

2-アミノ-4-クロロフェノールのマウスを用いた  
経口投与による 13 週間毒性試験（混餌試験）報告書

試験番号：0550

# APPENDICES

## APPENDICES

APPENDIX A 1	IDENTITY OF 2-AMINO-4-CHLOROPHENOL IN THE 13-WEEK FEED STUDY
APPENDIX A 2	STABILITY OF 2-AMINO-4-CHLOROPHENOL IN THE 13-WEEK FEED STUDY
APPENDIX A 3	CONCENTRATION OF 2-AMINO-4-CHLOROPHENOL IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY
APPENDIX A 4	HOMOGENEITY OF 2-AMINO-4-CHLOROPHENOL IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY
APPENDIX A 5	STABILITY OF 2-AMINO-4-CHLOROPHENOL IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY
APPENDIX B 1	CLINICAL OBSERVATION: MALE
APPENDIX B 2	CLINICAL OBSERVATION: FEMALE
APPENDIX C 1	BODY WEIGHT CHANGES: MALE
APPENDIX C 2	BODY WEIGHT CHANGES: FEMALE
APPENDIX D 1	FOOD CONSUMPTION CHANGES: MALE
APPENDIX D 2	FOOD CONSUMPTION CHANGES: FEMALE
APPENDIX E 1	CHEMICAL INTAKE CHANGES: MALE
APPENDIX E 2	CHEMICAL INTAKE CHANGES: FEMALE
APPENDIX F 1	HEMATOLOGY: MALE
APPENDIX F 2	HEMATOLOGY: FEMALE
APPENDIX G 1	BIOCHEMISTRY: MALE
APPENDIX G 2	BIOCHEMISTRY: FEMALE

## APPENDICES (CONTINUED)

APPENDIX H 1	URINALYSIS: MALE
APPENDIX H 2	URINALYSIS: FEMALE
APPENDIX I 1	GROSS FINDINGS: MALE: DEAD AND MORIBUND ANIMALS
APPENDIX I 2	GROSS FINDINGS: MALE: SACRIFICED ANIMALS
APPENDIX I 3	GROSS FINDINGS: FEMALE: DEAD AND MORIBUND ANIMALS
APPENDIX I 4	GROSS FINDINGS: FEMALE: SACRIFICED ANIMALS
APPENDIX J 1	ORGAN WEIGHT, ABSOLUTE: MALE
APPENDIX J 2	ORGAN WEIGHT, ABSOLUTE: FEMALE
APPENDIX K 1	ORGAN WEIGHT, RELATIVE: MALE
APPENDIX K 2	ORGAN WEIGHT, RELATIVE: FEMALE
APPENDIX L 1	HISTOPATHOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: MALE: DEAD AND MORIBUND ANIMALS
APPENDIX L 2	HISTOPATHOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: MALE: SACRIFICED ANIMALS
APPENDIX L 3	HISTOPATHOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: FEMALE: DEAD AND MORIBUND ANIMALS
APPENDIX L 4	HISTOPATHOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: FEMALE: SACRIFICED ANIMALS
APPENDIX M	METHODS, UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

## APPENDIX A 1

### IDENTITY OF 2-AMINO-4-CHLOROPHENOL IN THE 13-WEEK FEED STUDY

## IDENTITY OF 2-AMINO-4-CHLOROPHENOL IN THE 13-WEEK FEED STUDY

Test Substance : 2-Amino-4-chlorophenol (Wako Pure Chemical Industries, Ltd.)

Lot No. : CEQ0194

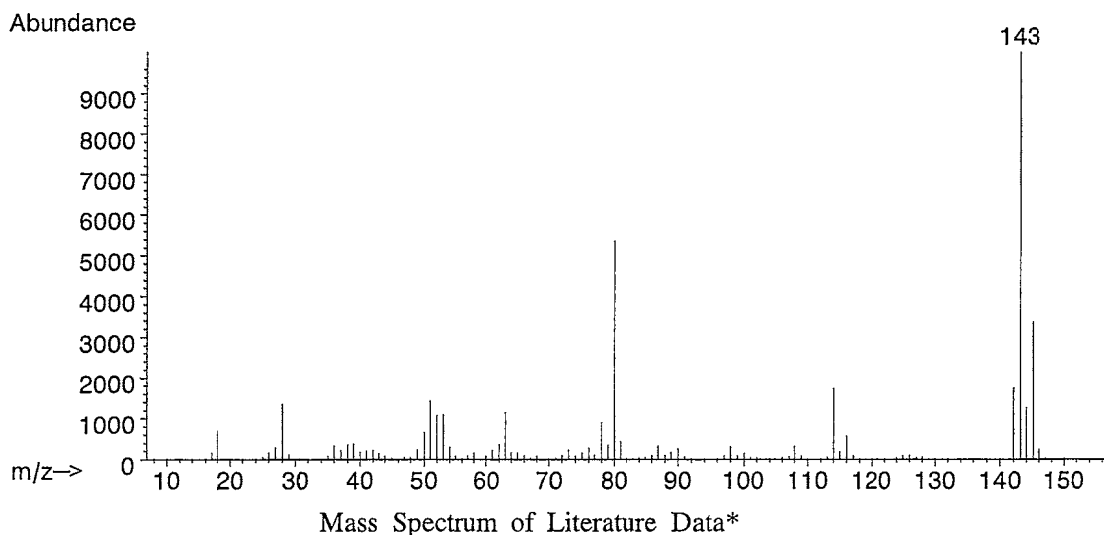
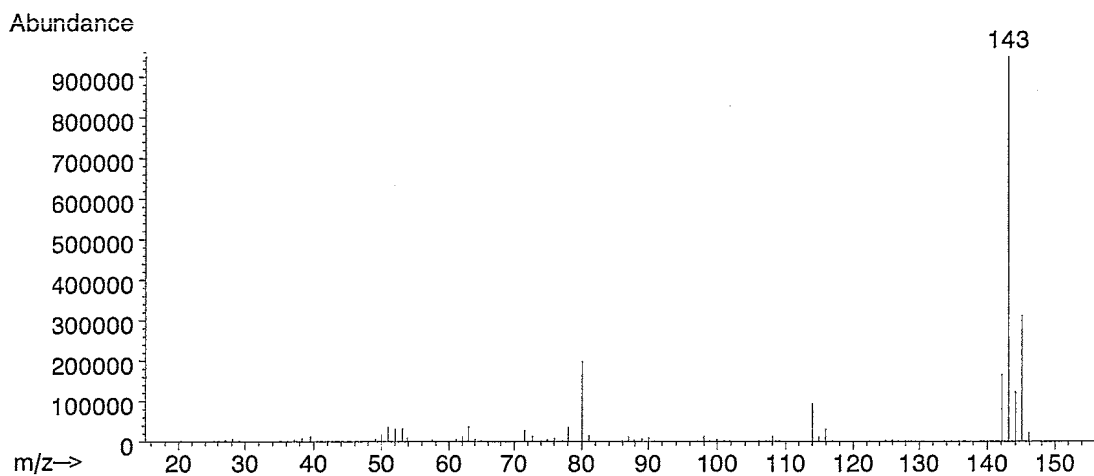
## 1. Spectral data

Mass Spectrometry

Instrument : Hewlett Packard 5989B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Result: The mass spectrum was consistent with literature spectrum.

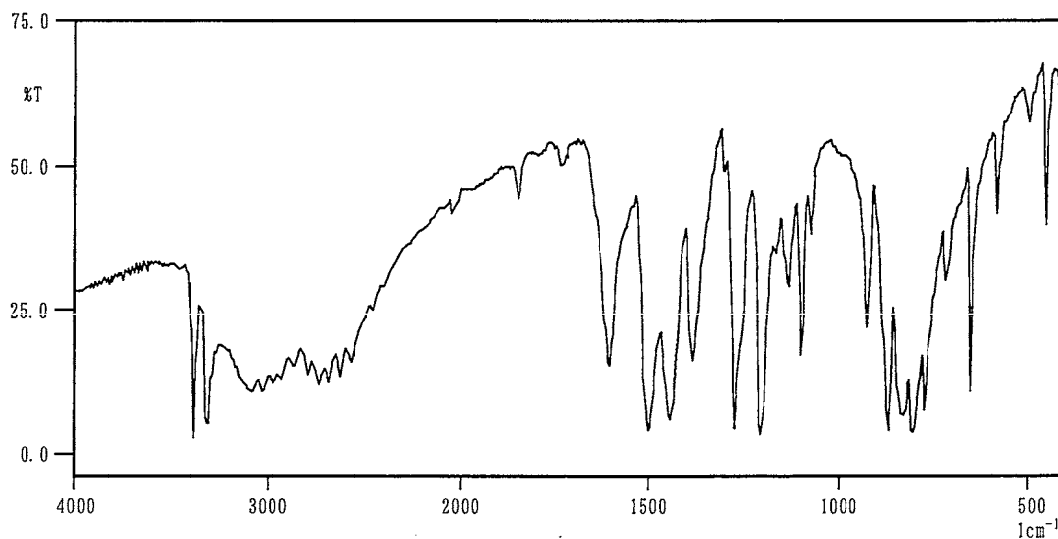
(\*McLafferty FW, ed. 1994. Wiley Registry of Mass Spectral Data. 6th ed.  
New York, NY : John Wiley and Sons.)

Infrared Spectrometry

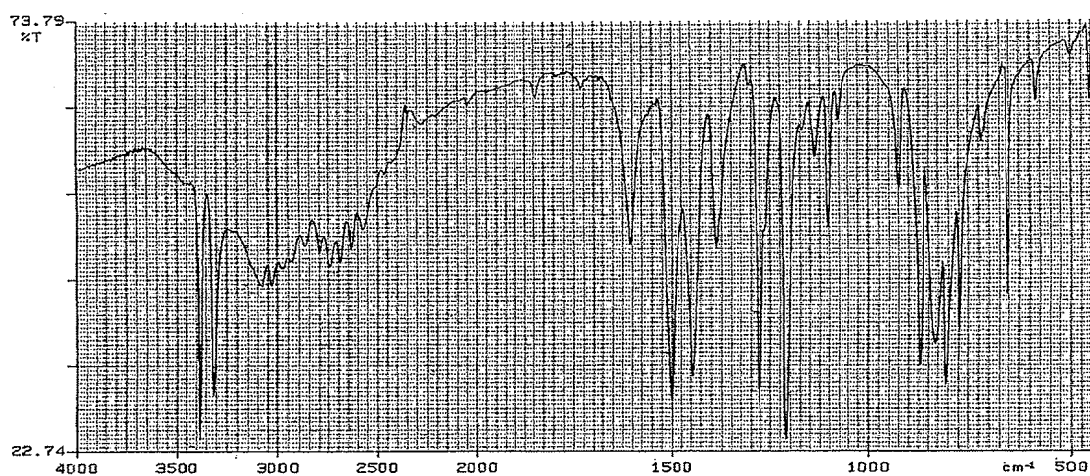
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution :  $2.0\text{ cm}^{-1}$



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-amino-4-chlorophenol by mass spectrum and infrared spectrum.

## APPENDIX A 2

### STABILITY OF 2-AMINO-4-CHLOROPHENOL IN THE 13-WEEK FEED STUDY

## STABILITY OF 2-AMINO-4-CHLOROPHENOL IN THE 13-WEEK FEED STUDY

Test Substance : 2-Amino-4-chlorophenol (Wako Pure Chemical Industries, Ltd.)

Lot No. : CEQ0194

1. Sample : This lot was used from 2004.7.30 to 2004.11.1. Test substance was stored in cold storage in a dark place.

## 2. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : DB-1 (0.25 mm $\phi$   $\times$  60 m)

Column Temperature : 100 °C  $\rightarrow$  (10 °C/min)  $\rightarrow$  250 °C (5 min)

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1  $\mu$ L

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
2004.07.27	1	12.373	100
2005.01.11	1	12.374	100

Result: Gas chromatography indicated one major peak (peak No.1) analyzed on 2004.7.27 and one major peak (peak No.1) analyzed on 2005.1.11. No new trace impurity peak in the test substance analyzed on 2005.1.11 was detected.

3. Conclusion: The test substance was stable for about 6 months in cold storage in a dark place.

## APPENDIX A 3

### CONCENTRATION OF 2-AMINO-4-CHLOROPHENOL IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

# CONCENTRATION OF 2-AMINO-4-CHLOROPHENOL IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

Date Analyzed	Target Concentration				
	512 <sup>a</sup>	1280	3200	8000	20000
2004.07.29	492 ( 96.1) <sup>b</sup>	1280 (100)	3170 ( 99.1)	8110 (101)	20400 (102)

<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 : 0.8 mL/min

Mobile Phase : Methanol : Acetonitrile : Phosphoric Acid  
(5 mM Octanesulfonic Acid Sodium Salt Monohydrate pH2.4) = 1 : 1 : 3

Detector : UV (284 nm)

Injection Volume : 10  $\mu$ L

## APPENDIX A 4

### HOMOGENEITY OF 2-AMINO-4-CHLOROPHENOL IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

# HOMOGENEITY OF 2-AMINO-4-CHLOROPHENOL IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

	Target Concentration				
	512 <sup>a</sup>	1280	3200	8000	20000
Coefficient Variation	2.30 <sup>b</sup>	2.71	2.05	2.58	2.66

<sup>a</sup> ppm

<sup>b</sup> % (n=7)

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 : 0.8 mL/min

Mobile Phase : Methanol : Acetonitrile : Phosphoric Acid  
(5 mM Octanesulfonic Acid Sodium Salt Monohydrate pH2.4) = 1 : 1 : 3

Detector : UV (284 nm)

Injection Volume : 10  $\mu$ L

## APPENDIX A 5

### STABILITY OF 2-AMINO-4-CHLOROPHENOL IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

# STABILITY OF 2-AMINO-4-CHLOROPHENOL IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

Date Prepared	Date Analyzed	Target Concentration	
		512 <sup>a</sup>	20000
2004.06.11	2004.06.11	484 (100 ) <sup>b</sup>	19900 (100 )
	2004.06.16 <sup>c</sup>	436 ( 90.1)	19600 ( 98.5)
	2004.06.25 <sup>d</sup>	477 ( 98.6)	19400 ( 97.5)

<sup>a</sup> ppm

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

<sup>c</sup> Animal room samples

<sup>d</sup> Cold storage 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 : 0.8 mL/min

Mobile Phase : Methanol : Acetonitrile : Phosphoric Acid

(5 mM Octanesulfonic Acid Sodium Salt Monohydrate pH2.4) = 1 : 1 : 3

Detector : UV (284 nm)

Injection Volume : 10  $\mu$ L

## APPENDIX B 1

### CLINICAL OBSERVATION : MALE

STUDY NO. : 0550  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : MALE

PAGE : 1

Clinical sign	Group Name	Administration Week-day												
		1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7
DEATH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	512 ppm	0	0	0	1	1	1	1	1	1	1	1	1	1
	1280 ppm	0	0	1	1	1	1	1	1	1	1	1	1	1
	3200 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	8000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	1	1	1	1	1	1	1	1
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	512 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1280 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	3200 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	8000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	1	0	0	0	0	0	0	0	0
SOILED PERI-GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	512 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1280 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	3200 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	8000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	1	0	0	0	0	0	0	0	0
INTERNAL MASS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	512 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1280 ppm	0	0	0	0	0	0	0	0	0	0	0	1	1
	3200 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	8000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
NON REMARKABLE	Control	10	10	10	10	10	10	10	10	10	10	10	10	10
	512 ppm	10	10	10	9	9	9	9	9	9	9	9	9	9
	1280 ppm	10	10	9	9	9	9	9	9	9	9	9	8	8
	3200 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	8000 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	20000 ppm	10	10	10	10	9	9	9	9	9	9	9	9	9

## APPENDIX B 2

### CLINICAL OBSERVATION : FEMALE

STUDY NO. : 0550  
ANIMAL : MOUSE B6D2F1/Cr1j[Crlj:BDF1]  
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : FEMALE

PAGE : 2

Clinical sign	Group Name	Administration Week-day												
		1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7
DEATH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	512 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1280 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	3200 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	8000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	2	3	3	3	3	3	3	3
SOILED	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	512 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1280 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	3200 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	8000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	1	2	0	0	0	0	0	0	0
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	512 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1280 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	3200 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	8000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	2	2	0	0	0	0	0	0	0
SOILED PERI-GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	512 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1280 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	3200 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	8000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	1	0	0	0	0	0	0	0	0
NON REMARKABLE	Control	10	10	10	10	10	10	10	10	10	10	10	10	10
	512 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	1280 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	3200 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	8000 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	20000 ppm	10	10	10	10	8	6	7	7	7	7	7	7	7

## APPENDIX C 1

### BODY WEIGHT CHANGES : MALE

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Cri:BDF1]  
 UNIT : g  
 REPORT TYPE : A1 13  
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 1

Group Name	Administration week						
	0	1	2	3	4	5	6
Control	23.8± 0.9	25.1± 0.9	26.4± 1.6	26.7± 1.9	27.2± 1.9	28.5± 1.8	28.2± 2.2
512 ppm	23.7± 0.9	24.8± 2.0	26.0± 2.4	26.1± 3.3	28.0± 1.4	29.1± 1.6	28.6± 1.9
1280 ppm	23.8± 0.9	25.0± 1.8	26.2± 1.8	26.3± 1.6	26.8± 1.7	28.0± 1.5	27.6± 1.4
3200 ppm	23.8± 0.8	24.6± 0.7	26.0± 1.0	26.1± 1.2	26.6± 1.3	28.0± 1.4	27.4± 1.6
8000 ppm	23.8± 0.9	24.5± 0.6	25.7± 0.9	26.1± 1.1	26.8± 1.2	27.6± 1.2	27.4± 1.4
20000 ppm	23.7± 1.0	22.3± 1.6**	24.2± 1.4*	24.6± 1.6	24.8± 1.9**	24.9± 3.4*	25.5± 1.0**

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

Test of Dunnett

(HAN260)

BATS 4

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 UNIT : g  
 REPORT TYPE : A1 13  
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 2

Group Name	Administration week						
	7	8	9	10	11	12	13
Control	29.1± 1.9	29.8± 2.0	30.4± 2.4	31.9± 2.0	31.8± 2.0	32.3± 2.3	32.9± 2.7
512 ppm	30.3± 2.0	31.0± 2.3	31.1± 2.6	32.1± 2.8	32.3± 2.5	32.9± 2.9	33.2± 3.0
1280 ppm	29.4± 1.3	29.7± 1.2	30.6± 1.7	31.5± 2.1	31.5± 2.3	31.2± 2.4	32.4± 2.4
3200 ppm	29.2± 1.7	29.7± 1.7	30.3± 1.4	31.1± 1.9	31.5± 1.6	31.5± 1.9	31.5± 3.1
8000 ppm	28.4± 1.3	28.8± 1.6	29.5± 1.5	30.4± 1.6	29.7± 2.7	30.8± 2.2	30.8± 2.7
20000 ppm	25.7± 1.2**	27.4± 1.3*	27.3± 1.6**	25.2± 1.4**	27.1± 2.2**	27.8± 1.1**	28.1± 1.1**

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

Test of Dunnett

(HAN260)

BATS 4

## APPENDIX C 2

### BODY WEIGHT CHANGES : FEMALE

STUDY NO. : 0550  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
UNIT : g  
REPORT TYPE : A1 13  
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)  
ALL ANIMALS

PAGE : 3

Group Name	Administration week						
	0	1	2	3	4	5	6
Control	18.8± 0.7	20.2± 1.2	21.0± 1.2	21.3± 0.8	21.3± 1.2	22.0± 1.1	20.8± 0.8
512 ppm	18.8± 0.8	20.2± 0.8	20.7± 0.8	20.5± 1.1	21.9± 1.0	22.3± 0.9	21.6± 0.3
1280 ppm	18.8± 0.7	19.4± 1.6	20.5± 1.3	20.7± 1.0	21.4± 0.8	22.4± 0.9	21.1± 0.8
3200 ppm	18.8± 0.8	20.0± 1.0	21.2± 1.2	20.5± 1.2	21.3± 1.4	22.0± 1.2	21.2± 1.4
8000 ppm	18.8± 0.7	19.9± 1.0	20.5± 0.6	20.9± 0.4	21.0± 0.8	21.8± 0.5	20.7± 0.8
20000 ppm	18.8± 0.7	18.6± 0.9**	20.2± 0.7	19.8± 0.7**	20.2± 0.9	20.1± 1.8	19.1± 1.9

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

Test of Dunnett

(HAN260)

BATS 4

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 UNIT : g  
 REPORT TYPE : A1 13  
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 4

Group Name	Administration week						
	7	8	9	10	11	12	13
Control	22.1± 1.3	21.7± 1.3	22.5± 1.1	22.5± 1.4	23.2± 1.3	23.6± 1.5	23.7± 1.3
512 ppm	22.6± 0.9	21.8± 0.6	22.3± 0.6	22.5± 0.8	23.8± 1.1	23.5± 1.6	23.8± 1.0
1280 ppm	22.3± 0.7	22.0± 0.8	22.9± 1.2	22.7± 0.8	23.4± 1.8	23.1± 1.7	23.9± 1.8
3200 ppm	22.5± 1.8	22.8± 1.3	22.9± 1.2	22.8± 1.3	23.2± 1.3	24.0± 1.6	24.2± 1.8
8000 ppm	21.8± 0.9	21.4± 0.9	22.7± 0.9	21.5± 1.4	22.6± 0.9	22.7± 0.8	22.5± 0.6
20000 ppm	20.8± 1.5	21.8± 0.6	22.8± 1.2	20.2± 0.9**	22.9± 1.7	23.0± 1.3	22.9± 0.9

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

Test of Dunnett

(HAN260)

BATS 4

## APPENDIX D 1

### FOOD CONSUMPTION CHANGES : MALE

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 UNIT : g  
 REPORT TYPE : A1 13  
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 1

Group Name	Administration week						
	1	2	3	4	5	6	7
Control	4.0± 0.3	3.6± 0.4	3.5± 0.5	3.6± 0.3	3.7± 0.3	3.9± 0.3	4.3± 0.4
512 ppm	3.9± 0.9	3.9± 0.8	3.6± 1.0	4.0± 0.5	4.2± 0.6	3.8± 0.5	4.3± 0.4
1280 ppm	4.0± 0.4	3.9± 0.7	3.6± 0.5	3.7± 0.4	3.8± 0.3	3.7± 0.4	4.3± 0.6
3200 ppm	3.9± 0.2	4.2± 0.3	3.7± 0.5	3.8± 0.7	4.1± 0.5	3.9± 0.6	4.3± 0.5
8000 ppm	4.0± 0.2	3.9± 0.2	3.8± 0.4	3.9± 0.7	3.9± 0.8	4.1± 0.3	4.0± 0.4
20000 ppm	3.8± 0.6	3.8± 0.4	3.5± 0.5	3.6± 0.4	3.6± 0.5	3.9± 0.7	3.3± 0.5**

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

Test of Dunnett

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 UNIT : g  
 REPORT TYPE : A1 13  
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 2

Group Name	Administration week					
	8	9	10	11	12	13
Control	4.1± 0.5	3.5± 0.5	4.1± 0.3	3.7± 0.5	3.9± 0.4	3.9± 0.4
512 ppm	4.3± 0.6	3.9± 0.5	4.1± 0.7	4.1± 0.4	4.1± 0.3	4.1± 0.4
1280 ppm	4.1± 0.4	4.1± 0.6	4.1± 0.4	3.9± 0.5	3.8± 0.6	4.0± 0.3
3200 ppm	4.4± 0.5	4.2± 0.6*	4.1± 0.5	4.4± 0.4	3.8± 0.5	3.8± 0.7
8000 ppm	4.1± 0.3	4.1± 0.6	4.3± 0.6	3.7± 0.6	4.2± 0.5	3.9± 0.6
20000 ppm	4.8± 0.5**	4.4± 0.5**	3.3± 0.9	4.1± 0.8	4.1± 0.7	3.6± 0.4

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

Test of Dunnett

## APPENDIX D 2

### FOOD CONSUMPTION CHANGES : FEMALE

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 UNIT : g  
 REPORT TYPE : A1 13  
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 3

Group Name	Administration week						
	1	2	3	4	5	6	7
Control	3.8± 0.5	3.6± 0.5	3.4± 0.3	3.3± 0.2	3.6± 0.3	3.4± 0.4	3.7± 0.3
512 ppm	3.7± 0.6	3.3± 0.2	3.4± 0.5	3.6± 0.4	3.7± 0.4	3.8± 0.5	4.1± 0.5
1280 ppm	3.2± 0.6	3.1± 0.3	3.3± 0.5	3.2± 0.4	3.6± 0.3	3.5± 0.3	3.5± 0.3
3200 ppm	3.5± 0.4	3.5± 0.5	3.1± 0.5	3.4± 0.3	3.5± 0.6	3.4± 0.5	3.9± 1.0
8000 ppm	3.5± 0.3	3.2± 0.2	3.4± 0.2	3.2± 0.4	3.5± 0.3	3.4± 0.3	3.6± 0.3
20000 ppm	3.5± 0.6	3.2± 0.4	3.1± 0.5	3.3± 0.5	3.4± 0.4	3.5± 0.6	3.3± 1.2

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

Test of Dunnett

(HAN260)

BATS 4

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 UNIT : g  
 REPORT TYPE : A1 13  
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 4

Group Name	Administration week					
	8	9	10	11	12	13
Control	3.8± 0.4	3.7± 0.6	3.6± 0.7	4.0± 0.5	3.9± 0.3	3.8± 0.6
512 ppm	3.8± 0.3	4.0± 0.4	3.8± 0.5	4.1± 0.4	3.9± 0.2	3.8± 0.3
1280 ppm	3.7± 0.2	3.9± 0.5	3.7± 0.6	3.9± 0.6	3.7± 0.3	3.7± 0.3
3200 ppm	4.0± 0.4	3.8± 0.3	3.7± 0.4	3.7± 0.4	3.8± 0.5	3.9± 0.4
8000 ppm	3.7± 0.2	4.0± 0.7	3.4± 0.7	3.5± 0.4	3.6± 0.5	3.4± 0.5
20000 ppm	4.3± 0.6	4.2± 0.6	3.1± 0.6	3.9± 0.7	3.5± 0.3	3.4± 0.5

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

Test of Dunnett

(HAN260)

BATS 4

## APPENDIX E 1

### CHEMICAL INTAKE CHANGES : MALE

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Cri:BDF1]  
 UNIT : g/kg/day  
 REPORT TYPE : A1 13  
 SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 1

Group Name	Administration (Week-Day)									
	1-7	2-7	3-7	4-7	5-7	6-7	7-7			
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000		
512 ppm	0.079± 0.014	0.076± 0.012	0.069± 0.014	0.073± 0.007	0.074± 0.010	0.068± 0.009	0.072± 0.006			
1280 ppm	0.203± 0.010	0.190± 0.031	0.174± 0.024	0.178± 0.018	0.175± 0.010	0.170± 0.017	0.189± 0.024			
3200 ppm	0.506± 0.025	0.511± 0.042	0.455± 0.069	0.454± 0.082	0.471± 0.059	0.459± 0.070	0.476± 0.061			
8000 ppm	1.320± 0.099	1.214± 0.058	1.149± 0.100	1.152± 0.186	1.134± 0.198	1.182± 0.074	1.139± 0.091			
20000 ppm	3.368± 0.423	3.131± 0.326	2.877± 0.409	2.905± 0.399	2.973± 0.662	3.056± 0.629	2.561± 0.438			

(IIAN300)

BAIS 4

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 UNIT : g/kg/day  
 REPORT TYPE : A1 13  
 SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 2

Group Name	Administration (Week-Day)									
	8-7		9-7		10-7		11-7		12-7	13-7
Control	0.000± 0.000		0.000± 0.000		0.000± 0.000		0.000± 0.000		0.000± 0.000	
512 ppm	0.072± 0.009		0.064± 0.007		0.066± 0.009		0.065± 0.005		0.064± 0.007	0.063± 0.007
1280 ppm	0.177± 0.019		0.173± 0.022		0.165± 0.016		0.160± 0.018		0.154± 0.021	0.158± 0.013
3200 ppm	0.470± 0.052		0.449± 0.077		0.422± 0.049		0.442± 0.036		0.384± 0.055	0.383± 0.046
8000 ppm	1.151± 0.098		1.116± 0.156		1.140± 0.172		0.981± 0.111		1.087± 0.128	1.006± 0.121
20000 ppm	3.485± 0.305		3.258± 0.337		2.602± 0.692		2.985± 0.447		2.978± 0.557	2.535± 0.247

(IAN300)

BAIS 4

## APPENDIX E 2

### CHEMICAL INTAKE CHANGES : FEMALE

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 UNIT : g/kg/day  
 REPORT TYPE : A1 13  
 SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 3

Group Name	Administration (Week-Day)									
	1-7	2-7	3-7	4-7	5-7	6-7	7-7			
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000		
512 ppm	0.094± 0.014	0.081± 0.005	0.085± 0.010	0.084± 0.008	0.086± 0.008	0.090± 0.011	0.094± 0.010			
1280 ppm	0.210± 0.024	0.196± 0.014	0.202± 0.029	0.192± 0.024	0.205± 0.015	0.211± 0.017	0.201± 0.020			
3200 ppm	0.558± 0.045	0.522± 0.055	0.491± 0.074	0.505± 0.040	0.503± 0.075	0.510± 0.054	0.553± 0.102			
8000 ppm	1.388± 0.082	1.232± 0.081	1.299± 0.093	1.231± 0.128	1.273± 0.105	1.310± 0.120	1.321± 0.077			
20000 ppm	3.712± 0.493	3.207± 0.285	3.090± 0.447	3.267± 0.495	3.351± 0.470	3.723± 0.844	3.124± 1.090			

(HAN300)

BAIS 4

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crl:BDF1]  
 UNIT : g/kg/day  
 REPORT TYPE : A1 13  
 SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 4

Group Name	Administration (Week-Day)									
	8-7		9-7		10-7		11-7		12-7	13-7
Control	0.000± 0.000		0.000± 0.000		0.000± 0.000		0.000± 0.000		0.000± 0.000	
512 ppm	0.088± 0.007		0.092± 0.008		0.087± 0.011		0.089± 0.007		0.084± 0.005	0.081± 0.006
1280 ppm	0.215± 0.015		0.218± 0.018		0.206± 0.033		0.211± 0.020		0.205± 0.016	0.198± 0.014
3200 ppm	0.556± 0.051		0.534± 0.044		0.516± 0.049		0.516± 0.050		0.510± 0.056	0.517± 0.060
8000 ppm	1.380± 0.110		1.420± 0.217		1.264± 0.211		1.241± 0.128		1.277± 0.188	1.209± 0.161
20000 ppm	3.925± 0.552		3.684± 0.450		3.085± 0.564		3.382± 0.439		3.033± 0.338	2.942± 0.462

(HAN300)

BAIS 4

## APPENDIX F 1

### HEMATOLOGY : MALE

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 MEASURE. TIME : 1  
 SEX : MALE

HEMATOLOGY (SUMMARY)  
 ALL ANIMALS ( 14W)

REPORT TYPE : A1

PAGE : 1

Group Name	NO. of Animals	RED BLOOD CELL 10 <sup>6</sup> /μl		HEMOGLOBIN g/dl		HEMATOCRIT %		MCV fl		MCH pg		MCHC g/dl		PLATELET 10 <sup>3</sup> /μl	
Control	9	10.52±	0.32	15.8±	0.5	47.6±	1.7	45.3±	0.8	15.1±	0.1	33.3±	0.7	1415±	71
512 ppm	9	10.66±	0.20	16.0±	0.3	48.0±	0.6	45.0±	0.4	15.1±	0.2	33.5±	0.3	1381±	83
1280 ppm	9	10.48±	0.38	15.6±	0.6	46.5±	1.4	44.4±	0.9	14.9±	0.3	33.5±	0.7	1363±	51
3200 ppm	10	10.20±	0.29	15.5±	0.6	46.3±	1.4	45.3±	0.8	15.1±	0.3	33.4±	0.3	1310±	94*
8000 ppm	10	9.78±	0.26**	15.2±	0.4*	44.6±	1.0*	45.6±	0.5	15.5±	0.2**	34.0±	0.4*	1401±	105
20000 ppm	9	9.21±	0.25**	16.1±	0.3	41.2±	0.4**	44.7±	1.2	17.5±	0.3**	39.2±	0.7**	1451±	105

Significant difference ; \* : P ≤ 0.05

\*\* : P ≤ 0.01

Test of Dunnett

(HCL070)

BAIS 4

STUDY NO. : 0550

ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]

MEASURE. TIME : 1

SEX : MALE

REPORT TYPE : A1

HEMATOLOGY (SUMMARY)

ALL ANIMALS ( 14W)

PAGE : 2

Group Name	NO. of Animals	RETICULOCYTE %	
Control	9	2.1±	0.3
512 ppm	9	2.0±	0.3
1280 ppm	9	2.3±	0.3
3200 ppm	10	2.6±	0.5
8000 ppm	10	3.7±	0.7**
20000 ppm	9	6.1±	1.4**

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

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 4

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Cri:BDF1]  
 MEASURE. TIME : 1  
 SEX : MALE

HEMATOLOGY (SUMMARY)  
 ALL ANIMALS ( 14W)

REPORT TYPE : A1

PAGE : 3

Group Name	NO. of Animals	WBC 1 O <sup>3</sup> /μl		Differential N-BAND		WBC (%) N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHER	
Control	9	2.37±	0.90	0±	1	12±	3	2±	1	0±	0	2±	1	83±	3	0±	0
512 ppm	9	2.78±	0.85	0±	0	14±	3	1±	1	0±	0	3±	2	82±	3	0±	0
1280 ppm	9	2.56±	1.63	0±	0	14±	4	2±	1	0±	0	3±	1	82±	5	0±	0
3200 ppm	10	1.77±	0.95	0±	1	13±	4	1±	1	0±	0	2±	1	83±	3	0±	0
8000 ppm	10	2.20±	1.32	1±	1	15±	4	1±	1*	0±	0	2±	1	82±	4	0±	0
20000 ppm	9	2.19±	1.16	1±	1	11±	3	0±	1*	0±	0	1±	1	86±	3	0±	0

Significant difference ; \* : P ≤ 0.05

\*\* : P ≤ 0.01

Test of Dunnett

(HCL070)

BAIS 4

## APPENDIX F 2

### HEMATOLOGY : FEMALE

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 MEASURE. TIME : 1  
 SEX : FEMALE

HEMATOLOGY (SUMMARY)  
 ALL ANIMALS ( 14W)

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	10	10.80±	0.29	16.5±	0.4	49.0±	1.1	45.3±	0.7	15.3±	0.1	33.8±	0.5	1224±	82
512 ppm	10	10.74±	0.34	16.3±	0.5	48.3±	1.2	44.9±	0.5	15.2±	0.1	33.8±	0.3	1243±	60
1280 ppm	10	10.67±	0.28	16.3±	0.5	47.8±	1.3	44.8±	0.4	15.3±	0.2	34.1±	0.3	1264±	99
3200 ppm	8	10.61±	0.21	16.1±	0.3	48.1±	1.1	45.3±	0.6	15.2±	0.1	33.5±	0.4	1286±	46
8000 ppm	10	10.12±	0.30**	15.7±	0.5**	46.5±	1.2**	45.9±	0.7	15.5±	0.2	33.7±	0.4	1312±	73
20000 ppm	7	9.68±	0.49**	16.8±	1.1	44.6±	2.5**	46.0±	0.8	17.3±	0.6**	37.6±	0.8**	1318±	182

Significant difference ; \* : P ≤ 0.05      \*\* : P ≤ 0.01

Test of Dunnett

(HCL070)

BAIS 4

STUDY NO. : 0550  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
MEASURE. TIME : 1  
SEX : FEMALE

HEMATOLOGY (SUMMARY)  
ALL ANIMALS ( 14W)

REPORT TYPE : A1

PAGE : 5

Group Name	NO. of Animals	RETICULOCYTE %	
Control	10	2.2±	0.6
512 ppm	10	2.2±	0.5
1280 ppm	10	1.9±	0.4
3200 ppm	8	2.5±	0.8
8000 ppm	10	4.1±	1.2**
20000 ppm	7	7.3±	1.4**

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

Test of Dunnett

(IICL070)

BAIS 4

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 MEASURE. TIME : 1  
 SEX : FEMALE

HEMATOLOGY (SUMMARY)  
 ALL ANIMALS ( 14W)

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		LYMPHO		OTHER	
Control	10	2.46±	1.03	0±	0	13±	3	1±	1	0±	0	3±	1	83±	2	0±	0
512 ppm	10	2.21±	0.91	0±	1	13±	3	1±	1	0±	0	2±	1	84±	4	0±	0
1280 ppm	10	2.16±	1.08	0±	0	13±	3	2±	2	0±	0	2±	1	84±	5	0±	0
3200 ppm	8	2.27±	0.93	1±	1	12±	3	2±	2	0±	0	2±	1	84±	3	0±	0
8000 ppm	10	1.45±	0.76	0±	0	17±	8	0±	1	0±	0	1±	1**	82±	7	0±	0
20000 ppm	7	2.89±	1.61	0±	0	15±	5	0±	1	0±	0	1±	1**	83±	5	0±	0

Significant difference ; \* : P ≤ 0.05

\*\* : P ≤ 0.01

Test of Dunnett

(HCL070)

BAIS 4

## APPENDIX G 1

BIOCHEMISTRY : MALE

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 MEASURE. TIME : 1  
 SEX : MALE

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS ( 14W)

REPORT TYPE : A1

PAGE : 1

Group Name	NO. of Animals	TOTAL PROTEIN g/dl		ALBUMIN g/dl		A/G RATIO		T-BILIRUBIN mg/dl		GLUCOSE mg/dl		T-CHOLESTEROL mg/dl		TRIGLYCERIDE mg/dl	
Control	10	5.2±	0.3	3.0±	0.1	1.4±	0.1	0.13±	0.02	217±	35	84±	10	27±	13
512 ppm	9	5.2±	0.1	3.0±	0.1	1.4±	0.1	0.14±	0.01	170±	45	83±	8	27±	12
1280 ppm	9	5.2±	0.3	2.9±	0.1	1.3±	0.1	0.14±	0.03	195±	37	85±	16	23±	8
3200 ppm	10	5.0±	0.2	2.8±	0.2	1.3±	0.2	0.13±	0.02	170±	45	78±	10	21±	11
8000 ppm	10	5.1±	0.1	3.0±	0.1	1.4±	0.1	0.15±	0.03	177±	38	77±	6	21±	7
20000 ppm	9	5.0±	0.2	2.9±	0.2	1.5±	0.1	0.16±	0.02*	173±	38	81±	8	19±	5

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

\*\* :  $P \leq 0.01$

Test of Dunnett

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 MEASURE. TIME : 1  
 SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS ( 14W)

PAGE : 2

Group Name	NO. of Animals	PHOSPHOLIPID mg/dl		AST IU/l		ALT IU/l		LDH IU/l		ALP IU/l		G-GTP IU/l		CK IU/l	
Control	10	169±	15	43±	3	16±	2	182±	39	142±	14	1±	0	47±	15
512 ppm	9	167±	16	48±	5	19±	2	203±	50	144±	10	1±	1	54±	20
1280 ppm	9	172±	29	48±	12	18±	5	214±	61	141±	9	1±	0	56±	24
3200 ppm	10	153±	19	45±	6	17±	1	208±	68	141±	6	1±	0	75±	72
8000 ppm	10	158±	13	46±	8	18±	4	234±	91	146±	14	1±	1	68±	38
20000 ppm	9	160±	15	49±	9	19±	4	243±	107	153±	31	1±	1	68±	38

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

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 4

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 MEASURE. TIME : 1  
 SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS ( 14W)

PAGE : 3

Group Name	NO. of Animals	UREA NITROGEN mg/dl		SODIUM mEq/l		POTASSIUM mEq/l		CHLORIDE mEq/l		CALCIUM mg/dl		INORGANIC PHOSPHORUS mg/dl	
Control	10	24.2±	5.3	152±	1	4.6±	0.8	121±	2	8.7±	0.3	7.1±	0.9
512 ppm	9	24.5±	5.4	151±	1	4.4±	0.3	121±	2	8.7±	0.2	7.0±	0.9
1280 ppm	9	25.7±	8.2	151±	1	4.4±	0.4	121±	2	8.8±	0.3	6.4±	0.5
3200 ppm	10	26.2±	5.3	151±	2	4.4±	0.1	122±	1	8.6±	0.3	7.2±	1.0
8000 ppm	10	24.8±	2.5	151±	2	4.7±	0.6	119±	4	8.5±	0.2	6.8±	1.2
20000 ppm	9	25.8±	3.5	153±	1	4.6±	0.4	120±	2	8.7±	0.3	7.1±	1.3

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

Test of Dunnett

(HCL074)

BAIS 4

## APPENDIX G 2

### BIOCHEMISTRY : FEMALE

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 MEASURE. TIME : 1  
 SEX : FEMALE  
 REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS ( 14W)

PAGE : 4

Group Name	NO. of Animals	TOTAL PROTEIN g/dl		ALBUMIN g/dl		A/G RATIO		T-BILIRUBIN mg/dl		GLUCOSE mg/dl		T-CHOLESTEROL mg/dl		TRIGLYCERIDE mg/dl	
Control	10	5.2±	0.2	3.2±	0.1	1.7±	0.1	0.14±	0.02	131±	23	72±	6	17±	3
512 ppm	9	5.2±	0.2	3.2±	0.2	1.6±	0.2	0.15±	0.06	140±	25	72±	10	18±	9
1280 ppm	10	5.1±	0.1	3.2±	0.1	1.8±	0.2	0.13±	0.01	136±	20	70±	7	17±	5
3200 ppm	8	5.2±	0.1	3.3±	0.1	1.7±	0.1	0.13±	0.01	153±	31	76±	15	18±	9
8000 ppm	10	5.1±	0.2	3.2±	0.1	1.7±	0.1	0.14±	0.04	142±	23	81±	12	21±	9
20000 ppm	7	5.3±	0.3	3.4±	0.1	1.8±	0.1	0.18±	0.05	180±	22**	93±	13**	17±	4

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

Test of Dunnett

(HCL074)

BAIS 4

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 MEASURE. TIME : 1  
 SEX : FEMALE

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS ( 14W)

REPORT TYPE : A1

PAGE : 5

Group Name	NO. of Animals	PHOSPHOLIPID mg/dl		AST I U / l		ALT I U / l		LDH I U / l		ALP I U / l		G-GTP I U / l		CK I U / l	
Control	10	143±	9	65±	15	23±	4	240±	70	223±	22	1±	0	111±	48
512 ppm	9	144±	14	59±	7	20±	2	256±	122	223±	21	1±	1	137±	187
1280 ppm	10	138±	12	63±	12	22±	4	229±	33	232±	20	1±	0	126±	65
3200 ppm	8	148±	25	57±	5	20±	3	226±	28	216±	28	1±	1	71±	16
8000 ppm	10	157±	19	69±	14	24±	4	284±	87	218±	27	1±	1	139±	46
20000 ppm	7	171±	18**	59±	14	20±	4	321±	188	203±	45	1±	1	163±	145

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

Test of Dunnett

(HCL074)

BAIS 4

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 MEASURE. TIME : 1  
 SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS ( 14W)

PAGE : 6

Group Name	NO. of Animals	UREA NITROGEN mg/dl		SODIUM mEq/l		POTASSIUM mEq/l		CHLORIDE mEq/l		CALCIUM mg/dl		INORGANIC PHOSPHORUS mg/dl	
Control	10	19.0±	2.4	152±	2	4.3±	0.2	121±	1	8.8±	0.2	6.6±	1.3
512 ppm	9	19.2±	2.0	151±	2	4.4±	0.5	121±	2	8.6±	0.3	5.9±	0.6
1280 ppm	10	19.0±	3.3	151±	2	4.4±	0.3	120±	2	8.7±	0.2	5.9±	0.8
3200 ppm	8	19.5±	2.0	151±	1	4.5±	0.3	122±	1	8.8±	0.2	5.8±	1.2
8000 ppm	10	20.2±	2.3	151±	1	4.4±	0.4	121±	1	8.6±	0.3	6.5±	1.2
20000 ppm	7	27.4±	8.0*	151±	1	4.5±	0.4	119±	2	8.8±	0.3	6.0±	1.4

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

Test of Dunnett

(HCL074)

BAIS 4

## APPENDIX H 1

### URINALYSIS : MALE

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 MEASURE. TIME : 1  
 SEX : MALE REPORT TYPE : A1

URINALYSIS

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	3	4	2	1		0	0	7	3	0	0		10	0	0	0	0	0		1	2	7	0	0	0		10	0	0	0	0	
512 ppm	9	0	0	0	5	3	1	0		0	0	9	0	0	0		9	0	0	0	0	0		2	2	5	0	0	0		9	0	0	0	0	
1280 ppm	9	0	0	2	3	1	1	2		0	1	8	0	0	0		9	0	0	0	0	0		3	4	2	0	0	0		9	0	0	0	0	
3200 ppm	10	0	1	1	2	3	3	0		0	0	10	0	0	0		10	0	0	0	0	0		5	3	2	0	0	0		10	0	0	0	0	
8000 ppm	10	0	4	0	1	2	2	1		0	4	6	0	0	0	*	10	0	0	0	0	0		6	3	1	0	0	0	*	10	0	0	0	0	
20000 ppm	9	0	2	5	1	1	0	0	*	0	8	1	0	0	0	**	9	0	0	0	0	0		6	3	0	0	0	0	**	9	0	0	0	0	

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

Test of CHI SQUARE

(HCL101)

BATS 4

STUDY NO. : 0550  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
MEASURE. TIME : 1  
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
512 ppm	9	9 0 0 0 0
1280 ppm	9	9 0 0 0 0
3200 ppm	10	10 0 0 0 0
8000 ppm	10	10 0 0 0 0
20000 ppm	9	9 0 0 0 0

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

Test of CHI SQUARE

(HCL101)

BAIS 4

## APPENDIX H 2

### URINALYSIS : FEMALE

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Cri:BDF1]  
 MEASURE. TIME : 1  
 SEX : FEMALE

URINALYSIS

REPORT TYPE : A1

PAGE : 3

Group Name	NO. of Animals	pH							CHI	Protein					CHI	Glucose					CHI	Ketone body					CHI	Occult blood				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+
Control	10	0	1	4	2	3	0	0		0	2	7	1	0	0		10	0	0	0	0	0		1	9	0	0	0	0		10	0	0	0	0
512 ppm	10	0	0	4	0	2	4	0		0	1	7	2	0	0		10	0	0	0	0	0		1	8	1	0	0	0		10	0	0	0	0
1280 ppm	10	0	1	1	4	2	2	0		0	3	5	2	0	0		10	0	0	0	0	0		0	10	0	0	0	0		10	0	0	0	0
3200 ppm	10	0	4	2	1	3	0	0		0	3	6	1	0	0		10	0	0	0	0	0		1	9	0	0	0	0		10	0	0	0	0
8000 ppm	10	0	1	3	4	0	2	0		0	5	4	1	0	0		10	0	0	0	0	0		0	7	3	0	0	0		10	0	0	0	0
20000 ppm	7	0	0	1	3	1	2	0		0	3	2	2	0	0		7	0	0	0	0	0		0	7	0	0	0	0		7	0	0	0	0

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

Test of CHI SQUARE

(HCL101)

BAIS 4

STUDY NO. : 0550  
ANIMAL : MOUSE B6D2F1/Cr1j[BDF1]  
MEASURE. TIME : 1  
SEX : FEMALE

URINALYSIS

REPORT TYPE : A1

PAGE : 4

Group Name	NO. of Animals	Urobilinogen ± + 2+ 3+ 4+ CHH
Control	10	10 0 0 0 0
512 ppm	10	10 0 0 0 0
1280 ppm	10	10 0 0 0 0
3200 ppm	10	10 0 0 0 0
8000 ppm	10	10 0 0 0 0
20000 ppm	7	7 0 0 0 0

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

Test of CHI SQUARE

(HCL101)

BAIS 4

## APPENDIX I 1

### GROSS FINDINGS : MALE DEAD AND MORIBUND ANIMALS

STUDY NO. : 0550  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : MALE

GROSS FINDINGS (SUMMARY)  
DEAD AND MORIBUND ANIMALS (0- 14W)

PAGE : 1

Organ	Findings	Group Name NO. of Animals	Control	512 ppm	1280 ppm	3200 ppm
			0 (%)	1 (%)	1 (%)	0 (%)
thymus	atrophic		- ( -)	0 ( 0)	1 (100)	- ( -)
spleen	dark		- ( -)	0 ( 0)	0 ( 0)	- ( -)
gl stomach	ulcer		- ( -)	0 ( 0)	0 ( 0)	- ( -)
kidney	enlarged		- ( -)	0 ( 0)	1 (100)	- ( -)
	white zone		- ( -)	0 ( 0)	1 (100)	- ( -)
	hydronephrosis		- ( -)	1 (100)	0 ( 0)	- ( -)
thoracic ca	pleural fluid		- ( -)	0 ( 0)	1 (100)	- ( -)

(HPT080)

BAIS 4

STUDY NO. : 0550  
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]  
REPORT TYPE : A1  
SEX : MALE

GROSS FINDINGS (SUMMARY)  
DEAD AND MORIBUND ANIMALS (0- 14W)

PAGE : 2

Organ	Findings	Group Name	8000 ppm	20000 ppm
		NO. of Animals	0 (%)	1 (%)
thymus	atrophic		- ( -)	1 (100)
spleen	dark		- ( -)	1 (100)
gl stomach	ulcer		- ( -)	1 (100)
kidney	enlarged		- ( -)	0 ( 0)
	white zone		- ( -)	0 ( 0)
	hydronephrosis		- ( -)	0 ( 0)
thoracic ca	pleural fluid		- ( -)	0 ( 0)

(HPT080)

BAIS 4

## APPENDIX I 2

### GROSS FINDINGS : MALE SACRIFICED ANIMALS

STUDY NO. : 0550  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : MALE

GROSS FINDINGS (SUMMARY)  
SACRIFICED ANIMALS ( 14W)

PAGE : 1

Organ	Findings	Group Name NO. of Animals	Control	512 ppm	1280 ppm	3200 ppm
			10 (%)	9 (%)	9 (%)	10 (%)
spleen	enlarged		0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
	dark		0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
	black zone		1 ( 10)	0 ( 0)	0 ( 0)	0 ( 0)
forestomach	thick		0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
kidney	hydronephrosis		1 ( 10)	1 ( 11)	2 ( 22)	0 ( 0)

(HPT080)

BAIS 4

STUDY NO. : 0550  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : MALE

GROSS FINDINGS (SUMMARY)  
SACRIFICED ANIMALS ( 14W)

PAGE : 2

Organ	Findings	Group Name	8000 ppm		20000 ppm	
		NO. of Animals	10	(%)	9	(%)
spleen	enlarged		0	( 0)	8	( 89)
	dark		0	( 0)	9	(100)
	black zone		0	( 0)	0	( 0)
forestomach	thick		0	( 0)	5	( 56)
kidney	hydronephrosis		0	( 0)	0	( 0)

(HPT080)

BAIS 4

## APPENDIX I 3

### GROSS FINDINGS : FEMALE DEAD AND MORIBUND ANIMALS

STUDY NO. : 0550  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : FEMALE

GROSS FINDINGS (SUMMARY)  
DEAD AND MORIBUND ANIMALS (0- 14W)

PAGE : 3

Organ	Findings	Group Name	Control	512 ppm	1280 ppm	3200 ppm
		NO. of Animals	0 (%)	0 (%)	0 (%)	0 (%)
thymus	atrophic		- ( -)	- ( -)	- ( -)	- ( -)
spleen	dark		- ( -)	- ( -)	- ( -)	- ( -)
forestomach	thick		- ( -)	- ( -)	- ( -)	- ( -)

(HPT080)

BAIS 4

STUDY NO. : 0550  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : FEMALE

GROSS FINDINGS (SUMMARY)  
DEAD AND MORIBUND ANIMALS (0- 14W)

PAGE : 4

Organ	Findings	Group Name	8000 ppm	20000 ppm
		NO. of Animals	0 (%)	3 (%)
thymus	atrophic		- ( -)	3 (100)
spleen	dark		- ( -)	2 ( 67)
forestomach	thick		- ( -)	2 ( 67)

(HPT080)

BAIS 4

## APPENDIX I 4

### GROSS FINDINGS : FEMALE SACRIFICED ANIMALS

STUDY NO. : 0550  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : FEMALE

GROSS FINDINGS (SUMMARY)  
SACRIFICED ANIMALS ( 14W)

PAGE : 3

Organ	Findings	Group Name NO. of Animals	Control		512 ppm		1280 ppm		3200 ppm	
			10	(%)	10	(%)	10	(%)	10	(%)
spleen	enlarged		0	( 0)	0	( 0)	0	( 0)	0	( 0)
	dark		0	( 0)	0	( 0)	0	( 0)	0	( 0)
	black zone		1	( 10)	0	( 0)	0	( 0)	0	( 0)
forestomach	thick		0	( 0)	0	( 0)	0	( 0)	0	( 0)
ovary	cyst		0	( 0)	0	( 0)	0	( 0)	0	( 0)

(HPT080)

BAIS 4

STUDY NO. : 0550  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : FEMALE

GROSS FINDINGS (SUMMARY)  
SACRIFICED ANIMALS ( 14W)

PAGE : 4

Organ	Findings	Group Name	8000 ppm		20000 ppm	
		NO. of Animals	10	(%)	7	(%)
spleen	enlarged		0	( 0)	7	(100)
	dark		0	( 0)	7	(100)
	black zone		0	( 0)	0	( 0)
forestomach	thick		2	( 20)	7	(100)
ovary	cyst		2	( 20)	0	( 0)

(HPT080)

BAIS 4

## APPENDIX J 1

ORGAN WEIGHT, ABSOLUTE : MALE

STUDY NO. : 0550  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : MALE  
UNIT: g

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

PAGE : 1

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	30.6± 2.4	0.038± 0.005	0.010± 0.002	0.229± 0.020	0.146± 0.015	0.146± 0.010
512 ppm	9	30.8± 2.6	0.035± 0.006	0.009± 0.001	0.205± 0.030	0.152± 0.011	0.149± 0.007
1280 ppm	9	30.1± 2.4	0.039± 0.009	0.010± 0.001	0.241± 0.027	0.149± 0.015	0.143± 0.011
3200 ppm	10	29.6± 3.1	0.033± 0.007	0.010± 0.001	0.228± 0.033	0.151± 0.018	0.145± 0.009
8000 ppm	10	28.7± 2.5	0.036± 0.006	0.010± 0.002	0.225± 0.028	0.149± 0.015	0.153± 0.016
20000 ppm	9	25.8± 1.0**	0.032± 0.003	0.009± 0.002	0.215± 0.028	0.143± 0.012	0.147± 0.012

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

Test of Dunnett

(HCL040)

BAIS 4

STUDY NO. : 0550  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : MALE  
UNIT: g

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

PAGE : 2

Group Name	NO. of Animals	KIDNEYS		SPLEEN		LIVER		BRAIN	
Control	10	0.419±	0.033	0.050±	0.005	1.094±	0.073	0.437±	0.009
512 ppm	9	0.447±	0.067	0.054±	0.008	1.126±	0.071	0.447±	0.013
1280 ppm	9	0.744±	0.733	0.054±	0.011	1.077±	0.101	0.448±	0.018
3200 ppm	10	0.407±	0.029	0.053±	0.008	1.088±	0.127	0.441±	0.010
8000 ppm	10	0.409±	0.028	0.067±	0.005**	1.116±	0.108	0.441±	0.014
20000 ppm	9	0.450±	0.031*	0.145±	0.023**	1.214±	0.068*	0.432±	0.014

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

Test of Dunnett

(HCL040)

BAIS 4

## APPENDIX J 2

ORGAN WEIGHT, ABSOLUTE : FEMALE

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE  
 UNIT: g

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

PAGE : 3

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	21.2± 1.3	0.040± 0.004	0.013± 0.001	0.028± 0.006	0.119± 0.008	0.139± 0.008
512 ppm	10	21.1± 1.2	0.039± 0.008	0.013± 0.003	0.027± 0.006	0.119± 0.004	0.145± 0.008
1280 ppm	10	21.0± 1.4	0.039± 0.004	0.012± 0.001	0.023± 0.002	0.116± 0.007	0.137± 0.008
3200 ppm	10	21.9± 1.6	0.042± 0.005	0.012± 0.001	0.027± 0.004	0.121± 0.011	0.148± 0.011
8000 ppm	10	20.5± 0.8	0.042± 0.007	0.013± 0.003	0.027± 0.009	0.119± 0.008	0.137± 0.009
20000 ppm	7	20.5± 0.7	0.039± 0.006	0.014± 0.002	0.023± 0.003	0.120± 0.006	0.138± 0.009

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

Test of Dunnett

(HCL040)

BAIS 4

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE  
 UNIT: g

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

PAGE : 4

Group Name	NO. of Animals	KIDNEYS		SPLEEN		LIVER		BRAIN	
Control	10	0.293±	0.014	0.054±	0.005	0.877±	0.027	0.459±	0.011
512 ppm	10	0.298±	0.012	0.057±	0.004	0.880±	0.047	0.456±	0.011
1280 ppm	10	0.284±	0.018	0.052±	0.006	0.857±	0.091	0.453±	0.013
3200 ppm	10	0.308±	0.020	0.056±	0.007	0.916±	0.090	0.464±	0.011
8000 ppm	10	0.292±	0.010	0.071±	0.013*	0.895±	0.071	0.454±	0.015
20000 ppm	7	0.315±	0.020*	0.153±	0.015**	1.036±	0.067**	0.446±	0.024

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

Test of Dunnett

(HCL040)

BAIS 4

## APPENDIX K 1

ORGAN WEIGHT, RELATIVE : MALE

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Cri:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE  
 UNIT: %

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

PAGE : 1

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	30.6± 2.4	0.124± 0.016	0.032± 0.009	0.753± 0.082	0.478± 0.049	0.479± 0.031
512 ppm	9	30.8± 2.6	0.113± 0.013	0.030± 0.003	0.670± 0.112	0.496± 0.048	0.487± 0.045
1280 ppm	9	30.1± 2.4	0.128± 0.023	0.032± 0.004	0.803± 0.087	0.499± 0.060	0.476± 0.039
3200 ppm	10	29.6± 3.1	0.111± 0.016	0.034± 0.006	0.778± 0.144	0.513± 0.052	0.495± 0.054
8000 ppm	10	28.7± 2.5	0.125± 0.013	0.034± 0.007	0.784± 0.084	0.522± 0.071	0.532± 0.029*
20000 ppm	9	25.8± 1.0**	0.125± 0.016	0.037± 0.007	0.830± 0.097	0.553± 0.051	0.572± 0.061**

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

Test of Dunnett

(HCL042)

BAIS 4

STUDY NO. : 0550  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : MALE  
UNIT: %

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

PAGE : 2

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.376± 0.135	0.162± 0.016	3.583± 0.193	1.438± 0.128
512 ppm	9	1.464± 0.299	0.177± 0.033	3.662± 0.230	1.458± 0.137
1280 ppm	9	2.583± 2.767	0.182± 0.047	3.579± 0.184	1.495± 0.103
3200 ppm	10	1.381± 0.070	0.178± 0.016	3.673± 0.144	1.505± 0.152
8000 ppm	10	1.427± 0.065	0.233± 0.014**	3.891± 0.204**	1.545± 0.125
20000 ppm	9	1.744± 0.136**	0.562± 0.091**	4.702± 0.207**	1.674± 0.103**

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

Test of Dunnett

(HCL042)

BAYS 4

## APPENDIX K 2

ORGAN WEIGHT, RELATIVE : FEMALE

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE  
 UNIT: %

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

PAGE : 3

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	21.2± 1.3	0.188± 0.020	0.063± 0.007	0.133± 0.030	0.561± 0.015	0.656± 0.021
512 ppm	10	21.1± 1.2	0.186± 0.031	0.063± 0.014	0.130± 0.032	0.562± 0.035	0.685± 0.050
1280 ppm	10	21.0± 1.4	0.186± 0.019	0.059± 0.009	0.109± 0.010	0.554± 0.031	0.657± 0.045
3200 ppm	10	21.9± 1.6	0.194± 0.024	0.057± 0.005	0.122± 0.020	0.553± 0.057	0.677± 0.060
8000 ppm	10	20.5± 0.8	0.205± 0.032	0.065± 0.015	0.130± 0.043	0.581± 0.045	0.672± 0.044
20000 ppm	7	20.5± 0.7	0.191± 0.026	0.066± 0.010	0.112± 0.018	0.584± 0.021	0.672± 0.057

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

Test of Dunnett

(HCL042)

BAIS 4

STUDY NO. : 0550  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : FEMALE  
UNIT: %

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

PAGE : 4

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.386± 0.045	0.254± 0.019	4.148± 0.141	2.171± 0.105
512 ppm	10	1.412± 0.092	0.268± 0.020	4.166± 0.175	2.161± 0.118
1280 ppm	10	1.356± 0.060	0.250± 0.019	4.085± 0.248	2.170± 0.120
3200 ppm	10	1.408± 0.081	0.257± 0.029	4.179± 0.229	2.126± 0.135
8000 ppm	10	1.426± 0.044	0.344± 0.053**	4.368± 0.231	2.220± 0.069
20000 ppm	7	1.538± 0.130*	0.744± 0.069**	5.043± 0.240**	2.173± 0.137

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

Test of Dunnett

(HCL042)

BAIS 4

## APPENDIX L 1

HISTOPATHOLOGICAL FINDINGS :  
NON-NEOPLASTIC LESIONS : MALE  
DEAD AND MORIBUND ANIMALS

STUDY NO. : 0550  
ANIMAL : MOUSE B6D2F1/Crj[Cri:BDF1]  
REPORT TYPE : A1  
SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
DEAD AND MORIBUND ANIMALS (0- 14W)

PAGE : 1

		Group Name No. of Animals on Study	Control 0				512 ppm 1				1280 ppm 1				3200 ppm 0			
Organ	Findings	Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
{Hematopoietic system}																		
thymus			< 0>				< 1>				< 1>				< 0>			
	atrophy		-	-	-	-	1	0	0	0	0	0	1	0	-	-	-	-
			( - )	( - )	( - )	( - )	(100)	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	(100)	( 0 )	( - )	( - )	( - )	( - )
spleen			< 0>				< 1>				< 1>				< 0>			
	deposit of hemosiderin		-	-	-	-	0	0	0	0	0	0	0	0	-	-	-	-
			( - )	( - )	( - )	( - )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( - )	( - )	( - )	( - )
	extramedullary hematopoiesis		-	-	-	-	0	0	0	0	0	0	0	0	-	-	-	-
			( - )	( - )	( - )	( - )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( - )	( - )	( - )	( - )
{Circulatory system}																		
heart			< 0>				< 1>				< 1>				< 0>			
	myocardial necrosis		-	-	-	-	0	0	0	0	0	1	0	0	-	-	-	-
			( - )	( - )	( - )	( - )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	(100)	( 0 )	( 0 )	( - )	( - )	( - )	( - )
	myocarditis		-	-	-	-	0	1	0	0	0	0	0	0	-	-	-	-
			( - )	( - )	( - )	( - )	( 0 )	(100)	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( - )	( - )	( - )	( - )
{Digestive system}																		
stomach			< 0>				< 1>				< 1>				< 0>			
	hyperplasia:forestomach		-	-	-	-	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																	

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0- 14W)

PAGE : 2

Organ	Findings	8000 ppm				20000 ppm			
		0				1			
		1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Hematopoietic system)									
thymus		< 0>				< 1>			
	atrophy	-	-	-	-	0	0	1	0
		( - )	( - )	( - )	( - )	( 0 )	( 0 )	(100)	( 0 )
spleen		< 0>				< 1>			
	deposit of hemosiderin	-	-	-	-	0	0	1	0
		( - )	( - )	( - )	( - )	( 0 )	( 0 )	(100)	( 0 )
	extramedullary hematopoiesis	-	-	-	-	0	0	1	0
		( - )	( - )	( - )	( - )	( 0 )	( 0 )	(100)	( 0 )
(Circulatory system)									
heart		< 0>				< 1>			
	myocardial necrosis	-	-	-	-	0	0	0	0
		( - )	( - )	( - )	( - )	( 0 )	( 0 )	( 0 )	( 0 )
	myocarditis	-	-	-	-	0	0	0	0
		( - )	( - )	( - )	( - )	( 0 )	( 0 )	( 0 )	( 0 )
(Digestive system)									
stomach		< 0>				< 1>			
	hyperplasia:forestomach	-	-	-	-	0	1	0	0
		( - )	( - )	( - )	( - )	( 0 )	(100)	( 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. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0- 14W)

PAGE : 3

Organ	Findings	Group Name	Control				512 ppm				1280 ppm				3200 ppm			
		No. of Animals on Study	0				1				1				0			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Urinary system)																		
kidney	hydronephrosis		< 0>				< 1>				< 1>				< 0>			
		-	-	-	-	0	0	1	0	0	0	1	0	-	-	-	-	
		( - )	( - )	( - )	( - )	( 0 )	( 0 )	( 100 )	( 0 )	( 0 )	( 0 )	( 100 )	( 0 )	( - )	( - )	( - )	( - )	
	mineralization:cortex		< 0>				< 0>				< 0>				< 0>			
		-	-	-	-	0	0	0	0	1	0	0	0	-	-	-	-	
		( - )	( - )	( - )	( - )	( 0 )	( 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	b : Number of animals with lesion																	
( c )	c : b / a * 100																	

(HPT150)

BAIS4

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
DEAD AND MORIBUND ANIMALS (0- 14W)

[illegible]

kidney									
					< 0>				< 1>
hydronephrosis	-	-	-	-		1	0	0	0
	( - )	( - )	( - )	( - )		(100)	( 0 )	( 0 )	( 0 )
mineralization:cortex	-	-	-	-		0	0	0	0
	( - )	( - )	( - )	( - )		( 0 )	( 0 )	( 0 )	( 0 )

(HPT150)

BAIS4

## APPENDIX L 2

HISTOPATHOLOGICAL FINDINGS :  
NON-NEOPLASTIC LESIONS : MALE  
SACRIFICED ANIMALS

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Crj[Crl:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS ( 14W)

PAGE : 1

Organ_____	Findings_____	Group Name No. of Animals on Study Grade	Control 10				512 ppm 9				1280 ppm 9				3200 ppm 10				
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	
<hr/>																			
{Respiratory system}																			
nasal cavit			<10>				< 9>				< 9>				<10>				
	eosinophilic change:respiratory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 20 )	( 0 )	( 0 )	( 0 )	
	respiratory metaplasia:olfactory epithelium		1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
		( 10 )	( 0 )	( 0 )	( 0 )	( 0 )	( 11 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
{Hematopoietic system}																			
spleen			<10>				< 9>				< 9>				<10>				
	deposit of hemosiderin		0	0	0	0	0	0	0	0	0	0	0	0	10	0	0	0	0 **
		( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 100 )	( 0 )	( 0 )	( 0 )	( 0 )	
	deposit of melanin		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		( 10 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	extramedullary hematopoiesis		1	0	0	0	2	0	0	0	0	5	0	0	0	10	0	0	0 **
		( 10 )	( 0 )	( 0 )	( 0 )	( 0 )	( 22 )	( 0 )	( 0 )	( 0 )	( 0 )	( 56 )	( 0 )	( 0 )	( 0 )	( 100 )	( 0 )	( 0 )	( 0 )
{Digestive system}																			
stomach			<10>				< 9>				< 9>				<10>				
	erosion:forestomach		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 )

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

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS ( 14W)

PAGE : 2

Organ	Findings	8000 ppm				20000 ppm			
		10				9			
		1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}									
nasal cavit	eosinophilic change:respiratory epithelium	<10>				< 9>			
		0	0	0	0	0	0	0	0
		( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
	respiratory metaplasia:olfactory epithelium	<10>				< 9>			
		0	0	0	0	0	0	0	0
		( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
{Hematopoietic system}									
spleen	deposit of hemosiderin	<10>				< 9>			
		10	0	0	0 **	0	9	0	0 **
		(100)	( 0)	( 0)	( 0)	( 0)	(100)	( 0)	( 0)
	deposit of melanin	<10>				< 9>			
		0	0	0	0	0	0	0	0
		( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
	extramedullary hematopoiesis	<10>				< 9>			
		2	8	0	0 **	0	0	9	0 **
		( 20)	( 80)	( 0)	( 0)	( 0)	( 0)	(100)	( 0)
{Digestive system}									
stomach	erosion:forestomach	<10>				< 9>			
		0	0	0	0	2	0	0	0
		( 0)	( 0)	( 0)	( 0)	( 22)	( 0)	( 0)	( 0)

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

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS ( 14W)

PAGE : 3

		Group Name	Control				512 ppm				1280 ppm				3200 ppm			
		No. of Animals on Study	10				9				9				10			
Organ	Findings	Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
stomach			<10>				< 9>				< 9>				<10>			
	ulcer:forestomach		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 )	( 10 )	( 0 )	( 0 )	( 0 )	( 0 )
			<10>				< 9>				< 9>				<10>			
	hyperplasia:forestomach		0	0	0	0	0	0	0	0	1	0	0	0	7	1	0	0 **
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 11 )	( 0 )	( 0 )	( 0 )	( 70 )	( 10 )	( 0 )	( 0 )
liver			<10>				< 9>				< 9>				<10>			
	deposit of hemosiderin		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
			<10>				< 9>				< 9>				<10>			
	granulation		1	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0
			( 10 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 22 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
			<10>				< 9>				< 9>				<10>			
	swelling:centeral		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 )
{Urinary system}																		
kidney			<10>				< 9>				< 9>				<10>			
	scar		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. : 0550  
 ANIMAL : MOUSE B6D2F1/Crj[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS ( 14W)

PAGE : 4

		Group Name	8000 ppm				20000 ppm			
		No. of Animals on Study	10				9			
Organ_____	Findings_____	Grade	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
<hr/>										
{Digestive system}										
stomach			<10>				< 9>			
	ulcer:forestomach		0	0	0	0	3	0	0	0
			( 0)	( 0)	( 0)	( 0)	( 33)	( 0)	( 0)	( 0)
	hyperplasia:forestomach		4	4	0	0 **	0	0	9	0 **
			( 40)	( 40)	( 0)	( 0)	( 0)	( 0)	(100)	( 0)
liver			<10>				< 9>			
	deposit of hemosiderin		0	0	0	0	9	0	0	0 **
			( 0)	( 0)	( 0)	( 0)	(100)	( 0)	( 0)	( 0)
	granulation		0	0	0	0	2	0	0	0
			( 0)	( 0)	( 0)	( 0)	( 22)	( 0)	( 0)	( 0)
	swelling:central		6	0	0	0 *	7	0	0	0 **
			( 60)	( 0)	( 0)	( 0)	( 78)	( 0)	( 0)	( 0)
{Urinary system}										
kidney			<10>				< 9>			
	scar		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 : 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. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS ( 14W)

PAGE : 5

Organ	Findings	Group Name No. of Animals on Study Grade	Control 10				512 ppm 9				1280 ppm 9				3200 ppm 10			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Urinary system)																		
kidney	inflammatory polyp		<10>				< 9>				< 9>				<10>			
			0	1	0	0	0	1	0	0	0	1	0	0	0	0	0	0
			( 0 )	( 10 )	( 0 )	( 0 )	( 0 )	( 11 )	( 0 )	( 0 )	( 0 )	( 11 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	hydronephrosis		0	1	0	0	0	0	1	0	0	0	2	0	0	0	0	0
			( 0 )	( 10 )	( 0 )	( 0 )	( 0 )	( 0 )	( 11 )	( 0 )	( 0 )	( 0 )	( 22 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
urin bladd	hyperplasia:transitional epithelium		<10>				< 9>				< 9>				<10>			
			0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 11 )	( 0 )	( 0 )	( 0 )	( 10 )	( 0 )	( 0 )	( 0 )
	swelling:transitional epithelium		0	0	0	0	0	0	0	0	1	0	0	0	5	0	0	0 *
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 11 )	( 0 )	( 0 )	( 0 )	( 50 )	( 0 )	( 0 )	( 0 )

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

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS ( 14W)

PAGE : 6

Organ	Findings	Group Name No. of Animals on Study Grade				8000 ppm 10				20000 ppm 9			
		1				2				3			
		4				1				2			
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}													
kidney		<10>				< 9>							
	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)
	hydronephrosis	0	0	1	0	0	0	0	0	0	0	0	0
		( 0)	( 0)	( 10)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)
urin bladd		<10>				< 9>							
	hyperplasia:transitional epithelium	4	0	0	0	8	0	0	0	0	0	0	**
		( 40)	( 0)	( 0)	( 0)	( 89)	( 0)	( 0)	( 0)	( 0)	( 0)	( 0)	
	swelling:transitional epithelium	5	4	0	0	1	8	0	0	0	0	0	**
		( 50)	( 40)	( 0)	( 0)	( 11)	( 89)	( 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)

BAIS4

## APPENDIX L 3

HISTOPATHOLOGICAL FINDINGS :  
NON-NEOPLASTIC LESIONS : FEMALE  
DEAD AND MORIBUND ANIMALS

STUDY NO. : 0550  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
DEAD AND MORIBUND ANIMALS (0- 14W)

PAGE : 5

Organ	Findings	Group Name	Control				512 ppm				1280 ppm				3200 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Hematopoietic system)																		
thymus			< 0>				< 0>				< 0>				< 0>			
	atrophy		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )
spleen			< 0>				< 0>				< 0>				< 0>			
	deposit of hemosiderin		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )
	extramedullary hematopoiesis		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )
(Digestive system)																		
tongue			< 0>				< 0>				< 0>				< 0>			
	inflammation		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )
stomach			< 0>				< 0>				< 0>				< 0>			
	erosion:forestomach		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )
	ulcer:forestomach		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )
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

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0- 14W)

PAGE : 6

Organ	Findings	Group Name		8000 ppm				20000 ppm			
		No. of Animals on Study		0				3			
		Grade		1	2	3	4	1	2	3	4
				(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Hematopoietic system)											
thymus	atrophy			< 0>				< 3>			
				-	-	-	-	0	0	3	0
				( - )	( - )	( - )	( - )	( 0 )	( 0 )	(100)	( 0 )
spleen	deposit of hemosiderin			< 0>				< 3>			
				-	-	-	-	0	3	0	0
				( - )	( - )	( - )	( - )	( 0 )	(100)	( 0 )	( 0 )
	extramedullary hematopoiesis			-	-	-	-	0	2	1	0
				( - )	( - )	( - )	( - )	( 0 )	( 67 )	( 33 )	( 0 )
(Digestive system)											
tongue	inflammation			< 0>				< 3>			
				-	-	-	-	1	0	0	0
				( - )	( - )	( - )	( - )	( 33 )	( 0 )	( 0 )	( 0 )
stomach	erosion:forestomach			< 0>				< 3>			
				-	-	-	-	2	0	0	0
				( - )	( - )	( - )	( - )	( 67 )	( 0 )	( 0 )	( 0 )
	ulcer:forestomach			-	-	-	-	2	0	0	0
				( - )	( - )	( - )	( - )	( 67 )	( 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

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0- 14W)

PAGE : 7

Organ	Findings	Group Name	Control				512 ppm				1280 ppm				3200 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Digestive system)																		
stomach	hyperplasia:forestomach		< 0>				< 0>				< 0>				< 0>			
			-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )	( - )
(Urinary system)																		
urin bladd	necrosis:transitional epithelium		< 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

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0- 14W)

PAGE : 8

Organ	Findings	8000 ppm				20000 ppm			
		0				3			
		1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

{Digestive system}

stomach	hyperplasia:forestomach	< 0>				< 3>			
		-	-	-	-	0	0	3	0
		( -)	( -)	( -)	( -)	( 0)	( 0)	(100)	( 0)

{Urinary system}

urin bladd	necrosis:transitional epithelium	< 0>				< 3>			
		-	-	-	-	0	2	0	0
		( -)	( -)	( -)	( -)	( 0)	( 67)	( 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)

BAIS4

## APPENDIX L 4

HISTOPATHOLOGICAL FINDINGS :  
NON-NEOPLASTIC LESIONS : FEMALE  
SACRIFICED ANIMALS

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS ( 14W)

PAGE : 7

Organ	Findings	Group Name No. of Animals on Study Grade	Control 10				512 ppm 10				1280 ppm 10				3200 ppm 10			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}																		
spleen			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		0	0	0	0	0	0	0	0	5	0	0	0 *	10	0	0	0 **
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 50 )	( 0 )	( 0 )	( 0 )	( 100 )	( 0 )	( 0 )	( 0 )
	deposit of melanin		1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			( 10 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 10 )	( 0 )	( 0 )	( 0 )
	extramedullary hematopoiesis		1	0	0	0	2	0	0	0	9	0	0	0 **	8	2	0	0 **
			( 10 )	( 0 )	( 0 )	( 0 )	( 20 )	( 0 )	( 0 )	( 0 )	( 90 )	( 0 )	( 0 )	( 0 )	( 80 )	( 20 )	( 0 )	( 0 )
{Digestive system}																		
stomach			<10>				<10>				<10>				<10>			
	erosion:forestomach		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 10 )	( 0 )	( 0 )
	ulcer:forestomach		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 )
	hyperplasia:forestomach		0	0	0	0	0	0	0	0	2	0	0	0	3	3	0	0 *
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 20 )	( 0 )	( 0 )	( 0 )	( 30 )	( 30 )	( 0 )	( 0 )
liver			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		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. : 0550  
 ANIMAL : MOUSE B6D2F1/Crlj[Crlj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS ( 14#)

PAGE : 8

Organ	Findings	Group Name		8000 ppm				20000 ppm			
		No. of Animals on Study		10				7			
		Grade		1	2	3	4	1	2	3	4
				(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}											
spleen				<10>				< 7>			
	deposit of hemosiderin			3 ( 30)	7 ( 70)	0 ( 0)	0 ** ( 0)	0 ( 0)	7 (100)	0 ( 0)	0 ** ( 0)
	deposit of melanin			0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
	extramedullary hematopoiesis			4 ( 40)	5 ( 50)	1 ( 10)	0 ** ( 0)	0 ( 0)	0 ( 0)	7 (100)	0 ** ( 0)
{Digestive system}											
stomach				<10>				< 7>			
	erosion:forestomach			1 ( 10)	0 ( 0)	0 ( 0)	0 ( 0)	1 ( 14)	0 ( 0)	0 ( 0)	0 ( 0)
	ulcer:forestomach			0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	3 ( 43)	1 ( 14)	0 ( 0)	0 * ( 0)
	hyperplasia:forestomach			5 ( 50)	3 ( 30)	2 ( 20)	0 ** ( 0)	0 ( 0)	0 ( 0)	7 (100)	0 ** ( 0)
liver				<10>				< 7>			
	deposit of hemosiderin			0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	7 (100)	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

STUDY NO. : 0550  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
SACRIFICED ANIMALS ( 14W)

PAGE : 9

Organ	Findings	Group Name No. of Animals on Study Grade	Control 10				512 ppm 10				1280 ppm 10				3200 ppm 10			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Digestive system)																		
liver	granulation		<10>				<10>				<10>				<10>			
			2	0	0	0	0	0	0	0	2	0	0	0	3	0	0	0
			( 20 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 20 )	( 0 )	( 0 )	( 0 )	( 30 )	( 0 )	( 0 )	( 0 )
(Urinary system)																		
urin bladd	hyperplasia:transitional epithelium		<10>				<10>				<10>				<10>			
			0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 10 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	necrosis:transitional epithelium		<10>				<10>				<10>				<10>			
			0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )
	swelling:transitional epithelium		<10>				<10>				<10>				<10>			
			0	0	0	0	0	0	0	0	2	0	0	0	7	0	0	0 **
			( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 20 )	( 0 )	( 0 )	( 0 )	( 70 )	( 0 )	( 0 )	( 0 )
(Endocrine system)																		
pituitary	cyst		<10>				<10>				<10>				<10>			
			0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
			( 0 )	( 0 )	( 0 )	( 0 )	( 10 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 0 )	( 10 )	( 0 )	( 0 )	( 0 )

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

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

b b : Number of animals with lesion

( c ) c : b / a \* 100

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

(HPT150)

BAIS4

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS ( 14W)

PAGE : 10

Organ	Findings	8000 ppm				20000 ppm			
		10				7			
		1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}									
liver									
	granulation	<10>				< 7>			
		2	0	0	0	2	0	0	0
		( 20)	( 0)	( 0)	( 0)	( 29)	( 0)	( 0)	( 0)
{Urinary system}									
urin bladd									
	hyperplasia:transitional epithelium	<10>				< 7>			
		0	0	0	0	4	0	0	0 *
		( 0)	( 0)	( 0)	( 0)	( 57)	( 0)	( 0)	( 0)
	necrosis:transitional epithelium	0	0	0	0	0	1	0	0
		( 0)	( 0)	( 0)	( 0)	( 0)	( 14)	( 0)	( 0)
	swelling:transitional epithelium	10	0	0	0 **	0	7	0	0 **
		(100)	( 0)	( 0)	( 0)	( 0)	(100)	( 0)	( 0)
{Endocrine system}									
pituitary									
	cyst	<10>				< 7>			
		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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$  Test of Chi Square

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS ( 14W)

PAGE : 11

		Group Name	Control				512 ppm				1280 ppm				3200 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
Organ	Findings		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
<hr/>																		
{Reproductive system}																		
ovary			<10>				<10>				<10>				<10>			
	cyst		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 )
<hr/>																		
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																		

(HPT150)

BAIS4

STUDY NO. : 0550  
 ANIMAL : MOUSE B6D2F1/Crj[Crl:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS ( 14W)

PAGE : 12

Organ	Findings	Group Name		8000 ppm				20000 ppm			
		No. of Animals on Study		10				7			
		Grade		1	2	3	4	1	2	3	4
				(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

{Reproductive system}

ovary

cyst

<10>				< 7>			
2	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

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

(HPT150)

BAIS4

## APPENDIX M

METHODS, UNITS AND DECIMAL PLACE FOR  
HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK  
FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

METHODS, UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY  
IN THE 13- WEEK FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

Item	Method	Unit	Decimal place
<b>Hematology</b>			
Red blood cell (RBC)	Light scattering method <sup>1)</sup>	$\times 10^6/\mu\text{L}$	2
Hemoglobin(Hgb)	Cyanmethemoglobin method <sup>1)</sup>	g/dL	1
Hematocrit(Hct)	Calculated as $\text{RBC} \times \text{MCV}/10$ <sup>1)</sup>	%	1
Mean corpuscular volume(MCV)	Light scattering method <sup>1)</sup>	fL	1
Mean corpuscular hemoglobin(MCH)	Calculated as $\text{Hgb}/\text{RBC} \times 10$ <sup>1)</sup>	pg	1
Mean corpuscular hemoglobin concentration (MCHC)	Calculated as $\text{Hgb}/\text{Hct} \times 100$ <sup>1)</sup>	g/dL	1
Platelet	Light scattering method <sup>1)</sup>	$\times 10^3/\mu\text{L}$	0
Reticulocyte	Light scattering method <sup>1)</sup>	%	1
White blood cell(WBC)	Light scattering method <sup>1)</sup>	$\times 10^3/\mu\text{L}$	2
Differential WBC	Pattern recognition method <sup>2)</sup> (Wright staining)	%	0
<b>Biochemistry</b>			
Total protein(TP)	Biuret method <sup>3)</sup>	g/dL	1
Albumin (Alb)	BCG method <sup>3)</sup>	g/dL	1
A/G ratio	Calculated as $\text{Alb}/(\text{TP} - \text{Alb})$ <sup>3)</sup>	—	1
T-bilirubin	Alkaline azobilirubin method <sup>3)</sup>	mg/dL	2
Glucose	GlcK·G-6-PDH method <sup>3)</sup>	mg/dL	0
T-cholesterol	CE·COD·POD method <sup>3)</sup>	mg/dL	0
Triglyceride	LPL·GK·GPO·POD method <sup>3)</sup>	mg/dL	0
Phospholipid	PLD·ChOD·POD method <sup>3)</sup>	mg/dL	0
Aspartate aminotransferase (AST)	JSCC method <sup>3)</sup>	IU/L	0
Alanine aminotransferase (ALT)	JSCC method <sup>3)</sup>	IU/L	0
Lactate dehydrogenase (LDH)	SFBC method <sup>3)</sup>	IU/L	0
Alkaline phosphatase (ALP)	GSCC method <sup>3)</sup>	IU/L	0
$\gamma$ -Glutamyl transpeptidase ( $\gamma$ -GTP)	JSCC method <sup>3)</sup>	IU/L	0
Creatine kinase (CK)	JSCC method <sup>3)</sup>	IU/L	0
Urea nitrogen	Urease·GLDH method <sup>3)</sup>	mg/dL	1
Sodium	Ion selective electrode method <sup>3)</sup>	mEq/L	0
Potassium	Ion selective electrode method <sup>3)</sup>	mEq/L	1
Chloride	Ion selective electrode method <sup>3)</sup>	mEq/L	0
Calcium	OCPC method <sup>3)</sup>	mg/dL	1
Inorganic phosphorus	PNP·XOD·POD method <sup>3)</sup>	mg/dL	1

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

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

3) Automatic analyzer (Hitachi 7080 : Hitachi,Ltd.)