blood cell (RBC)	Light scattering method <sup>1)</sup>
Hemoglobin (Hgb)	Cyanmethemoglobin method <sup>1)</sup>
Hematocrit (Hct)	Calculated as $RBC \times MCV / 10$ <sup>1)</sup>
Mean corpuscular volume (MCV)	Light scattering method <sup>1)</sup>
Mean corpuscular hemoglobin (MCH)	Calculated as $Hgb / RBC \times 10$ <sup>1)</sup>
Mean corpuscular hemoglobin concentration (MCHC)	Calculated as $Hgb / Hct \times 100$ <sup>1)</sup>
Platelet	Light scattering method <sup>1)</sup>
White blood cell (WBC)	Light scattering method <sup>1)</sup>
Differential WBC	Pattern recognition method <sup>2)</sup> (Wright staining)
<b>Biochemistry</b>	
Total protein (TP)	Biuret method <sup>3)</sup>
Albumin (Alb)	BCG method <sup>3)</sup>
A/G ratio	Calculated as $Alb / (TP - Alb)$ <sup>3)</sup>
T-bilirubin	Alkaline azobilirubin method <sup>3)</sup>
Glucose	GlcK · G-6-PDH method <sup>3)</sup>
T-cholesterol	CE · COD · POD method <sup>3)</sup>
Triglyceride	LPL · GK · GPO · POD method <sup>3)</sup>
Phospholipid	PLD · ChOD · POD method <sup>3)</sup>
Glutamic oxaloacetic transaminase (GOT)	JSCC method <sup>3)</sup>
Glutamic pyruvic transaminase (GPT)	JSCC method <sup>3)</sup>
Lactate dehydrogenase (LDH)	SFBC method <sup>3)</sup>
Alkaline phosphatase (ALP)	GSCC method <sup>3)</sup>
$\gamma$ -Glutamyl transpeptidase ( $\gamma$ -GTP)	L- $\gamma$ -Glutamyl-p-nitroanilide method <sup>3)</sup>
Creatine phosphokinase (CPK)	JSCC method <sup>3)</sup>
Urea nitrogen	Urease · GLDH method <sup>3)</sup>
Sodium	Ion selective electrode method <sup>3)</sup>
Potassium	Ion selective electrode method <sup>3)</sup>
Chloride	Ion selective electrode method <sup>3)</sup>
Calcium	OCPC method <sup>3)</sup>
Inorganic phosphorus	PNP · XOD · POD method <sup>3)</sup>
<b>Urinalysis</b>	
pH, Protein, Glucose, Ketone body, Occult Blood, Urobilinogen	Urinalysis reagent paper method <sup>4)</sup>

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
<b>Hematology</b>		
Red blood cell (RBC)	$\times 10^6 / \mu\text{L}$	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	$\times 10^3 / \mu\text{L}$	0
White blood cell (WBC)	$\times 10^3 / \mu\text{L}$	2
Differential WBC	%	0
<b>Biochemistry</b>		
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
$\gamma$ -Glutamyl transpeptidase ( $\gamma$ -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