2-アミノ-4-クロロフェノールのラットを用いた 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:0549

# **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                                       |
| APPENDIX I 2 | GROSS FINDINGS: FEMALE                                     |
| 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   |
| APPENDIX L 2 | HISTOPATHOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: FEMALE |
|              |  |

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

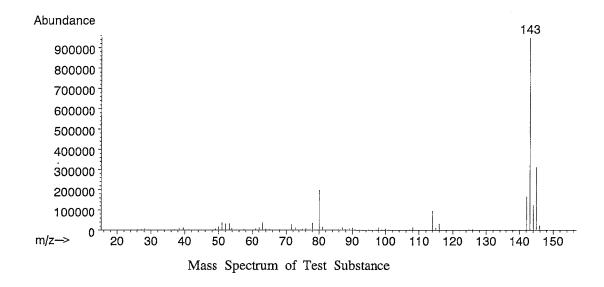
#### 1. Spectral data

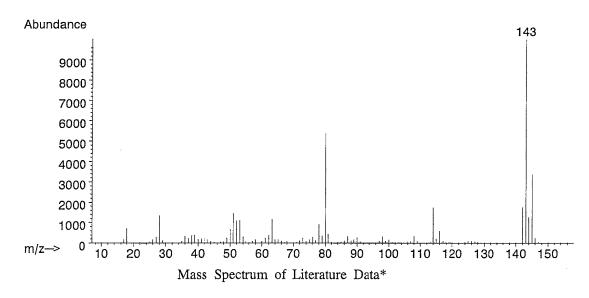
#### Mass Spectrometry

Instrument : Hewlett Packard 5989B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV





Result: The mass spectrum was consistent with literature spectrum.

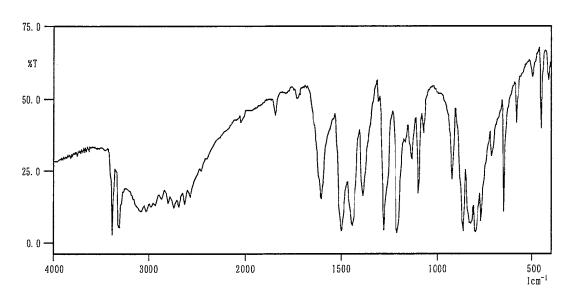
(\*McLafferty FW, ed. 1994. Wiley Registry of Mass Spectral Data. 6th ed. New York, NY: John Wiley and Sons.)

#### Infrared Spectrometry

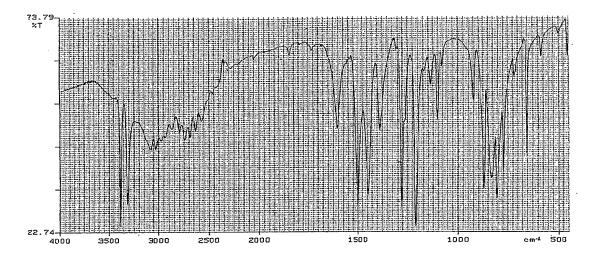
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 2.0 cm<sup>-1</sup>



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 2004.9.24 to 2004.12.27. 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 $\phi$  × 60 m)

Column Temperature : 100  $^{\circ}$  C  $\rightarrow$  (10  $^{\circ}$  C/min)  $\rightarrow$  250  $^{\circ}$  C (5 min)

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 µL

| Date (date analyzed) | Peak No. | Retention Time (min) | Area<br>(%) |
|----------------------|----------|----------------------|-------------|
| 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

|               |                          | Target Concentration |            |            |             |  |  |  |  |  |  |  |  |
|---------------|--------------------------|----------------------|------------|------------|-------------|--|--|--|--|--|--|--|--|
| Date Analyzed | 512ª                     | 1280                 | 3200       | 8000       | 20000       |  |  |  |  |  |  |  |  |
| 2004.09.23    | 498 ( 97.3) <sup>b</sup> | 1250 ( 97.7)         | 3350 (105) | 8080 (101) | 20600 (103) |  |  |  |  |  |  |  |  |

<sup>&</sup>lt;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 ℃

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 μL

## 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 |      |      |      |       |  |  |  |  |  |
|-----------------------|----------------------|------|------|------|-------|--|--|--|--|--|
|                       | 512ª                 | 1280 | 3200 | 8000 | 20000 |  |  |  |  |  |
| Coefficient Variation | 1.62 <sup>b</sup>    | 2.85 | 1.62 | 2.16 | 3.77  |  |  |  |  |  |

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 $\phi$  × 15 cm)

Column Temperature

: 40 ℃

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 µL

<sup>&</sup>lt;sup>a</sup> ppm
<sup>b</sup> % (n=7)

## 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

|               |                         | Target Co               | oncentration  |
|---------------|-------------------------|-------------------------|---------------|
| Date Prepared | Date Analyzed           | 512ª                    | 20000         |
| 2004.06.11    | 2004.06.11              | 484 (100 ) <sup>b</sup> | 19900 (100 )  |
|               | 2004.06.16°             | 437 ( 90.3)             | 19600 ( 98.5) |
|               | 2004.06.25 <sup>d</sup> | 477 ( 98.6)             | 19400 ( 97.5) |

a ppm

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 $\phi$  × 15 cm)

Column Temperature: 40 ℃

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 μL

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

<sup>&</sup>lt;sup>c</sup> Animal room samples

d Cold storage samples

# APPENDIX B 1

CLINICAL OBSERVATION: MALE

# CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrl;[F344/DuCrj]
REPORT TYPE : A1 13

SEX : MALE

PAGE: 1

| Clinical sign | Group Name | Admini | stration W | eek-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 |
| COLORED       | Control    | 0      | 0          | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
|               | 512 ppm    | ō      | 0          | 0       | Ö   | Ö   | Ö   | 0   | 0   | Ö   | 0    | Ô    | 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 ррш  | 0      | 10         | 10      | 2   | 4   | 4   | 4   | 4   | 4   | 4    | 6    | 6    | 6    |
| ON 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     | 0          | 0       | 8   | 6   | 6   | 6   | 6   | 6   | 6    | 4    | 4    | 4    |

(HAN190)

## APPENDIX B 2

CLINICAL OBSERVATION: FEMALE

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]

REPORT TYPE : A1 13

SEX : FEMALE

PAGE: 2

| Clinical sign        | Group Name | Admini | stration W | eek-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 |
|                      |            |        |            |         |     |     |     |     |     |     |      |      |      |      |
| OLORED               | 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      | 2          | 2       | 2   | 2   | 2   | 2   | 2   | 2   | 2    | 2    | 2    | 2    |
|                      | muq 0008   | 0      | 0          | 0       | 2   | 2   | 2   | 2   | 2   | 2   | 2    | 2    | 2    | 2    |
|                      | 20000 ppm  | 2      | 6          | 6       | 7   | 7   | 7   | 7   | 7   | 7   | 7    | 7    | 7    | 7    |
| OILED 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 ррт   | 0      | 0          | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
|                      | 8000 ppm   | 0      | 1          | 2       | 3   | 3   | 3   | 3   | 3   | 3   | 3    | 3    | 3    | 3    |
|                      | 20000 ppm  | 0      | 0          | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
| CORNEAL OPACITY      | 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   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 1    |
| 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     | 8          | 8       | 8   | 8   | 8   | 8   | 8   | 8   | 8    | 8    | 8    | 8    |
|                      | 8000 ppm   | 10     | 9          | 8       | 5   | 5   | 5   | 5   | 5   | 5   | 5    | 5    | 5    | 5    |
|                      | 20000 ppm  | 8      | 4          | 4       | 3   | 3   | 3   | 3   | 3   | 3   | 3    | 3    | 3    | 3    |

(HAN190)

# APPENDIX C 1

BODY WEIGHT CHANGES: MALE

STUDY NO. : 0549 ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]

BODY WEIGHT CHANGES ALL ANIMALS

(SUMMARY)

UNIT : g
REPORT TYPE : A1 13

SEX : MALE

PAGE: 1

| oup Name              | Admini    | stratio | n week      |     | Administration week |             |            |               |      |                |      |      |      |      |  |  |  |
|-----------------------|-----------|---------|-------------|-----|---------------------|-------------|------------|---------------|------|----------------|------|------|------|------|--|--|--|
| ,,,,,                 | 0         |         | 1           |     | 2                   |             | 3          |               | 4    |                | 5    |      | 6    |      |  |  |  |
| Control               | 123 ±     | 4       | 153±        | 6   | 188±                | 9           | 210±       | 9             | 229± | 11             | 245± | 12   | 260土 | 13   |  |  |  |
| 512 ppm               | 123±      | 4       | 152±        | 5   | 198±                | 44          | 205±       | 7             | 220± | 9              | 238± | 8    | 252± | 10   |  |  |  |
| 1280 ppm              | 123±      | 4       | 152±        | 4   | 185±                | 6           | 209±       | 6             | 226± | 7              | 242± | 9    | 257± | 8    |  |  |  |
| 3200 ppm              | 123±      | 4       | 151±        | 4   | 186±                | 5           | 206±       | 5             | 221± | 5              | 237± | 7    | 253± | 6    |  |  |  |
| 8000 ppm              | 123±      | 4       | 150±        | 5   | 181上                | 5           | 200±       | 4 <b>*</b> *  | 212± | 7 <b>*</b> * . | 223± | 10** | 240± | 12** |  |  |  |
| 20000 ррт             | 123±      | 4       | 132±        | 5** | 161±                | 6 <b>**</b> | 181±       | 6 <b>≯</b> >* | 192± | 8**            | 202± | 10** | 216± | 11** |  |  |  |
| Significant differenc | ne; *:P≤0 | . 05    | **: P ≤ 0.0 | )T  |                     |             | Test of Du | unnatt        |      |                |      |      | x    |      |  |  |  |

(HAN260)

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]

230± 11\*\*

UNIT : g REPORT TYPE : A1 13

SEX : MALE

BODY WEIGHT CHANGES ALL ANIMALS

(SUMMARY)

Group Name Administration week\_ 7 9 10 11 12 13 Control 273± 14 286土 15 296± 14 307± 15 314± 15 323± 17 330± 16 512 ppm 267± 10  $281 \pm 10$ 292± 11 301 ± 11 309± 11 317± 11 325± 13

| 1280 ppm | 274± | 9    | 289± | 9    | 300± | 9   | 309± | 10   | 318± | 11  | 327± | 11  | 334± | 11  |
|----------|------|------|------|------|------|-----|------|------|------|-----|------|-----|------|-----|
| 3200 ppm | 269± | 8    | 283± | 8    | 296± | 10  | 306± | 10   | 316± | 11  | 325± | 11  | 332± | 9   |
| 8000 ррш | 255土 | 12** | 270± | 12** | 280± | 15* | 290± | 14** | 298± | 14* | 307生 | 14* | 312土 | 17* |
|          |      |      |      |      |      |     |      |      |      |     |      |     |      |     |

262± 10\*\*

271± 10\*\*

278士 11\*\*

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

253± 10\*\*

241± 10\*\*

(HAN260)

20000 ppm

BAIS 4

285± 10\*\*

PAGE: 2

# APPENDIX C 2

BODY WEIGHT CHANGES: FEMALE

ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]

UNIT : g

REPORT TYPE : A1 13

SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS

PAGE: 3

| oup Name               | Admini    | stration | week         |             |      |             |             |      |      |     |      |     |      |              |
|------------------------|-----------|----------|--------------|-------------|------|-------------|-------------|------|------|-----|------|-----|------|--------------|
|                        | 0         |          | 1            |             | 2    |             | 3           |      | 4    |     | 5    |     | 6    |              |
| Control                | 99±       | 3        | 113±         | 4           | 127± | 4           | 135±        | 4    | 141± | 5   | 149± | 6   | 152土 | 5            |
| 512 ppm                | 99±       | 3        | 115±         | 5           | 129± | 6           | 137±        | 7    | 144± | 7   | 152± | 8   | 157± | 9            |
| 1280 ppm               | 99±       | 3        | 112±         | 3           | 127± | 4           | 135±        | 6    | 142± | 5   | 148± | 8   | 153± | 8            |
| 3200 ppm               | 99±       | 3        | 113±         | 4           | 125± | 5           | 134±        | 6    | 141± | 5   | 147± | 6   | 151± | 7            |
| 8000 ppm               | 99 土      | 3        | 111±         | 4           | 123生 | 6           | 129±        | 6    | 134土 | б   | 141土 | 8   | 145土 | 9            |
| 20000 ppm              | 99±       | 3        | 104±         | 4 <b>**</b> | 118± | 5 <b>**</b> | 125±        | 5**  | 129± | 5** | 135± | 7** | 140± | 7 <b>*</b> * |
|                        |           |          |              |             |      |             |             |      |      |     |      |     |      |              |
| Significant difference | ce; *:P≤( | . 05     | ** : P ≤ 0.0 | 1           |      |             | Test of Dur | mett |      |     |      |     |      | •            |

(HAN260)

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]

UNIT : g

REPORT TYPE : A1 13

(SUMMARY)

BODY WEIGHT CHANGES

ALL ANIMALS

| 7<br>155± | 6                    | 8                             |  | 9  |  | 10  |   | 11  |   | 12   |  | 13  |   |
|-----------|----------------------|-------------------------------|--|--|--|---|---|---|---|--|--|---|---|
| 155土      | 6                    |                               |  |  |  |   |   |   |   |  |  |   |   |
|           |                      | 158±                          | 6  | 162±   | 7  | 167±  | 7   | 169生  | 7   | 172±   | 8  | 174土  | 8   |
| 160±      | 11                   | 162±                          | 12   | 166±   | 14   | 170±  | 14  | 174±  | 15  | 176±   | 15   | 178±  | 15  |
| 156±      | . 8                  | 158±                          | 10   | 164±   | 10   | 167±  | 10  | 171±  | 11  | 172±   | 9  | 175±  | 12  |
| 156±      | 7                    | 159±                          | 8  | 162±   | 8  | 166±  | 7   | 168生  | 9   | 170±   | 7  | 172±  | 7   |
| 149±      | 9                    | 153上                          | 9  | 156±   | 9  | 159土  | 10  | 162土  | 11  | 164土   | 11   | 167±  | 11  |
| 143±      | 7**                  | 147±                          | 8*   | 149±   | <b>7</b> ∗   | 151±  | 8**   | 156±  | 8*  | 158±   | 8*   | 161±  | 9*  |
|           |                      |                               |  |  |  |   |   |   |   |  |  |   |   |
|           | 156±<br>156±<br>149± | 156± 8 156± 7 149± 9 143± 7** | 156± 8 158±  156± 7 159±  149± 9 153±  143± 7** 147± | 156± 8 158± 10  156± 7 159± 8  149± 9 153± 9  143± 7** 147± 8* | 156± 8 158± 10 164±  156± 7 159± 8 162±  149± 9 153± 9 156±  143± 7** 147± 8* 149± | 156±       8       158±       10       164±       10         156±       7       159±       8       162±       8         149±       9       153±       9       156±       9         143±       7**       147±       8*       149±       7* | 156±       8       158±       10       164±       10       167±         156±       7       159±       8       162±       8       166±         149±       9       153±       9       156±       9       159±         143±       7**       147±       8*       149±       7*       151± | 156±       8       158±       10       164±       10       167±       10         156±       7       159±       8       162±       8       166±       7         149±       9       153±       9       156±       9       159±       10         143±       7**       147±       8*       149±       7*       151±       8** | 156±       8       158±       10       164±       10       167±       10       171±         156±       7       159±       8       162±       8       166±       7       168±         149±       9       153±       9       156±       9       159±       10       162±         143±       7**       147±       8*       149±       7*       151±       8**       156± | 156±       8       158±       10       164±       10       167±       10       171±       11         156±       7       159±       8       162±       8       166±       7       168±       9         149±       9       153±       9       156±       9       159±       10       162±       11         143±       7**       147±       8*       149±       7*       151±       8**       156±       8* | 156±       8       158±       10       164±       10       167±       10       171±       11       172±         156±       7       159±       8       162±       8       166±       7       168±       9       170±         149±       9       153±       9       156±       9       159±       10       162±       11       164±         143±       7**       147±       8*       149±       7*       151±       8**       156±       8*       158± | 156± 8 158± 10 164± 10 167± 10 171± 11 172± 9  156± 7 159± 8 162± 8 166± 7 168± 9 170± 7  149± 9 153± 9 156± 9 159± 10 162± 11 164± 11  143± 7** 147± 8* 149± 7* 151± 8** 156± 8* 158± 8* | 156± 8 158± 10 164± 10 167± 10 171± 11 172± 9 175±  156± 7 159± 8 162± 8 166± 7 168± 9 170± 7 172±  149± 9 153± 9 156± 9 159± 10 162± 11 164± 11 167±  143± 7** 147± 8* 149± 7* 151± 8** 156± 8* 158± 8* 161± |

(HAN260)

## APPENDIX D 1

FOOD CONSUMPTION CHANGES: MALE

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

UNIT : g

REPORT TYPE : A1 13

SEX : MALE

PAGE: 1

| oup Name             | Administration week |              |                      |                 |             |             |              |
|----------------------|---------------------|--------------|----------------------|-----------------|-------------|-------------|--------------|
|                      | 1                   | 2            | 3                    | 4               | 5           | 6           | 7            |
| Control              | 13.5± 0.7           | 14.1± 0.8    | 13.9± 0.7            | 14.4± 0.8       | 14.4± 0.9   | 14.4± 1.0   | 14.5± 1.0    |
| 512 ppm              | 13.2± 0.7           | 13.2± 0.7*   | 13.7± 0.7            | 13.8± 0.8       | 14.0± 0.7   | 14.2± 0.7   | 14.3± 0.9    |
| 1280 ppm             | 13.4± 0.8           | 13.8± 0.7    | 13.7± 0.8            | 14.1± 0.6       | 14.1± 0.7   | 14.5± 0.9   | 14.7± 0.6    |
| 3200 ррт             | 13.4± 0.5           | 14.1± 0.7    | 14.0± 0.7            | 14.1± 0.7       | 13.8± 0.5   | 14.3± 0.4   | 14.5± 0.8    |
| 8000 ppm             | 13.0± 0.5           | 13.6± 0.5    | 13.5 ± 0.4           | 13.7± 0.6       | 13.1± 0.9** | 13.5 ± 0.9  | 13.8生 0.9    |
| 20000 ррт            | 11.1± 0.6★★         | 12.4± 0.6**  | 12.9± 0.7 <b>*</b> * | 12.8± 0.6**     | 12.3± 0.7** | 12.7± 0.8** | 13.0± 0.7**  |
| Significant differen | nce; *: P ≤ 0.05    | **: P ≤ 0.01 |                      | Test of Dunnett |             |             | 144 AND 41 A |

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]

UNIT : g

REPORT TYPE : A1 13

SEX : MALE

PAGE: 2

| p Name                  | 8           | 9             | 10          |                 |             | Administration week |  |  |  |  |  |  |  |
|-------------------------|-------------|---------------|-------------|-----------------|-------------|---------------------|--|--|--|--|--|--|--|
|                         |             |               | 10          | 11              | 12          | 13                  |  |  |  |  |  |  |  |
| Control                 | 14.4± 0.8   | 14.2± 0.7     | 14.3± 0.7   | 14.2± 0.9       | 14.4± 1.0   | 14.4± 0.9           |  |  |  |  |  |  |  |
| 512 ppm                 | 14.0± 0.9   | 14.1± 0.8     | 14.1± 0.6   | 13.9± 0.8       | 14.3± 0.9   | 14.1± 0.8           |  |  |  |  |  |  |  |
| 1280 ppm                | 14.3± 0.7   | 14.3± 0.7     | 14.3± 0.6   | 14.5± 0.7       | 14.2± 0.6   | 14.2± 0.7           |  |  |  |  |  |  |  |
| 3200 ррш                | 14.4± 0.7   | 14.5± 0.8     | 14.6± 0.5   | 14.6± 0.6       | 14.9± 0.5   | 14.7± 0.8           |  |  |  |  |  |  |  |
| 8000 ppm                | 14.1± 0.8   | 13.6± 0.9     | 13.7± 0.9   | 13.8± 0.7       | 13.8± 0.9   | 13.6± 1.7           |  |  |  |  |  |  |  |
| 20000 ррт               | 12.9± 0.8≯≠ | 13.2± 0.6*    | 13.1± 0.8★★ | 13.2生 0.6***    | 13.1± 0.8** | 13.2± 0.6*          |  |  |  |  |  |  |  |
| Significant difference; | *: P ≤ 0.05 | ** : P ≤ 0.01 |             | Test of Dunnett |             |                     |  |  |  |  |  |  |  |

## APPENDIX D 2

FOOD CONSUMPTION CHANGES: FEMALE

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

UNIT : g

REPORT TYPE : A1 13

SEX : FEMALE

PAGE: 3

| oup Name             | Administration   | week          |               |                 |           |           |               |
|----------------------|------------------|---------------|---------------|-----------------|-----------|-----------|---------------|
|                      | 1                | 2             | 3             | 4               | 5         | 6         | 7             |
| Control              | 9.7± 0.5         | 9.9± 0.4      | $9.9 \pm 0.6$ | 9.9± 0.8        | 10.3± 0.8 | 9.9± 0.6  | $9.7 \pm 0.8$ |
| 512 ppm              | 9.9± 0.5         | 9.9± 0.8      | 10.1± 0.9     | 10.3± 0.8       | 10.3± 0.9 | 9.8± 0.9  | 9.9± 0.8      |
| 1280 ppm             | 9.4± 0.6         | 9.7± 0.7      | 10.0± 0.6     | 10.2± 1.0       | 10.4± 1.1 | 10.1± 0.8 | 9.7± 1.1      |
| 3200 ррт             | 9.9± 0.4         | 9.4± 0.5      | 9.7± 0.7      | 10.2± 0.5       | 9.9± 0.7  | 9.8± 0.6  | 9.8± 0.8      |
| 8000 ррш             | 9.3 ± 0.5        | 9.4± 0.6      | 9.2± 0.8      | 9.6± 0.8        | 9.7± 0.8  | 9.1± 0.9  | 9.1± 0.7      |
| 20000 ppm            | 9.4± 0.7         | 9.2± 0.7      | 9.5± 0.4      | 9.0± 0.7        | 9.3± 0.7* | 9.0± 0.9  | 8.8± 0.7      |
| - T.D                |                  |               |               |                 |           |           |               |
| Significant differen | rce; *: P ≤ 0.05 | ** : P ≤ 0.01 |               | Test of Dunnett |           |           |               |

(HAN260)

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

UNIT : g
REPORT TYPE : A1 13

SEX : FEMALE

PAGE: 4

| oup Name             | Administration  | week          |          |                 |          |          |  |
|----------------------|-----------------|---------------|----------|-----------------|----------|----------|--|
|                      | 8               | 9             | 10       | 11              | 12       | 13       |  |
| Control              | 9.5± 0.5        | 9.5± 0.5      | 9.4± 0.6 | 9.3± 0.5        | 9.3± 0.6 | 9.2± 0.5 |  |
| 512 ppm              | 9.0± 1.1        | 9.2± 1.1      | 9.4± 0.9 | 9.5± 1.1        | 9.6± 0.8 | 9.2± 0.9 |  |
| 1280 ppm             | 9.3± 1.1        | 9.7± 1.2      | 9.7± 1.1 | 9.6± 1.1        | 9.3± 1.0 | 9.4± 1.1 |  |
| 3200 ррт             | 9.2± 0.6        | 9.3± 0.6      | 9.3± 0.5 | 8.9± 0.4        | 9.2± 0.6 | 8.9± 0.5 |  |
| 8000 ppm             | 9.0± 0.6        | 9.1± 0.5      | 9.0± 0.7 | 9.0± 0.8        | 9.0± 0.7 | 8.9± 0.9 |  |
| 20000 ррт            | 9.0± 0.5        | 8.7± 0.7      | 8.6± 0.6 | 9.0± 0.6        | 9.0± 0.6 | 8.9± 0.8 |  |
| Significant differen | ve; *: P ≤ 0.05 | ** : P ≤ 0.01 |          | Test of Dunnett |          |          |  |

(HAN260)

# APPENDIX E 1

CHEMICAL INTAKE CHANGES: MALE

CHEMICAL INTAKE CHANGES (SUMMARY)

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]

rlj[F344/DuCrj] ALL ANIMALS

UNIT : g/kg/day REPORT TYPE : A1 13

SEX : MALE

PAGE: 1

| oup Name  | Administration | (weeks)      |              |              | *            |              |               |
|-----------|----------------|--------------|--------------|--------------|--------------|--------------|---------------|
|           | 1              | 2            | 3            | 4            | 5            | 6            | 7             |
| Control   | 0.000± 0.000   | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000生 0.000 | 0.000± 0.000 | 0.000± 0.000  |
| 512 ppm   | 0.044± 0.002   | 0.035± 0.005 | 0.034± 0.001 | 0.032± 0.001 | 0.030± 0.001 | 0.029± 0.001 | 0.027± 0.001  |
| 1280 ppm  | 0.113± 0.005   | 0.095± 0.003 | 0.084± 0.003 | 0.080± 0.002 | 0.075± 0.001 | 0.072± 0.002 | 0.069± 0.001  |
| 3200 ppm  | 0.284± 0.011   | 0.242± 0.008 | 0.218± 0.009 | 0.204± 0.008 | 0.186± 0.005 | 0.181± 0.004 | 0.172± 0.008  |
| 8000 ppm  | 0.694± 0.018   | 0.600± 0.012 | 0.540± 0.019 | 0.520± 0.022 | 0.469± 0.014 | 0.451± 0.014 | 0.433 ± 0.018 |
| 20000 ppm | 1.681 ± 0.065  | 1.540± 0.048 | 1.425± 0.064 | 1.333± 0.077 | 1.216± 0.024 | 1.174± 0.042 | 1.127± 0.037  |

(HAN300)

CHEMICAL INTAKE CHANGES (SUMMARY)

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g / kg / d a y
REPORT TYPE : A1 13

ALL ANIMALS

SEX : MALE

PAGE: 2

| Group Name | Administration | (weeks)      |              |              |              |              |  |
|------------|----------------|--------------|--------------|--------------|--------------|--------------|--|
|            | 8              | 9            | 10           | 11           | 12           | 13           |  |
| Control    | 0.000± 0.000   | 0.000± 0.000 | 0.000± 0.000 | 0.000生 0.000 | 0.000± 0.000 | 0.000± 0.000 |  |
| 512 ppm    | 0.026± 0.001   | 0.025± 0.001 | 0.024± 0.001 | 0.023± 0.001 | 0.023± 0.001 | 0.022± 0.001 |  |
| 1280 ppm   | 0.064± 0.002   | 0.061± 0.002 | 0.059± 0.001 | 0.058± 0.001 | 0.056± 0.002 | 0.054± 0.002 |  |
| 3200 ppm   | 0.163± 0.006   | 0.156± 0.005 | 0.153± 0.003 | 0.149± 0.005 | 0.146± 0.004 | 0.142± 0.007 |  |
| 8000 ppm   | 0.417± 0.021   | 0.389± 0.014 | 0.380± 0.016 | 0.372± 0.014 | 0.361± 0.013 | 0.348± 0.033 |  |
| 20000 ррш  | 1.070± 0.067   | 1.043± 0.049 | 0.997± 0.056 | 0.972± 0.036 | 0.940± 0.050 | 0.925± 0.044 |  |
|            |                |              |              |              |              |              |  |

(IIAN300)

## APPENDIX E 2

CHEMICAL INTAKE CHANGES: FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY) ALL ANIMALS

ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
UNIT : g/kg/day
REPORT TYPE : A1 13

SEX : FEMALE

| Group Name | Administration    | (weeks)           |              |                   |                   |                   |                   |
|------------|-------------------|-------------------|--------------|-------------------|-------------------|-------------------|-------------------|
|            | 1                 | 2                 | 3            | 4                 | 5                 | 6                 | 7                 |
|            |                   |                   |              |                   |                   |                   |                   |
| Control    | $0.000 \pm 0.000$ | $0.000 \pm 0.000$ | 0.000± 0.000 | $0.000 \pm 0.000$ | $0.000 \pm 0.000$ | $0.000 \pm 0.000$ | 0.000± 0.000      |
|            |                   |                   |              |                   |                   |                   |                   |
| 512 ppm    | 0.044± 0.003      | $0.039 \pm 0.002$ | 0.038± 0.003 | $0.037 \pm 0.002$ | $0.035 \pm 0.002$ | 0.032± 0.002      | 0.032± 0.002      |
|            |                   |                   |              |                   |                   |                   |                   |
| 1280 ppm   | 0.107± 0.005      | 0.098± 0.007      | 0.095± 0.003 | 0.092± 0.007      | 0.090± 0.006      | $0.085 \pm 0.004$ | $0.080 \pm 0.006$ |
| 3200 ppm   | 0.280± 0.007      | 0.241± 0.008      | 0.0004 0.010 | 0.232± 0.009      | 0.017 + 0.000     | 0.007 ± 0.000     | 0.000-1- 0.011    |
| 3200 ppiii | 0.200 ± 0.001     | 0.241 = 0.006     | 0.232± 0.010 | 0.232± 0.009      | 0.217± 0.009      | 0.207± 0.009      | 0.202± 0.011      |
| 8000 ppm   | 0.674± 0.029      | 0.614± 0.031      | 0.567± 0.031 | 0.569± 0.030      | 0.548± 0.022      | 0.502± 0.033      | 0.491± 0.022      |
|            |                   |                   |              |                   |                   |                   |                   |
| 20000 ppm  | 1.807± 0.089      | 1.566± 0.108      | 1.519± 0.075 | 1.398± 0.069      | 1.367± 0.064      | 1.283± 0.076      | 1.230± 0.064      |
|            |                   |                   |              |                   |                   |                   |                   |
|            |                   |                   |              |                   |                   |                   |                   |

(IIAN300)

BAIS 4

PAGE: 3

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g / kg / d a y
REPORT TYPE : A1 13

SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)

ALL ANIMALS

| Group Name | Administration | (weeks)      |              |              |              |              |  |
|------------|----------------|--------------|--------------|--------------|--------------|--------------|--|
|            | 8              | 9            | 10           | 11           | 12           | 13           |  |
| Control    | 0.000± 0.000   | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 |  |
| 512 ppm    | 0.028± 0.002   | 0.029± 0.001 | 0.029± 0.001 | 0.028± 0.001 | 0.028± 0.001 | 0.026± 0.001 |  |
| 1280 ppm   | 0.075± 0.005   | 0.076± 0.006 | 0.075± 0.006 | 0.072± 0.005 | 0.069± 0.005 | 0.069± 0.005 |  |
| 3200 ppm   | 0.187± 0.010   | 0.184± 0.009 | 0.179± 0.007 | 0.171± 0.010 | 0.174± 0.011 | 0.165± 0.009 |  |
| 8000 ppm   | 0.470± 0.012   | 0.467± 0.019 | 0,455± 0,021 | 0.445± 0.017 | 0.439± 0.020 | 0.424± 0.028 |  |
| 20000 ppm  | 1. 234± 0. 044 | 1.165± 0.059 | 1.142± 0.058 | 1.152± 0.038 | 1.136± 0.029 | 1.111± 0.039 |  |
|            |                |              |              |              |              |              |  |

(IIAN300)

BAIS 4

PAGE: 4

## APPENDIX F 1

HEMATOLOGY: MALE

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]

MEASURE. TIME: 1

HEMATOLOGY (SUMMARY) ALL ANIMALS ( 14W)

| oup Name  | NO. of<br>Animals | RED BLO | OOD CELL | HEMOGLO<br>g/dl | DBIN  | HEMATOC<br>% | CRIT  | MCV<br>f l |       | MCH<br>pg |        | MCHC<br>g/dl |        | PLATELET<br>1 0³/µ |      |
|-----------|-------------------|---------|----------|-----------------|-------|--------------|-------|------------|-------|-----------|--------|--------------|--------|--------------------|------|
| Control   | 10                | 9.34±   | 0. 17    | 16.3±           | 0.3   | 45.6±        | 0.6   | 48.8±      | 0.6   | 17.5±     | 0.4    | 35.8±        | 0.6    | 687±               | 53   |
| 512 ppm   | 10                | 9.40±   | 0. 19    | 16.4±           | 0.3   | 45.9±        | 1.0   | 48.9±      | 0.6   | 17.4±     | 0.2    | 35.6±        | 0.4    | 680±               | 29   |
| 1280 ppm  | 10                | 9.32±   | 0. 17    | 16.2±           | 0. 2  | 45.5±        | 0.8   | 48.9±      | 0.6   | 17.4±     | 0.2    | 35.6±        | 0.6    | 711±               | 40   |
| 3200 ppm  | 10                | 8.97±   | 0.13**   | 15.6±           | 0.3** | 44.5±        | 0.9*  | 49.6±      | 0.5*  | 17.4±     | 0.3    | 35.1±        | 0.5**  | 745±               | 64*  |
| mqq 0008  | 10                | 8.56±   | 0.17**   | 15.3±           | 0.3** | 44.0±        | 0.6** | 51.4±      | 0.7** | 17.8±     | 0.2**  | 34.7生        | 0. 3** | 796土               | 60** |
| 20000 թթա | 10                | 7.82±   | 0.15**   | 14.6±           | 0.2** | 42.3±        | 0.8** | 54.0±      | 0.6** | 18.7±     | 0. 2** | 34.5±        | 0. 3** | 748±               | 42*  |

(HCL070) BAIS 4

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1

HEMATOLOGY (SUMMARY) ALL ANIMALS ( 14W)

| SEX : MALE  | REPORT 1          | TYPE: A1     |        |                 |        |         |         |      |      | PAGE: 2 |
|-------------|-------------------|--------------|--------|-----------------|--------|---------|---------|------|------|---------|
| Group Name  | NO. of<br>Animals | RETICUI<br>% | LOCYTE | metiiemogl<br>% | OBIN . | <br>    |         |      |      |         |
| Control     | 10                | 1.8±         | 0. 1   | 0.3±            | 0. 1   |         |         |      |      |         |
| 512 ppm     | 10                | 1.8±         | 0. 2   | 0.3±            | 0.1    |         |         |      |      |         |
| 1280 ppm    | 10                | 2.0±         | 0. 2*  | 0.3±            | 0. 1   |         |         |      |      |         |
| 3200 ppm    | 10                | 2.6±         | 0. 2** | 0.5±            | 0. 1   |         |         |      |      |         |
| 8000 ppm    | 10                | 3.8±         | 0.3**  | 0.8±            | 0. 3** |         |         |      |      |         |
| 20000 թբա   | 10                | 5.6±         | 0. 2** | 1.0±            | 0. 2** |         |         |      |      |         |
| Significant | difference;       | *: P ≤ (     | 0.05 * | * : P ≤ 0.01    |        | Test of | Dunnett | <br> | <br> |         |
| (HCL070)    |                   |              |        |                 |        |         |         | <br> | <br> | DATE    |

(HCL070)

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]

MEASURE. TIME: 1

SEX : MALE

REPORT TYPE : A1

HEMATOLOGY (SUMMARY) ALL ANIMALS ( 14W)

PAGE: 3 Group Name NO. of WBC Differential WBC (%) Animals  $10^{3}/\mu l$ N-BAND N-SEG EOSINO BASO MONO LYMPHO OTHER Control 10 4.54± 1.14 0± 19± 0 3  $1\pm$ 0± 0  $3\pm$ 2 77 ± 0土 0 512 ppm 10 4.81 ± 0.87  $0\pm$ 0 17± 3 土 1  $0\pm$ 0  $3\pm$ 78± 0± 0 1280 ppm 10 5.11 ± 0.93 0± 0 18± 3 1± 0± 0  $3\pm$ 2 78±  $0\pm$ 0 3200 ppm 10 4.82± 1.04 0± 0 20土 3 i± 1 0± 0 3± 2 76± 0 0± 8000 ppm 10 5.03± 0.85 0<u>+</u> 0 17± 1± 0土 3 -1-79<u>-1-</u> <u>1-</u>0 0 1 20000 ppm 10 4.94± 0.98 Ο± 16± 4 1± 1 0± 0 3± 2 80 ±  $0\pm$ 0 Significant difference;  $*: P \leq 0.05$ \*\* : P ≤ 0.01 Test of Dunnett

(HCL070)

## APPENDIX F 2

HEMATOLOGY: FEMALE

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]

MEASURE. TIME: 1

SEX : FEMALE

REPORT TYPE : A1

HEMATOLOGY (SUMMARY) ALL ANIMALS ( 14W)

PAGE: 4 Group Name NO. of RED BLOOD CELL HEMOGLOBIN HEMATOCRIT MCV MCH MCHC PLATELET Animals 1 05/µl g/dl % f £ g/dl 103/µl рg Control 10 8.76± 0.23  $16.3 \pm$ 0.5 44.5± 1.1  $50.9 \pm$ 0.5 18.6± 0.1 36.5± 740± 0.5 33 43.8± 1.0 512 ppm 10  $8.60 \pm 0.21$ 16.0± 0.4  $50.9 \pm$ 0.6 18.6± 0.1  $36.6 \pm$ 0.3 724± 60 1280 ppm 10 8.50 ± 0.16\* 15.9± 0.3 43.8± 0.6 0.6\* 18.7 $\pm$  0.2  $51.6 \pm$  $36.3 \pm$ 0.4  $776 \pm$ 53 3200 ppm 10 8.20± 0.22\*\* 15.6± 0.4\*\* 43.6± 1.3 53.2生 0.6\*\* 19.0± 0.2\*\*  $35.8 \pm$ 0.4\*\* 763± 61 8000 ppm 10 7.75± 0.25\*\* 15.0 $\pm$ 0.4\*\* 41.9± 1.2\*\*  $54.1 \pm$ 0.4\*\* 19.4土 0.3\*\*  $35.8 \pm$ 0.4\*\* 869± 85\*\* 20000 ppm 10 7.14± 0.16\*\* 14.1± 0.3\*\*  $40.0 \pm$ 0.8\*\* 56.1 $\pm$ 0.5\*\* 19.8± 0.3\*\*  $35.4 \pm$ 0.5\*\* 848± 65\*\* Significant difference;  $*: P \leq 0.05$ \*\*:  $P \leq 0.01$ Test of Dunnett

(HCL070)

STUDY NO. : 0549
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
MEASURE. TIME : 1

SEX : FEMALE

REPORT TYPE : A1

HEMATOLOGY (SUMMARY) ALL ANIMALS ( 14W)

| oup Name    | NO. of<br>Animals | RETICUI<br>% | OCYTE   | METHEMOG<br>% | LOBIN |               |        |   |      |    |
|-------------|-------------------|--------------|---------|---------------|-------|---------------|--------|---|------|----|
| Control     | 10                | 1.7±         | 0. 2    | 0.3±          | 0. 1  |               |        |   |      |    |
| 512 ppm     | 10                | 1.7±         | 0.2     | 0.3±          | 0.1   |               |        |   |      |    |
| 1280 ppm    | 10                | 2.1±         | 0.2     | 0.3±          | 0.0   |               |        |   |      |    |
| 3200 ppm    | 10                | 2.5±         | 0.4**   | 0.3±          | 0. 1  |               |        |   |      |    |
| 8000 ppm    | 10                | 3.7±         | 0. 7**  | 0.7±          | 0.3   |               |        | · |      |    |
| 20000 ррт   | 10                | 5.7±         | 0.7**   | 1.0±          | 0.3** |               | •      |   |      |    |
| Significant | difference;       | *: P ≤ 0     | ). 05 * | * : P ≤ 0.01  |       | <br>Test of D | unnett |   | <br> |    |
| CL070)      |                   |              |         |               | ****  | <br>          |        |   | <br> | BA |

PAGE: 5

HEMATOLOGY (SUMMARY) ALL ANIMALS ( 14W)

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1

SEX : FEMALE

REPORT TYPE : A1

PAGE: 6

| roup Name | NO. of<br>Animals | ₩BC<br>1 0³/1 |       | Dif<br>N-BAND | ferentia | 1 WBC (%<br>N-SEG | n) | EOSINO |              | BAS0 |   | MONO             | , | LYMPHO |   | OTHER |    |
|-----------|-------------------|---------------|-------|---------------|----------|-------------------|----|--------|--------------|------|---|------------------|---|--------|---|-------|----|
|           |                   |               |       |               |          |                   |    |        |              |      |   |                  |   |        |   |       |    |
| Control   | 10                | 2. 45±        | 0. 70 | 0±            | 0        | 17±               | 4  | 1±     | 1            | 0±   | 0 | 4 <del>1</del> : | 2 | 78±    | 5 | 0生    | 0  |
| 512 ppm   | 10                | 2.66±         | 1. 20 | 0±            | 0        | 18±               | 4  | 1±     | 1            | 0±   | 0 | 3±               | 2 | 77±    | 5 | 0±    | 0  |
| 1280 ppm  | 10                | 2.52±         | 0.78  | 0±            | 0        | 17±               | 3  | 2±     | 1            | 0±   | 0 | 4±               | 2 | 78±    | 3 | 0±    | 0  |
| 3200 ppm  | 10                | 2.49±         | 0. 47 | 0±            | 0        | 18±               | 3  | 1±     | ı            | 0±   | 0 | <u>4±</u>        | 2 | 78±    | 4 | 0±    | 0  |
| 8000 ppm  | 10                | 2.86±         | 0.82  | 0±            | 0        | 17±               | 4  | ι±     | 1            | 0±   | 0 | 3±               | 2 | 79土    | 4 | 0±    | 0  |
| 20000 թբm | 10                | 3. 22±        | 1. 25 | 0±            | 0        | 18±               | 4  | 1±     | 1            | 0±   | 0 | <b>4</b> ±       | 2 | 78±    | 5 | 0±    | 0  |
|           | difference ;      |               |       | 0±<br>**: P ≦ |          | 18±               | 4  |        | 1<br>of Dunr |      | 0 | 4±<br>           | 2 | 78±    | 5 |       | ;± |

BAIS 4 (HCL070)

# APPENDIX G 1

BIOCHEMISTRY: MALE

BIOCHEMISTRY (SUMMARY) ALL ANIMALS ( 14W)

ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

PAGE: 1

| oup Name  | NO. of<br>Animals | TOTAL F<br>g/dl |      | ALBUMIN<br>g∕dl | ı    | A/G RAT | 10   | T-BILI<br>mg/dl |         | GLUCOSE<br>mg/dl |    | T-CHOLES<br>mg/dl | STEROL | TRIGLYC<br>mg/dl | ERIDE |
|-----------|-------------------|-----------------|------|-----------------|------|---------|------|-----------------|---------|------------------|----|-------------------|--------|------------------|-------|
| Control   | 10                | 6.3±            | 0.2  | 3.5±            | 0.1  | 1.3±    | 0.1  | 0.11±           | 0.01    | 210±             | 22 | 65±               | 4      | 60 <u>-</u> 1-   | 15    |
| 512 ppm   | 10                | 6.4±            | 0.2  | 3.5±            | 0.1  | 1.3±    | 0.1  | 0.12±           | 0.01    | 214±             | 18 | 63±               | 4      | 68±              | 16    |
| 1280 ppm  | 10                | 6.4±            | 0. 1 | 3.5±            | 0.1  | 1.2±    | 0.1  | 0.12±           | 0.01    | 213±             | 15 | 62±               | 5      | 63±              | 20    |
| 3200 ppm  | 10                | 6.5±            | 0. 1 | 3.6±            | 0.1  | 1.2±    | 0.0  | 0.12±           | 0.01    | 221±             | 19 | 63±               | 5      | 66±              | 16    |
| 8000 ppm  | 10                | 6.4±            | 0. 1 | 3.5±            | 0. 1 | 1.3±    | 0. 1 | 0.12±           | 0.01    | 206±             | 12 | 62±               | 4      | 56土              | 23    |
| 20000 թթա | 10                | 6.5±            | 0.2  | 3.6±            | 0. 1 | 1.2±    | 0. 1 | 0.16±           | 0. 02** | 201±             | 12 | 73±               | 6**    | 54±              | 16    |

(HCL074)

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]

MEASURE. TIME: 1

SEX : MALE

REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY) ALL ANIMALS ( 14W)

PAGE: 2 Group Name NO. of PHOSPHOLIPID AST ALT LDH ALP G-GTP CK mg/dl Animals IU/l IU/2 IU/l IU/l IU/l IU/2 Control 10 115士 7 56± 109± 45 16 215± 74  $242\pm$ 15 1土 1 112± 11 10 115± 122± 512 ppm 34 59± 13 227± 48 248± 15  $1 \pm$ 109± 11 1280 ppm 10 116± 9 110± 37  $53 \pm$ 12  $205\pm$ 67  $252\pm$ 10 1± 108± 14 3200 ppm 10 118± 8 131± 68  $59\pm$ 20 257± 134 250± 22  $2\pm$ 118± 21 8000 ppm 10 115± 7 99± 28  $45\pm$ 10 177± 46  $242 \pm$ 25  $2\pm$ 1 100土 11 20000 ppm 10  $130 \pm$ 7\*\* 84± 10 35± 3\*\* 160± 45  $225\pm$ 27  $4\pm$ 1\*\* 94± 14\* Significant difference ;  $*: P \leq 0.05$ \*\* :  $P \leq 0.01$ Test of Dunnett

(IICL074)

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]

MEASURE. TIME: 1

SEX : MALE

REPORT TYPE : AI

BIOCHEMISTRY (SUMMARY) ALL ANIMALS ( 14W)

Group Name NO. of UREA NITOROGEN CREATININE SODIUM POTASSIUM CHLORIDE CALCIUM INORGANIC PHOSPHORUS Animals mg/dl mg/dl m Eq / L m Eq/2  $mEq/\ell$ mg/dl mg/dl Control 10 18.4± 1.2  $0.5\pm$ 0.1 141±  $3.4\pm 0.2$ 1 104土 1  $10.2 \pm 0.2$ 5.3± 0.6 512 ppm 10 18.5 $\pm$ 1.0  $0.5 \pm$ 0.1 141±  $3.3 \pm$ 0.2 104± 10.2± 0.2 5.5± 0.5 1280 ppm 0.2 10 18.5± 1.8  $0.5 \pm$ 0.1 142±  $3.4\pm 0.2$ 104±  $10.3 \pm$ 5.4生 0.5 3200 ppm 10 18.9± 1.3  $0.6 \pm$ 0.1  $142 \pm$ 3.4生 0.2 104± 10.3± 0.2 5.5± 0.5 8000 ppm 10 18.4± 2.0 0.5± 0.1 141± 1 3.5± 0.2 104± 10.2± 0.3  $5.5 \pm$ 0.6 20000 ppm 10 18.9± 1.9 0.5± 0.1 141± 1 3.8± 0.2\*\* 103± 10.4± 0.2 5.7± 0.5 Significant difference;  $*: P \leq 0.05$ \*\* :  $P \leq 0.01$ Test of Dunnett

PAGE: 3

(HCL074)

## APPENDIX G 2

BIOCHEMISTRY: FEMALE

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]

MEASURE. TIME: 1 SEX: FEMALE

REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY) ALL ANIMALS ( 14W)

| oup Name  | NO. of<br>Animals | TOTAL P<br>g/dl | ROTEIN | ALBUMIN<br>g/dl |      | A/G RAT | 10    | T-BILI<br>mg/dl |       | GLUCOSE<br>mg/dl |      | T-CHOLES<br>mg/dl | STEROL | TRIGLYCE<br>mg/dl | RIDE |
|-----------|-------------------|-----------------|--------|-----------------|------|---------|-------|-----------------|-------|------------------|------|-------------------|--------|-------------------|------|
| Control   | 10                | 6. 3土           | 0.2    | 3.5±            | 0. 1 | 1.2±    | 0. 1  | 0.14±           | 0.02  | 151±             | 16   | 75±               | 6      | 14±               | 4    |
| 512 ppm   | 10                | 6.2±            | 0.2    | 3.5±            | 0. 1 | 1.3±    | 0.1   | 0.14±           | 0.02  | 152±             | 11   | 74±               | 5      | 14±               | 4    |
| 1280 ppm  | 10                | 6.3±            | 0.2    | 3.5±            | 0.1  | 1.3±    | 0.1   | 0.14±           | 0.03  | 151±             | 16   | 79±               | 3      | 16±               | 7    |
| 3200 ppm  | 10                | 6.2±            | 0.2    | 3.4±            | 0.1  | 1.3±    | 0.1   | 0.19±           | 0.14  | 143±             | 17   | 75±               | 4      | 14±               | 4    |
| 8000 ppm  | 10                | 6.3±            | 0.2    | 3.6±            | 0. 1 | 1.4±    | 0.1** | 0.15±           | 0.02  | 162±             | 10   | 82±               | 6**    | 11±               | 7    |
| 20000 ppm | 10                | 6.3±            | 0.2    | 3.5±            | 0.1  | 1.3±    | 0. 1  | 0.17±           | 0.02* | 180±             | 20** | 93 <del>±</del>   | 6**    | 16±               | 5    |

PAGE: 4

(IICL074) BAIS 4

BIOCHEMISTRY (SUMMARY) ALL ANIMALS ( 14W)

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]

MEASURE. TIME: 1 SEX : FEMALE

REPORT TYPE : A1

PAGE: 5

| oup Name  | NO. of<br>Animals | PHOSPHOI<br>mg/dL | LIPID | AST<br>IU/1 |    | ALT<br>IU/L | !   | LDH<br>I U/ | 2   | ALP<br>IU/£ | !  | G-GTP<br>I U/2 |     | I U/A | 2   |
|-----------|-------------------|-------------------|-------|-------------|----|-------------|-----|-------------|-----|-------------|----|----------------|-----|-------|-----|
| Control   | 10                | 140±              | 11    | 87±         | 12 | 40±         | 5   | 261±        | 84  | 179±        | 21 | 2±             | 1   | 127±  | 23  |
| 512 ppm   | 10                | 139±              | 9     | 80±         | 10 | 37±         | 3   | 266±        | 190 | 188±        | 26 | 2±             | 1   | 134±  | 50  |
| 1280 ppm  | 10                | 150±              | 8     | 78±         | 9  | 37±         | 6   | 252±        | 154 | 174土        | 24 | 1±             | 1   | 126±  | 46  |
| 3200 ppm  | 10                | 141 ±             | 6     | 81±         | 18 | 34±         | 6*  | 427±        | 605 | 187±        | 18 | 2±             | 1   | 179±  | 120 |
| 8000 ppm  | 10                | 150±              | 11    | 90±         | 33 | 37±         | 13* | 268±        | 110 | 186±        | 17 | 3±             | 1** | 125±  | 29  |
| 20000 ppm | 10                | 158±              | 8**   | 86±         | 11 | 34±         | 5   | 294±        | 155 | 191±        | 19 | 7±             | 2** | 126±  | 41  |

BAIS 4 (HCL074)

BIOCHEMISTRY (SUMMARY) ALL ANIMALS ( 14W)

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1

SEX : FEMALE

REPORT TYPE : AI

PAGE: 6

| oup Name  | NO. of<br>Animals | UREA NIT<br>mg/dl | OROGEN | CREATIN<br>mg/dl | INE  | SODIUM<br>m Eq/l |   | POTASSI<br>m Eq/ |     | CHLORIDE<br>m Eq / L |   | CALCIUN<br>mg/dl | [    | INORGAN<br>mg/dl  | IC PHOSPHORU |
|-----------|-------------------|-------------------|--------|------------------|------|------------------|---|------------------|-----|----------------------|---|------------------|------|-------------------|--------------|
| Control   | 10                | 19.0生             | 1. 0   | 0.5±             | 0.1  | 141±             | 1 | 3.5±             | 0.3 | 105±                 | 2 | 9.8±             | 0.3  | 5. 2土             | 1.0          |
| 512 ppm   | 10                | 19.0±             | 1.6    | 0.5±             | 0.1  | 141±             | 1 | 3.6±             | 0.2 | 105±                 | 2 | 9.9±             | 0.3  | 5.2±              | 0.8          |
| 1280 ppm  | 10                | 18.0±             | 2.4    | 0.6±             | 0.1  | 141生             | 2 | 3.5±             | 0.3 | 105±                 | 2 | 9.7±             | 0.3  | 5.0±              | 0.8          |
| 3200 ppm  | 10                | 17.7±             | 2.0    | 0.6±             | 0. 1 | 140±             | 2 | 3.8±             | 0.5 | 106±                 | 2 | 9.7±             | 0.3  | 5.6±              | 0.7          |
| 8000 ppm  | 10                | 19.1±             | 1.3    | 0.6生             | 0.1  | 141±             | 1 | 3.6±             | 0.3 | 105±                 | 1 | 9.7±             | 0. 4 | 5. 1 <del>'</del> | 0.8          |
| 20000 ррш | 10                | 20.6±             | 1. 3   | 0.5±             | 0.0  | 140±             | 1 | 3.7±             | 0.3 | 105±                 | 1 | 9.8±             | 0.3  | 5.2±              | 0. 7         |

(HCL074)

## APPENDIX H 1

URINALYSIS: MALE

URINALYSIS

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]

10

MEASURE. TIME: 1

8000 ppm

20000 ppm

SEX : MALE

REPORT TYPE : A1

| NO. of  | pf]                 |                              |                |                         |                      |   |   |   |   | P:  | rote  | in_   |   |  |   |  | G1   | uco   | se.   |   |  |   |   | Ket  | one  | body   | r  |  |   |   | Bili  | uhir   | 1  |   |  |  |  |
|---------|---------------------|------------------------------|----------------|-------------------------|----------------------|---|---|---|---|---|---|---|---|--|---|--|--|---|---|---|--|---|---|--|--|--|--|--|---|---|---|--|--|---|--|--|--|
| Animals | 5.                  | 0 6                          | 6.0            | 6.5                     | 7.0                  | 7.5   | 8.0   | 8.5   | CHI   | _   | - ±   | +   | 2+  | 3+   | 4+  | CHI  | _  | ±   | +   | 2+  | 3+ 4   | 4+ CH)  |   |  |  |  |  | 4+   | CIII                                    |   |   |  |  | CIII                                    |  |  |  |
|         |                     |                              |                |                         |                      |   |   |   |   |   |   |   |   |  |   |  |  |   |   |   |  |   |   |  |  |  |  |  |   |   |   |  |  |   |  |  | -  |
| 10      | 0                   | 1                            | 0              | 0                       | 0                    | 0   | 4   | 6   |   |   | 0 (   | 6   | 4   | 0  | 0   |  | 10   | 0   | 0   | 0   | 0  | 0   |   | 0  | 3  | 7 (  | 0  | 0  |   |   | 10  | 0  | 0  |   |  |  |  |
| 10      | 0                   | ,                            | 0              | 0                       | 0                    | 0   | 3   | 7   |   |   | 0 (   | 8 (   | 2   | 0  | 0   |  | 10   | 0   | 0   | 0   | 0  | 0   |   | 0  | 6  | 4 (  | 0  | 0  |   |   | 10  | 0  | 0  |   |  |  |  |
| 10      | O                   | 1                            | 0              | 0                       | 0                    | 0   | 4   | 6   |   |   | 0 1   | . 7   | 2   | 0  | 0   |  | 10   | 0   | 0   | 0   | 0  | 0   |   | 2  | 4  | 4 (  | 0  | 0  |   |   | 10  | 0  | 0  |   |  |  |  |
| 10      | 0                   | <b>;</b>                     | 0              | 0                       | 0                    | 0   | 2   | 8   |   | :   | 0 (   | 10  | 0   | 0  | 0   | *  | 10   | 0   | 0   | 0   | 0  | 0   |   | 0  | 8  | 2 (  | 0  | 0  | *                                       |   | 10  | 0  | 0  |   |  |  |  |
|         | Animals  10  10  10 | Animals 5.  10 0  10 0  10 0 | 10 0 10 0 10 0 | 10 0 0 10 10 0 0 10 0 0 | 10 0 0 0 10 10 0 0 0 | Animals 5.0 6.0 6.5 7.0  10 0 0 0 0  10 0 0 0 0  10 0 0 0 0 | Animals 5.0 6.0 6.5 7.0 7.5  10 0 0 0 0 0 0  10 0 0 0 0 0 | Animals 5.0 6.0 6.5 7.0 7.5 8.0  10 0 0 0 0 0 4  10 0 0 0 0 0 3  10 0 0 0 0 0 4 | Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5  10 0 0 0 0 0 4 6  10 0 0 0 0 0 3 7  10 0 0 0 0 0 4 6 | Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI  10 0 0 0 0 0 4 6 10 0 0 0 0 3 7 10 0 0 0 0 0 4 6 | Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI  10 0 0 0 0 0 4 6  10 0 0 0 0 3 7  10 0 0 0 0 0 4 6 | Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI — ± | Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI — ± +  10 0 0 0 0 0 4 6 0 0 6  10 0 0 0 0 0 3 7 0 0 8  10 0 0 0 0 0 4 6 0 1 7 | Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI — ± + 2+  10 0 0 0 0 0 4 6 0 0 6 4  10 0 0 0 0 0 3 7 0 0 8 2  10 0 0 0 0 0 4 6 0 1 7 2 | Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI — ± + 2+ 3+  10 0 0 0 0 0 4 6 0 0 6 4 0  10 0 0 0 0 0 3 7 0 0 8 2 0  10 0 0 0 0 0 4 6 0 1 7 2 0 | Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI — ± + 2+ 3+ 4+  10 0 0 0 0 0 4 6 0 0 6 4 0 0  10 0 0 0 0 0 3 7 0 0 8 2 0 0  10 0 0 0 0 0 4 6 0 1 7 2 0 0 | Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI — ± + 2+ 3+ 4+ CHI  10 0 0 0 0 0 4 6 0 0 6 4 0 0  10 0 0 0 0 0 3 7 0 0 8 2 0 0  10 0 0 0 0 0 4 6 0 1 7 2 0 0 | Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI — ± + 2+ 3+ 4+ CHI —  10 0 0 0 0 0 4 6 0 0 6 4 0 0 10  10 0 0 0 0 0 3 7 0 0 8 2 0 0 10  10 0 0 0 0 0 4 6 0 1 7 2 0 0 10 | Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI — ± + 2+ 3+ 4+ CHI — ±  10 0 0 0 0 0 4 6 0 0 6 4 0 0 10 0  10 0 0 0 0 0 3 7 0 0 8 2 0 0 10 0  10 0 0 0 0 0 4 6 0 1 7 2 0 0 10 0 | Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI — ± + 2+ 3+ 4+ CHI — ± +  10 0 0 0 0 0 4 6 0 0 6 4 0 0 10 0 0  10 0 0 0 0 0 3 7 0 0 8 2 0 0 10 0 0  10 0 0 0 0 0 4 6 0 1 7 2 0 0 10 0 0 | Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI — ± + 2+ 3+ 4+ CHI — ± + 2+  10 0 0 0 0 0 4 6 0 0 6 4 0 0 10 0 0 0  10 0 0 0 0 0 3 7 0 0 8 2 0 0 10 0 0 0  10 0 0 0 0 0 4 6 0 1 7 2 0 0 10 0 0 | Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI — ± + 2+ 3+ 4+ CHI — ± + 2+ 3+ 4  10 0 0 0 0 0 4 6 0 0 6 4 0 0 10 0 0 0 0  10 0 0 0 0 0 3 7 0 0 8 2 0 0 10 0 0 0 0  10 0 0 0 0 0 4 6 0 1 7 2 0 0 10 0 0 0 0 | Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI — ± + 2+ 3+ 4+ CHI — ± + 2+ 3+ 4+ CH  10 0 0 0 0 0 4 6 0 0 6 4 0 0 10 0 0 0 0 0  10 0 0 0 0 0 3 7 0 0 8 2 0 0 10 0 0 0 0  10 0 0 0 0 0 4 6 0 1 7 2 0 0 10 0 0 0 0 0 | Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI — ± + 2+ 3+ 4+ CHI — ± + 2+ 3+ 4+ CHI  10 0 0 0 0 0 4 6 0 0 6 4 0 0 10 0 0 0 0 0  10 0 0 0 0 0 3 7 0 0 8 2 0 0 10 0 0 0 0  10 0 0 0 0 0 4 6 0 1 7 2 0 0 10 0 0 0 0 | Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI — ± + 2+ 3+ 4+ CHI — ± + 2+ 3+ 4+ CHI — 10 0 0 0 0 0 4 6 0 0 6 4 0 0 10 0 0 0 0 0 0 0 0 10 0 0 0 0 0 0 | Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI — ± + 2+ 3+ 4+ CHI — ± + 2+ 3+ 4+ CHI — ± - ± -  10 0 0 0 0 0 4 6 0 0 6 4 0 0 10 0 0 0 0 0 0 0 0 3  10 0 0 0 0 0 8 2 0 0 10 0 0 0 0 6  10 0 0 0 0 0 4 6 0 1 7 2 0 0 10 0 0 0 0 0 2 4 | Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI — ± + 2+ 3+ 4+ CHI — ± + 2+ 3+ | Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI — ± + 2+ 3+ 4+ CHI — ± + 2+ 3+ | Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI | Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI | Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI — ± + 2+ 3+ 4+ CHI  10 0 0 0 0 0 0 0 4 6 0 0 0 6 4 0 0 10 0 0 0 0 0 0 0 0 0 0 10 0 0 0 0 | Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI — ± + 2+ 3+ 4+ CHI — + 2+ 3+ 4+ CHI — ± + 2+ 3+ 4 | Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI — ± + 2+ 3+ 4+ CHI — ± + 2+ 3+ | Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI | Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI — ± + 2+ 3+ 4+ CHI — + 2+ 3+ 4+ CHI — + 2+ 3 | Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI — ± + 2+ 3+ 4+ CHI — + 2+ 3+ 4+ CHI — + 2+ 3+ 4+ CHI — + 2+ | Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI — ± + 2+ 3+ 4+ CHI — + 2+ 3+ |

10 0 0 0 0 0

10 0 0 0 0 0

2 6 2 0 0 0

7 2 1 0 0 0 \*\*

10 0 0 0

0 10 0 0 \*\*

0 3 7 0 0 0 \*

0 10 0 0 0 0 \*\*

PAGE: 1

Significant difference ; \*:  $P \le 0.05$  \*\*:  $P \le 0.01$  Test of CHI SQUARE

0 0 0 0 2 4 4

0 0 0 1 6 2 1 \*

(HCL101) BAIS 4

URINALYSIS

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]

MEASURE. TIME: 1

SEX : MALE

REPORT TYPE : A1

| Group Name  | NO. of<br>Animals | Occult blood $-\pm +2+3+$ CHI | Urobilinogen<br>± + 2+ 3+ 4+ CHI |                    |      |
|-------------|-------------------|-------------------------------|----------------------------------|--------------------|------|
|             |                   |                               |                                  |                    |      |
| Control     | 10                | 9 1 0 0 0                     | 10 0 0 0 0                       |                    |      |
| 512 ppm     | 10                | 10 0 0 0 0                    | 10 0 0 0 0                       |                    |      |
| 1280 ppm    | 10                | 10 0 0 0 0                    | 10 0 0 0 0                       |                    |      |
| 3200 ppm    | 10                | 9 0 1 0 0                     | 10 0 0 0 0                       |                    |      |
| 8000 ppm    | 10                | 10 0 0 0 0                    | 10 0 0 0 0                       |                    |      |
| 20000 ppm   | 10                | 10 0 0 0 0                    | 10 0 0 0 0                       |                    |      |
|             |                   |                               |                                  |                    |      |
| Significant | difference        | ; *: P ≤ 0.05 **              | $: P \leq 0.01$                  | Test of CHI SQUARE |      |
| (HCL101)    |                   |                               |                                  |                    | BAIS |

PAGE: 2

## APPENDIX H 2

URINALYSIS: FEMALE

URINALYSIS

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1

SEX : FEMALE

REPORT TYPE : A1

PAGE: 3

| oup Name  | NO. of  | Hu   |     |     |      |     |     |     |     | Prot | ein |     |    |       | ( | luce | se_ |    |      |        | Ket | one | bod | lv |      |     |          | Bi! | iru | oin   |   |     |
|-----------|---------|------|-----|-----|------|-----|-----|-----|-----|------|-----|-----|----|-------|---|------|-----|----|------|--------|-----|-----|-----|----|------|-----|----------|-----|-----|-------|---|-----|
|           | Animals | 5. 0 | 6.0 | 6.5 | 7. 0 | 7.5 | 8.0 | 8.5 | CHI | - =  |     |     | 3+ | 4+ CH |   |      |     | 2+ | 3+ 4 | 4+ CHI |     |     |     |    | + 4+ | · C | HI       |     |     | 2+ 3- | + | CHI |
| Control   | 10      | 0    | 0   | 0   | 0    | 0   | 8   | 2   |     | 0    | 4 8 | 5 ( | 0  | 0     | : | .0 ( | 0   | 0  | 0    | 0      | 4   | 6   | 0   | 0  | 0 0  | )   |          | 10  | 0   | 0 (   | 0 |     |
| 512 ppm   | 10      | 0    | 0   | 0   | 0    | 0   | 1   | 9   | **  | 0    | 4 6 | 5 ( | 0  | 0     | : | .0   | 0   | 0  | 0    | 0      | 6   | 4   | 0   | 0  | 0 0  | )   |          | 10  | 0   | 0 0   | 0 |     |
| 1280 ppm  | 10      | 0    | 0   | 0   | 0    | 0   | 2   | 8   | **  | 0    | 4 6 | 6 ( | 0  | 0     |   | .0   | 0   | 0  | 0    | 0      | 6   | 4   | 0   | 0  | 0 0  | )   |          | 10  | 0   | 0 (   | 0 |     |
| 3200 ppm  | 10      | 0    | 0   | 0   | 0    | 0   | 1   | 9   | **  | 0    | 7 : | 3 ( | 0  | 0     |   | .0   | 0   | 0  | 0    | 0      | 6   | 4   | 0   | 0  | 0 0  | )   |          | 10  | 0   | 0 (   | 0 |     |
| mqq 0008  | 10      | 0    | 0   | 0   | 0    | 0   | . 3 | 7   | *   | 2    | 6 2 | 2 ( | 0  | 0     |   | .0   | 0   | 0  | 0    | 0      | 7   | 3   | 0   | 0  | 0 0  | )   |          | 7   | 3   | 0 (   | 0 |     |
| 20000 ррв | 10      | 0    | 0   | 0   | 0    | 0   | 10  | 0   |     | i    | 7 2 | 2 ( | 0  | 0     |   | 0    | 0   | 0  | 0    | 0 .    | 10  | 0   | 0   | 0  | 0 0  | ) * | <b>*</b> | 2   | 8   | 0     | 0 | **  |

(HCL101) BAIS 4

URINALYSIS

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

| Group Name  | NO. of<br>Animals | Occult blood<br>- ± + 2+ 3+ CHI | Urobilinogen<br>± + 2+ 3+ 4+ CHI |                    |        |
|-------------|-------------------|---------------------------------|----------------------------------|--------------------|--------|
| 0 . 1       | 10                | 10.0.0.0                        | 10.000                           |                    |        |
| Control     | 10                | 10 0 0 0 0                      | 10 0 0 0 0                       |                    |        |
| 512 ppm     | 10                | 10 0 0 0 0                      | 10 0 0 0 0                       |                    |        |
| 1280 ppm    | 10                | 10 0 0 0 0                      | 10 0 0 0 0                       |                    |        |
| 3200 ppm    | 10                | 10 0 0 0 0                      | 10 0 0 0 0                       |                    |        |
| 8000 ppm    | 10                | 10 0 0 0 0                      | 10 0 0 0 0                       |                    |        |
| 20000 ppm   | 01                | 10 0 0 0 0                      | 10 0 0 0 0                       |                    |        |
| Significant | difference        | ; *: P ≤ 0.05 **                | : P ≤ 0.01                       | Test of CHI SQUARE |        |
|             | . difference      | , 1 = 0.00                      | . 1 = 0.01                       | rest of one odough |        |
| (HCL101)    |                   |                                 |                                  |                    | RATS 4 |

PAGE: 4

BAIS 4 (HCL101)

## APPENDIX I 1

GROSS FINDINGS: MALE

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]

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

REPORT TYPE : A1

SEX : MALE

| rgan      | Findings   | Group Name<br>NO. of Animals | Control<br>10 (%) | 512 ppm<br>10 (%) | 1280 ppm<br>10 (%) | 3200 ppm<br>10 (%) |
|-----------|------------|------------------------------|-------------------|-------------------|--------------------|--------------------|
| pleen     | enlarged   |                              | 0 ( 0)            | 0 ( 0)            | 0 ( 0)             | 0 ( 0)             |
| restomach | ulcer      |                              | 0 ( 0)            | 0 ( 0)            | 0 ( 0)             | 0 ( 0)             |
|           | thick      |                              | 0 (0)             | 0 ( 0)            | 0 ( 0)             | 0 ( 0)             |
| iver      | herniation |                              | 0 ( 0)            | 2 (20)            | 0 ( 0)             | 1 (10)             |

(HPT080)

BAIS 4

PAGE: 1

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

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1 SEX : MALE

PAGE: 2

| Organ       | Findings   | Group Name 8000 ppm<br>NO. of Animals 10 (%) | 20000 ppm<br>10 (%) |        |
|-------------|------------|--|---------------------|--------|
| spleen      | enlarged   | 0 ( 0)                                       | 10 (100)            |        |
| forestomach | ulcer      | 0 ( 0)                                       | 1 (10)              |        |
|             | thick      | 1 (10)                                       | 10 (100)            |        |
| liver       | herniation | 2 (20)                                       | 1 (10)              |        |
|             |            |  |                     |        |
| (HPT080)    |            |  |                     | BAIS 4 |

## APPENDIX I 2

GROSS FINDINGS : FEMALE

RAT F344/DuCrlCrlj[F344/DuCrj]

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

ANIMAL : RAT REPORT TYPE : A1

SEX : FEMALE

PAGE: 3

| gan       | Findings   | Group Name Control NO. of Animals 10 (%) | 512 ppm<br>10 (%) | 1280 ppm<br>10 (%) | 3200 ppm<br>10 (%) |
|-----------|------------|--|-------------------|--------------------|--------------------|
| leen      | enlarged   | 0 ( 0)                                   | 0 ( 0)            | 0 ( 0)             | 0 ( 0)             |
| restomach | ulcer      | 0 ( 0)                                   | 0 ( 0)            | 0 ( 0)             | 0 ( 0)             |
|           | thick      | 0 ( 0)                                   | 0 ( 0)            | 0 ( 0)             | 0 ( 0)             |
| er        | herniation | 2 (20)                                   | 4 (40)            | 1 (10)             | 1 (10)             |
| n bladd   | white zone | 0 ( 0)                                   | 0 ( 0)            | 1 (10)             | 0 ( 0)             |
| e         | turbid     | 0 ( 0)                                   | 0 ( 0)            | 0 ( 0)             | 0 ( 0)             |

(HPT080)

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]

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

REPORT TYPE : A1
SEX : FEMALE

PAGE: 4

| Organ       | Findings   | Group Name 8000 ppm<br>NO. of Animals 10 (%) | 20000 ppm<br>10 (%) |      |
|-------------|------------|--|---------------------|------|
| ,           |            | 0 ( 0)                                       | 10 (100)            |      |
| spleen      | enlarged   | 0 ( 0)                                       | 10 (100)            |      |
| forestomach | ulcer      | 0 ( 0)                                       | 2 ( 20)             |      |
|             | thick      | 0 ( 0)                                       | 10 (100)            |      |
| liver       | herniation | 1 (10)                                       | 1 (10)              |      |
| urin bladd  | white zone | 0 ( 0)                                       | 0 ( 0)              |      |
| eye         | turbid     | 0 ( 0)                                       | 1 (10)              |      |
|             |            |  |                     | ·    |
| (HPT080)    |            |  |                     | BAIS |

## APPENDIX J 1

ORGAN WEIGHT, ABSOLUTE: MALE

STUDY NO.: 0549
ANIMAL: RAT F344/DuCrlCrlj[F344/DuCrj]

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

REPORT TYPE : A1

SEX : MALE UNIT: g

PAGE: 1

| oup Name    | NO. of<br>Animals | Body      | Weight | THYM       | JS     | ADRE   | NALS   | TEST       | ES     | HEAR            | T        | LUNG   | S      |
|-------------|-------------------|-----------|--------|------------|--------|--------|--------|------------|--------|-----------------|----------|--------|--------|
| Control     | 10                | 310±      | 16     | 0.224±     | 0.031  | 0.047± | 0.003  | 3.058±     | 0. 115 | 0. 926 <u>+</u> | 0. 034   | 0.964± | 0.038  |
| 512 ppm     | 10                | 304±      | 12     | 0.229±     | 0. 028 | 0.048± | 0.004  | 3.069±     | 0.068  | 0.912±          | 0. 044   | 0.976± | 0.048  |
| 1280 ppm    | 10                | 313±      | 11     | 0.226±     | 0.023  | 0.048± | 0.004  | 3.086±     | 0.065  | 0.932±          | 0.031    | 0.991± | 0.052  |
| 3200 ррш    | 10                | 311±      | 9      | 0.218±     | 0.020  | 0.048± | 0.003  | 3.077±     | 0. 144 | 0.932±          | 0. 035   | 0.975± |        |
| 8000 ppm    | 10                | 291±      | 17**   | 0.203±     | 0.028  | 0.046生 | 0.002  | 3.089±     | 0.051  | 0.908±          | 0. 045   | 0.968± | 0.036  |
| 20000 ррт   | 10                | 266±      | 11**   | 0.190±     | 0.019* | 0.042± | 0.002* | 3.057±     | 0. 089 | 0.858±          | 0. 025** | 0.910± | 0.040* |
| Significant | difference;       | *: P ≤ 0. | 05 **  | : P ≤ 0.01 |        |        | Test   | of Dunnett |        |                 |          |        |        |
| CI 040)     |                   |           |        |            |        |        |        |            |        |                 |          |        |        |

(HCL040)

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]

REPORT TYPE : A1

SEX : MALE UNIT: g

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

| oup Name  | NO. of<br>Animals | KIDî   | NEYS   | SPLI   | BEN     | LIVI   | GR     | BRA    |          |  |
|-----------|-------------------|--------|--------|--------|---------|--------|--------|--------|----------|--|
| Control   | 10                | 1.836± | 0.066  | 0.579± | 0. 022  | 7.419± | 0. 467 | 1.959± | 0. 043   |  |
| 512 ppm   | 10                | 1.820± | 0. 069 | 0.562± | 0. 025  | 7.353± | 0. 488 | 1.960± | 0. 023   |  |
| 1280 ppm  | 10                | 1.864± | 0.068  | 0.597± | 0.029   | 7.523± | 0. 422 | 1.954± | 0.031    |  |
| 3200 ppm  | 10                | 1.927± | 0.080* | 0.638± | 0.034   | 7.872± | 0. 439 | 1.956± | 0. 033   |  |
| 8000 ppm  | 10                | 1.922± | 0.073* | 0.748± | 0.058** | 7.485± | 0.514  | 1.947± | 0.041    |  |
| 20000 ppm | 10                | 1.871± | 0.081  | 1.211± | 0.061** | 7.892± | 0. 263 | 1.899± | 0. 027★★ |  |

(HCL040)

## APPENDIX J 2

ORGAN WEIGHT, ABSOLUTE: FEMALE

ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]

REPORT TYPE : A1 SEX : FEMALE UNIT: g ORGAN WEIGHT: ABSOLUTE (SUMMARY) SURVIVAL ANIMALS ( 14W)

PAGE: 3

| oup Name  | NO. of<br>Animals |      |    | ТНҮМС   | MUS ADRENALS |        | NALS    | OVARIES |         | HEART  |        | LUNG   |        |
|-----------|-------------------|------|----|---------|--------------|--------|---------|---------|---------|--------|--------|--------|--------|
| Control   | 10                | 160± | 8  | 0.178±  | 0.016        | 0.052± | 0.002   | 0.104±  | 0. 007  | 0.584± | 0.014  | 0.710± | 0. 027 |
| 512 ppm   | 10                | 165± | 15 | 0. 185± | 0. 026       | 0.052± | 0.004   | 0.104±  | 0.014   | 0.593± | 0. 036 | 0.739± | 0.048  |
| 1280 ppm  | 10                | 162± | 10 | 0.172±  | 0.019        | 0.050± | 0.004   | 0.101±  | 0.009   | 0.592± | 0.038  | 0.718± | 0.043  |
| 3200 ppm  | 10                | 159± | 6  | 0.175±  | 0.016        | 0.048± | 0.003   | 0.100±  | 0.016   | 0.577± | 0.035  | 0.708± | 0.022  |
| 8000 ppm  | 10                | 154士 | 10 | 0.168土  | 0.011        | 0.049± | 0.003   | 0.097±  | 0.012   | 0.573± | 0.037  | 0.709± | 0. 033 |
| 20000 ppm | 10                | 149± | 9* | 0.166±  | 0. 026       | 0.047± | 0.003** | 0.088±  | 0.006** | 0.579± | 0.046  | 0.695± | 0.048  |

(HCL040)

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]

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

REPORT TYPE : A1 SEX : FEMALE

UNIT: g

| oup Name  | NO. of<br>Animals |        |        | SPLI   | SPLEEN            |         | LIVER    |        | IN     |  |   |  |
|-----------|-------------------|--------|--------|--------|-------------------|---------|----------|--------|--------|--|---|--|
| Control   | 10                | 1.062土 | 0. 031 | 0.376± | 0. 026            | 3. 739± | 0. 186   | 1.800± | 0. 028 |  |   |  |
| 512 ppm   | 10                | 1.099生 | 0.053  | 0.379± | 0. 032            | 3.813±  | 0. 345   | 1.800± | 0. 039 |  | • |  |
| 1280 ppm  | 10                | 1.069± | 0.080  | 0.381± | 0.025             | 3.871±  | 0. 432   | 1.804± | 0. 033 |  |   |  |
| 3200 ppm  | 10                | 1.055± | 0.034  | 0.408± | 0.027             | 3.820±  | 0. 162   | 1.792± | 0. 033 |  |   |  |
| 8000 ppm  | 10                | 1.060± | 0.041  | 0.481± | Ö. 029 <b>*</b> * | 3.880±  | 0. 268   | 1.768生 | 0. 029 |  |   |  |
| 20000 ppm | 10                | 1.090± | 0.063  | 0.740± | 0.064**           | 4.439±  | 0. 313** | 1.765± | 0. 038 |  |   |  |

(HCL040)

## APPENDIX K 1

ORGAN WEIGHT, RELATIVE : MALE

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1

SEX : MALE UNIT: %

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

PAGE: 1

| oup Name    | NO. of<br>Animals |          |         | THYMUS       | ADRENALS     | TESTES         | HEART          | LUNGS          |  |
|-------------|-------------------|----------|---------|--------------|--------------|----------------|----------------|----------------|--|
| Control     | 10                | 310±     | 16      | 0.072± 0.008 | 0.015± 0.001 | 0.989± 0.058   | 0.299± 0.017   | 0.311± 0.016   |  |
| 512 ppm     | 10                | 304±     | 12      | 0.075± 0.008 | 0.016± 0.001 | 1.011± 0.045   | 0.300± 0.012   | 0.321± 0.015   |  |
| 1280 ppm    | 10                | 313±     | 11      | 0.072± 0.006 | 0.015± 0.001 | 0.988± 0.044   | 0.298± 0.010   | 0.317± 0.013   |  |
| 3200 ppm    | 10                | 311±     | 9       | 0.070± 0.006 | 0.015± 0.001 | 0.991± 0.042   | 0.300± 0.012   | 0.314± 0.009   |  |
| 8000 ppm    | 10                | 291土     | 17**    | 0.070± 0.007 | 0.016± 0.001 | 1.064± 0.063** | 0.312± 0.007   | 0.333± 0.017** |  |
| 20000 ppm   | 10                | 266±     | 11**    | 0.071± 0.005 | 0.016± 0.001 | 1.152± 0.055** | 0.323± 0.011** | 0.343± 0.017** |  |
| Significant | difference;       | *: P ≤ 0 | . 05 ** | : P ≤ 0.01   | Tes          | t of Dunnett   |                |                |  |

(HCL042)

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1

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

SEX : MALE UNIT: %

PAGE: 2

| oup Name    | NO. of<br>Animals | KIDNEYS          | SPLEEN         | LIVER          | BRAIN         |  |
|-------------|-------------------|------------------|----------------|----------------|---------------|--|
| Control     | 10                | 0.593± 0.014     | 0.187± 0.006   | 2.394± 0.093   | 0.633 ± 0.030 |  |
| 512 ppm     | 10                | 0.599± 0.015     | 0.185± 0.006   | 2. 418± 0. 077 | 0.646± 0.022  |  |
| 1280 ppm    | 10                | 0.596± 0.018     | 0.191± 0.008   | 2.404± 0.074   | 0.626± 0.026  |  |
| 3200 ppm    | 10                | 0.620± 0.025*    | 0.205± 0.010   | 2.532± 0.083** | 0.630± 0.016  |  |
| 8000 ppm    | 10                | 0.661± 0.027**   | 0.257± 0.009** | 2.570± 0.077** | 0.671土 0.042* |  |
| 20000 ppm   | 10                | 0.704± 0.022**   | 0.456± 0.024** | 2.972± 0.109** | 0.716± 0.029★ |  |
| Significant | difference;       | * : P ≤ 0.05 **: | P ≤ 0.01       | Test           | of Dunnott    |  |
| ICL042)     |                   |                  |                |                |               |  |

### APPENDIX K 2

ORGAN WEIGHT, RELATIVE : FEMALE

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1

SEX: FEMALE UNIT: %

ORGAN WEIGHT: RELATIVE (SUMMARY)

SURVIVAL ANIMALS ( 14W)

PAGE: 3

| oup Name  | NO. of<br>Animals |      | Veight<br>(g) | THYMUS       | ADRENALS     | OVARIES       | HEART         | LUNGS        |  |
|-----------|-------------------|------|---------------|--------------|--------------|---------------|---------------|--------------|--|
| Control   | 10                | 160± | 8             | 0.111± 0.010 | 0.032± 0.002 | 0.065± 0.003  | 0.366± 0.016  | 0.444± 0.023 |  |
| 512 ppm   | 10                | 165± | 15            | 0.112± 0.011 | 0.032± 0.002 | 0.063± 0.008  | 0.361± 0.017  | 0.450± 0.027 |  |
| 1280 ppm  | 10                | 162± | 10            | 0.106± 0.007 | 0.031± 0.002 | 0.062± 0.004  | 0.367± 0.018  | 0.445± 0.025 |  |
| 3200 ppm  | 10                | 159± | 6             | 0.111± 0.011 | 0.030± 0.002 | 0.063± 0.011  | 0.363± 0.015  | 0.446± 0.025 |  |
| 8000 ppm  | 10                | 154土 | 10            | 0.110± 0.008 | 0.032± 0.003 | 0.063 ± 0.005 | 0.372 ± 0.014 | 0.461± 0.024 |  |
| 20000 ppm | 10                | 149士 | 9*            | 0.111± 0.013 | 0.032± 0.003 | 0.060± 0.005  | 0.390± 0.023* | 0.468± 0.023 |  |

ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]

RAT F344/DuCrlCrlj[F344/DuCrj]

REPORT TYPE : A1 SEX : FEMALE UNIT: % ORGAN WEIGHT: RELATIVE (SUMMARY)
SURVIVAL ANIMALS ( 14W)

| oup Name  | NO. of<br>Animals | KIDNEYS        | SPLEEN         | LIVER          | BRAIN        |  |
|-----------|-------------------|----------------|----------------|----------------|--------------|--|
| Control   | 10                | 0.664± 0.028   | 0.235± 0.012   | 2.335± 0.086   | 1.127± 0.072 |  |
| 512 ppm   | 10                | 0.670± 0.040   | 0.231± 0.009   | 2.315± 0.080   | 1.100± 0.089 |  |
| 1280 ppm  | 10                | 0.661± 0.026   | 0.236± 0.011   | 2.390± 0.147   | 1.120± 0.062 |  |
| 3200 ррш  | 10                | 0.665± 0.027   | 0.257± 0.019   | 2.407± 0.083   | 1.130± 0.051 |  |
| 8000 ppm  | 10                | 0.689生 0.040   | 0.299± 0.009** | 2.517± 0.093** | 1.150± 0.067 |  |
| 20000 ppm | 10                | 0.734± 0.016** | 0.498± 0.020★★ | 2.990± 0.132** | 1.192± 0.065 |  |

(HCL042)

BAIS 4

## APPENDIX L 1

HISTOPATHOLOGICAL FINDINGS:

NON-NEOPLASTIC LESIONS : MALE

HISTOPATHOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

: RAT F344/DuCrlCrlj[F344/DuCrj]

REPORT TYPE : A1

ANIMAL

SEX

: MALE

ALL ANIMALS (0- 14W)

Group Name Control 512 ppm 1280 ppm 3200 ppm No. of Animals on Study 10 10 10 10 Grade 3 3 (%) Findings\_ (%) (%) (%) (%) (%) (%) (%) (%) {Respiratory system} nasal cavit <10> <10> <10> <10> 0 0 inflammation: foreign body 0 0 0 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) respiratory metaplasia:gland 3 0 0 0 0 0 0 0 5 0 0 0 3 0 0 0 (30) (0) (0) (0) (0)(0)(0)(0) (50) (0) (0) (0) (30) (0) (0) (0) lung <10> <10> <10> <10> 0 0 hemorrhage 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (10) (0) (0) (0) (0)(0)(0)(0) accumulation of foamy cells 0 0 0 0 0 0 (10) (0) (0) (0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) {Hematopoietic system} spleen <10> <10> <10> <10> 0 0 deposit of hemosiderin 0 0 0 0 0 0 0 0 10 0 0 0 \*\* (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (100) ( 0) ( 0) ( 0) extramedullary hematopoiesis 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) (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 Significant difference ; \* :  $P \le 0.05$  \*\* :  $P \le 0.01$  Test of Chi Square

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

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1

SEX : MALE

| Organ                               | No   | oup Name 8000 ppm of Animals on Study 10 ade 1 2 3 4 (%) (%) (%) (%) | 20000 ppm<br>10<br>1 2 3 4<br>(%) (%) (%) (%) |  |
|-------------------------------------|--|--|---|--|
| {Respiratory                        | system}  |  |   |  |
| nasal cavit                         | inflammation:foreign body  | <10> 2 0 0 0 ( 20) ( 0) ( 0) ( 0)                                    | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)        |  |
|                                     | respiratory metaplasia:gland   | 2 0 0 0 (20) (20) (0) (0)  | 4 0 0 0<br>(40) ( 0) ( 0) ( 0)                |  |
| lung                                | hemorrhage   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                       | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)        |  |
|                                     | accumulation of foamy cells  | 0 0 0 0 0 (0)  | 0 0 0 0 0 ( 0) ( 0)                           |  |
| {Hematopoieti                       | ic system)   |  |   |  |
| spleen                              | deposit of hemosiderin   | 10 0 0 0 **<br>(100) ( 0) ( 0) ( 0)                                  | 10 0 0 0 **<br>(100) ( 0) ( 0) ( 0)           |  |
|                                     | extramedullary hematopoiesis   | 10 0 0 0 *** (100) ( 0) ( 0) ( 0)                                    | 10 0 0 0 *** (100) ( 0) ( 0) ( 0)             |  |
| Grade <u>&gt; b (c) Significant</u> | 1: Slight 2: Moderate 3: a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 difference; *: $P \le 0.05$ **: $P \le 0$ |  |   |  |

(HPT150)

: RAT F344/DuCrlCrlj[F344/DuCrj]

HISTOPATHOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0- 14W)

REPORT TYPE : A1 SEX : MALE

ANIMAL

512 ppm Group Name Control 1280 ppm 3200 ppm No. of Animals on Study 10 10 10 10 Grade Findings\_ (%) (%) (%) (%) (%) (Hematopoietic system) spleen <10> <10> <10> engorgement of erythrocyte 0 0 0 0 0 0 0 0 0 10 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (100) ( 0) ( 0) ( 0) {Circulatory system} heart <10> inflammatory infiltration 0 0 0 0 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (10) (0) (0) (0) (0)(0)(0)(0) {Digestive system} stomach <10> <10> <10> 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) hyperplasia: 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) liver <10> <10> <10> <10> hermiation 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 (0).(0)(0)(0) (20) (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 ь b: Number of animals with lesion (c) c:b/a \* 100 Significant difference;  $*: P \le 0.05$   $**: P \le 0.01$  Test of Chi Square

(HPT150)

: RAT F344/DuCrlCrlj[F344/DuCrj]

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

HISTOPATHOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0- 14W)

REPORT TYPE : A1 SEX : MALE

ANIMAL

Group Name 20000 ppm 8000 ppm No. of Animals on Study 10 10 Grade Organ\_ Findings\_ (%) (%) (%) (%) (Hematopoietic system) spleen <10> engorgement of erythrocyte 0 0 0 \*\* (100) ( 0) ( 0) ( 0) (0)(100)(0)(0) {Circulatory system} heart inflammatory infiltration 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) {Digestive system} stomach <10> ulcer:forestomach 0 0 0 (0)(0)(0)(0) (0)(10)(0)(0) hyperplasia: forestomach 0 \*\* (30) (70) (0) (0) (0)(0)(100)(0) liver <10> <10> herniation 0 0 0 1 0 0 0 (20) (0) (0) (0) (10) (0) (0) (0) Grade l : Slight 2 : Moderate 3 : Marked 4 : Severe くぉ> a : Number of animals examined at the site b b: Number of animals with lesion (c) c : b / a \* 100

(HPT150)

: RAT F344/DuCrlCrlj[F344/DuCrj]

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

REPORT TYPE : A1

ANIMAL

SEX : MALE

Group Name Control 512 ppm 1280 ppm 3200 ppm No. of Animals on Study 10 10 10 10 Grade 3 Organ\_ Findings\_ (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (Digestive system) liver <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) granulation 0 0 0 0 0 0 0 0 (10) (0) (0) (0) (10) (0) (0) (0) (0)(0)(0)(0) (0)(0)(0)(0) (Urinary system) kidney <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) eosinophilic body 10 0 0 0 10 0 0 0 10 10 0 (100) ( 0) ( 0) ( 0) (100) ( 0) ( 0) ( 0) (100) ( 0) ( 0) ( 0) (100) ( 0) ( 0) ( 0) urin bladd <10> <10> <10> <10> squamous cell metaplasia 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) transitional cell hyperplasia 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 b (c) c:b/a \* 100 Significant difference ; \* :  $P \le 0.05$  \*\* :  $P \le 0.01$  Test of Chi Square

ANIMAL

HISTOPATHOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

: RAT F344/DuCr1Cr1j[F344/DuCrj]

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

ALL ANIMALS (0- 14W)

REPORT TYPE : A1
SEX : MALE

Group Name mqq 0008 20000 ppm No. of Animals on Study 10 10 Grade Organ\_ Findings\_ (%) (%) (%) (%) (%) (%) (Digestive system) liver <10> deposit of hemosiderin 0 0 0 10 0 0 0 \*\* (0)(0)(0)(0) (100) ( 0) ( 0) ( 0) granulation 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) {Urinary system} kidnev <10>> <10> deposit of hemosiderin 0 0 \*\* 10 0 0 0 \*\* (100) ( 0) ( 0) ( 0) (70) (0) (0) (0) eosinophilic body 0 0 10 0 0 0 (100) ( 0) ( 0) ( 0) (100) ( 0) ( 0) ( 0) urin bladd <10> <10> squamous cell metaplasia 0 0 0 0 1 0 0 0 (0)(0)(0)(0) (10) (0) (0) (0) transitional cell hyperplasia 0 0 0 0 4 5 0 0 \*\* (0)(0)(0)(0) (40) (50) (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)

ANIMAL

: RAT F344/DuCrlCrlj[F344/DuCrj]

HISTOPATHOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0- 14W)

REPORT TYPE : A1

SEX : MALE

Group Name Control 512 ppm 3200 ppm 1280 ppm No. of Animals on Study 10 10 10 10 Grade Findings\_ (%) (%) (%) (%) (%) (Urinary system) urin bladd <10> <10> <10> swelling:transitional epithelium 0 0 0 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) {Endocrine system} pituitary <10> <10> Rathke pouch 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) adrenal <10> <10> <10> <10> hyperplasia:cortical cell 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(10)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (Reproductive system) prostate <10> <10> <10> inflammatory infiltration 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (10) (0) (0) (0) (0)(0)(0)(0) 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:b/a\*100 Significant difference ; \* :  $P \le 0.05$  \*\* :  $P \le 0.01$  Test of Chi Square

(HPT150)

BAIS4

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0- 14W)

REPORT TYPE : A1 SEX : MALE

| Organ                                |   | Group Name 8000 ppm No. of Animals on Study 10 Grade 1 2 3 4 (%) (%) (%) (%) | 20000 ppm<br>10<br>1 2 3 4<br>(%) (%) (%) (%) |       |
|--------------------------------------|---|--|---|-------|
| {Urinary sys                         | stem}   |  |   |       |
| urin bladd                           | swelling:transitional epithelium  | ( 0) ( 0) ( 0) ( 0)  | 3 6 0 0 *** ( 30) ( 60) ( 0) ( 0)             |       |
| {Endocrine s                         | system)   |  |   |       |
| pituitary                            | Rathke pouch  | <10> 2 0 0 0 ( 20) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |       |
| adrenal                              | hyperplasia:cortical cell   | <10> 0 0 0 0 0 0 0 0 0 0 0   | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)        |       |
| {Reproductive                        | ve system)  |  |   |       |
| prostate                             | inflammatory infiltration   | <10> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |       |
| Grade <a>a&gt;</a> b (c) Significant | 1: Slight 2: Moderate 3 a: Number of animals examined at the si b: Number of animals with lesion c: b/a*100 difference; *: P ≤ 0.05 **: P ≤ |  |   |       |
| (HPT150)                             |   |  |   | RATSA |

### APPENDIX L 2

HISTOPATHOLOGICAL FINDINGS:

NON-NEOPLASTIC LESIONS : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj] ALL ANIMALS (0- 14W)

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

REPORT TYPE : A1

SEX : FEMALE

Odinithin dan

| Organ         | Findings                     | Group Name   Control No. of Animals on Study   10   Grade   1   2   3   4     (%)   (%)   (%)   (%) | 512 ppm<br>10<br>1 2 3 4<br>(%) (%) (%) (%) | 1280 ppm<br>10<br>1 2 3 4<br>(%) (%) (%) | 3200 ppm<br>10<br>1 2 3 4<br>(%) (%) (%) (%) |
|---------------|------------------------------|---|---|--|--|
| {Respiratory  | system)                      |   |   |  |  |
| nasal cavit   | inflammatory infiltration    | (10)<br>1 0 0 0<br>(10) (0) (0) (0)   | (10)<br>1 0 0 0<br>( 10) ( 0) ( 0) ( 0)     | (10)<br>1 0 0 0<br>(10) (0) (0) (0)      | (10)<br>1 0 0 0<br>( 10) ( 0) ( 0) ( 0)      |
|               | respiratory metaplasia:gland | 4 0 0 0<br>(40) ( 0) ( 0) ( 0)  | 4 0 0 0<br>(40) ( 0) ( 0) ( 0)              | 0 0 0 0 0 (0) (0) (0)                    | 0 0 0 0 0 (0) (0)                            |
| lung          | inflammatory infiltration    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0 0<br>0 0 0 0                        | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |
| {Hematopoieti | c system)                    |   |   |  |  |
| bone marrow   | granulation                  | 1 0 0 0 0 (10) (10) (0) (0)   | (10)<br>0 0 0 0<br>(0) (0) (0) (0)          | (10)<br>0 0 0 0<br>(0) (0) (0) (0)       | 0 I 0 0 0 (0) (0)                            |
| spleen        | deposit of hemosiderin       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | (10)<br>0 0 0 0<br>(0) (0) (0) (0)          | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | (10)<br>10 0 0 0 ***<br>(100) ( 0) ( 0) ( 0) |
|               | extramedullary 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)                          |

HISTOPATHOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1

ALL ANIMALS (0- 14W)

| INDI OILI | 1111 | ٠ | nı     |
|-----------|------|---|--------|
| SEX       |      | : | FEMALE |

| Organ               | No  | oup Name 8000 ppm  of Animals on Study 10  ade 1 2 3 4 (%) (%) (%) (%)                 | 20000 ppm<br>10<br>1 2 3 4<br>(%) (%) (%) (%)  |  |
|---------------------|---|--|--|--|
| (Respiratory        | system)   |  |  |  |
| nasal cavit         | inflammatory infiltration   | 1 0 0 0<br>( 10) ( 0) ( 0) ( 0)  | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |  |
|                     | respiratory metaplasia:gland  | 2 0 0 0 0 (20) ( 20) ( 0) ( 0)   | 2 0 0 0<br>(20) (0) (0) (0)  |  |
| lung                | inflammatory infiltration   | ( 0) ( 0) ( 0) ( 0)<br>0 0 0 0<br><10>   | 1 0 0 0<br>(10) (0) (0) (0)  |  |
| {Hematopoiet        | ic system)  |  |  |  |
| bone marrow         | granulation   | <10> 2 0 0 0 ( 20) ( 0) ( 0) ( 0)  | \( \lambda 10 \) \( \lambda 0 \) \( \lambda 10 \) \( \lambda 10 \) \( \lambda 10 \) \( \lambda 0 \) \( \lambda |  |
| spleen              | deposit of hemosiderin  | \( \lambda 10 \rangle \) \( 10  0  0 \rightarrow ** \) \( (100)  (0)  (0)  (0)  (0) \) | 10 0 0 0 ***<br>(100) ( 0) ( 0) ( 0)   |  |
|                     | extramedullary hematopoiesis  | 10 0 0 0 ***<br>(100) ( 0) ( 0) ( 0)   | 10 0 0 0 **<br>(100) ( 0) ( 0) ( 0)  |  |
| Grade <a> b (c)</a> | 1: Slight 2: Moderate 3: a: Number of animals examined at the sit b: Number of animals with lesion c: b/a * 100 | Marked 4 : Severe  |  |  |

(HPT150)

HISTOPATHOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj] ALL ANIMALS (0- 14W)

REPORT TYPE : A1 SEX

: FEMALE

| Organ               | No   | Oup Name         Control           of Animals on Study         10           ade         1         2         3           (%)         (%)         (%) | 512 ppm<br>10<br>4 1 2 3 4<br>(%) (%) (%) (%) | 1280 ppm<br>10<br>1 2 3 4<br>(%) (%) (%) (%) | 3200 ppm<br>10<br>1 2 3 4<br>(%) (%) (%) (%) |
|---------------------|--|---|---|--|--|
| {Hematopoieti       | c system)  |   |   |  |  |
| spleen              | engorgement of erythrocyte   | (10)<br>0 0 0<br>( 0) ( 0) ( 0) (   | 0       | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)       | (10)<br>10 0 0 0 ***<br>(100) ( 0) ( 0) ( 0) |
| {Digestive sy       | stem)  |   |   |  |  |
| stomach             | erosion:forestomach  | (10)<br>0 0 0<br>( 0) ( 0) ( 0) (   | 0 0 0 0 0 0<br>0) ( 0) ( 0) ( 0) ( 0)         | <10> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0           | <pre></pre>                                  |
|                     | ulcer:forestomach  | 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 0 0 (0) (0)                            | 0 0 0 0 0 ( 0) ( 0)                          |
| large intes         | mineralization   | \( \lambda 10 > \) \( 1 \) \( 0 \) \( 10 \) \( 0 \) \( 0 \) \( 0 \)   | 0 0 0 0 0<br>0) ( 0) ( 0) ( 0) ( 0)           | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)       | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)       |
| liver               | herniation   | 2 0 0 (20) (0) (0) (  | 0 4 0 0 0<br>0) (40) (0) (0) (0)              | 1 0 0 0<br>( 10) ( 0) ( 0) ( 0)              | (10)<br>1 0 0 0<br>(10) (0) (0) (0)          |
| Grade <a> b (c)</a> | 1: Slight 2: Moderate 3: a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 | Marked 4: Severe  |   |  |  |

HISTOPATHOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0- 14W)

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj] REPORT TYPE : A1

SEX : FEMALE

PAGE: 12

| Organ                           |   | oup Name 8000 ppm of Animals on Study 10 ade 1 2 3 4 (%) (%) (%) (%) | 20000 ppm<br>10<br>1 2 3 4<br>(%) (%) (%) (%) |  |
|---------------------------------|---|--|---|--|
| {Hematopoieti                   | ic system)  |  |   |  |
| spleen                          | engorgement of erythrocyte  | <10> 10 0 0 0 *** (100) ( 0) ( 0) ( 0)                               | <10><br>0 10 0 0 **<br>( 0) (100) ( 0) ( 0)   |  |
| {Digestive sy                   | ystem)  |  |   |  |
| stomach                         | erosion:forestomach   | <10> 0 0 0 0 0 0 0 0 0 0 0 0 0 0                                     | <10> 2 0 0 0 (20) (0) (0) (0)                 |  |
|                                 | ulcer:forestomach   | 0 0 0 0 0 (0) (0)  | 1 1 0 0<br>(10) (10) (0) (0)                  |  |
|                                 | hyperplasia:forestomach   | 3 7 0 0 ***<br>(30) (70) (0) (0)                                     | 0 0 10 0 *** ( 0) ( 0) (100) ( 0)             |  |
| large intes                     | mineralization  | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                               | <10> 0 0 0 0 0 0 0 0 0 0 0 0 0                |  |
| liver                           | herniation  | <10><br>1 0 0 0<br>( 10) ( 0) ( 0) ( 0)                              | <10> 1 0 0 0 ( 10) ( 0) ( 0) ( 0)             |  |
| Grade <a> b (c) Significant</a> | 1 : Slight 2 : Moderate 3 : a : Number of animals examined at the site b : Number of animals with lesion c : b / a * 100 difference ; * : $P \le 0.05$ ** : $P \le 0$ | Marked 4: Severe  01 Test of Chi Square                              |   |  |
| (HPT150)                        | ·   |  |   |  |

(Digestive system)

{Urinary system}

kidney

liver

ANIMAL

HISTOPATHOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

: RAT F344/DuCrlCrlj[F344/DuCrj]

ALL ANIMALS (0- 14W)

REPORT TYPE : A1 : FEMALE SEX

Findings\_

granulation

hyaline cast

3200 ppm Group Name Control 512 ppm 1280 ppm No. of Animals on Study 10 10 10 10 Grade (%) (%) (%) (%) (%) (%) <10> <10> <10> 0 0 0 0 0 0 0 0 0 0 0 0 0 deposit of hemosiderin (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) 1 0 0 0 1 0 0 0 0 0 0 (10) (0) (0) (0) (10) (0) (0) (0) (10) (0) (0) (0) (20) (0) (0) (0) <10> <10> <10> 0 0 0 0 0 0 0 0 0 0 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)(0) (0)(0)(0)(0) (0)(0)(0)(0) 2 0 0 0 0 0 0 0 1 0 0 0 mineralization:cortico-medullary junction 2 0 0 0 (20) (0) (0) (0) (0)(0)(0)(0) (10) (0) (0) (0) (20) (0) (0) (0) <10> <10> <10> <10> 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 : Number of animals examined at the site < a >

swelling:transitional epithelium

b: Number of animals with lesion

(c) c:b/a \* 100

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

0 0 0

(0)(0)(0)(0)

(HPT150)

b

urin bladd

(0)(0)(0)(0)

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

PAGE: 14

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]

REPORT TYPE : A1

ALL ANIMALS (0- 14W)

SEX : FEMALE

| Organ                              | Group Nome<br>No. of Anim<br>Grade<br>Findings   | 8000 ppm nals on Study 10 10 1 2 3 4 (%) (%) (%) | 20000 ppm<br>10<br>1 2 3 4<br>(%) (%) (%) (%)  |  |
|------------------------------------|--|--|--|--|
| {Digestive sy                      | vstem)   |  |  |  |
| liver                              | deposit of hemosiderin   | (0) (0) (0) (0)                                  | (10)<br>10   |  |
|                                    | granulation  | 1 0 0 0 0 (10) (10) (10)                         | 0 0 0 0 0 (0) (0)  |  |
| {Urinary syst                      | tem)   |  |  |  |
| kidney                             | deposit of hemosiderin   | 9 0 0 0 **<br>( 90) ( 0) ( 0) ( 0)               | \( \lambda \) 10 \( 0 \) 0 \( 0 \) \( \text{100} \) \( \text{100} \) \( \text{0} \) \( \text{0} \) \( \text{0} \) \( \text{0} \) |  |
|                                    | hyaline cast   | 1 0 0 0 0 (10) (10) (10)                         | 0 0 0 0 0 (0) (0) (0)  |  |
|                                    | mineralization:cortico-medullary junction  | 2 0 0 0 0 (20) (0) (0)                           | 0 0 0 0 0 (0) (0) (0)  |  |
| urin bladd                         | swelling:transitional epithelium   | (10)<br>0 0 0 0<br>(0) (0) (0) (0)               | <10> 4 1 0 0 * (40) (10) (0) (0)   |  |
| Grade <a> b (c) Significant of</a> | I: Slight 2: Moderate 3: Marked a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 difference; *: P ≤ 0.05 **: P ≤ 0.01 | 4 : Severe                                       |  |  |

HISTOPATHOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]

REPORT TYPE : A1
SEX : FEMALE

ALL ANIMALS (0- 14W)

| rganFindings              | Group Name<br>No. of Anim<br>Grade | Control als on Study 10  1 2 3  (%) (%) (%) | 4 <u>1</u> (%) | 512 ppm<br>10<br>2 3 4<br>(%) (%) (%) | 1280 ppm<br>10<br>1 2 3 4<br>(%) (%) (%) (%) | 3200 ppn<br>10<br>1 2 3 4<br>(%) (%) (%) (%) |
|---------------------------|------------------------------------|---|----------------|---------------------------------------|--|--|
| pecial sense organs/appe  | ndage)                             |   |                |                                       |  |  |
| ve<br>degenerati          | on:cornea                          | <10><br>0 0 0<br>( 0) ( 0) ( 0) (           | 0 0            | <10><br>0 0 0<br>( 0) ( 0) ( 0)       | <10><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)       | <10> 0 0 0 0 0 0 0 0 0 0 0                   |
| order gl<br>granulatio    | n                                  | 0 0 0<br>( 0) ( 0) ( 0) (                   | 0 0            | <10><br>0 0 0<br>( 0) ( 0) ( 0)       | (10)<br>i 0 0 0<br>(10) (0) (0) (0)          | (10) (0) (0) (0)                             |
| b b: Number c c : b / a * |                                    | 4 : Severe                                  |                |                                       |  |  |

HISTOPATHOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

PAGE: 16

ALL ANIMALS (0- 14W)

ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]
REPORT TYPE : A1
SEX : FEMALE

: FEMALE

| Organ                               |  | Group Name 8000 ppm  No. of Animals on Study 10  Grade 1 2 3 4  (%) (%) (%) (%) | 20000 ppm<br>10<br>1 2 3 4<br>(%) (%) (%) (%) |  |
|-------------------------------------|--|---|---|--|
| (Special ser                        | nse organs/appendage}  |   |   |  |
| eye                                 | degeneration:cornea  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | (10)<br>1 0 0 0<br>(10) (0) (0) (0)           |  |
| Harder gl                           | granulation  | 2 0 0 0<br>( 20) ( 0) ( 0) ( 0)   | ( 0) ( 0) ( 0) ( 0)<br>0 0 0 0<br>( 0) ( 0) ( |  |
| Grade <a>&gt; b (c) Significant</a> | I: Slight 2: Moderate 3 a: Number of animals examined at the si b: Number of animals with lesion c: b / a * 100 difference; * : P ≤ 0.05 **: P ≤ |   |   |  |
| (HPT150)                            |  |   |   |  |

#### 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<br>place |
|--|--|------------------------------|------------------|
| Hematology   |  |                              |                  |
| Red blood cell (RBC)                               | Light scattering method <sup>1)</sup>            | $	imes 10^6/\mu\mathrm{L}$   | 2                |
| Hemoglobin(Hgb)                                    | Cyanmethemoglobin method 1)                      | g/dL                         | 1                |
| Methemoglobin                                      | Multiple-wavelength Spectrophotometric method 4) | %                            | 1                |
| Hematocrit(Hct)                                    | Calculated as RBC×MCV/10 10                      | %                            | 1                |
| Mean corpuscular volume(MCV)                       | Light scattering method 1)                       | fL                           | 1                |
| Mean corpuscular hemoglobin(MCH)                   | Calculated as Hgb/RBC×10 <sup>1)</sup>           | pg                           | 1                |
| Mean corpuscular hemoglobin concentration          | Calculated as Hgb/Hct×100 1)                     | g/dL                         | 1                |
| (MCHC)   |  |                              |                  |
| Platelet   | Light scattering method 1)                       | $	imes 10^3 / \mu  	ext{L}$  | 0                |
| Reticulocyte                                       | Light scattering method 1)                       | %                            | 1                |
| White blood cell(WBC)                              | Light scattering method 1)                       | $	imes 10^3 / \mu\mathrm{L}$ | 2                |
| Differential WBC                                   | Pattern recognition method 2)                    | %                            | 0                |
|  | (Wright staining)                                |                              |                  |
| Biochemistry                                       |  |                              |                  |
| Total protein(TP)                                  | Biuret method 3)                                 | g/dL                         | 1                |
| Albumin (Alb)                                      | BCG method 3)                                    | g/dL                         | 1                |
| A/G ratio  | Calculated as Alb/(TP-Alb) 3)                    |                              | 1                |
| T-bilirubin  | Alkaline azobilirubin method 3)                  | mg/dL                        | 2                |
| Glucose  | GlcK·G-6-PDH method 3)                           | mg/dL                        | 0                |
| T-cholesterol                                      | CE·COD·POD method 3)                             | mg/dL                        | 0                |
| Triglyceride                                       | LPL·GK·GPO·POD method 3)                         | mg/dL                        | 0                |
| Phospholipid                                       | PLD·ChOD·POD method 3)                           | mg/dL                        | 0                |
| Aspartate aminotransferase (AST)                   | JSCC method 3)                                   | IU/L                         | 0                |
| Alanine aminotransferase (ALT)                     | JSCC method 3)                                   | IU/L                         | 0                |
| Lactate dehydrogenase (LDH)                        | SFBC method 3)                                   | IU/L                         | 0                |
| Alkaline phosphatase (ALP)                         | GSCC method 3)                                   | IU/L                         | 0                |
| $\gamma$ -Glutamyl transpeptidase ( $\gamma$ -GTP) | JSCC method 3)                                   | IU/L                         | 0                |
| Creatine kinase (CK)                               | JSCC method 3)                                   | IU/L                         | 0                |
| Urea nitrogen                                      | Urease GLDH method 3)                            | mg/dL                        | 1                |
| Creatinine   | Jaffe 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 3)                | mEq/L                        | 0                |
| Calcium  | OCPC method 3)                                   | mg/dL                        | 1                |
| Inorganic phosphorus                               | PNP·XOD·POD method 3)                            | 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.)
- 4) CO-oximeter (CIBA · CORNING 270 : Bayer Corporation)