

2-フェノキシエタノールのラットを用いた経口投与  
による2週間毒性試験（混水試験）報告書

試験番号： 0453

## APPENDICES

## APPENDICES

APPENDIX A 1	CLINICAL OBSERVATION: SUMMARY, RAT: MALE ( 2-WEEK STUDY )
APPENDIX A 2	CLINICAL OBSERVATION: SUMMARY, RAT: FEMALE ( 2-WEEK STUDY )
APPENDIX B 1	BODY WEIGHT CHANGES: SUMMARY, RAT: MALE ( 2-WEEK STUDY )
APPENDIX B 2	BODY WEIGHT CHANGES: SUMMARY, RAT: FEMALE ( 2-WEEK STUDY )
APPENDIX C 1	WATER CONSUMPTION CHANGES: SUMMARY, RAT: MALE ( 2-WEEK STUDY )
APPENDIX C 2	WATER CONSUMPTION CHANGES: SUMMARY, RAT: FEMALE ( 2-WEEK STUDY )
APPENDIX D 1	FOOD CONSUMPTION CHANGES: SUMMARY, RAT: MALE ( 2-WEEK STUDY )
APPENDIX D 2	FOOD CONSUMPTION CHANGES: SUMMARY, RAT: FEMALE ( 2-WEEK STUDY )
APPENDIX E 1	CHEMICAL INTAKE CHANGES: SUMMARY, RAT: MALE ( 2-WEEK STUDY )
APPENDIX E 2	CHEMICAL INTAKE CHANGES: SUMMARY, RAT: FEMALE ( 2-WEEK STUDY )
APPENDIX F 1	HEMATOLOGY: SUMMARY, RAT: MALE ( 2-WEEK STUDY )
APPENDIX F 2	HEMATOLOGY: SUMMARY, RAT: FEMALE ( 2-WEEK STUDY )
APPENDIX G 1	BIOCHEMISTRY: SUMMARY, RAT: MALE ( 2-WEEK STUDY )
APPENDIX G 2	BIOCHEMISTRY: SUMMARY, RAT: FEMALE ( 2-WEEK STUDY )
APPENDIX H 1	URINALYSIS: SUMMARY, RAT: MALE ( 2-WEEK STUDY )
APPENDIX H 2	URINALYSIS: SUMMARY, RAT: FEMALE ( 2-WEEK STUDY )

## APPENDICES (CONTINUED)

APPENDIX I 1	GROSS FINDINGS: SUMMARY, RAT: MALE: ALL ANIMALS ( 2-WEEK STUDY )
APPENDIX I 2	GROSS FINDINGS: SUMMARY, RAT: FEMALE: ALL ANIMALS ( 2-WEEK STUDY )
APPENDIX J 1	ORGAN WEIGHT: ABSOLUTE: SUMMARY, RAT: MALE ( 2-WEEK STUDY )
APPENDIX J 2	ORGAN WEIGHT: ABSOLUTE: SUMMARY, RAT: FEMALE ( 2-WEEK STUDY )
APPENDIX K 1	ORGAN WEIGHT: RELATIVE: SUMMARY, RAT: MALE ( 2-WEEK STUDY )
APPENDIX K 2	ORGAN WEIGHT: RELATIVE: SUMMARY, RAT: FEMALE ( 2-WEEK STUDY )
APPENDIX L 1	HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY, RAT: MALE: ALL ANIMALS ( 2-WEEK STUDY )
APPENDIX L 2	HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY, RAT: FEMALE: ALL ANIMALS ( 2-WEEK STUDY )
APPENDIX M 1	IDENTITY OF 2-PHENOXYETHANOL IN THE 2-WEEK DRINKING WATER STUDY
APPENDIX M 2	STABILITY OF 2-PHENOXYETHANOL IN THE 2-WEEK DRINKING WATER STUDY
APPENDIX M 3	CONCENTRATION OF 2-PHENOXYETHANOL IN FORMULATED WATER IN THE 2-WEEK DRINKING WATER STUDY
APPENDIX M 4	STABILITY OF 2-PHENOXYETHANOL IN FORMULATED WATER IN THE 2-WEEK DRINKING WATER STUDY
APPENDIX N 1	METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS IN THE 2-WEEK DRINKING WATER STUDY OF 2-PHENOXYETHANOL
APPENDIX O 1	UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK DRINKING WATER STUDY OF 2-PHENOXYETHANOL

## APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, RAT : MALE  
(2-WEEK STUDY)

STUDY NO. : 0453  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : MALE

PAGE : 1

Clinical sign	Group Name	Administration Week-day			
		1-3	1-7	2-3	2-7
SOILED PERI GENITALIA	Control	0	0	0	0
	1600ppm	0	0	0	0
	4000ppm	0	0	0	0
	10000ppm	0	0	0	0
	17500ppm	0	0	1	0
	25000ppm	0	5	5	4
ABNORMAL GROWTH OF TEETH	Control	0	0	0	0
	1600ppm	0	0	0	0
	4000ppm	0	1	0	0
	10000ppm	0	0	0	0
	17500ppm	0	0	0	0
	25000ppm	0	0	0	0

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## APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, RAT : FEMALE  
(2-WEEK STUDY)

STUDY NO. : 0453  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : FEMALE

PAGE : 2

Clinical sign	Group Name	Administration Week-day			
		1-3	1-7	2-3	2-7
SOILED	Control	0	0	0	0
	1600ppm	0	0	0	0
	4000ppm	0	0	0	0
	10000ppm	0	0	0	0
	17500ppm	0	1	1	0
	25000ppm	0	4	4	2
PILOERECTION	Control	0	0	0	0
	1600ppm	0	0	0	0
	4000ppm	0	0	0	0
	10000ppm	1	0	0	0
	17500ppm	2	1	1	1
	25000ppm	4	4	4	4
SOILED PERI GENITALIA	Control	0	0	0	0
	1600ppm	0	0	0	0
	4000ppm	0	0	1	2
	10000ppm	0	1	2	2
	17500ppm	3	3	4	4
	25000ppm	5	5	5	5
OLIGO-STOOL	Control	0	0	0	0
	1600ppm	0	0	0	0
	4000ppm	0	0	0	0
	10000ppm	0	0	0	0
	17500ppm	0	1	0	0
	25000ppm	5	5	5	0

## APPENDIX B 1

BODY WEIGHT CHANGES : SUMMARY, RAT : MALE  
(2-WEEK STUDY)



STUDY NO. : 0453  
 ANIMAL : RAT F344/DuCrj  
 UNIT : g  
 REPORT TYPE : A1 2  
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 1

Group Name	Administration		week-day							
	0-0		1-3		1-7		2-3		2-7	
Control	125±	4	137±	6	155±	5	165±	5	179±	7
1600ppm	125±	4	139±	4	157±	6	170±	7	186±	7
4000ppm	125±	4	137±	5	151±	10	162±	12	171±	19
10000ppm	126±	4	134±	4	147±	6	161±	6	172±	6
17500ppm	125±	4	123±	2**	139±	3**	150±	4**	161±	4
25000ppm	125±	4	111±	5**	111±	7**	124±	7**	139±	7**

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

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## APPENDIX B 2

### BODY WEIGHT CHANGES : SUMMARY, RAT : FEMALE (2-WEEK STUDY)

STUDY NO. : 0453  
 ANIMAL : RAT F344/DuCrj  
 UNIT : g  
 REPORT TYPE : A1 2  
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 2

Group Name	Administration week-day									
	0-0		1-3		1-7		2-3		2-7	
Control	101±	3	107±	4	113±	5	119±	3	124±	2
1600ppm	102±	2	108±	3	115±	3	120±	3	125±	4
4000ppm	101±	3	107±	3	113±	3	118±	5	123±	5
10000ppm	101±	4	103±	9	111±	7	116±	7	122±	9
17500ppm	101±	3	95±	3**	100±	9**	105±	6**	110±	2
25000ppm	101±	3	87±	3**	77±	4**	80±	6**	91±	5**

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

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## APPENDIX C 1

### WATER CONSUMPTION CHANGES : SUMMARY, RAT : MALE (2-WEEK STUDY)

STUDY NO. : 0453  
 ANIMAL : RAT F344/DuCrj  
 UNIT : g  
 REPORT TYPE : A1 2  
 SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 1

Group Name	Administration week-day(effective)			
	1-3(3)	1-7(4)	2-3(3)	2-7(4)
Control	18.9± 2.5	17.9± 1.2	17.8± 0.7	18.5± 1.0
1600ppm	17.7± 0.6	18.3± 1.1	18.2± 1.0	19.6± 1.7
4000ppm	16.9± 1.0	17.4± 0.9	17.2± 1.0	16.8± 2.0
10000ppm	13.0± 0.9	13.7± 0.7**	14.3± 0.7**	14.5± 0.8**
17500ppm	11.2± 3.6*	16.4± 1.4	13.8± 0.9**	14.4± 0.6**
25000ppm	6.2± 1.2**	11.6± 1.9**	16.0± 0.9*	15.1± 0.9**

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

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## APPENDIX C 2

### WATER CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE (2-WEEK STUDY)

STUDY NO. : 0453  
 ANIMAL : RAT F344/DuCrj  
 UNIT : g  
 REPORT TYPE : A1 2  
 SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 2

Group Name	Administration week-day(effective)			
	1-3(3)	1-7(4)	2-3(3)	2-7(4)
Control	15.8± 1.4	16.1± 0.9	14.8± 1.3	15.7± 2.2
1600ppm	15.4± 0.9	15.7± 1.1	14.4± 1.2	14.9± 1.6
4000ppm	16.3± 4.7	14.3± 1.3	19.6± 14.8	17.8± 10.4
10000ppm	10.6± 1.9	12.5± 0.9*	11.2± 1.0*	12.0± 1.2*
17500ppm	7.6± 1.9*	12.6± 2.3*	11.3± 3.4	10.9± 1.1**
25000ppm	5.0± 0.5**	6.9± 2.6**	11.3± 0.6*	13.0± 1.0

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

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## APPENDIX D 1

### FOOD CONSUMPTION CHANGES : SUMMARY, RAT : MALE (2-WEEK STUDY)



STUDY NO. : 0453  
 ANIMAL : RAT F344/DuCrj  
 UNIT : g  
 REPORT TYPE : A1 2  
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 1

Group Name	Administration week-day(effective)			
	1-3(3)	1-7(4)	2-3(3)	2-7(4)
Control	13.3± 0.9	14.0± 0.8	14.2± 0.6	14.8± 1.1
1600ppm	13.5± 0.6	14.0± 0.6	15.0± 0.9	15.8± 1.2
4000ppm	13.1± 0.7	13.5± 1.3	13.8± 1.2	13.5± 2.6
10000ppm	11.5± 0.7**	12.2± 0.5*	13.0± 0.5	13.5± 0.3
17500ppm	9.5± 0.5**	11.1± 0.8**	12.4± 0.5*	13.2± 0.6
25000ppm	7.6± 0.6**	6.9± 1.0**	9.8± 0.9**	12.1± 0.8*

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

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## APPENDIX D 2

### FOOD CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE (2-WEEK STUDY)

STUDY NO. : 0453  
 ANIMAL : RAT F344/DuCrj  
 UNIT : g  
 REPORT TYPE : A1 2  
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 2

Group Name	Administration week-day(effective)			
	1-3(3)	1-7(4)	2-3(3)	2-7(4)
Control	9.8± 0.7	10.1± 0.3	9.8± 0.1	10.3± 0.2
1600ppm	10.5± 0.8	10.6± 0.6	10.2± 0.5	10.5± 0.8
4000ppm	9.9± 0.7	10.0± 0.7	9.9± 0.6	10.0± 0.7
10000ppm	8.5± 1.2	9.6± 0.6	9.2± 0.3	9.7± 0.8
17500ppm	6.9± 0.7**	7.4± 1.6	8.3± 0.7	8.9± 0.9*
25000ppm	5.5± 0.7**	3.8± 1.6*	6.2± 0.9**	8.8± 0.8*

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

Test of Dunnett

## APPENDIX E 1

CHEMICAL INTAKE CHANGES : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0453  
ANIMAL : RAT F344/DuCrj  
UNIT : g/kg/day  
REPORT TYPE : A1 2  
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)  
ALL ANIMALS

PAGE : 1

Group Name	Administration (Week-Day)			
	1-3	1-7	2-3	2-7
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
1600ppm	0.204± 0.007	0.186± 0.007	0.171± 0.006	0.168± 0.012
4000ppm	0.494± 0.019	0.464± 0.015	0.428± 0.036	0.394± 0.007
10000ppm	0.969± 0.056	0.931± 0.040	0.892± 0.035	0.843± 0.055
17500ppm	1.592± 0.509	2.060± 0.147	1.616± 0.115	1.563± 0.090
25000ppm	1.385± 0.238	2.604± 0.337	3.237± 0.102	2.736± 0.205

## APPENDIX E 2

CHEMICAL INTAKE CHANGES : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0453  
 ANIMAL : RAT F344/DuCrj  
 UNIT : g/kg/day  
 REPORT TYPE : A1 2  
 SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 2

Group Name	Administration (Week-Day)			
	1-3	1-7	2-3	2-7
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
1600ppm	0.228± 0.010	0.219± 0.010	0.192± 0.015	0.191± 0.020
4000ppm	0.608± 0.162	0.507± 0.037	0.653± 0.458	0.573± 0.307
10000ppm	1.024± 0.108	1.123± 0.125	0.959± 0.085	0.986± 0.073
17500ppm	1.384± 0.329	2.193± 0.280	1.910± 0.669	1.732± 0.192
25000ppm	1.435± 0.109	2.196± 0.730	3.533± 0.293	3.610± 0.437

## APPENDIX F 1

HEMATOLOGY : SUMMARY, RAT : MALE

(2-WEEK STUDY)



STUDY NO. : 0453  
ANIMAL : RAT F344/DuCrj  
MEASURE. TIME : 1  
SEX : MALE

HEMATOLOGY (SUMMARY)  
ALL ANIMALS ( 2W)

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>9</sup> /μl	
Control	5	7.93±	0.13	15.0±	0.2	41.3±	0.7	52.1±	0.5	18.9±	0.2	36.3±	0.2	980±	123
1600ppm	5	7.63±	0.15	14.6±	0.2	40.2±	0.7	52.7±	0.5	19.1±	0.1	36.2±	0.2	900±	39
4000ppm	5	7.94±	0.50	15.3±	0.9	41.8±	2.3	52.7±	0.8	19.2±	0.2*	36.5±	0.3	852±	36
10000ppm	4	7.70±	0.35	14.9±	0.6	41.2±	1.8	53.5±	0.3*	19.3±	0.1**	36.2±	0.3	865±	37
17500ppm	5	7.77±	0.26	15.2±	0.5	42.0±	1.0	54.0±	0.8**	19.5±	0.2**	36.1±	0.5	749±	46**
25000ppm	4	7.51±	0.29	14.6±	0.5	40.3±	1.4	53.6±	0.7**	19.4±	0.1**	36.2±	0.3	685±	26**

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

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STUDY NO. : 0453  
ANIMAL : RAT F344/DuCrj  
MEASURE. TIME : 1  
SEX : MALE

HEMATOLOGY (SUMMARY)  
ALL ANIMALS ( 2W)

REPORT TYPE : A1

PAGE : 2

Group Name	NO. of Animals	RETICULOCYTE %		PROTHROMBIN TIME s e c		APTT s e c	
Control	5	3.2±	0.5	15.4±	0.5	20.6±	1.7
1600ppm	5	3.4±	0.2	14.9±	0.4	20.0±	2.2
4000ppm	5	2.7±	0.9	15.4±	0.4	22.0±	1.1
10000ppm	4	3.0±	0.1	15.0±	0.6	21.4±	3.2
17500ppm	5	3.0±	0.3	15.3±	0.6	20.8±	2.7
25000ppm	4	3.3±	0.3	15.7±	0.6	20.8±	1.2

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

Test of Dunnett

STUDY NO. : 0453  
 ANIMAL : RAT F344/DuCrj  
 MEASURE. TIME : 1  
 SEX : MALE

HEMATOLOGY (SUMMARY)  
 ALL ANIMALS ( 2W)

REPORT TYPE : A1

PAGE : 3

Group Name	NO. of Animals	WBC 10 <sup>3</sup> /μl		Differential N-BAND		WBC (%) N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHER	
Control	5	5.49±	1.48	1±	1	15±	4	1±	1	0±	0	1±	0	83±	4	0±	0
1600ppm	5	4.27±	1.54	1±	1	15±	0	1±	1	0±	0	2±	1	81±	1	0±	0
4000ppm	5	3.57±	0.86	1±	1	16±	4	0±	1	0±	0	1±	0	81±	4	0±	0
10000ppm	4	4.48±	0.93	1±	1	15±	4	1±	1	0±	0	3±	1*	81±	6	0±	1
17500ppm	5	3.96±	1.00	2±	1	15±	2	0±	1	0±	0	1±	0	82±	4	0±	0
25000ppm	4	3.86±	0.35	2±	1	17±	3	2±	1	0±	0	1±	1	79±	2	0±	0

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

\*\* :  $P \leq 0.01$

Test of Dunnett

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## APPENDIX F 2

HEMATOLOGY : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0453  
 ANIMAL : RAT F344/DuCrj  
 MEASURE. TIME : 1  
 SEX : FEMALE

HEMATOLOGY (SUMMARY)  
 ALL ANIMALS ( 2W)

REPORT TYPE : A1

PAGE : 4

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	5	8.00±	0.36	15.6±	0.6	41.8±	1.5	52.2±	1.1	19.4±	0.4	37.2±	0.2	824±	36
1600ppm	4	7.98±	0.11	15.3±	0.3	40.9±	0.5	51.2±	0.5	19.1±	0.2	37.3±	0.3	708±	74*
4000ppm	5	8.17±	0.17	15.8±	0.3	42.3±	0.8	51.8±	0.5	19.3±	0.1	37.3±	0.2	806±	64
10000ppm	5	7.96±	0.34	15.3±	0.7	41.7±	1.6	52.4±	0.4	19.2±	0.2	36.7±	0.5	780±	85
17500ppm	5	7.81±	0.38	15.0±	0.8	41.4±	1.8	53.0±	0.5	19.2±	0.2	36.2±	0.7*	667±	58**
25000ppm	5	7.76±	0.42	14.8±	0.7	41.1±	2.6	53.0±	0.6	19.0±	0.2	35.9±	0.6**	669±	45**

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

Test of Dunnett

STUDY NO. : 0453  
ANIMAL : RAT F344/DuCrj  
MEASURE. TIME : 1  
SEX : FEMALE

REPORT TYPE : A1

HEMATOLOGY (SUMMARY)  
ALL ANIMALS ( 2W)

PAGE : 5

Group Name	NO. of Animals	RETICULOCYTE %		PROTHROMBIN TIME s e c		APTT s e c	
Control	5	1.8±	0.3	16.3±	0.3	19.0±	1.1
1600ppm	4	1.8±	0.3	16.0±	0.3	18.4±	2.1
4000ppm	5	1.6±	0.4	16.5±	0.6	18.6±	0.8
10000ppm	5	1.7±	0.0	16.7±	0.4	19.0±	1.0
17500ppm	5	2.0±	0.4	16.6±	0.5	19.0±	0.4
25000ppm	5	1.2±	1.0	16.8±	0.5	16.9±	2.0

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

Test of Dunnett

STUDY NO. : 0453  
ANIMAL : RAT F344/DuCrj  
MEASURE. TIME : 1  
SEX : FEMALE

HEMATOLOGY (SUMMARY)  
ALL ANIMALS ( 2W)

REPORT TYPE : A1

PAGE : 6

Group Name	NO. of Animals	WBC 10 <sup>3</sup> /μl		Differential N-BAND		WBC (%) N-SEG		EOSINO		BASO		MONO		LYMPHIO		OTHER	
Control	5	3.95±	2.14	1±	0	14±	3	1±	0	0±	0	3±	1	81±	4	0±	0
1600ppm	4	2.78±	0.28	1±	1	14±	1	1±	0	0±	0	2±	1	83±	2	0±	1
4000ppm	5	3.15±	0.55	1±	1	15±	3	2±	2	0±	0	2±	1	81±	5	0±	0
10000ppm	5	3.24±	1.22	0±	1	16±	6	1±	1	0±	0	1±	1	81±	7	0±	0
17500ppm	5	3.40±	1.10	1±	1	18±	5	2±	1	0±	0	2±	2	77±	7	0±	0
25000ppm	5	3.65±	0.64	1±	1	19±	5	2±	1	0±	0	3±	2	74±	6	1±	1

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

\*\* :  $P \leq 0.01$

Test of Dunnett

## APPENDIX G 1

BIOCHEMISTRY : SUMMARY, RAT : MALE

(2-WEEK STUDY)



STUDY NO. : 0453  
 ANIMAL : RAT F344/DuCrj  
 MEASURE. TIME : 1  
 SEX : MALE

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS ( 2W)

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		PHOSPHOLIPID mg/dl	
Control	5	5.8±	0.1	3.6±	0.1	1.7±	0.0	0.12±	0.02	197±	12	65±	3	145±	8
1600ppm	5	5.6±	0.1	3.6±	0.1	1.7±	0.1	0.12±	0.01	199±	12	64±	2	146±	6
4000ppm	5	5.7±	0.1	3.6±	0.0	1.7±	0.1	0.11±	0.02	206±	15	59±	7	135±	7
10000ppm	4	5.8±	0.1	3.6±	0.1	1.7±	0.1	0.12±	0.01	196±	22	67±	3	153±	4
17500ppm	5	5.8±	0.1	3.7±	0.1	1.8±	0.1	0.12±	0.01	187±	9	69±	5	155±	10
25000ppm	4	5.8±	0.2	3.7±	0.1	1.8±	0.1	0.14±	0.01	180±	11	76±	4**	157±	12

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

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 4

STUDY NO. : 0453  
 ANIMAL : RAT F344/DuCrj  
 MEASURE. TIME : 1  
 SEX : MALE

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS ( 2W)

REPORT TYPE : A1

PAGE : 2

Group Name	NO. of Animals	GOT I U / ℓ		GPT I U / ℓ		LDH I U / ℓ		G-GTP I U / ℓ		CPK I U / ℓ		UREA NITROGEN mg / dℓ		CREATININE mg / dℓ	
Control	5	54±	3	35±	2	197±	67	1±	1	165±	33	16.5±	2.4	0.4±	0.0
1600ppm	5	50±	4	35±	3	202±	124	2±	1	168±	28	18.2±	2.1	0.4±	0.0
4000ppm	5	50±	7	33±	3	229±	138	2±	0	152±	25	19.1±	2.3	0.4±	0.0
10000ppm	4	52±	7	34±	1	323±	215	2±	2	180±	67	17.8±	1.0	0.4±	0.0
17500ppm	5	43±	9	33±	2	261±	68	2±	1	149±	13	20.1±	2.1*	0.4±	0.0
25000ppm	4	56±	9	39±	2	305±	30	1±	1	156±	17	22.9±	1.7**	0.4±	0.1

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

Test of Dunnett

(HCL074)

BAIS 4

STUDY NO. : 0453  
 ANIMAL : RAT F344/DuCrj  
 MEASURE. TIME : 1  
 SEX : MALE

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS ( 2W)

REPORT TYPE : A1

PAGE : 3

Group Name	NO. of Animals	SODIUM mEq/ℓ		POTASSIUM mEq/ℓ		CHLORIDE mEq/ℓ		CALCIUM mg/dℓ		INORGANIC PHOSPHORUS mg/dℓ	
Control	5	139±	1	4.6±	0.1	102±	0	10.7±	0.2	8.5±	0.7
1600ppm	5	139±	2	4.5±	0.1	102±	1	10.9±	0.1	8.4±	0.5
4000ppm	5	138±	2	4.6±	0.5	103±	1	10.6±	0.4	7.7±	0.7
10000ppm	4	139±	2	4.5±	0.3	103±	1	10.8±	0.1	8.4±	0.6
17500ppm	5	139±	1	4.4±	0.4	103±	2	10.7±	0.1	7.7±	0.4
25000ppm	4	138±	2	4.7±	0.3	102±	1	10.6±	0.3	7.4±	0.5*

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

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 4

## APPENDIX G 2

BIOCHEMISTRY : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0453  
 ANIMAL : RAT F344/DuCrj  
 MEASURE. TIME : 1  
 SEX : FEMALE

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS ( 2W)

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		PHOSPHOLIPID mg/dl	
Control	5	5.5±	0.1	3.4±	0.1	1.7±	0.1	0.16±	0.04	186±	11	72±	3	145±	5
1600ppm	4	5.4±	0.1	3.4±	0.2	1.7±	0.1	0.16±	0.04	191±	5	76±	9	150±	12
4000ppm	5	5.6±	0.1	3.5±	0.1	1.6±	0.1	0.14±	0.02	188±	8	71±	7	142±	15
10000ppm	5	5.4±	0.1	3.4±	0.1	1.7±	0.1	0.13±	0.02	186±	6	69±	2	141±	5
17500ppm	5	5.4±	0.1	3.4±	0.1	1.7±	0.1	0.13±	0.01	178±	9	72±	7	140±	14
25000ppm	5	5.6±	0.1	3.6±	0.1	1.9±	0.2	0.15±	0.02	164±	8**	71±	3	146±	8

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

Test of Dunnett

STUDY NO. : 0453  
 ANIMAL : RAT F344/DuCrj  
 MEASURE. TIME : 1  
 SEX : FEMALE

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS ( 2W)

REPORT TYPE : A1

PAGE : 5

Group Name	NO. of Animals	GOT I U / ℓ		GPT I U / ℓ		LDH I U / ℓ		G-GTP I U / ℓ		CPK I U / ℓ		UREA NITROGEN mg / dl		CREATININE mg / dl	
Control	5	59±	5	30±	2	530±	267	2±	1	202±	66	17.7±	1.8	0.4±	0.0
1600ppm	4	65±	4	35±	3	469±	203	2±	1	188±	33	17.3±	1.4	0.4±	0.0
4000ppm	5	62±	5	32±	3	494±	250	2±	1	212±	72	22.4±	7.0	0.4±	0.0
10000ppm	5	57±	6	34±	3	258±	87	2±	1	149±	18	19.2±	3.1	0.4±	0.0
17500ppm	5	58±	4	33±	5	235±	28	2±	1	149±	25	20.6±	4.5	0.4±	0.0
25000ppm	5	73±	10**	50±	11**	319±	140	3±	1	172±	34	30.6±	4.3**	0.4±	0.0

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

Test of Dunnett

(HCL074)

BAIS 4

STUDY NO. : 0453  
 ANIMAL : RAT F344/DuCrj  
 MEASURE. TIME : 1  
 SEX : FEMALE

REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS ( 2W)

PAGE : 6

Group Name	NO. of Animals	SODIUM mEq/ℓ		POTASSIUM mEq/ℓ		CHLORIDE mEq/ℓ		CALCIUM mg/dℓ		INORGANIC PHOSPHORUS mg/dℓ	
Control	5	138±	3	4.2±	0.3	105±	2	10.3±	0.2	7.0±	1.2
1600ppm	4	138±	1	4.1±	0.2	104±	1	10.2±	0.3	7.2±	0.6
4000ppm	5	139±	3	3.9±	0.5	105±	2	10.4±	0.2	6.5±	0.9
10000ppm	5	137±	1	4.1±	0.4	105±	3	10.4±	0.2	6.2±	1.1
17500ppm	5	138±	2	4.0±	0.3	107±	3	10.2±	0.2	6.2±	1.2
25000ppm	5	141±	1	4.2±	0.3	108±	3	10.5±	0.2	6.0±	1.0

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

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 4

## APPENDIX H 1

URINALYSIS : SUMMARY, RAT : MALE

(2-WEEK STUDY)



STUDY NO. : 0453

ANIMAL : RAT F344/DuCrj

MEASURE. TIME : 1

SEX : MALE

REPORT TYPE : A1

## URINALYSIS

PAGE : 1

Group Name	NO. of Animals	pH_____							Protein_____					Glucose_____					Ketone body_____					Bilirubin_____		
		5.0	6.0	6.5	7.0	7.5	8.0	8.5	-	±	+	2+	3+	4+	-	±	+	2+	3+	4+	-	±	+	2+	3+	
Control	5	0	0	0	0	0	5	0	0	0	5	0	0	0	5	0	0	0	0	0	5	0	0	0	0	
1600ppm	5	0	0	0	0	0	4	1	0	0	5	0	0	0	5	0	0	0	0	0	5	0	0	0	0	
4000ppm	5	0	0	0	0	1	4	0	0	1	4	0	0	0	5	0	0	0	0	0	4	1	0	0	0	
10000ppm	5	0	0	0	0	0	5	0	0	0	5	0	0	0	5	0	0	0	0	0	4	1	0	0	0	
17500ppm	5	0	0	0	0	3	2	0	0	0	5	0	0	0	5	0	0	0	0	0	4	1	0	0	0	
25000ppm	5	0	2	2	1	0	0	0	0	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	0	

(HCL101)

BAIS 4

STUDY NO. : 0453  
ANIMAL : RAT F344/DuCrj  
MEASURE TIME : 1  
SEX : MALE

URINALYSIS

REPORT TYPE : A1

PAGE : 2

Group Name	NO. of Animals	Occult blood - ± + 2+ 3+	Urobilinogen ± + 2+ 3+ 4+
Control	5	5 0 0 0 0	5 0 0 0 0
1600ppm	5	5 0 0 0 0	5 0 0 0 0
4000ppm	5	5 0 0 0 0	5 0 0 0 0
10000ppm	5	5 0 0 0 0	5 0 0 0 0
17500ppm	5	5 0 0 0 0	5 0 0 0 0
25000ppm	5	5 0 0 0 0	5 0 0 0 0

(HCL101)

BAIS 4

## APPENDIX H 2

URINALYSIS : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0453

ANIMAL : RAT F344/DuCrj

MEASURE. TIME : 1

SEX : FEMALE

REPORT TYPE : A1

## URINALYSIS

PAGE : 3

Group Name	NO. of Animals	pH							Protein						Glucose						Ketone body						Bilirubin			
		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	5	0	0	0	0	0	5	0	0	4	1	0	0	0	5	0	0	0	0	0	5	0	0	0	0	0	5	0	0	0
1600ppm	5	0	0	0	0	1	4	0	0	2	3	0	0	0	5	0	0	0	0	0	5	0	0	0	0	0	5	0	0	0
4000ppm	5	0	0	0	0	1	3	1	0	3	2	0	0	0	5	0	0	0	0	0	5	0	0	0	0	0	5	0	0	0
10000ppm	5	0	0	0	0	0	5	0	0	2	3	0	0	0	5	0	0	0	0	0	5	0	0	0	0	0	5	0	0	0
17500ppm	5	0	0	0	2	2	1	0	0	4	1	0	0	0	5	0	0	0	0	0	5	0	0	0	0	0	5	0	0	0
25000ppm	5	0	3	2	0	0	0	0	0	5	0	0	0	0	5	0	0	0	0	0	5	0	0	0	0	0	5	0	0	0

(HCL101)

BAIS 4

STUDY NO. : 0453

ANIMAL : RAT F344/DuCrj

MEASURE. TIME : 1

SEX : FEMALE

REPORT TYPE : A1

URINALYSIS

PAGE : 4

Group Name	NO. of Animals	Occult blood					Urobilinogen				
		-	±	+	2+	3+	±	+	2+	3+	4+
Control	5	5	0	0	0	0	5	0	0	0	0
1600ppm	5	5	0	0	0	0	5	0	0	0	0
4000ppm	5	5	0	0	0	0	5	0	0	0	0
10000ppm	5	5	0	0	0	0	5	0	0	0	0
17500ppm	5	5	0	0	0	0	5	0	0	0	0
25000ppm	5	5	0	0	0	0	5	0	0	0	0

(HCL101)

BAIS 4

## APPENDIX I 1

GROSS FINDINGS : SUMMARY, RAT : MALE : ALL ANIMALS  
(2-WEEK STUDY)

STUDY NO. : 0453  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 1

Organ	Findings	Group Name	Control	1600ppm	4000ppm	10000ppm
		NO. of Animals	5 (%)	5 (%)	5 (%)	5 (%)
liver	herniation		0 ( 0)	0 ( 0)	1 ( 20)	0 ( 0)

(HPT080)

BAIS 4

STUDY NO. : 0453  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 2

Organ	Findings	Group Name	17500ppm	25000ppm
		NO. of Animals	5 (%)	5 (%)
liver	herniation		0 ( 0 )	0 ( 0 )

(HPT080)

BAIS 4



## APPENDIX I 2

GROSS FINDINGS : SUMMARY, RAT : FEMALE : ALL ANIMALS  
(2-WEEK STUDY)

STUDY NO. : 0453  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 3

Organ	Findings	Group Name NO. of Animals	Control 5 (%)	1600ppm 5 (%)	4000ppm 5 (%)	10000ppm 5 (%)
liver	herniation		1 ( 20)	2 ( 40)	1 ( 20)	1 ( 20)

(HPT080)

BAIS 4

STUDY NO. : 0453  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 4

Organ_____	Findings_____	Group Name NO. of Animals	17500ppm 5 (%)	25000ppm 5 (%)
liver	herniation		1 ( 20)	1 ( 20)

(HPT080)

BAIS 4

## APPENDIX J 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : MALE  
(2-WEEK STUDY)

STUDY NO. : 0453  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : MALE  
UNIT: g

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

PAGE : 1

Group Name	NO. of Animals	Body Weight		THYMUS		ADRENALS		TESTES		HEART		LUNGS	
Control	5	179±	7	0.326±	0.022	0.040±	0.005	2.395±	0.086	0.665±	0.032	0.774±	0.023
1600ppm	5	186±	7	0.341±	0.025	0.039±	0.005	2.406±	0.132	0.659±	0.015	0.783±	0.029
4000ppm	5	171±	19	0.315±	0.046	0.045±	0.006	2.372±	0.114	0.634±	0.081	0.728±	0.052
10000ppm	5	172±	6	0.321±	0.018	0.038±	0.003	2.368±	0.042	0.632±	0.034	0.751±	0.056
17500ppm	5	161±	4	0.304±	0.021	0.041±	0.002	2.270±	0.137	0.594±	0.023	0.704±	0.040
25000ppm	5	139±	7**	0.247±	0.026**	0.033±	0.007	1.972±	0.353*	0.510±	0.022**	0.650±	0.057**

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

Test of Dunnett

(HCL040)

BAIS 4

STUDY NO. : 0453  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : MALE  
UNIT: g

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

PAGE : 2

Group Name	NO. of Animals	KIDNEYS		SPLEEN		LIVER		BRAIN		THYROID	
Control	5	1.357±	0.040	0.452±	0.050	7.242±	0.546	1.659±	0.055	0.019±	0.003
1600ppm	5	1.375±	0.064	0.465±	0.011	7.878±	0.397	1.700±	0.069	0.021±	0.006
4000ppm	5	1.331±	0.176	0.412±	0.059	7.039±	1.219	1.687±	0.033	0.019±	0.003
10000ppm	5	1.436±	0.050	0.420±	0.034	7.711±	0.141	1.679±	0.009	0.018±	0.002
17500ppm	5	1.390±	0.046	0.381±	0.018	6.931±	0.365	1.662±	0.042	0.019±	0.003
25000ppm	5	1.303±	0.085	0.342±	0.008**	6.345±	0.612	1.611±	0.026	0.020±	0.004

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

Test of Dunnett

(HCL040)

BAIS 4

## APPENDIX J 2

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : FEMALE  
(2-WEEK STUDY)

STUDY NO. : 0453  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : FEMALE  
UNIT: g

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

PAGE : 3

Group Name	NO. of Animals	Body Weight		THYMUS		ADRENALS		OVARIES		HEART		LUNGS	
Control	5	124±	2	0.276±	0.022	0.047±	0.012	0.076±	0.013	0.479±	0.033	0.638±	0.025
1600ppm	5	125±	4	0.293±	0.023	0.042±	0.007	0.066±	0.006	0.489±	0.012	0.638±	0.033
4000ppm	5	123±	5	0.282±	0.030	0.044±	0.003	0.074±	0.008	0.486±	0.040	0.604±	0.044
10000ppm	5	122±	9	0.274±	0.024	0.041±	0.003	0.070±	0.008	0.473±	0.040	0.605±	0.039
17500ppm	5	110±	2	0.253±	0.036	0.038±	0.003	0.068±	0.012	0.442±	0.015	0.572±	0.017*
25000ppm	5	91±	5**	0.133±	0.046**	0.031±	0.005*	0.048±	0.003**	0.366±	0.021**	0.498±	0.023**

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

Test of Dunnett

(HCL040)

BAIS 4



STUDY NO. : 0453  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : FEMALE  
UNIT: g

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

PAGE : 4

Group Name	NO. of Animals	KIDNEYS		SPLEEN		LIVER		BRAIN		THYROID	
Control	5	0.974±	0.037	0.328±	0.017	4.562±	0.365	1.585±	0.030	0.020±	0.005
1600ppm	5	0.995±	0.067	0.326±	0.012	4.599±	0.389	1.590±	0.039	0.016±	0.002
4000ppm	5	0.997±	0.015	0.321±	0.027	4.583±	0.148	1.574±	0.040	0.015±	0.001
10000ppm	5	1.020±	0.037	0.321±	0.026	4.600±	0.333	1.573±	0.011	0.018±	0.003
17500ppm	5	1.024±	0.026	0.293±	0.011	4.513±	0.207	1.579±	0.036	0.017±	0.002
25000ppm	5	0.943±	0.038	0.216±	0.025**	4.269±	0.155	1.536±	0.049	0.017±	0.002

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

Test of Dunnett

(HCL040)

BAIS 4

## APPENDIX K 1

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : MALE  
(2-WEEK STUDY)

STUDY NO. : 0453  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : MALE  
UNIT: %

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

PAGE : 1

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	5	179± 7	0.183± 0.017	0.023± 0.002	1.339± 0.036	0.372± 0.019	0.433± 0.013
1600ppm	5	186± 7	0.183± 0.016	0.021± 0.002	1.293± 0.056	0.354± 0.015	0.421± 0.013
4000ppm	5	171± 19	0.184± 0.011	0.026± 0.002	1.404± 0.186	0.371± 0.012	0.428± 0.019
10000ppm	5	172± 6	0.186± 0.007	0.022± 0.002	1.375± 0.056	0.366± 0.014	0.436± 0.043
17500ppm	5	161± 4	0.189± 0.014	0.026± 0.001	1.407± 0.066	0.369± 0.021	0.437± 0.015
25000ppm	5	139± 7**	0.178± 0.015	0.024± 0.004	1.417± 0.215	0.368± 0.018	0.468± 0.020

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

Test of Dunnett

(HCL042)

BAIS 4

STUDY NO. : 0453  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : MALE  
UNIT: %

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

PAGE : 2

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN	THYROID
Control	5	0.759± 0.009	0.253± 0.027	4.043± 0.183	0.928± 0.042	0.011± 0.002
1600ppm	5	0.739± 0.019	0.250± 0.008	4.234± 0.066	0.916± 0.072	0.011± 0.003
4000ppm	5	0.778± 0.030	0.241± 0.010	4.097± 0.291	0.997± 0.106	0.011± 0.002
10000ppm	5	0.834± 0.047	0.244± 0.017	4.478± 0.183**	0.975± 0.038	0.010± 0.001
17500ppm	5	0.862± 0.012	0.237± 0.010	4.297± 0.132	1.031± 0.008	0.012± 0.002
25000ppm	5	0.940± 0.026**	0.247± 0.012	4.572± 0.251**	1.164± 0.047**	0.015± 0.003

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

Test of Dunnett

(HCL042)

BAIS 4

## APPENDIX K 2

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : FEMALE  
(2-WEEK STUDY)

STUDY NO. : 0453  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1  
SEX : FEMALE  
UNIT: %

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

PAGE : 3

Group Name	NO. of Animals	Body Weight (g)		THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	5	124±	2	0.222± 0.018	0.038± 0.009	0.061± 0.010	0.385± 0.026	0.513± 0.014
1600ppm	5	125±	4	0.235± 0.014	0.034± 0.004	0.053± 0.004	0.393± 0.011	0.512± 0.020
4000ppm	5	123±	5	0.229± 0.017	0.036± 0.003	0.060± 0.006	0.396± 0.031	0.492± 0.024
10000ppm	5	122±	9	0.225± 0.017	0.033± 0.004	0.058± 0.004	0.389± 0.030	0.497± 0.026
17500ppm	5	110±	2	0.229± 0.029	0.035± 0.003	0.062± 0.011	0.402± 0.011	0.520± 0.016
25000ppm	5	91±	5**	0.145± 0.041**	0.034± 0.005	0.053± 0.006	0.404± 0.024	0.551± 0.040

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

Test of Dunnett

(HCL042)

BAIS 4

STUDY NO. : 0453  
 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1  
 SEX : FEMALE  
 UNIT: %

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

PAGE : 4

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN	THYROID
Control	5	0.784± 0.022	0.264± 0.016	3.671± 0.253	1.276± 0.009	0.016± 0.004
1600ppm	5	0.798± 0.037	0.262± 0.005	3.688± 0.257	1.277± 0.031	0.013± 0.001
4000ppm	5	0.813± 0.032	0.261± 0.016	3.734± 0.097	1.282± 0.042	0.012± 0.002
10000ppm	5	0.838± 0.037	0.263± 0.008	3.774± 0.149	1.295± 0.097	0.015± 0.002
17500ppm	5	0.931± 0.036**	0.267± 0.007	4.105± 0.231*	1.436± 0.045	0.016± 0.002
25000ppm	5	1.042± 0.056**	0.238± 0.018*	4.722± 0.298**	1.701± 0.130**	0.019± 0.003

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

Test of Dunnett

(HCL042)

BAIS 4

APPENDIX L 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : ALL ANIMALS

(2-WEEK STUDY)



STUDY NO. : 0453  
 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1  
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0- 2W)

PAGE : 1

Organ	Findings	Control				1600ppm				4000ppm				10000ppm			
		5				5				5				5			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Hematopoietic system)																	
bone marrow		< 5>				< 5>				< 5>				< 5>			
	decreased hematopoiesis	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 )
(Digestive system)																	
liver		< 5>				< 5>				< 5>				< 5>			
	herniation	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 20 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
(Endocrine system)																	
pituitary		< 5>				< 5>				< 5>				< 5>			
	Ratlike pouch	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 20 )	( 0 )	( 0 )	( 0 )
thyroid		< 5>				< 5>				< 5>				< 5>			
	ultimibranchial body remanet	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 20 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
(Reproductive system)																	
prostate		< 5>				< 5>				< 5>				< 5>			
	inflammation	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 20 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )

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

STUDY NO. : 0453  
 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1  
 SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0- 2W)

PAGE : 2

Organ	Findings	Group Name		17500ppm				25000ppm			
		No. of Animals on Study		5				5			
		Grade		1	2	3	4	1	2	3	4
				(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Hematopoietic system)											
bone marrow	decreased hematopoiesis			< 5>				< 5>			
				0	0	0	0	5	0	0	0
				( 0 )	( 0 )	( 0 )	( 0 )	(100)	( 0 )	( 0 )	( 0 )
(Digestive system)											
liver	herniation			< 5>				< 5>			
				0	0	0	0	0	0	0	0
				( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
(Endocrine system)											
pituitary	Rathke pouch			< 5>				< 5>			
				0	0	0	0	0	0	0	0
				( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
thyroid	ultimibranhial body remanet			< 5>				< 5>			
				0	0	0	0	0	0	0	0
				( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
(Reproductive system)											
prostate	inflammation			< 5>				< 5>			
				0	0	0	0	0	0	0	0
				( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )

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

APPENDIX L 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : ALL ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0453  
 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0- 2W)

PAGE : 3

		Group Name	Control				1600ppm				4000ppm				10000ppm			
		No. of Animals on Study	5				5				5				5			
Organ	Findings	Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}																		
bone marrow			< 5>				< 5>				< 5>				< 5>			
	decreased hematopoiesis		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 )
{Digestive system}																		
liver			< 5>				< 5>				< 5>				< 5>			
	herniation		1	0	0	0	2	0	0	0	1	0	0	0	1	0	0	0
			( 20 )	( 0 )	( 0 )	( 0 )	( 40 )	( 0 )	( 0 )	( 0 )	( 20 )	( 0 )	( 0 )	( 0 )	( 20 )	( 0 )	( 0 )	( 0 )
	perivascular inflammation		1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			( 20 )	( 0 )	( 0 )	( 0 )	( 20 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
{Urinary system}																		
kidney			< 5>				< 5>				< 5>				< 5>			
	mineralization:cortico-medullary junction		2	0	0	0	1	0	0	0	1	0	0	0	2	0	0	0
			( 40 )	( 0 )	( 0 )	( 0 )	( 20 )	( 0 )	( 0 )	( 0 )	( 20 )	( 0 )	( 0 )	( 0 )	( 40 )	( 0 )	( 0 )	( 0 )
{Endocrine system}																		
thyroid			< 5>				< 5>				< 5>				< 5>			
	ultimibranchial body remanet		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 20 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
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																	

STUDY NO. : 0453  
 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0- 2W)

PAGE : 4

		Group Name				17500ppm				25000ppm				
		No. of Animals on Study				5				5				
Organ	Findings	Grade	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Hematopoietic system)														
bone marrow			< 5>				< 5>							
	decreased hematopoiesis		0	0	0	0	0	5	0	0	0	100	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 100 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
(Digestive system)														
liver			< 5>				< 5>							
	herniation		1	0	0	0	1	0	0	0	20	0	0	0
			( 20 )	( 0 )	( 0 )	( 0 )	( 20 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	perivascular inflammation		0	0	0	0	1	0	0	0	20	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 20 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
(Urinary system)														
kidney			< 5>				< 5>							
	mineralization:cortico-medullary junction		0	0	0	0	1	0	0	0	20	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 20 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
(Endocrine system)														
thyroid			< 5>				< 5>							
	ultimibranchial body remanet		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													

(HPT150)

BAIS4

## APPENDIX M 1

### IDENTITY OF 2-PHENOXYETHANOL IN THE 2-WEEK DRINKING WATER STUDY

## IDENTITY OF 2-PHENOXYETHANOL IN THE 2-WEEK DRINKING WATER STUDY

Test Substance : 2-Phenoxyethanol (Wako Pure Chemical Industries, Ltd.)

Lot No. : WAR5157

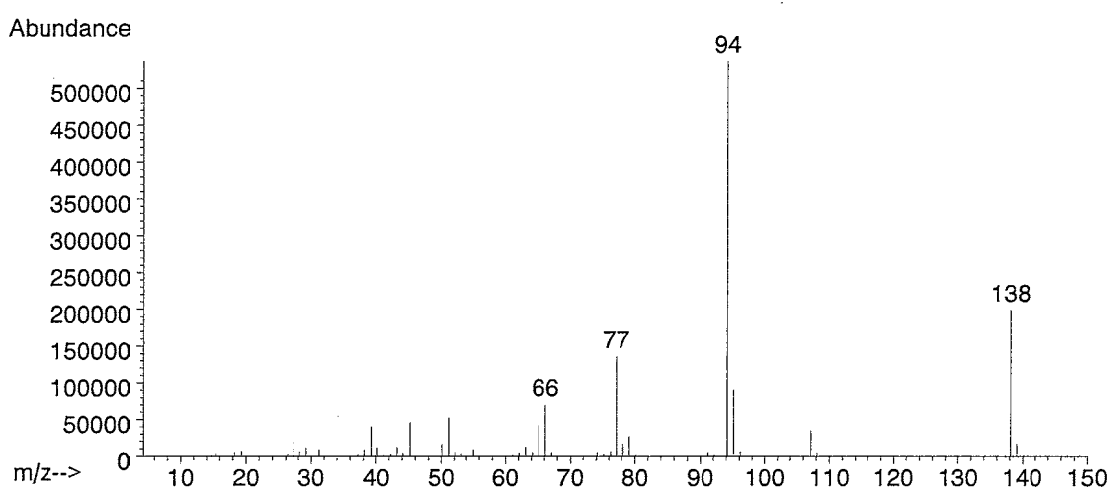
## 1. Spectral Data

Mass Spectrometry

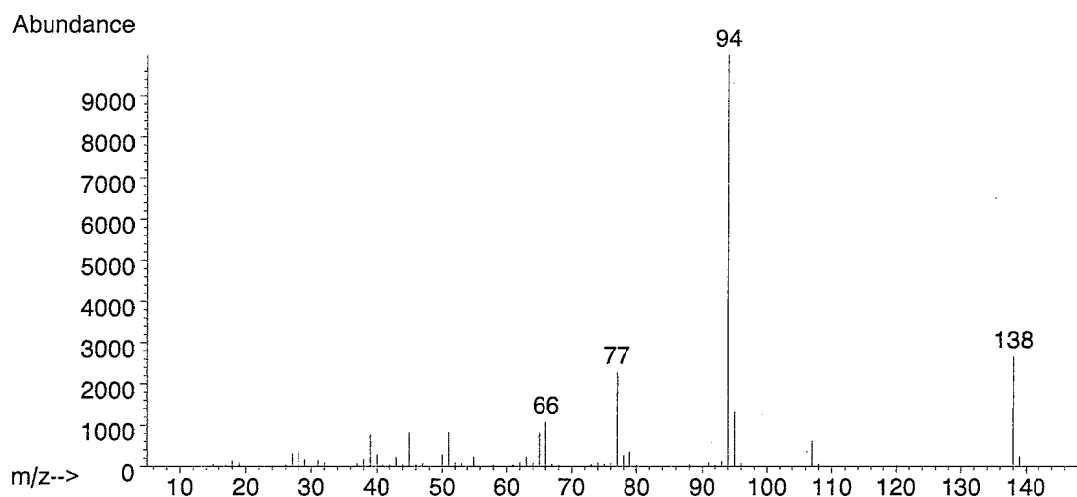
Instrument : Hewlett Packard 5989B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance



Mass Spectrum of Literature Data\*

Result: The mass spectrum was consistent with literature spectrum.

(\*McLafferty, F.W. (1994)

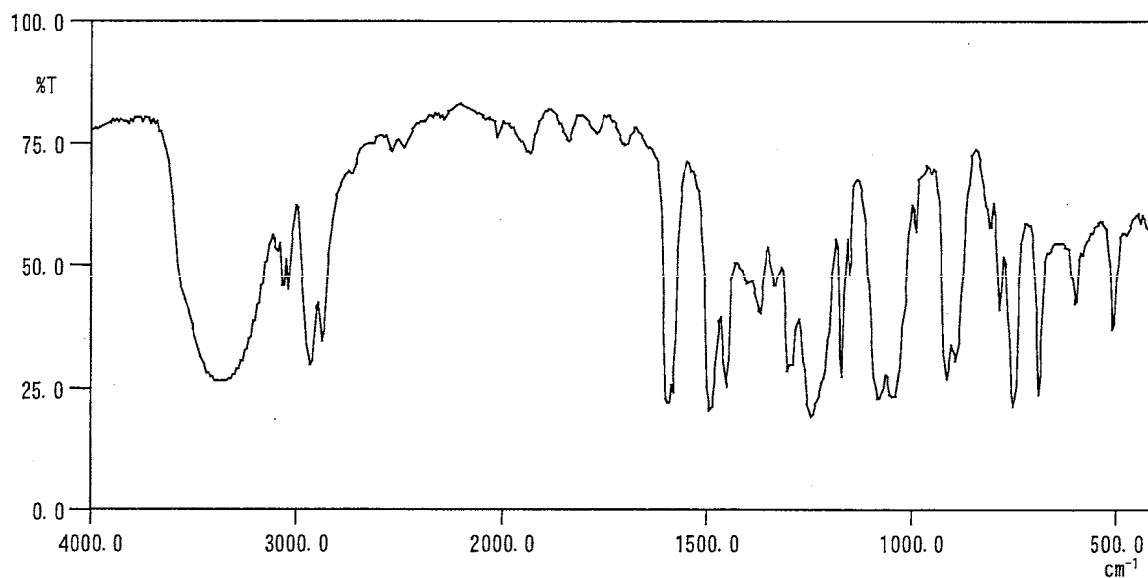
Wiley Registry of Mass Spectral Data, 6<sup>th</sup> edition. Entry Number 25888  
John Wiley and Sons, Inc. New York)

## Infrared Spectrometry

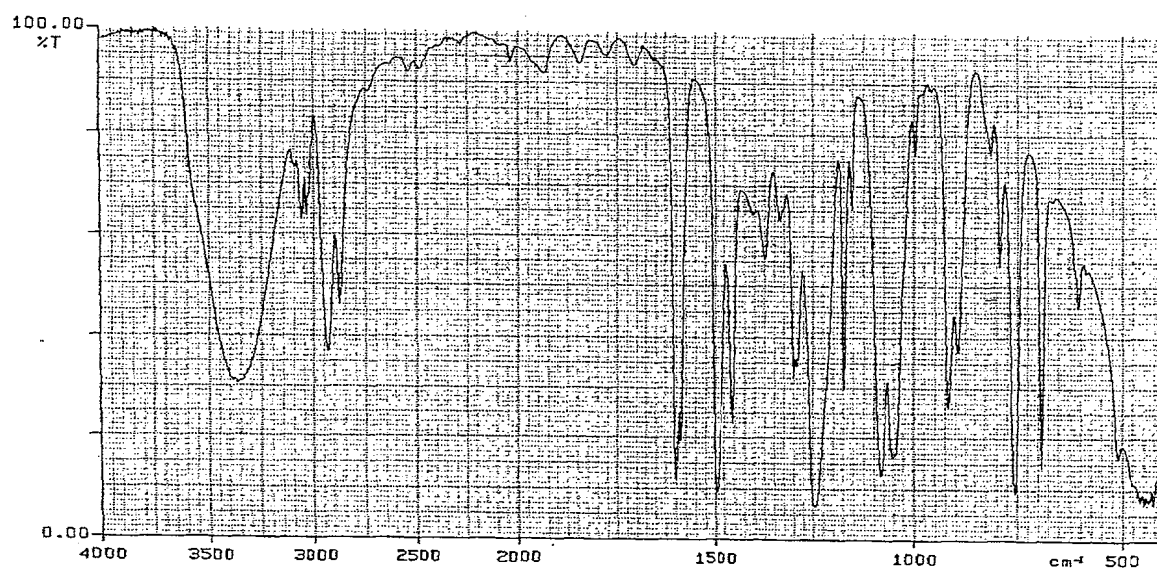
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

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



Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data\*

Result: The infrared spectrum was consistent with literature spectrum.

(\*Performed by Wako Pure Chemical Industries, Ltd.)

2. Conclusion: The test substance was identified as 2-phenoxyethanol by mass spectrum and infrared spectrum.



## APPENDIX M 2

### STABILITY OF 2-PHENOXYETHANOL IN THE 2-WEEK DRINKING WATER STUDY

## STABILITY OF 2-PHENOXYETHANOL IN THE 2-WEEK DRINKING WATER STUDY

Test Substance : 2-Phenoxyethanol (Wako Pure Chemical Industries, Ltd.)  
Lot No. : WAR5157  
1. Sample : This lot was used from 2002.6.25 to 2002.7.9. Test substance was stored in a dark place at room temperature.

## 2. High Performance Liquid Chromatography

Instrument : Shimadzu LC-10 High Performance Liquid Chromatograph  
Column : TSK GEL ODS-80TM (4.6 mm $\phi$   $\times$  15 cm)  
Column Temperature : 40 °C  
Flow Rate : 1 mL/min  
Mobile Phase : Acetonitrile : Distilled Water = 4 : 6  
Detector : UV (271 nm)  
Injection Volume : 10  $\mu$ L

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
2002.05.21	1	3.571	100
2002.07.18	1	3.601	100

Result: High performance liquid chromatography indicated one major peak (peak No.1) analyzed on 2002.5.21 and one major peak (peak No.1) analyzed on 2002.7.18. No new trace impurity peak in the test substance analyzed on 2002.7.18 was detected.

3. Conclusion: The test substance was stable for about 2 months in a dark place at room temperature.

## APPENDIX M 3

### CONCENTRATION OF 2-PHENOXYETHANOL IN FORMULATED WATER IN THE 2-WEEK DRINKING WATER STUDY

# CONCENTRATION OF 2-PHENOXYETHANOL IN FORMULATED WATER IN THE 2-WEEK DRINKING WATER STUDY

Date Analyzed	Target Concentration				
	1600 <sup>a</sup>	4000	10000	17500	25000
2002.06.25	1590 ( 99.4) <sup>b</sup>	4010 (100)	9990 ( 99.9)	17300 ( 98.9)	25200 (101)

<sup>a</sup> ppm

<sup>b</sup> %

Analytical Method : The samples were analyzed by high performance liquid chromatography.

Instrument : Shimadzu LC-10 High Performance Liquid Chromatograph

Column : TSK GEL ODS-80TM (4.6 mm $\phi$   $\times$  15 cm)

Column Temperature : 40 °C

Flow Rate : 1 mL/min

Mobile Phase : Acetonitrile : Distilled Water = 4 : 6

Detector : UV (271 nm)

Injection Volume : 10  $\mu$ L

## APPENDIX M 4

### STABILITY OF 2-PHENOXYETHANOL IN FORMULATED WATER IN THE 2-WEEK DRINKING WATER STUDY

# STABILITY OF 2-PHENOXYETHANOL IN FORMULATED WATER IN THE 2-WEEK DRINKING WATER STUDY

Date Prepared	Date Analyzed	Target Concentration	
		100 <sup>a</sup>	25000
2002.05.15	2002.05.15	97.3 (100) <sup>b</sup>	24600 (100)
	2002.05.20 <sup>c</sup>	98.7 (101)	25700 (104)

<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 high performance liquid chromatography.

Instrument : Shimadzu LC-10 High Performance Liquid Chromatograph  
 Column : TSK GEL ODS-80TM (4.6 mm $\phi$   $\times$  15 cm)  
 Column Temperature : 40 °C  
 Flow Rate : 1 mL/min  
 Mobile Phase : Acetonitrile : Distilled Water = 4 : 6  
 Detector : UV (271 nm)  
 Injection Volume : 10  $\mu$ L

## APPENDIX N 1

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS  
IN THE 2-WEEK DRINKING WATER STUDY OF 2-PHENOXYETHANOL

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS  
IN THE 2-WEEK DRINKING WATER STUDY OF 2-PHENOXYETHANOL

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>
Reticulocyte	Light scattering method <sup>1)</sup>
Prothrombin time	Quick one stage method <sup>2)</sup>
Activated partial thromboplastin time (APTT)	Ellagic acid activated method <sup>2)</sup>
White blood cell (WBC)	Light scattering method <sup>1)</sup>
Differential WBC	Pattern recognition method <sup>3)</sup> (Wright staining)
<b>Biochemistry</b>	
Total protein (TP)	Biuret method <sup>4)</sup>
Albumin (Alb)	BCG method <sup>4)</sup>
A/G ratio	Calculated as $Alb / (TP - Alb)$ <sup>4)</sup>
T-bilirubin	Alkaline azobilirubin method <sup>4)</sup>
Glucose	GlcK · G-6-PDH method <sup>4)</sup>
T-cholesterol	CE · COD · POD method <sup>4)</sup>
Phospholipid	PLD · ChOD · POD method <sup>4)</sup>
Glutamic oxaloacetic transaminase (GOT)	JSCC method <sup>4)</sup>
Glutamic pyruvic transaminase (GPT)	JSCC method <sup>4)</sup>
Lactate dehydrogenase (LDH)	SFBC method <sup>4)</sup>
$\gamma$ -Glutamyl transpeptidase ( $\gamma$ -GTP)	$\gamma$ -Glutamyl-p-nitroanilide method <sup>4)</sup>
Creatine phosphokinase (CPK)	JSCC method <sup>4)</sup>
Urea nitrogen	Urease · GLDH method <sup>4)</sup>
Creatinine	Jaffe method <sup>4)</sup>
Sodium	Ion selective electrode method <sup>4)</sup>
Potassium	Ion selective electrode method <sup>4)</sup>
Chloride	Ion selective electrode method <sup>4)</sup>
Calcium	OCPC method <sup>4)</sup>
Inorganic phosphorus	PNP · XOD · POD method <sup>4)</sup>
<b>Urinalysis</b>	
pH, Protein, Glucose, Ketone body, Bilirubin, Occult Blood, Urobilinogen	Urinalysis reagent paper method <sup>5)</sup>

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

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

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

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

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



## APPENDIX O 1

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

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

Item	Unit	Decimal Place
<b>Hematology</b>		
Red blood cell (RBC)	$\times 10^6 / \mu\text{L}$	2
Hemoglobin (Hgb)	g/dL	1
Hematocrit (Hct)	%	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
Reticulocyte	%	1
Prothrombin time	sec	1
Activated partial thromboplastin time (APTT)	sec	1
White blood cell (WBC)	$\times 10^3 / \mu\text{L}$	2
Differential WBC	%	0
<b>Biochemistry</b>		
Total protein (TP)	g/dL	1
Albumin (Alb)	g/dL	1
A/G ratio	—	1
T-bilirubin	mg/dL	2
Glucose	mg/dL	0
T-cholesterol	mg/dL	0
Phospholipid	mg/dL	0
Glutamic oxaloacetic transaminase (GOT)	IU/L	0
Glutamic pyruvic transaminase (GPT)	IU/L	0
Lactate dehydrogenase (LDH)	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