

ジクロロメタンのマウスを用いた  
吸入による 13 週間毒性試験報告書

試験番号 : 0258

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## APPENDIX A 1

CLINICAL OBSERVATION :SUMMARY, MOUSE : MALE  
(13-WEEK STUDY)

STUDY NO. : 0258  
ANIMAL : MOUSE BDF1  
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : MALE

PAGE : 1

Clinical sign	Group Name	Administration Week-day													
		0-0	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
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
CRUSTA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	8000 ppm	0	0	0	0	0	1	1	0	0	0	0	0	0	1

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## APPENDIX B 1

### BODY WEIGHT CHANGES :SUMMARY, MOUSE : MALE (13-WEEK STUDY)

STUDY NO. : 0258  
 ANIMAL : MOUSE BDF1  
 UNIT : g  
 REPORT TYPE : A1 13  
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 1

Group Name	Administration week-day						
	0-0	1-7	2-7	3-7	4-7	5-7	6-7
Control	22.2± 0.7	24.0± 0.8	25.0± 0.6	26.2± 0.9	26.9± 0.8	27.5± 0.9	28.5± 1.0
500 ppm	22.1± 0.8	23.8± 0.9	24.8± 1.2	25.8± 1.2	26.5± 1.1	27.0± 1.3	27.5± 1.2
1000 ppm	22.4± 1.0	23.7± 0.8	24.6± 1.1	25.4± 0.9	26.1± 1.1	26.6± 1.4	27.4± 1.5
2000 ppm	22.3± 0.8	24.2± 0.8	25.1± 0.9	26.0± 0.9	26.7± 1.0	27.2± 1.2	27.5± 1.2
4000 ppm	22.4± 0.5	24.3± 0.7	25.4± 0.8	26.1± 1.0	27.0± 1.3	27.7± 1.1	28.4± 0.9
8000 ppm	22.0± 0.6	22.5± 0.8**	24.1± 0.8	25.3± 1.1	26.2± 1.1	26.9± 0.9	27.4± 1.1

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

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STUDY NO. : 0258  
 ANIMAL : MOUSE BDF1  
 UNIT : g  
 REPORT TYPE : A1 13  
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 2

Group Name	Administration week-day						
	7-7	8-7	9-7	10-7	11-7	12-7	13-6
Control	29.1± 1.2	29.8± 1.2	30.7± 1.1	31.5± 1.5	32.0± 1.5	32.7± 1.5	33.0± 1.6
500 ppm	28.3± 1.4	29.0± 1.5	29.4± 1.5	30.1± 1.4	30.4± 1.2	31.0± 1.4	32.1± 1.5
1000 ppm	27.7± 1.5*	28.2± 1.7*	28.9± 2.0	30.0± 2.1	30.4± 2.0	30.8± 2.4	31.7± 2.4
2000 ppm	27.4± 1.4*	28.3± 1.6	28.6± 2.2	29.0± 2.2	30.1± 2.2	30.5± 2.6	31.8± 2.4
4000 ppm	28.8± 0.8	29.8± 0.7	29.9± 1.2	30.7± 1.2	31.0± 1.5	31.7± 1.7	33.0± 1.7
8000 ppm	27.9± 1.0	28.9± 1.5	29.5± 1.9	30.0± 2.0	30.4± 2.2	30.8± 2.1	31.9± 1.9

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. : 0258  
ANIMAL : MOUSE BDF1  
UNIT : g  
REPORT TYPE : A1 13  
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)  
ALL ANIMALS

PAGE : 3

Group Name	Administration week-day						
	0-0	1-7	2-7	3-7	4-7	5-7	6-7
Control	18.5± 0.5	19.8± 0.7	20.9± 0.9	21.5± 0.5	22.1± 1.0	22.3± 0.8	23.6± 1.0
500 ppm	18.6± 0.8	19.9± 0.9	20.7± 0.5	21.5± 1.1	22.4± 0.8	22.9± 1.2	23.8± 0.9
1000 ppm	18.2± 0.5	19.7± 0.8	20.5± 0.8	21.4± 0.7	22.2± 0.9	22.7± 0.6	23.5± 0.9
2000 ppm	18.7± 0.6	19.7± 0.8	20.6± 1.2	21.7± 1.1	22.3± 1.0	22.0± 1.2	23.1± 1.3
4000 ppm	18.7± 0.8	19.8± 0.7	20.4± 0.7	21.1± 0.7	22.3± 0.8	22.4± 0.9	22.9± 0.7
8000 ppm	18.4± 0.7	18.2± 1.1**	19.2± 0.3**	19.7± 0.3**	20.5± 0.8**	21.1± 0.8*	21.4± 0.7**

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

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STUDY NO. : 0258  
 ANIMAL : MOUSE BDF1  
 UNIT : g  
 REPORT TYPE : A1 13  
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 4

Group Name	Administration week-day						
	7-7	8-7	9-7	10-7	11-7	12-7	13-6
Control	24.2± 1.4	24.2± 1.4	24.1± 0.8	24.7± 0.8	25.2± 1.0	26.0± 1.2	26.0± 1.8
500 ppm	24.4± 0.9	24.4± 1.4	24.9± 1.0	25.1± 1.3	26.0± 1.7	25.5± 1.0	26.1± 1.1
1000 ppm	23.6± 0.5	24.3± 1.3	24.8± 0.8	24.7± 0.9	25.1± 0.5	25.1± 0.9	25.3± 1.0
2000 ppm	23.7± 1.2	23.7± 1.2	25.1± 1.6	24.1± 1.5	24.8± 1.3	24.8± 1.2	25.8± 1.3
4000 ppm	23.5± 0.5	24.0± 1.2	24.3± 0.7	24.7± 0.8	24.5± 0.8	24.9± 1.0	25.5± 1.2
8000 ppm	22.0± 0.9**	21.8± 1.1**	22.4± 1.0**	22.6± 1.1**	22.5± 0.8**	23.1± 1.1**	23.5± 1.1**

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

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## APPENDIX C 1

### FOOD CONSUMPTION CHANGES : SUMMARY, MOUSE : MALE (13-WEEK STUDY)

STUDY NO. : 0258  
 ANIMAL : MOUSE BDF1  
 UNIT : g  
 REPORT TYPE : A1 13  
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 1

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	4.4± 0.2	4.4± 0.2	4.4± 0.2	4.4± 0.3	4.5± 0.3	4.5± 0.2	4.7± 0.3
500 ppm	4.5± 0.3	4.5± 0.7	4.4± 0.2	4.4± 0.2	4.5± 0.2	4.5± 0.2	4.8± 0.4
1000 ppm	4.3± 0.3	4.4± 0.4	4.4± 0.3	4.4± 0.3	4.5± 0.4	4.6± 0.4	4.3± 0.3
2000 ppm	4.5± 0.2	4.4± 0.2	4.5± 0.2	4.4± 0.3	4.3± 0.2	4.4± 0.2	4.1± 0.3**
4000 ppm	4.5± 0.2	4.5± 0.2	4.9± 0.2**	5.1± 0.3**	4.9± 0.5	5.0± 0.6	4.5± 0.3
8000 ppm	3.8± 0.4**	4.6± 0.3	4.8± 0.4**	4.8± 0.4	4.9± 0.3	4.9± 0.4	4.6± 0.4

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

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STUDY NO. : 0258  
 ANIMAL : MOUSE 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)	13-6(6)
Control	4.6± 0.3	4.6± 0.3	4.5± 0.2	4.6± 0.2	4.5± 0.2	4.5± 0.3
500 ppm	4.5± 0.2	4.6± 0.3	4.5± 0.3	4.6± 0.4	4.6± 0.4	4.7± 0.3
1000 ppm	4.7± 0.3	4.8± 0.5	4.6± 0.4	4.5± 0.3	4.5± 0.4	4.5± 0.3
2000 ppm	4.5± 0.4	4.5± 0.5	4.3± 0.4	4.5± 0.3	4.4± 0.4	4.5± 0.3
4000 ppm	5.1± 0.5*	4.7± 0.4	4.9± 0.4	4.9± 0.6	5.1± 0.6*	5.2± 0.3**
8000 ppm	5.1± 0.5*	4.7± 0.5	5.0± 0.5*	5.0± 0.5	5.0± 0.4	5.5± 0.4**

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

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## APPENDIX C 2

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



STUDY NO. : 0258  
 ANIMAL : MOUSE 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	3.6± 0.2	3.8± 0.1	3.9± 0.2	4.2± 0.2	4.3± 0.2	4.4± 0.2	4.7± 0.2
500 ppm	3.8± 0.2	4.0± 0.2	4.3± 0.3**	4.5± 0.3*	4.6± 0.4	4.8± 0.4	5.0± 0.3*
1000 ppm	3.6± 0.3	4.0± 0.1	4.1± 0.1	4.3± 0.2	4.4± 0.2	4.7± 0.4	4.8± 0.4
2000 ppm	3.9± 0.3	4.2± 0.3**	4.2± 0.3**	4.2± 0.2	4.2± 0.3	4.5± 0.3	4.4± 0.2
4000 ppm	3.7± 0.3	3.9± 0.2	4.5± 0.4**	4.5± 0.3*	4.4± 0.4	4.5± 0.5	4.2± 0.3**
8000 ppm	3.3± 0.3*	3.8± 0.4	4.1± 0.2	4.2± 0.3	4.4± 0.4	4.3± 0.3	4.1± 0.3**

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

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STUDY NO. : 0258  
 ANIMAL : MOUSE BDF1  
 UNIT : g  
 REPORT TYPE : A1 13  
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 4

Group Name	Administration week-day(effective)		10-7(7)	11-7(7)	12-7(7)	13-6(6)
	8-7(7)	9-7(7)				
Control	4.5± 0.3	4.4± 0.2	4.4± 0.1	4.5± 0.3	4.4± 0.3	4.5± 0.3
500 ppm	4.8± 0.2	4.9± 0.3*	4.7± 0.3	5.0± 0.3**	4.6± 0.3	5.0± 0.4
1000 ppm	4.8± 0.4*	4.9± 0.3*	4.4± 0.4	4.6± 0.4	4.5± 0.4	4.5± 0.4
2000 ppm	4.7± 0.2	4.8± 0.4*	4.4± 0.3	4.6± 0.3	4.6± 0.5	4.8± 0.3
4000 ppm	4.5± 0.4	4.4± 0.3	4.5± 0.3	4.5± 0.4	4.2± 0.4	4.7± 0.6
8000 ppm	4.3± 0.3	4.1± 0.3	4.1± 0.3	4.2± 0.4	4.3± 0.5	4.5± 0.5

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

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## APPENDIX D 1

HEMATOLOGY : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0258  
 ANIMAL : MOUSE BDF1  
 SAMPLING DATE : 013-7  
 SEX : MALE

HEMATOLOGY (SUMMARY)  
 SURVIVAL ANIMALS ( 13)

REPORT TYPE : A1

PAGE : 1

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	10	10.76±	0.25	15.8±	0.4	49.4±	1.5	45.9±	0.7	14.7±	0.3	32.1±	0.7	1405±	62
500 ppm	10	11.02±	0.31	16.7±	0.5**	52.0±	1.8**	47.1±	0.5**	15.2±	0.1	32.2±	0.5	1427±	116
1000 ppm	10	10.92±	0.31	16.5±	0.4**	50.9±	1.6	46.6±	0.8*	15.1±	0.4	32.5±	0.5	1439±	107
2000 ppm	10	10.79±	0.17	16.6±	0.3**	51.1±	1.1	47.4±	0.7**	15.4±	0.3**	32.5±	0.4	1285±	434
4000 ppm	10	10.58±	0.32	16.4±	0.3**	50.2±	1.3	47.5±	0.3**	15.5±	0.2**	32.7±	0.4	1344±	77
8000 ppm	10	10.30±	0.36**	16.0±	0.5	49.9±	2.0	48.4±	0.4**	15.5±	0.2**	32.1±	0.4	1535±	95*

Significant difference ; \* :  $P \leq 0.05$

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 3

STUDY NO. : 0258  
 ANIMAL : MOUSE BDF1  
 SAMPLING DATE : 013-7  
 SEX : MALE

REPORT TYPE : A1

HEMATOLOGY (SUMMARY)  
 SURVIVAL ANIMALS ( 13)

PAGE : 2

Group Name	NO. of Animals	WBC 10 <sup>3</sup> /μl		Differential N-BAND		WBC (%) N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHERS	
Control	10	1.60±	0.95	0±	0	17±	5	2±	2	0±	0	4±	2	77±	6	0±	0
500 ppm	10	1.72±	1.08	0±	0	15±	4	2±	2	0±	0	3±	2	80±	6	0±	0
1000 ppm	10	1.51±	1.14	0±	0	16±	4	1±	1	0±	0	3±	2	80±	4	0±	0
2000 ppm	10	1.45±	0.88	0±	0	14±	7	1±	2	0±	0	3±	2	81±	6	0±	0
4000 ppm	10	1.18±	0.91	0±	0	16±	5	1±	2	0±	0	4±	2	79±	6	0±	0
8000 ppm	10	1.18±	0.86	0±	0	19±	8	1±	1	0±	0	4±	2	78±	9	0±	0

Significant difference ; \* :  $P \leq 0.05$

\*\* :  $P \leq 0.01$

Test of Dunnett

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## APPENDIX D 2

HEMATOLOGY : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0258  
 ANIMAL : MOUSE BDF1  
 SAMPLING DATE : 013-7  
 SEX : FEMALE

REPORT TYPE : A1

HEMATOLOGY (SUMMARY)  
 SURVIVAL ANIMALS ( 13)

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	10	10.70± 0.59	16.1± 0.9	49.4± 2.9	46.1± 0.5	15.1± 0.3	32.7± 0.5	1216± 89
500 ppm	10	10.64± 0.29	16.8± 0.4	50.1± 1.6	47.1± 0.6**	15.8± 0.5**	33.5± 1.3	1297± 86
1000 ppm	10	10.75± 0.25	16.8± 0.4	50.5± 1.4	46.9± 0.5**	15.6± 0.2*	33.2± 0.5	1313± 75
2000 ppm	10	10.75± 0.34	16.8± 0.4	50.6± 1.8	47.0± 0.5**	15.6± 0.2*	33.2± 0.6	1283± 82
4000 ppm	10	10.48± 0.45	16.3± 0.6	48.8± 2.0	46.6± 0.6	15.5± 0.3	33.3± 0.6	1280± 58
8000 ppm	9	9.72± 0.71**	16.0± 0.4	46.5± 3.5*	47.9± 0.5**	16.5± 1.1**	34.5± 2.3**	1343± 146

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

Test of Dunnett

(HCL070)

BAIS 3

STUDY NO. : 0258  
 ANIMAL : MOUSE BDF1  
 SAMPLING DATE : 013-7  
 SEX : FEMALE

REPORT TYPE : A1

HEMATOLOGY (SUMMARY)  
 SURVIVAL ANIMALS ( 13)

PAGE : 4

Group Name	NO. of Animals	WBC 10 <sup>3</sup> /μl		Differential N-BAND		WBC (%) N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHERS	
Control	10	0.88±	0.83	0±	0	24±	14	0±	1	0±	0	2±	1	74±	14	0±	0
500 ppm	10	0.84±	0.82	0±	0	21±	8	0±	0	0±	0	2±	2	77±	7	0±	0
1000 ppm	10	0.82±	0.81	0±	0	19±	4	0±	1	0±	0	2±	1	78±	5	0±	0
2000 ppm	10	1.26±	0.97	0±	0	17±	9	1±	1	0±	0	2±	1	80±	8	0±	0
4000 ppm	10	0.86±	0.60	0±	0	15±	7	1±	1	0±	0	4±	3	80±	7	0±	0
8000 ppm	9	0.86±	0.44	0±	0	23±	18	1±	1	0±	0	3±	2	73±	17	0±	0

Significant difference ; \* :  $P \leq 0.05$

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS3



## APPENDIX E 1

BIOCHEMISTRY : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0258  
ANIMAL : MOUSE BDF1  
SAMPLING DATE : 014-1  
SEX : MALE

BIOCHEMISTRY (SUMMARY)  
SURVIVAL ANIMALS ( 13)

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	5.4±	0.1	3.0±	0.1	1.3±	0.0	0.40±	0.12	226±	63	78±	5	74±	14
500 ppm	10	5.4±	0.2	3.1±	0.1	1.3±	0.1	0.37±	0.12	191±	43	69±	8	58±	13
1000 ppm	10	5.2±	0.2	3.0±	0.1	1.4±	0.1	0.38±	0.09	191±	47	67±	11*	54±	13*
2000 ppm	10	5.2±	0.2	3.0±	0.2	1.4±	0.2**	0.34±	0.08	211±	40	68±	8*	60±	16
4000 ppm	10	5.1±	0.3*	3.0±	0.2	1.4±	0.1*	0.39±	0.11	227±	47	67±	13*	59±	20
8000 ppm	10	5.1±	0.3*	2.9±	0.2	1.4±	0.1*	0.40±	0.14	224±	44	73±	7	48±	10**

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

Test of Dunnett

STUDY NO. : 0258  
ANIMAL : MOUSE BDF1  
SAMPLING DATE : 014-1  
SEX : MALE

REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)  
SURVIVAL ANIMALS ( 13)

PAGE : 2

Group Name	NO. of Animals	GOT I U / ℓ		GPT I U / ℓ		LDH I U / ℓ		ALP I U / ℓ		CPK I U / ℓ		UREA NITROGEN mg / dl		SODIUM mEq / ℓ	
Control	10	53±	9	18±	2	217±	25	177±	16	43±	7	26.1±	5.2	154±	1
500 ppm	10	54±	12	18±	2	228±	28	189±	12	48±	9	23.5±	4.0	154±	1
1000 ppm	10	50±	9	18±	2	213±	36	177±	7	47±	16	24.6±	6.5	154±	2
2000 ppm	10	46±	6	20±	7	208±	42	182±	12	47±	18	24.3±	5.1	154±	1
4000 ppm	10	47±	5	18±	3	213±	17	187±	14	41±	10	20.5±	3.1*	155±	2
8000 ppm	10	44±	4	17±	2	183±	24	168±	28	41±	10	17.0±	2.4**	155±	2

Significant difference ; \* :  $P \leq 0.05$

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS3

STUDY NO. : 0258  
 ANIMAL : MOUSE BDF1  
 SAMPLING DATE : 014-1  
 SEX : MALE

REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)  
 SURVIVAL ANIMALS ( 13)

PAGE : 3

Group Name	NO. of Animals	POTASSIUM mEq/ℓ		CHLORIDE mEq/ℓ		CALCIUM mg/dℓ		INORGANIC PHOSPHORUS mg/dℓ	
Control	10	4.6±	0.5	123±	3	8.8±	0.3	7.6±	1.2
500 ppm	10	4.5±	0.3	123±	2	8.7±	0.3	7.5±	0.9
1000 ppm	10	4.5±	0.5	123±	2	8.7±	0.3	7.5±	0.8
2000 ppm	10	4.6±	0.6	123±	3	8.7±	0.3	7.7±	1.6
4000 ppm	10	4.3±	0.5	124±	3	8.7±	0.3	7.7±	0.5
8000 ppm	10	4.4±	0.5	124±	2	8.8±	0.3	7.8±	1.2

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

Test of Dunnett

(HCL074)

BAIS3

## APPENDIX E 2

BIOCHEMISTRY : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0258  
 ANIMAL : MOUSE BDF1  
 SAMPLING DATE : 014-1  
 SEX : FEMALE

REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)  
 SURVIVAL ANIMALS ( 13)

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	5.5±	0.2	3.4±	0.1	1.5±	0.1	0.30±	0.09	184±	29	71±	11	49±	15
500 ppm	10	5.6±	0.2	3.4±	0.1	1.6±	0.1	0.32±	0.07	188±	28	61±	6*	41±	8
1000 ppm	10	5.6±	0.2	3.5±	0.2	1.6±	0.1	0.35±	0.08	179±	30	59±	7*	42±	8
2000 ppm	10	5.5±	0.2	3.4±	0.1	1.6±	0.1	0.36±	0.12	182±	37	62±	9	45±	9
4000 ppm	10	5.2±	0.1**	3.2±	0.1	1.6±	0.1	0.31±	0.11	174±	30	63±	6	44±	7
8000 ppm	9	5.1±	0.2**	3.2±	0.1*	1.6±	0.1	0.37±	0.11	194±	36	71±	7	48±	9

Significant defference ; \* :  $P \leq 0.05$

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS3

STUDY NO. : 0258  
 ANIMAL : MOUSE BDF1  
 SAMPLING DATE : 014-1  
 SEX : FEMALE

REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)  
 SURVIVAL ANIMALS ( 13)

PAGE : 5

Group Name	NO. of Animals	GOT IU / ℓ		GPT IU / ℓ		LDH IU / ℓ		ALP IU / ℓ		CPK IU / ℓ		UREA NITROGEN mg / dl		SODIUM mEq / ℓ	
Control	10	72±	28	21±	4	281±	144	307±	38	88±	102	21.1±	4.3	154±	2
500 ppm	10	66±	10	22±	3	271±	62	309±	34	63±	24	21.2±	3.3	154±	1
1000 ppm	10	70±	11	25±	5	261±	61	317±	28	77±	50	20.8±	2.6	154±	1
2000 ppm	10	61±	9	24±	4	230±	45	289±	37	55±	32	20.5±	2.1	155±	1
4000 ppm	10	62±	7	24±	4	236±	36	270±	23	46±	13	16.6±	2.5**	155±	2
8000 ppm	9	81±	47	29±	10	276±	115	275±	29	70±	46	16.3±	3.0**	155±	2

Significant defference ; \* :  $P \leq 0.05$

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 3

STUDY NO. : 0258  
ANIMAL : MOUSE BDF1  
SAMPLING DATE : 014-1  
SEX : FEMALE

REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)  
SURVIVAL ANIMALS ( 13)

PAGE : 6

Group Name	NO. of Animals	POTASSIUM mEq/ℓ		CHLORIDE mEq/ℓ		CALCIUM mg/dℓ		INORGANIC PHOSPHORUS mg/dℓ	
Control	10	4.4±	0.4	122±	3	8.8±	0.3	7.6±	1.0
500 ppm	10	4.4±	0.3	124±	2	8.8±	0.3	7.2±	0.5
1000 ppm	10	4.3±	0.3	122±	4	8.7±	0.3	6.8±	0.6
2000 ppm	10	4.2±	0.6	123±	3	8.8±	0.3	7.1±	1.0
4000 ppm	10	4.1±	0.6	122±	3	8.8±	0.3	6.9±	1.2
8000 ppm	9	4.0±	0.5	123±	3	8.7±	0.3	8.5±	1.2

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

Test of Dunnett

(HCL074)

BAIS3



## APPENDIX F 1

URINALYSIS : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0258  
 ANIMAL : MOUSE BDF1  
 SAMPLING DATE : 013-3  
 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	4	3		0	1	8	1	0	0		10	0	0	0	0	0		0	6	3	1	0	0		10	0	0	0	0	
500 ppm	10	0	0	2	1	4	3	0		0	2	7	1	0	0		10	0	0	0	0	0		0	6	3	1	0	0		10	0	0	0	0	
1000 ppm	10	0	0	0	0	2	7	1		0	2	7	1	0	0		10	0	0	0	0	0		0	7	3	0	0	0		10	0	0	0	0	
2000 ppm	10	0	0	1	0	1	7	1		0	2	8	0	0	0		10	0	0	0	0	0		0	6	4	0	0	0		10	0	0	0	0	
4000 ppm	10	0	0	1	0	1	6	2		0	1	9	0	0	0		10	0	0	0	0	0		3	6	1	0	0	0		10	0	0	0	0	
8000 ppm	10	0	0	0	1	3	5	1		0	3	6	1	0	0		10	0	0	0	0	0		1	7	2	0	0	0		9	1	0	0	0	

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

Test of CHI SQUARE

(HCL101)

BAIS3

STUDY NO. : 0258  
ANIMAL : MOUSE BDF1  
SAMPLING DATE : 013-3  
SEX : MALE

URINALYSIS

REPORT TYPE : A1

PAGE : 2

Group Name	NO. of Animals	Urobilinogen ± + 2+ 3+ 4+ CHI
Control	10	10 0 0 0 0
500 ppm	10	10 0 0 0 0
1000 ppm	10	10 0 0 0 0
2000 ppm	10	10 0 0 0 0
4000 ppm	10	10 0 0 0 0
8000 ppm	10	10 0 0 0 0

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

Test of CHI SQUARE

(HCL101)

BAIS3

## APPENDIX F 2

URINALYSIS : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0258  
 ANIMAL : MOUSE BDF1  
 SAMPLING DATE : 013-3  
 SEX : FEMALE

REPORT TYPE : A1

# URINALYSIS

PAGE : 3

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	2	0	5	3	0		0	3	7	0	0	0		10	0	0	0	0	0		0	8	2	0	0	0		10	0	0	0	0	
500 ppm	10	0	0	1	2	4	3	0		0	8	2	0	0	0	*	10	0	0	0	0	0		0	10	0	0	0	0		10	0	0	0	0	
1000 ppm	10	0	0	0	0	5	5	0		0	3	7	0	0	0		10	0	0	0	0	0		1	9	0	0	0	0		10	0	0	0	0	
2000 ppm	10	0	0	0	0	2	7	1		0	4	6	0	0	0		10	0	0	0	0	0		1	9	0	0	0	0		10	0	0	0	0	
4000 ppm	10	0	0	1	1	0	8	0	*	0	6	4	0	0	0		10	0	0	0	0	0		2	8	0	0	0	0		10	0	0	0	0	
8000 ppm	9	0	3	1	1	1	2	1		0	8	1	0	0	0	**	9	0	0	0	0	0		1	8	0	0	0	0		9	0	0	0	0	

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

Test of CHI SQUARE

(HCL101)

BAIS3

STUDY NO. : 0258  
ANIMAL : MOUSE BDF1  
SAMPLING DATE : 013-3  
SEX : FEMALE

URINALYSIS

REPORT TYPE : A1

PAGE : 4

Group Name	NO. of Animals	Urobilinogen					CHI
		±	+	2+	3+	4+	
Control	10	10	0	0	0	0	0
500 ppm	10	10	0	0	0	0	0
1000 ppm	10	10	0	0	0	0	0
2000 ppm	10	10	0	0	0	0	0
4000 ppm	10	10	0	0	0	0	0
8000 ppm	9	9	0	0	0	0	0

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

Test of CHI SQUARE

(HCL101)

BAIS3

## APPENDIX G 1

GROSS FINDINGS : SUMMARY, MOUSE : MALE : SACRIFICED ANIMALS  
(13-WEEK STUDY)

STUDY NO. : 0258  
ANIMAL : MOUSE BDF1  
REPORT TYPE : A1  
SEX : MALE

GROSS FINDINGS (SUMMARY)  
SACRIFICED ANIMALS ( 13W)

PAGE : 1

Organ	Findings	Group Name NO. of Animals	Control		500 ppm		1000 ppm		2000 ppm	
			10	(%)	10	(%)	10	(%)	10	(%)
skin/app	scab		0	( 0)	0	( 0)	0	( 0)	0	( 0)
spleen	black zone		0	( 0)	0	( 0)	3	( 30)	1	( 10)
kidney	hydronephrosis		0	( 0)	0	( 0)	0	( 0)	0	( 0)
testis	atrophic		0	( 0)	0	( 0)	1	( 10)	0	( 0)

(HPT080)

BAIS 3



STUDY NO. : 0258  
ANIMAL : MOUSE BDF1  
REPORT TYPE : A1  
SEX : MALE

GROSS FINDINGS (SUMMARY)  
SACRIFICED ANIMALS ( 13W)

PAGE : 2

Organ_____	Findings_____	Group Name NO. of Animals	4000 ppm		8000 ppm	
			10	(%)	10	(%)
skin/app	scab		0	( 0)	1	( 10)
spleen	black zone		0	( 0)	0	( 0)
kidney	hydronephrosis		1	( 10)	0	( 0)
testis	atrophic		0	( 0)	0	( 0)

(HPT080)

BAIS3

## APPENDIX G 2

GROSS FINDINGS : SUMMARY, MOUSE : FEMALE : DEAD AND MORIBUND ANIMALS  
(13-WEEK STUDY)

STUDY NO. : 0258  
ANIMAL : MOUSE BDF1  
REPORT TYPE : A1  
SEX : FEMALE

GROSS FINDINGS (SUMMARY)  
DEAD AND MORIBUND ANIMALS (0- 13W)

PAGE : 1

Organ	Findings	Group Name	Control	500 ppm	1000 ppm	2000 ppm
		NO. of Animals	0 (%)	0 (%)	0 (%)	0 (%)
lung	red		- ( -)	- ( -)	- ( -)	- ( -)
pleura	deformed		- ( -)	- ( -)	- ( -)	- ( -)

(HPT080)

BAIS3

STUDY NO. : 0258  
ANIMAL : MOUSE BDF1  
REPORT TYPE : A1  
SEX : FEMALE

GROSS FINDINGS (SUMMARY)  
DEAD AND MORIBUND ANIMALS (0- 13W)

PAGE : 2

Organ	Findings	Group Name	4000 ppm	8000 ppm
		NO. of Animals	0 (%)	1 (%)
lung	red		- ( -)	1 (100)
pleura	deformed		- ( -)	1 (100)

(HPT080)

BAIS 3

## APPENDIX G 3

GROSS FINDINGS : SUMMARY, MOUSE : FEMALE : SACRIFICED ANIMALS  
(13-WEEK STUDY)

STUDY NO. : 0258  
ANIMAL : MOUSE BDF1  
REPORT TYPE : A1  
SEX : FEMALE

GROSS FINDINGS (SUMMARY)  
SACRIFICED ANIMALS ( 13W)

PAGE : 3

Organ	Findings	Group Name		Control		500 ppm		1000 ppm		2000 ppm	
		NO. of Animals		10	(%)	10	(%)	10	(%)	10	(%)
spleen	black zone			2	( 20)	2	( 20)	1	( 10)	0	( 0)

(HPT080)

BAIS 3

STUDY NO. : 0258  
ANIMAL : MOUSE BDF1  
REPORT TYPE : A1  
SEX : FEMALE

GROSS FINDINGS (SUMMARY)  
SACRIFICED ANIMALS ( 13W)

PAGE : 4

Organ	Findings	Group Name NO. of Animals	4000 ppm 10 (%)	8000 ppm 9 (%)
spleen	black zone		0 ( 0)	1 ( 11)

(HPT080)

BAIS 3

## APPENDIX H 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOUSE : MALE  
(13-WEEK STUDY)



STUDY NO. : 0258  
 ANIMAL : MOUSE BDF1  
 REPORT TYPE : A1  
 SEX : MALE  
 UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)  
 SURVIVAL ANIMALS ( 13)

PAGE : 1

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	29.5± 1.5	0.035± 0.006	0.007± 0.002	0.186± 0.039	0.161± 0.009	0.153± 0.012
500 ppm	10	28.4± 1.7	0.038± 0.007	0.006± 0.001	0.194± 0.033	0.162± 0.012	0.155± 0.006
1000 ppm	10	28.0± 2.3	0.036± 0.006	0.006± 0.001	0.197± 0.046	0.161± 0.015	0.156± 0.006
2000 ppm	10	28.3± 2.3	0.034± 0.004	0.006± 0.002	0.210± 0.016	0.154± 0.012	0.160± 0.006
4000 ppm	10	29.5± 1.6	0.039± 0.003	0.008± 0.001	0.191± 0.016	0.156± 0.010	0.165± 0.011
8000 ppm	10	28.2± 1.7	0.030± 0.004	0.008± 0.002	0.162± 0.025	0.162± 0.013	0.183± 0.015**

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

Test of Dunnett

(HCL040)

BAIS 3

STUDY NO. : 0258  
ANIMAL : MOUSE BDF1  
REPORT TYPE : A1  
SEX : MALE  
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)  
SURVIVAL ANIMALS ( 13)

PAGE : 2

Group Name	NO. of Animals	KIDNEYS		SPLEEN		LIVER		BRAIN	
Control	10	0.449±	0.020	0.047±	0.005	1.185±	0.071	0.438±	0.014
500 ppm	10	0.442±	0.023	0.045±	0.005	1.192±	0.091	0.441±	0.009
1000 ppm	10	0.445±	0.029	0.045±	0.005	1.178±	0.079	0.438±	0.009
2000 ppm	10	0.432±	0.025	0.047±	0.004	1.224±	0.079	0.442±	0.006
4000 ppm	10	0.530±	0.288	0.048±	0.007	1.304±	0.088*	0.443±	0.023
8000 ppm	10	0.511±	0.049	0.044±	0.007	1.422±	0.131**	0.460±	0.018*

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

Test of Dunnett

(HCL040)

BAIS3

## APPENDIX H 2

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOUSE : FEMALE  
(13-WEEK STUDY)

STUDY NO. : 0258  
ANIMAL : MOUSE BDF1  
REPORT TYPE : A1  
SEX : FEMALE  
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)  
SURVIVAL ANIMALS ( 13)

PAGE : 3

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	22.0± 1.6	0.042± 0.006	0.011± 0.003	0.025± 0.004	0.130± 0.007	0.151± 0.009
500 ppm	10	22.1± 0.8	0.043± 0.007	0.011± 0.002	0.026± 0.007	0.135± 0.008	0.150± 0.007
1000 ppm	10	21.5± 0.8	0.041± 0.006	0.011± 0.002	0.026± 0.003	0.132± 0.007	0.153± 0.007
2000 ppm	10	22.0± 1.3	0.046± 0.006	0.010± 0.001	0.024± 0.004	0.129± 0.009	0.161± 0.011
4000 ppm	10	22.0± 0.9	0.041± 0.005	0.009± 0.001*	0.022± 0.004	0.121± 0.006	0.161± 0.012
8000 ppm	9	20.7± 1.1	0.036± 0.006	0.010± 0.001	0.020± 0.004	0.123± 0.010	0.159± 0.013

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

Test of Dunnett

(HCL040)

BAIS3

STUDY NO. : 0258  
 ANIMAL : MOUSE BDF1  
 REPORT TYPE : A1  
 SEX : FEMALE  
 UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)  
 SURVIVAL ANIMALS ( 13)

PAGE : 4

Group Name	NO. of Animals	KIDNEYS		SPLEEN		LIVER		BRAIN	
Control	10	0.302±	0.015	0.056±	0.008	0.962±	0.087	0.452±	0.013
500 ppm	10	0.309±	0.011	0.055±	0.006	1.001±	0.041	0.455±	0.006
1000 ppm	10	0.301±	0.014	0.053±	0.006	0.975±	0.041	0.450±	0.012
2000 ppm	10	0.305±	0.016	0.058±	0.009	1.032±	0.072	0.449±	0.014
4000 ppm	10	0.302±	0.014	0.053±	0.005	1.073±	0.056**	0.441±	0.012
8000 ppm	9	0.326±	0.018**	0.041±	0.005**	1.191±	0.092**	0.453±	0.013

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

Test of Dunnett

(HCL040)

BAIS 3

## APPENDIX I 1

ORGAN WEIGHT, RELATIVE : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0258  
ANIMAL : MOUSE BDF1  
REPORT TYPE : A1  
SEX : MALE  
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)  
SURVIVAL ANIMALS ( 13)

PAGE : 1

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	29.5± 1.5	0.121± 0.022	0.023± 0.006	0.633± 0.126	0.546± 0.045	0.520± 0.061
500 ppm	10	28.4± 1.7	0.133± 0.021	0.023± 0.005	0.682± 0.117	0.569± 0.046	0.546± 0.037
1000 ppm	10	28.0± 2.3	0.129± 0.013	0.023± 0.004	0.701± 0.144	0.575± 0.036	0.560± 0.045
2000 ppm	10	28.3± 2.3	0.121± 0.014	0.022± 0.007	0.745± 0.082	0.545± 0.046	0.568± 0.042
4000 ppm	10	29.5± 1.6	0.131± 0.009	0.026± 0.006	0.650± 0.046	0.529± 0.039	0.561± 0.036
8000 ppm	10	28.2± 1.7	0.105± 0.013	0.028± 0.008	0.576± 0.100	0.575± 0.025	0.650± 0.045**

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

Test of Dunnett

(HCL042)

BAIS 3

STUDY NO. : 0258  
ANIMAL : MOUSE BDF1  
REPORT TYPE : A1  
SEX : MALE  
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)  
SURVIVAL ANIMALS ( 13)

PAGE : 2

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.526± 0.102	0.160± 0.018	4.021± 0.155	1.490± 0.104
500 ppm	10	1.558± 0.085	0.159± 0.016	4.194± 0.258	1.556± 0.092
1000 ppm	10	1.593± 0.098	0.163± 0.016	4.217± 0.138	1.577± 0.144
2000 ppm	10	1.531± 0.096	0.167± 0.013	4.331± 0.175*	1.572± 0.125
4000 ppm	10	1.807± 1.015	0.164± 0.023	4.429± 0.252**	1.508± 0.106
8000 ppm	10	1.810± 0.090**	0.155± 0.023	5.044± 0.289**	1.637± 0.096

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

Test of Dunnett

(HCL042)

BAIS3



## APPENDIX I 2

ORGAN WEIGHT, RELATIVE : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0258  
 ANIMAL : MOUSE BDF1  
 REPORT TYPE : A1  
 SEX : FEMALE  
 UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)  
 SURVIVAL ANIMALS ( 13)

PAGE : 3

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	22.0± 1.6	0.189± 0.017	0.051± 0.008	0.113± 0.020	0.594± 0.032	0.690± 0.045
500 ppm	10	22.1± 0.8	0.194± 0.027	0.050± 0.008	0.119± 0.027	0.612± 0.031	0.677± 0.036
1000 ppm	10	21.5± 0.8	0.189± 0.023	0.053± 0.008	0.121± 0.013	0.613± 0.037	0.711± 0.043
2000 ppm	10	22.0± 1.3	0.211± 0.024	0.046± 0.006	0.109± 0.021	0.586± 0.031	0.731± 0.047
4000 ppm	10	22.0± 0.9	0.184± 0.022	0.039± 0.005**	0.102± 0.018	0.550± 0.024*	0.730± 0.049
8000 ppm	9	20.7± 1.1	0.173± 0.027	0.047± 0.005	0.098± 0.017	0.596± 0.040	0.765± 0.042**

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

Test of Dunnett

(HCL042)

BAIS 3

STUDY NO. : 0258  
ANIMAL : MOUSE BDF1  
REPORT TYPE : A1  
SEX : FEMALE  
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)  
SURVIVAL ANIMALS ( 13)

PAGE : 4

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.379± 0.063	0.255± 0.019	4.375± 0.165	2.066± 0.163
500 ppm	10	1.402± 0.066	0.248± 0.020	4.528± 0.055	2.062± 0.077
1000 ppm	10	1.401± 0.048	0.244± 0.022	4.537± 0.087	2.096± 0.082
2000 ppm	10	1.387± 0.036	0.265± 0.031	4.696± 0.135**	2.046± 0.114
4000 ppm	10	1.368± 0.054	0.241± 0.018	4.869± 0.170**	2.003± 0.064
8000 ppm	9	1.574± 0.077**	0.200± 0.018**	5.748± 0.304**	2.189± 0.098

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

Test of Dunnett

(HCL042)

BAIS3

APPENDIX J 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : MALE : SACRIFICED ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0258  
 ANIMAL : MOUSE BDF1  
 REPORT TYPE : A1  
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS ( 13W)

PAGE : 1

Organ	Findings	Group Name No. of Animals on Study Grade	Control 10				500 ppm 10				1000 ppm 10				2000 ppm 10			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Integumentary system/appandage]																		
skin/app	inflammation		<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 )
[Respiratory system]																		
lung	hemorrhage		<10>				<10>				<10>				<10>			
			1	0	0	0	0	0	0	0	1	0	0	0	4	0	0	0
			( 10 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 10 )	( 0 )	( 0 )	( 0 )	( 40 )	( 0 )	( 0 )	( 0 )
[Hematopoietic system]																		
spleen	deposit of melanin		<10>				<10>				<10>				<10>			
			0	0	0	0	0	0	0	0	3	0	0	0	1	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 30 )	( 0 )	( 0 )	( 0 )	( 10 )	( 0 )	( 0 )	( 0 )
[Digestive system]																		
liver	vacuolic change:peripheral		<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 )

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

STUDY NO. : 0258  
 ANIMAL : MOUSE BDF1  
 REPORT TYPE : A1  
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS ( 13W)

PAGE : 2

Organ	Findings	Group Name No. of Animals on Study Grade	4000 ppm				8000 ppm			
			10				10			
			1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

[Integumentary system/appandage]

skin/app	inflammation	<10>				<10>			
		0	0	0	0	2	0	0	0
		( 0)	( 0)	( 0)	( 0)	( 20)	( 0)	( 0)	( 0)

[Respiratory system]

lung	hemorrhage	<10>				<10>			
		2	0	0	0	2	0	0	0
		( 20)	( 0)	( 0)	( 0)	( 20)	( 0)	( 0)	( 0)

[Hematopoietic system]

spleen	deposit of melanin	<10>				<10>			
		0	0	0	0	0	0	0	0
		( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)

[Digestive system]

liver	vacuolic change:peripheral	<10>				<10>			
		0	0	0	0	3	0	0	0
		( 0)	( 0)	( 0)	( 0)	( 30)	( 0)	( 0)	( 0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b b : Number of animals with lesion

( c ) c : b / a \* 100

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

STUDY NO. : 0258  
ANIMAL : MOUSE BDF1  
REPORT TYPE : A1  
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
SACRIFICED ANIMALS ( 13W)

PAGE : 3

Organ	Findings	Group Name No. of Animals on Study Grade	Control 10				500 ppm 10				1000 ppm 10				2000 ppm 10			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																		
kidney			<10>				<10>				<10>				<10>			
	basophilic change		1 ( 10)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 10)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
	inflammatory polyp		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)
	vacuolization of proximal tubule		9 ( 90)	0 ( 0)	0 ( 0)	0 ( 0)	2 ( 20)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 10)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
	hydronephrosis		0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
[Endocrine system]																		
pituitary			<10>				<10>				<10>				<10>			
	cyst		2 ( 20)	0 ( 0)	0 ( 0)	0 ( 0)	2 ( 20)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b : 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. : 0258  
 ANIMAL : MOUSE BDF1  
 REPORT TYPE : A1  
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS ( 13W)

PAGE : 4

Organ	Findings	4000 ppm				8000 ppm			
		10				10			
		1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]									
kidney		<10>				<10>			
	basophilic change	0	0	0	0	1	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 10 )	( 0 )	( 0 )	( 0 )
	inflammatory polyp	1	0	0	0	0	0	0	0
		( 10 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	vacuolization of proximal tubule	0	0	0	0 **	0	0	0	0 **
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	hydronephrosis	0	0	1	0	0	0	0	0
		( 0 )	( 0 )	( 10 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
[Endocrine system]									
pituitary		<10>				<10>			
	cyst	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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$  Test of Chi Square



APPENDIX J 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : FEMALE : DEAD AND MORIBUND ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0258  
 ANIMAL : MOUSE BDF1  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0- 13W)

PAGE : 1

Organ	Findings	Group Name	Control				500 ppm				1000 ppm				2000 ppm			
		No. of Animals on Study	0				0				0				0			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
lung			< 0>				< 0>				< 0>				< 0>			
	congestion		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )
	hemorrhage		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )
[Digestive system]																		
liver			< 0>				< 0>				< 0>				< 0>			
	vacuolic change:peripheral		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )
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																	
(HPT150)																		

BAIS3

STUDY NO. : 0258  
 ANIMAL : MOUSE BDF1  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0- 13W)

PAGE : 2

		Group Name				4000 ppm				8000 ppm			
		No. of Animals on Study				0				1			
		Grade											
Organ_____	Findings_____					1	2	3	4				
						(%)	(%)	(%)	(%)				
						(%)	(%)	(%)	(%)	1	2	3	4
						(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

[Respiratory system]

Lung	congestion	< 0>				< 1>			
		-	-	-	-	0	0	1	0
		( - )	( - )	( - )	( - )	( 0 )	( 0 )	( 100 )	( 0 )
	hemorrhage	-	-	-	-	1	0	0	0
		( - )	( - )	( - )	( - )	( 100 )	( 0 )	( 0 )	( 0 )

[Digestive system]

Liver	vacuolic change:peripheral	< 0>				< 1>			
		-	-	-	-	1	0	0	0
		( - )	( - )	( - )	( - )	( 100 )	( 0 )	( 0 )	( 0 )

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

(HPT150)

BA1S3

APPENDIX J 3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : FEMALE : SACRIFICED ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0258  
ANIMAL : MOUSE BDF1  
REPORT TYPE : A1  
SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
SACRIFICED ANIMALS ( 13W)

PAGE : 5

Organ	Findings	Group Name No. of Animals on Study				Control 10				500 ppm 10				1000 ppm 10				2000 ppm 10			
		Grade																			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																					
nasal cavity	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 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	eosinophilic change:respiratory 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 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
lung	hemorrhage	1	0	0	0	3	0	0	0	2	0	0	0	3	0	0	0	3	0	0	0
		( 10 )	( 0 )	( 0 )	( 0 )	( 30 )	( 0 )	( 0 )	( 0 )	( 20 )	( 0 )	( 0 )	( 0 )	( 30 )	( 0 )	( 0 )	( 0 )	( 30 )	( 0 )	( 0 )	( 0 )
[Hematopoietic system]																					
spleen	deposit of melanin	2	0	0	0	2	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
		( 20 )	( 0 )	( 0 )	( 0 )	( 20 )	( 0 )	( 0 )	( 0 )	( 10 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
[Digestive system]																					
liver	granulation	1	0	0	0	1	0	0	0	0	0	0	0	2	0	0	0	2	0	0	0
		( 10 )	( 0 )	( 0 )	( 0 )	( 10 )	( 0 )	( 0 )	( 0 )	( 0 )	( 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

STUDY NO. : 0258  
 ANIMAL : MOUSE BDF1  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS ( 13W)

PAGE : 6

Organ	Findings	4000 ppm				8000 ppm			
		10				9			
		1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]									
nasal cavit	eosinophilic change:olfactory epithelium	<10>				< 9>			
		1	0	0	0	0	0	0	0
		( 10)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
	eosinophilic change:respiratory epithelium	<10>				< 9>			
		0	1	0	0	0	0	0	0
		( 0)	( 10)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
lung	hemorrhage	<10>				< 9>			
		2	0	0	0	2	0	0	0
		( 20)	( 0)	( 0)	( 0)	( 22)	( 0)	( 0)	( 0)
[Hematopoietic system]									
spleen	deposit of melanin	<10>				< 9>			
		0	0	0	0	1	0	0	0
		( 0)	( 0)	( 0)	( 0)	( 11)	( 0)	( 0)	( 0)
[Digestive system]									
liver	granulation	<10>				< 9>			
		0	0	0	0	1	0	0	0
		( 0)	( 0)	( 0)	( 0)	( 11)	( 0)	( 0)	( 0)

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

STUDY NO. : 0258  
 ANIMAL : MOUSE BDF1  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS ( 13W)

PAGE : 7

Organ_____	Findings_____	Group Name	Control				500 ppm				1000 ppm				2000 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
<hr/>																		
[Digestive system]																		
liver			<10>				<10>				<10>				<10>			
	vacuolic change:peripheral		0	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0 *
			( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 50)	( 0)	( 0)	( 0)	( 0)
 [Endocrine system]																		
thyroid			<10>				<10>				<10>				<10>			
	ultimibranchial body remanet		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			( 0)	( 0)	( 0)	( 0)	( 10)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)

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)

BAISS

STUDY NO. : 0258  
 ANIMAL : MOUSE BDF1  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS ( 13W)

PAGE : 8

		4000 ppm				8000 ppm			
		10				9			
		Grade				Grade			
Organ_____	Findings_____	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

[Digestive system]

Liver	vacuolic change:peripheral	<10>				< 9>			
		10	0	0	0 **	2	7	0	0 **
		(100)	( 0)	( 0)	( 0)	( 22)	( 78)	( 0)	( 0)

[Endocrine system]

thyroid	ultimibranchial body remanet	<10>				< 9>			
		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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$  Test of Chi Square

(HPT150)

BA153



APPENDIX K 1

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS : SUMMARY

MOUSE : MALE : ALL ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0258  
ANIMAL : MOUSE Crj:BDF1  
REPORT TYPE : A1  
SEX : MALE

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)  
ALL ANIMALS (0- 13W)

PAGE : 1

Organ	Findings	Group Name No. of animals on Study	Control 10	500 ppm 10	1000 ppm 10	2000 ppm 10
-------	----------	---------------------------------------	---------------	---------------	----------------	----------------

[Respiratory system]

Lung	bronchiolar-alveolar adenoma	<10> 0 ( 0%)	<10> 0 ( 0%)	<10> 0 ( 0%)	<10> 0 ( 0%)
------	------------------------------	-----------------	-----------------	-----------------	-----------------

< a >      a : Number of animals examined at the site  
b ( c )      b : Number of animals with neoplasm      c : b / a \* 100

(HPT085)

BA1S3

STUDY NO. : 0258  
ANIMAL : MOUSE Crj:BDF1  
REPORT TYPE : A1  
SEX : MALE

HISTOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)  
ALL ANIMALS (0- 13W)

PAGE : 2

Organ	Findings	Group Name No. of animals on Study	4000 ppm 10	8000 ppm 10
-------	----------	---------------------------------------	----------------	----------------

[Respiratory system]

lung	bronchiolar-alveolar adenoma	<10> 0 ( 0%)	<10> 1 ( 10%)
------	------------------------------	-----------------	------------------

< a >	a : Number of animals examined at the site	
b ( c )	b : Number of animals with neoplasm	c : b / a * 100

(HPT085)

BA1S3

## APPENDIX L 1

### IDENTITY OF DICHLOROMETHANE IN THE 13-WEEK INHALATION STUDY

## IDENTITY OF DICHLOROMETHANE IN THE 13-WEEK INHALATION STUDY

A. Lot No. APR5259

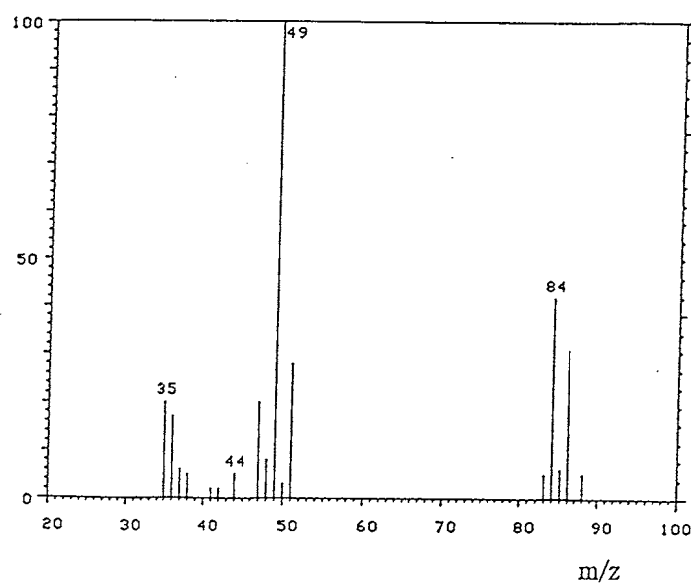
## 1. Spectral data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI(Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Results: The mass spectrum was consistent with literature spectrum.

<u>Determined Values</u>	<u>Literature Values*</u>
Fragment Peak(m/z)	Fragment Peak(m/z)
35	35
49	49
84	84

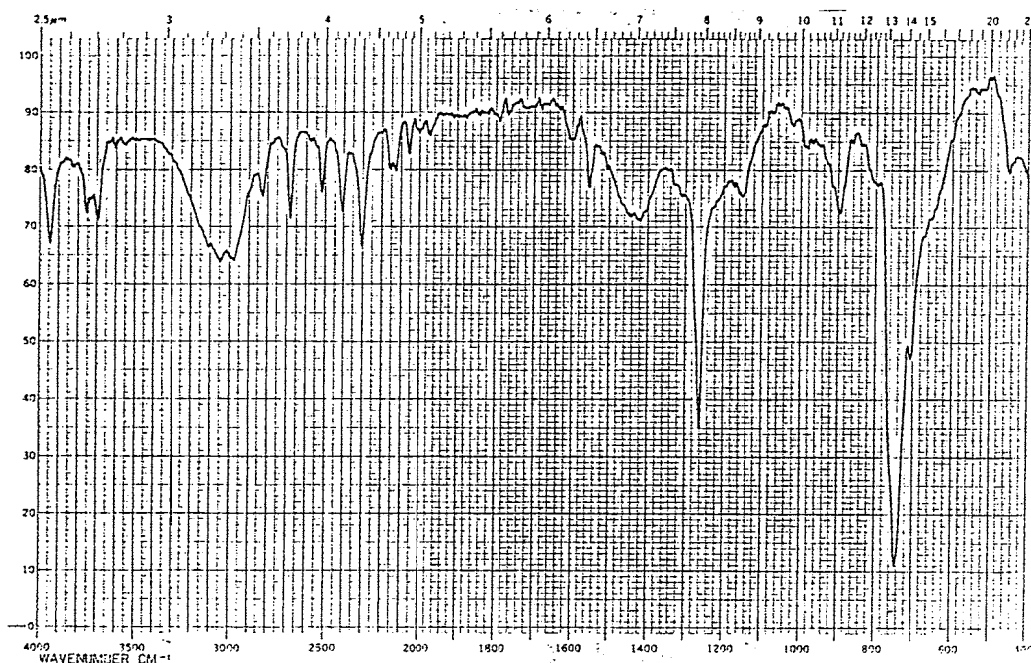
(\*EPA/NIH Mass Spectral Data Base (1978) Vol. 1, p. 33.)

Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr Liquid Cell

Slit : Medium



Infrared Spectrum of Test Substance

Results: The infrared spectrum was consistent with literature spectrum.

<u>Determined Values</u>	<u>Literature Values*</u>
Wave Number( $\text{cm}^{-1}$ )	Wave Number( $\text{cm}^{-1}$ )
430~ 480	
650~ 840	650~ 850
870~ 940	870~ 940
970~1000	970~1000
1120~1180	1130~1180
1200~1340	1200~1350
1370~1500	1380~1500
1530~1570	1540~1570
1580~1630	1580~1630
2040~2090	2050~2090
2100~2190	2120~2190
2250~2360	2280~2370
2380~2460	2400~2460
2500~2550	2500~2560
2650~2730	2650~2730
2800~2860	2800~2860
2900~3200	2900~3200
3650~3730	3670~3750
3730~3800	3750~3800
3900~4000	3900~4000

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

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

B. Lot No. APR5260

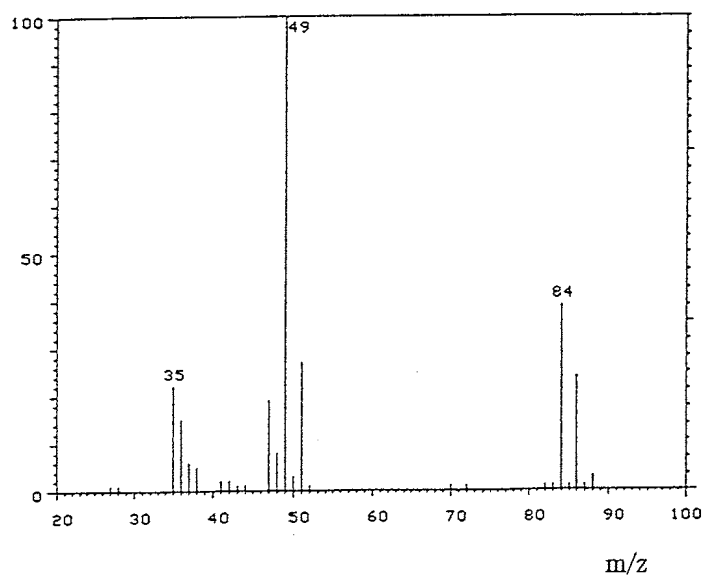
## 1. Spectral data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI(Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Results: The mass spectrum was consistent with literature spectrum.

<u>Determined Values</u>	<u>Literature Values</u> *
Fragment Peak(m/z)	Fragment Peak(m/z)
35	35
49	49
84	84

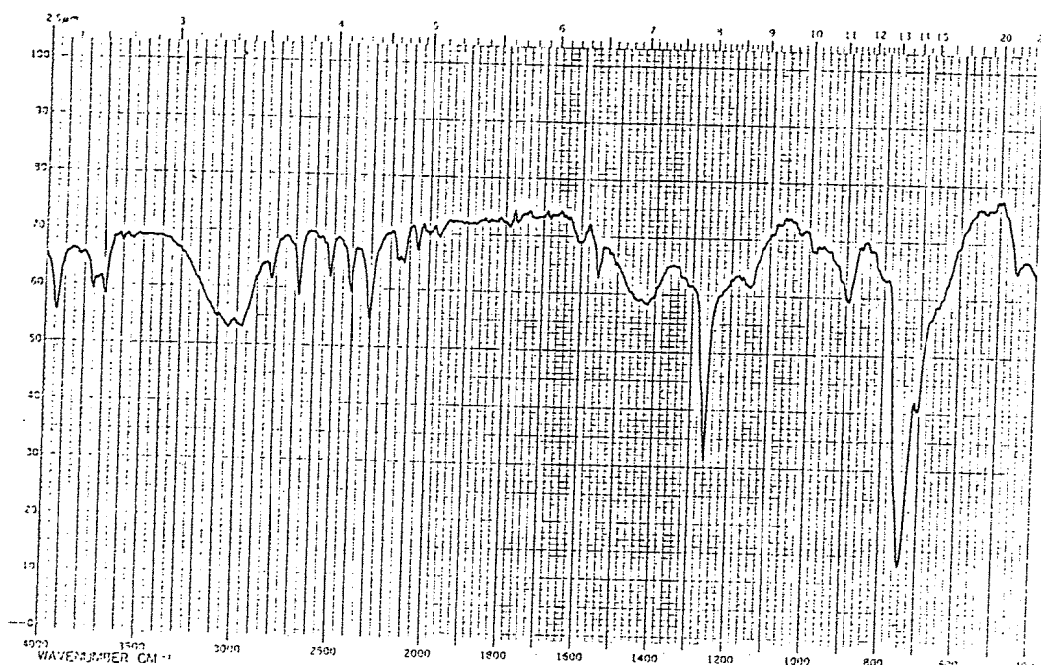
(\*EPA/NIH Mass Spectral Data Base (1978) Vol. 1, p. 33.)

Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr Liquid Cell

Slit : Medium



Infrared Spectrum of Test Substance

Results: The infrared spectrum was consistent with literature spectrum.

<u>Determined Values</u>	<u>Literature Values</u> *
Wave Number( $\text{cm}^{-1}$ )	Wave Number( $\text{cm}^{-1}$ )
430~ 480	
650~ 840	650~ 850
870~ 940	870~ 940
970~1000	970~1000
1120~1180	1130~1180
1200~1340	1200~1350
1370~1500	1380~1500
1530~1570	1540~1570
1580~1630	1580~1630
2040~2090	2050~2090
2100~2190	2120~2190
2250~2360	2280~2370
2380~2460	2400~2460
2500~2550	2500~2560
2650~2730	2650~2730
2800~2860	2800~2860
2900~3200	2900~3200
3650~3730	3670~3750
3730~3800	3750~3800
3900~4000	3900~4000

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

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



## APPENDIX L 2

### STABILITY OF DICHLOROMETHANE IN THE 13-WEEK INHALATION STUDY

## STABILITY OF DICHLOROMETHANE IN THE 13-WEEK INHALATION STUDY

A. Lot No. APR5259

1. Sample: This lot was used from 1994.1.25 to 1994.2.4. Test substance was stored in a dark place at room temperature.

## 2. Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr Liquid Cell

Slit : Medium

Results: The result of infrared spectrum did not change when before and after the lot of study.

<u>1994.01.11(date analyzed)</u>	<u>1994.02.08(date analyzed)</u>
Wave Number( $\text{cm}^{-1}$ )	Wave Number( $\text{cm}^{-1}$ )
430~ 480	430~ 480
650~ 840	650~ 840
870~ 940	870~ 940
970~1000	970~1000
1120~1180	1120~1180
1200~1340	1200~1340
1370~1500	1370~1500
1530~1570	1530~1570
1580~1630	1580~1630
2040~2090	2040~2090
2100~2190	2100~2190
2250~2360	2250~2360
2380~2460	2380~2460
2500~2550	2500~2550
2650~2730	2650~2730
2800~2860	2800~2860
2900~3200	2900~3200
3650~3730	3650~3730
3730~3800	3730~3800
3900~4000	3900~4000

## 3. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : Methyl Silicone(0.2 mm  $\phi$   $\times$  50 m)Column Temperature : 60  $^{\circ}\text{C}$ 

Flow Rate : 1 ml/min

Detector : FID(Flame Ionization Detector)

Injection Volume : 1  $\mu\text{l}$

Results: Gas chromatography indicated one major peak (peak No.1) and one impurity (peak No.2 < 1% of total area) analyzed at 1994.1.11 and one major peak (peak No.1) and one impurity (peak No.2 < 1% of total area) analyzed at 1994.2.8. No new trace impurity peak in the test substance analyzed at 1994.2.8 was detected.

Date (date analyzed)	Peak No.	Retention Time(min)	Area Count
1994.01.11	1	3.303	64234
	2	3.41	10
1994.02.08	1	3.302	64221
	2	3.407	8

4. Conclusions: The test substance was stable for about 1 month in a dark place at room temperature.

B. Lot No. APR5260

1. Sample: This lot was used from 1994.2.7 to 1994.4.25 Test substance was stored in a dark place at room temperature.

## 2. Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr Liquid Cell

Slit : Medium

Results: The result of infrared spectrum did not change when before and after the lot of study.

<u>1994.02.01(date analyzed)</u>	<u>1994.04.28(date analyzed)</u>
Wave Number( $\text{cm}^{-1}$ )	Wave Number( $\text{cm}^{-1}$ )
430~ 480	430~ 480
650~ 840	650~ 840
870~ 940	870~ 940
970~1000	970~1000
1120~1180	1120~1180
1200~1340	1200~1340
1370~1500	1370~1500
1530~1570	1530~1570
1580~1630	1580~1630
2040~2090	2040~2090
2100~2190	2100~2190
2250~2360	2250~2360
2380~2460	2380~2460
2500~2550	2500~2550
2650~2730	2650~2730
2800~2860	2800~2860
2900~3200	2900~3200
3650~3730	3650~3730
3730~3800	3730~3800
3900~4000	3900~4000

## 3. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

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

Column Temperature : 60 °C

Flow Rate : 1 ml/min

Detector : FID(Flame Ionization Detector)

Injection Volume : 1  $\mu$ l

Results: Gas chromatography indicated one major peak (peak No.1) and one impurity (peak No.2 < 1% of total area) analyzed at 1994.2.1 and one major peak (peak No.1) and one impurity (peak No.2 < 1% of total area) analyzed at 1994.4.28. No new trace impurity peak in the test substance analyzed at 1994.4.28 was detected.

Date (date analyzed)	Peak No.	Retention Time(min)	Area Count
1994.02.01	1	3.305	65049
	2	3.41	7
1994.04.28	1	3.302	64232
	2	3.407	9

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

## APPENDIX M 1

### CONCENTRATION OF DICHLOROMETHANE IN THE INHALATION CHAMBER OF THE 13-WEEK INHALATION STUDY

# CONCENTRATION OF DICHLOROMETHANE IN INHALATION CHAMBER

Group Name	Concentration(ppm)	
	Mean $\pm$	S.D.
Control	0.0 $\pm$	0.0
500ppm	501.9 $\pm$	1.3
1,000ppm	1,007.8 $\pm$	3.7
2,000ppm	2,000.9 $\pm$	8.8
4,000ppm	4,002.6 $\pm$	10.0
8,000ppm	8,001.3 $\pm$	22.0

## APPENDIX M 2

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER  
IN THE 13-WEEK INHALATION STUDY OF DICHLOROMETHANE



# ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 13-WEEK INHALATION STUDY OF DICHLOROMETHANE

Group Name	Temperature(°C) Mean $\pm$ S.D.	Humidity(%) Mean $\pm$ S.D.	Ventilation Rate(L/min) Mean $\pm$ S.D.	Room Air Change(time/h) Mean
Control	22.1 $\pm$ 0.1	55.9 $\pm$ 0.8	103.9 $\pm$ 0.2	12.0
500ppm	20.9 $\pm$ 0.1	57.2 $\pm$ 1.4	104.2 $\pm$ 0.3	12.0
1,000ppm	21.1 $\pm$ 0.1	56.6 $\pm$ 1.1	104.2 $\pm$ 0.2	12.0
2,000ppm	21.2 $\pm$ 0.1	55.9 $\pm$ 1.0	104.4 $\pm$ 0.2	12.0
4,000ppm	21.2 $\pm$ 0.3	54.8 $\pm$ 0.9	104.3 $\pm$ 0.1	12.0
8,000ppm	21.0 $\pm$ 0.1	54.8 $\pm$ 0.6	104.0 $\pm$ 0.3	12.0

## APPENDIX N 1

### METHODS FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK INHALATION STUDY OF DICHLOROMETHANE

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS IN THE  
13- WEEK INHALATION STUDY OF DICHLOROMETHANE

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> (May-Grunwald-Giemsa 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	Michaelson method <sup>3)</sup>
Glucose	Enzymatic method (HK-G-6-PDH) <sup>3)</sup>
T-cholesterol	Enzymatic method (CEH-COD-POD) <sup>3)</sup>
Triglyceride	Enzymatic method (GK-GPO-POD) <sup>3)</sup>
Glutamic oxaloacetic transaminase (GOT)	UV-Rate method <sup>3)</sup>
Glutamic pyruvic transaminase (GPT)	UV-Rate method <sup>3)</sup>
Lactate dehydrogenase (LDH)	UV-Rate method <sup>3)</sup>
Alkaline phosphatase (ALP)	p-Nitrophenylphosphate method <sup>3)</sup>
Creatine phosphokinase (CPK)	UV-Rate method <sup>3)</sup>
Urea nitrogen	Enzymatic method (Urease-GLDH) <sup>3)</sup>
Sodium	Flame photometry <sup>4)</sup>
Potassium	Flame photometry <sup>4)</sup>
Chloride	Coulometric titration <sup>4)</sup>
Calcium	OCPC method <sup>3)</sup>
Inorganic phosphorus	Enzymatic method (SPL-PGM-G-6-PDH) <sup>3)</sup>
<b>Urinalysis</b>	
pH, Protein, Glucose, Ketone body, Occult Blood, Urobilinogen	Urinalysis reagent paper method <sup>5)</sup>

1) Automatic blood cell analyzer (Technicon H-1 : Technicon Instruments Corporation, USA)

2) Automatic blood cell differential analyzer (Hitachi 8200 : Hitachi, Ltd., Japan)

3) Automatic analyzer (Hitachi 705 : Hitachi, Ltd., Japan)

4) Flame photometer (Hitachi 750 : Hitachi, Ltd., Japan)

5) Ames reagent strips for urinalysis (Uro-Labstix : Miles-Sankyo Co., Ltd., Japan)

## APPENDIX N 2

UNISTS AND DECIMAL PLACEFOR HEMAYOLOGY AND  
BIOCHEMISTRY IN THE 13-WEEK INHALATION STUDY OF DICHLOROMETHANE

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE  
13– WEEK INHALATION STUDY OF DICHLOROMETHANE

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 transaminase (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
Creatinine	mg/dL	1
Sodium	mEq/L	0
Potassium	mEq/L	1
Chloride	mEq/L	0
Calcium	mg/dL	1
Inorganic phosphorus	mg/dL	1