

1,2-ジクロロプロパンのマウスを用いた  
吸入によるがん原性試験報告書

試験番号：0458

# APPENDICES

## APPENDICES

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## APPENDIX A 1

### IDENTITY OF 1,2-DICHLOROPROPANE IN THE 2-YEAR INHALATION STUDY

## IDENTITY OF 1,2-DICHLOROPROPANE IN THE 2-YEAR INHALATION STUDY

Test Substance : 1,2-Dichloropropane (Wako Pure Chemical Industries, Ltd.)

A. Lot No. : WAH4634

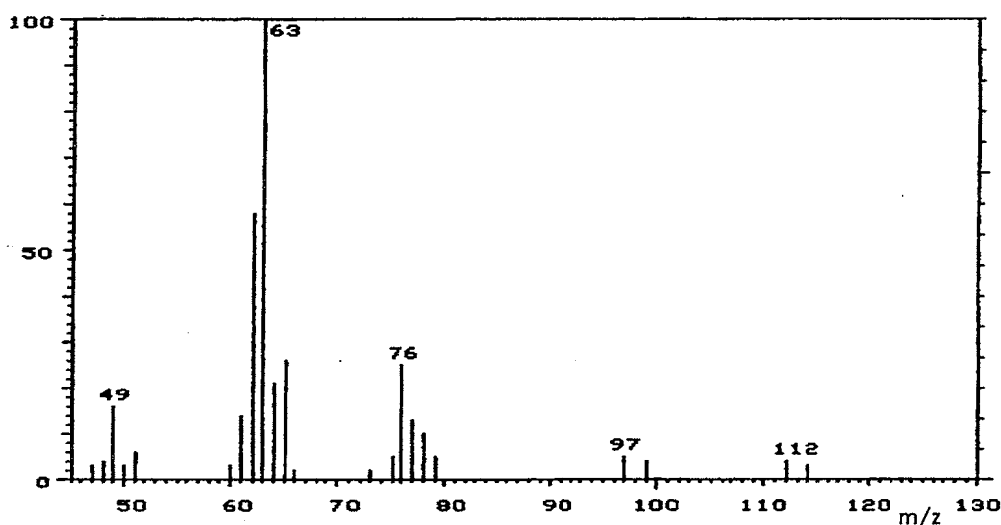
## 1. Spectral Data

Mass Spectrometry

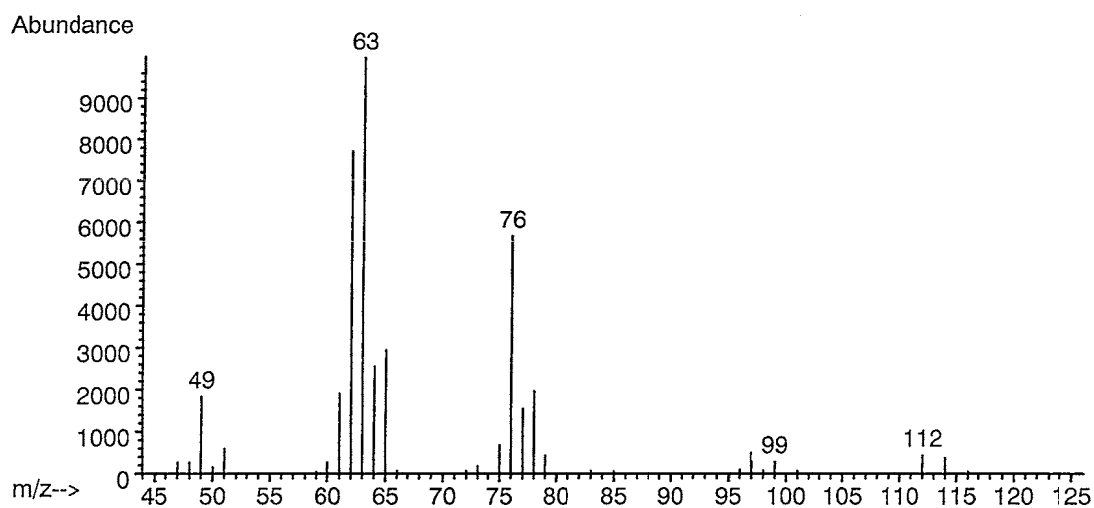
Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance



Mass Spectrum of Literature Data\*

Result: The mass spectrum was consistent with literature spectrum.

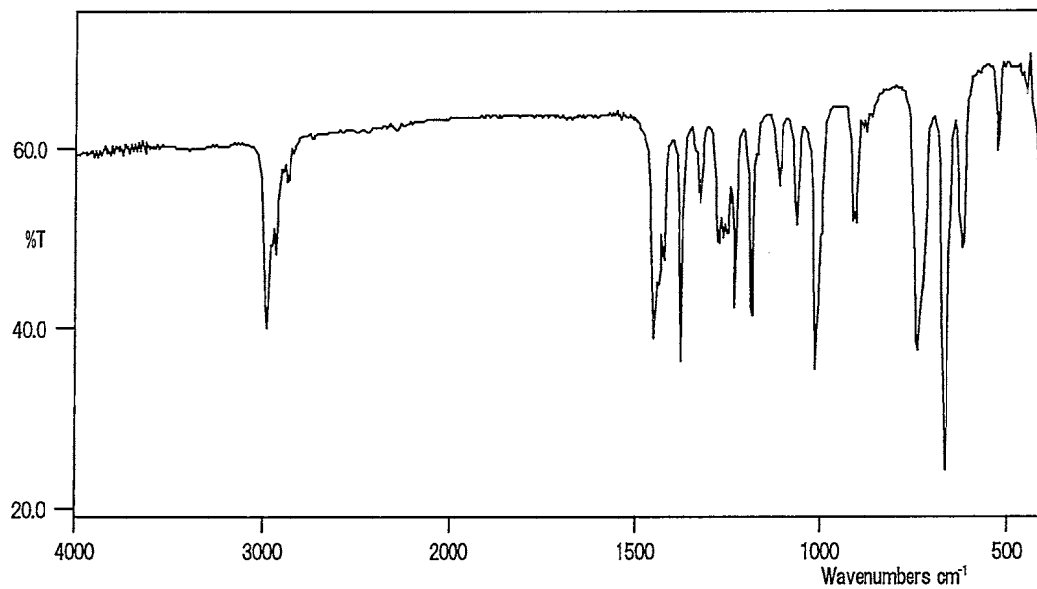
(\*McLafferty FW, ed. 1994. Wiley Registry of Mass Spectral Data. 6th ed. New York, NY:John Wiley and Sons.)

## Infrared Spectrometry

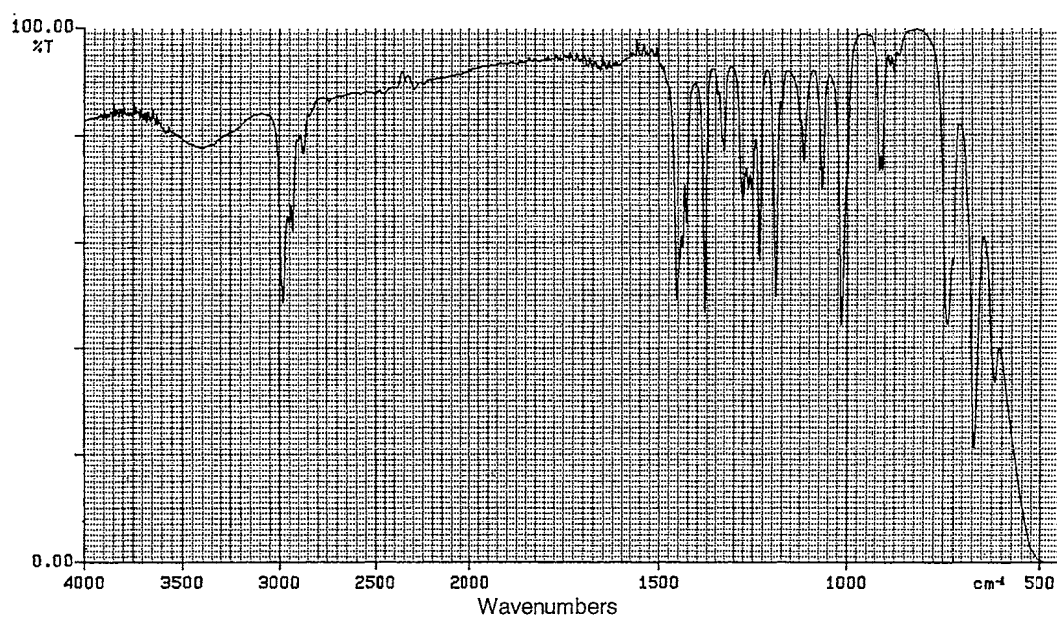
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 4  $\text{cm}^{-1}$



Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data\*

Result: The infrared spectrum was consistent with literature spectrum.

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

2. Conclusion: The test substance was identified as 1,2-dichloropropane by the mass spectrum and the infrared spectrum.

B. Lot No. : PKP5800

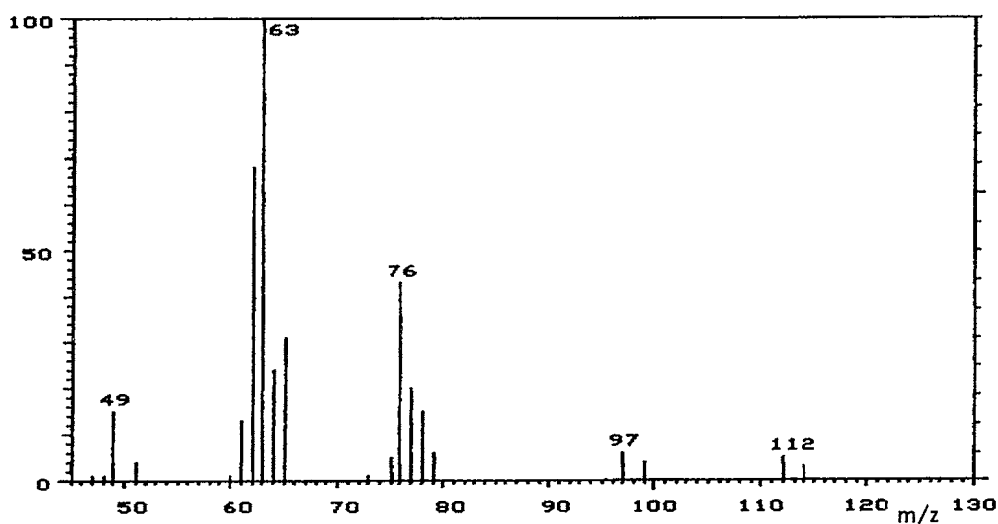
# 1. Spectral Data

## Mass Spectrometry

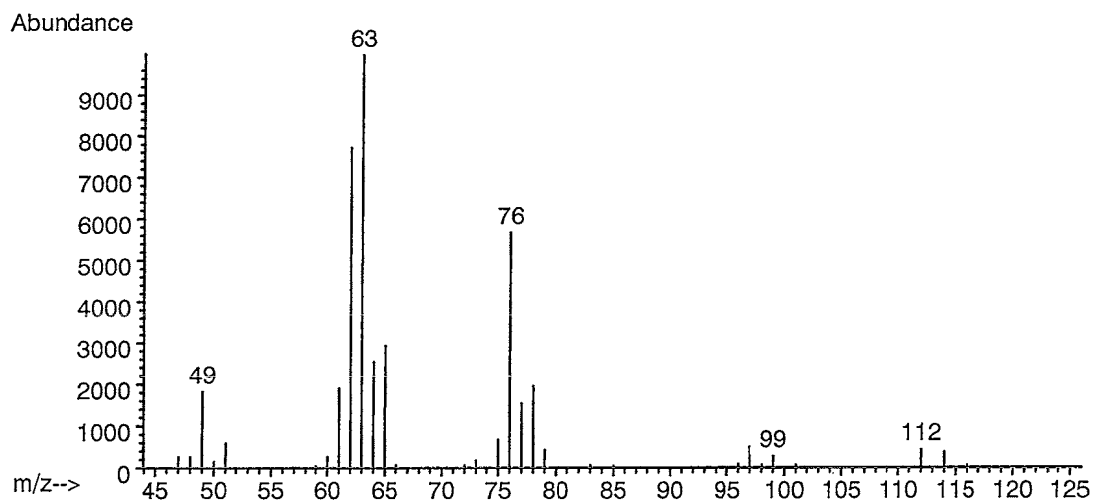
Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance



Mass Spectrum of Literature Data\*

Result: The mass spectrum was consistent with literature spectrum.

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

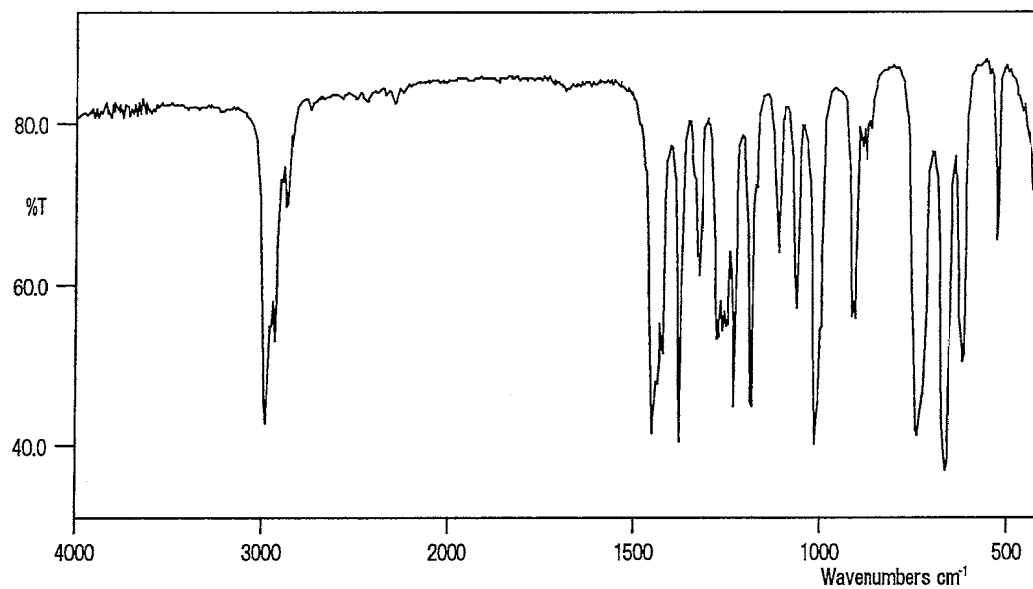


## Infrared Spectrometry

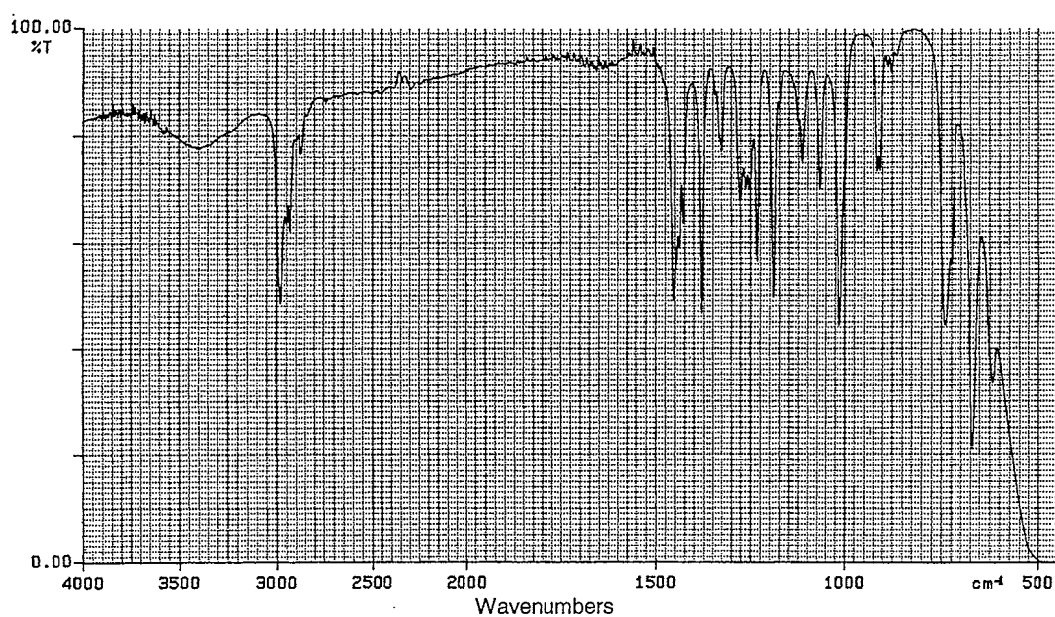
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 4  $\text{cm}^{-1}$



Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data\*

Result: The infrared spectrum was consistent with literature spectrum.  
(\*Performed by the Wako Pure Chemical Industries, Ltd.)

2. Conclusion: The test substance was identified as 1,2-dichloropropane by the mass spectrum and the infrared spectrum.

C. Lot No. : CER5780

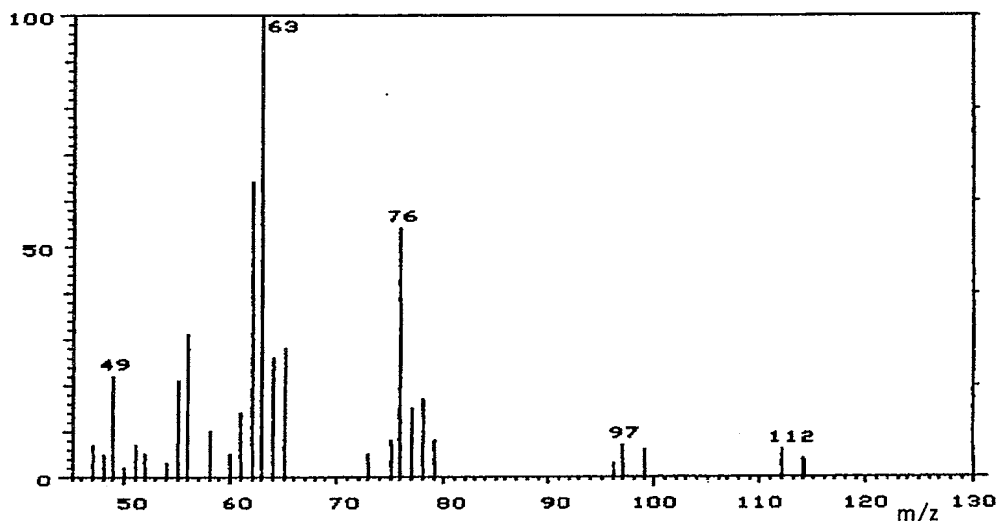
1. Spectral Data

Mass Spectrometry

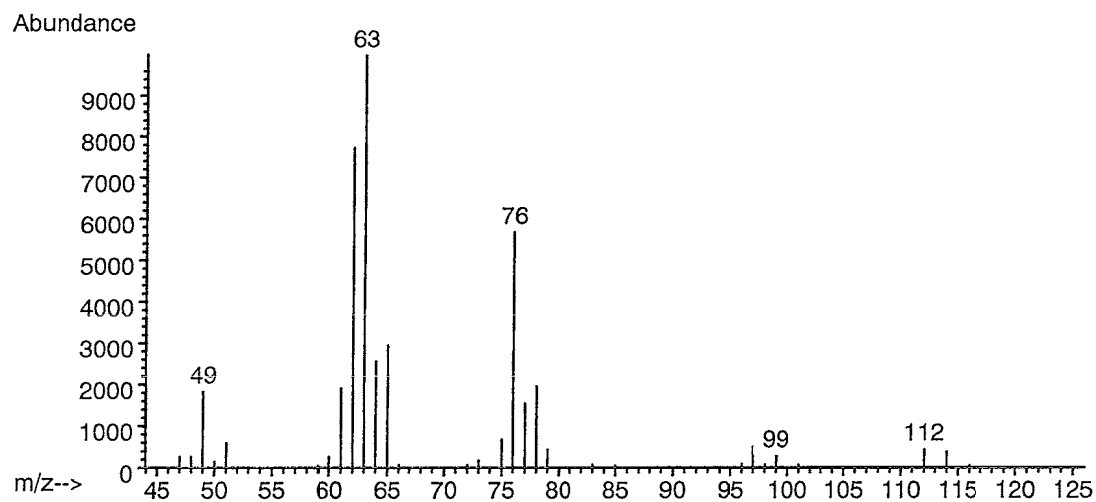
Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance



Mass Spectrum of Literature Data\*

Result: The mass spectrum was consistent with literature spectrum.

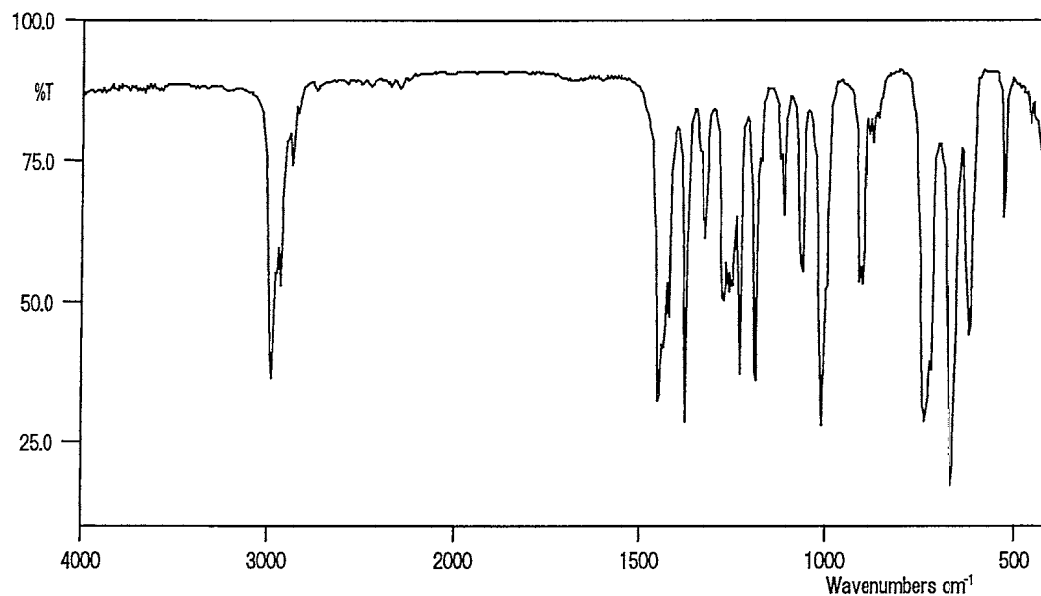
(\*McLafferty FW, ed. 1994. Wiley Registry of Mass Spectral Data. 6th ed.  
New York, NY:John Wiley and Sons.)

Infrared Spectrometry

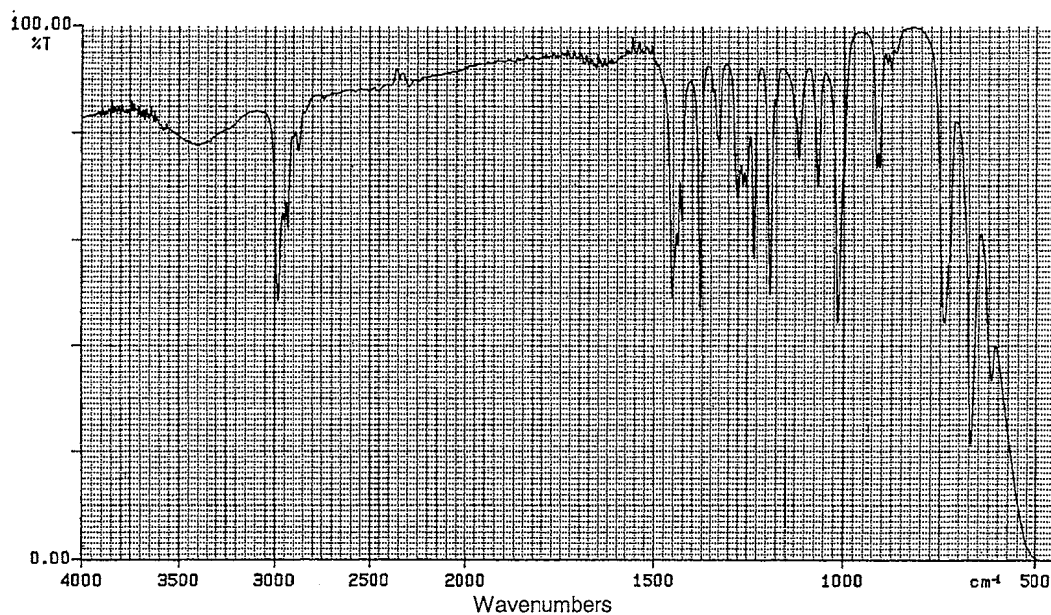
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 4  $\text{cm}^{-1}$



Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data\*

Result: The infrared spectrum was consistent with literature spectrum.

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

2. Conclusion: The test substance was identified as 1,2-dichloropropane by the mass spectrum and the infrared spectrum.

D. Lot No. : CEM1032

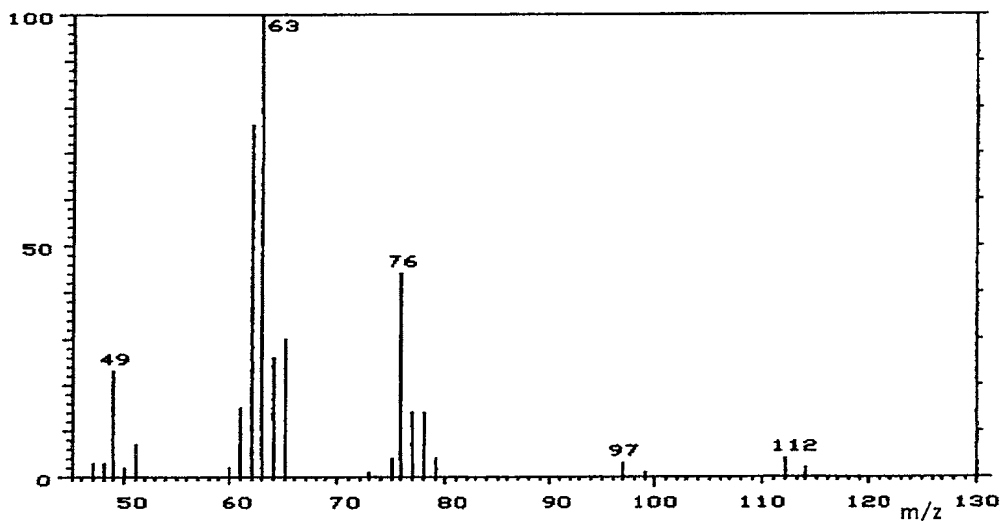
1. Spectral Data

Mass Spectrometry

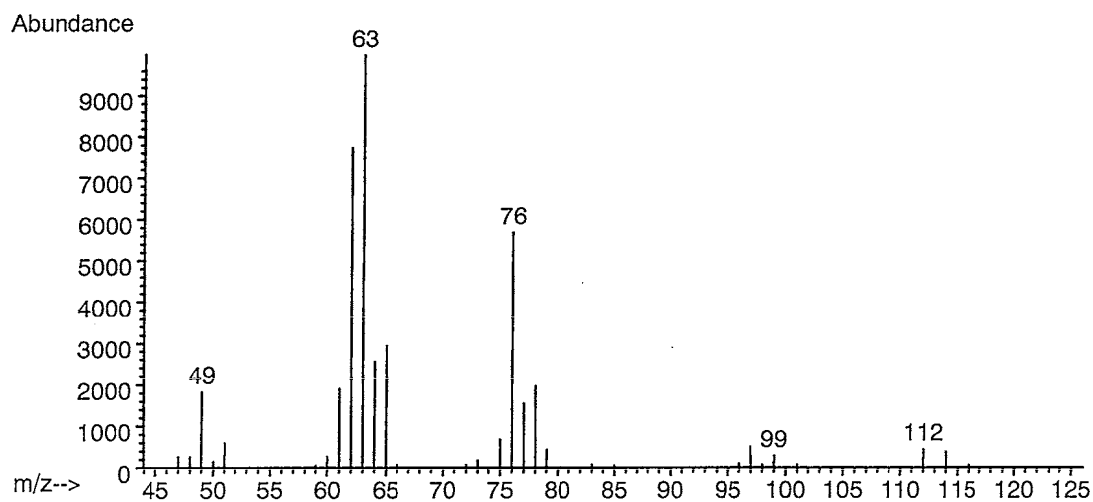
Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance



Mass Spectrum of Literature Data\*

Result: The mass spectrum was consistent with literature spectrum.

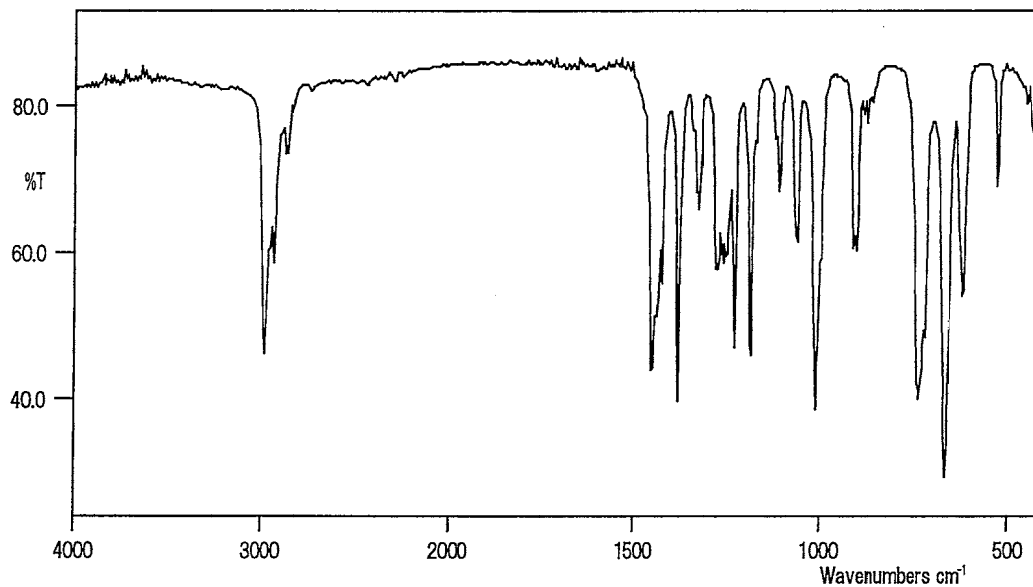
(\*McLafferty FW, ed. 1994. Wiley Registry of Mass Spectral Data. 6th ed.  
New York, NY:John Wiley and Sons.)

Infrared Spectrometry

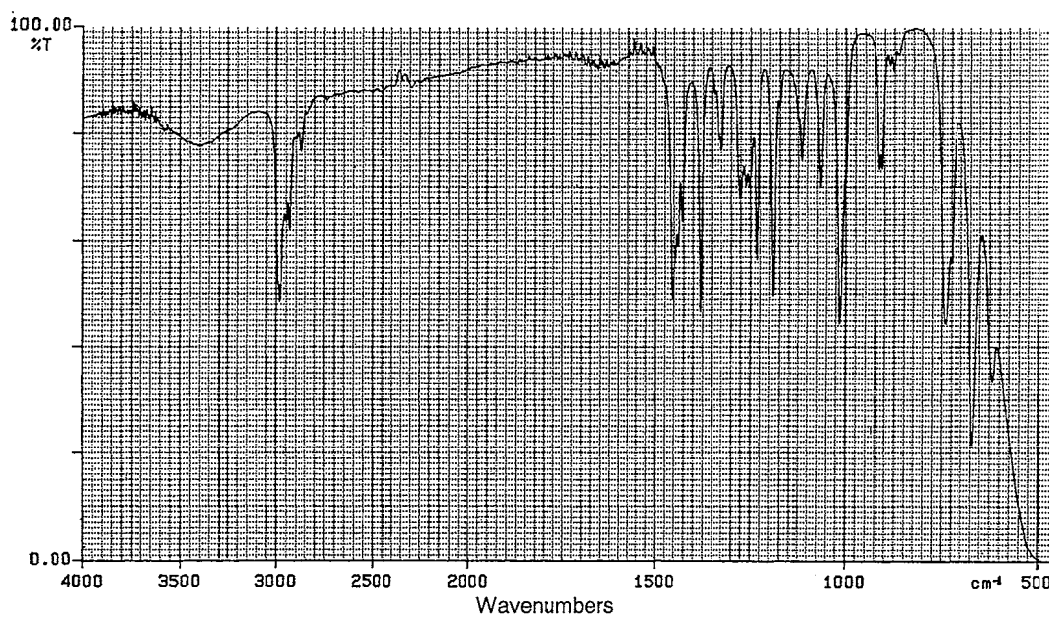
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution :  $4\text{ cm}^{-1}$



Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data\*

Result: The infrared spectrum was consistent with literature spectrum.

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

2. Conclusion: The test substance was identified as 1,2-dichloropropane by the mass spectrum and the infrared spectrum.

## APPENDIX A 2

### STABILITY OF 1,2-DICHLOROPROPANE IN THE 2-YEAR INHALATION STUDY

## STABILITY OF 1,2-DICHLOROPROPANE IN THE 2-YEAR INHALATION STUDY

Test Substance : 1,2-Dichloropropane (Wako Pure Chemical Industries, Ltd.)

A. Lot No. : WAH4634

1. Sample : This lot was used from 2002.10.25 to 2003.5.12. Test substance was stored in a dark place at room temperature.

## 2. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : Methyl Silicone ( 0.53 mm  $\phi$   $\times$  60 m)

Column Temperature: 100° C

Flow Rate : 15 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1  $\mu$ L

| Date<br>(date analyzed) | Peak No. | Retention Time<br>(min) | Area<br>(%) |
|-------------------------|----------|-------------------------|-------------|
| 2002.10.17              | 1        | 3.474                   | 99.97       |
|                         | 2        | 4.875                   | 0.03        |
| 2003.05.14              | 1        | 3.475                   | 99.97       |
|                         | 2        | 4.872                   | 0.03        |

Result: Gas chromatography indicated one major peak (peak No.1) and one impurity (peak No. 2 < 0.5% of total area) analyzed on 2002.10.17 and one major peak (peak No.1) and one impurity (peak No. 2 < 0.5% of total area) analyzed on 2003.5.14. No new trace impurity peak in the test substance analyzed on 2003.5.14 was detected.

3. Conclusion: The test substance was stable for about 6 months in a dark place at room temperature.

B. Lot No. : PKP5800

1. Sample : This lot was used from 2003.5.13 to 2004.3.2. Test substance was stored in a dark place at room temperature.

2. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : Methyl Silicone ( 0.53 mm $\phi$   $\times$  60 m)

Column Temperature: 100° C

Flow Rate : 15 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1  $\mu$ L

| Date<br>(date analyzed) | Peak No. | Retention Time<br>(min) | Area<br>(%) |
|-------------------------|----------|-------------------------|-------------|
| 2003.05.12              | 1        | 3.476                   | 99.99       |
|                         | 2        | 4.873                   | 0.01        |
| 2004.03.08              | 1        | 3.406                   | 99.99       |
|                         | 2        | 4.775                   | 0.01        |

Result: Gas chromatography indicated one major peak (peak No.1) and one impurity (peak No. 2 < 0.5% of total area) analyzed on 2003.5.12 and one major peak (peak No.1) and one impurity (peak No. 2 < 0.5% of total area) analyzed on 2004.3.8. No new trace impurity peak in the test substance analyzed on 2004.3.8 was detected.

3. Conclusion: The test substance was stable for about 9 months in a dark place at room temperature.



C. Lot No. : CER5780

1. Sample : This lot was used from 2004.3.3 to 2004.7.13. Test substance was stored in a dark place at room temperature.

2. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : Methyl Silicone ( 0.53 mm  $\phi$   $\times$  60 m)

Column Temperature: 100° C

Flow Rate : 15 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1  $\mu$ L

| Date<br>(date analyzed) | Peak No. | Retention Time<br>(min) | Area<br>(%) |
|-------------------------|----------|-------------------------|-------------|
| 2004.03.02              | 1        | 3.412                   | 99.81       |
|                         | 2        | 4.781                   | 0.19        |
| 2004.07.16              | 1        | 3.359                   | 99.81       |
|                         | 2        | 4.715                   | 0.19        |

Result: Gas chromatography indicated one major peak (peak No.1) and one impurity (peak No. 2 < 0.5% of total area) analyzed on 2004.3.2 and one major peak (peak No.1) and one impurity (peak No. 2 < 0.5% of total area) analyzed on 2004.7.16. No new trace impurity peak in the test substance analyzed on 2004.7.16 was detected.

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

D. Lot No. : CEM1032

1. Sample : This lot was used from 2004.7.14 to 2004.10.21. Test substance was stored in a dark place at room temperature.

2. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : Methyl Silicone ( 0.53 mm $\phi$   $\times$  60 m)

Column Temperature: 100° C

Flow Rate : 15 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1  $\mu$ L

| Date<br>(date analyzed) | Peak No. | Retention Time<br>(min) | Area<br>(%) |
|-------------------------|----------|-------------------------|-------------|
| 2004.07.13              | 1        | 3.363                   | 99.98       |
|                         | 2        | 4.719                   | 0.02        |
| 2004.11.02              | 1        | 3.359                   | 99.98       |
|                         | 2        | 4.716                   | 0.02        |

Result: Gas chromatography indicated one major peak (peak No.1) and one impurity (peak No. 2 < 0.5% of total area) analyzed on 2004.7.13 and one major peak (peak No.1) and one impurity (peak No. 2 < 0.5% of total area) analyzed on 2004.11.2. No new trace impurity peak in the test substance analyzed on 2004.11.2 was detected.

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

## APPENDIX B

# ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 2-YEAR  
INHALATION STUDY OF 1,2-DICHLOROPROPANE

| Group Name | Temperature<br>(°C) | Humidity<br>(%) | Ventilation Rate<br>(L/min) | Air Change<br>(time/h) |
|------------|---------------------|-----------------|-----------------------------|------------------------|
|            | Mean $\pm$ S.D.     | Mean $\pm$ S.D. | Mean $\pm$ S.D.             | Mean                   |
| Control    | 23.0 $\pm$ 0.0      | 53.9 $\pm$ 1.3  | 740.2 $\pm$ 6.1             | 12.0                   |
| 32 ppm     | 23.0 $\pm$ 0.0      | 56.0 $\pm$ 1.4  | 742.4 $\pm$ 5.9             | 12.0                   |
| 80 ppm     | 23.0 $\pm$ 0.1      | 55.4 $\pm$ 1.4  | 742.3 $\pm$ 6.8             | 12.0                   |
| 200 ppm    | 23.0 $\pm$ 0.1      | 55.1 $\pm$ 1.4  | 741.9 $\pm$ 7.2             | 12.0                   |

## APPENDIX C 1

### CLINICAL OBSERVATION : MALE

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : MALE

PAGE : 1

| Clinical sign      | Group Name | Administration Week-day |     |     |     |     |     |     |     |     |      |      |      |      |      |
|--------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|------|
|                    |            | 1-7                     | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 | 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 | 14-7 |
| DEATH              | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| MORIBUND SACRIFICE | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| HUNCHBACK POSITION | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| PARALYTIC GAIT     | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| ROTATING           | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| WASTING            | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| SOILED             | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| PILOBRECTION       | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 1   | 1   | 1   | 0    | 0    | 0    | 1    | 0    |
|                    | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : MALE

PAGE : 2

| Clinical sign      | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|--------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                    |            | 15-7                    | 16-7 | 17-7 | 18-7 | 19-7 | 20-7 | 21-7 | 22-7 | 23-7 | 24-7 | 25-7 | 26-7 | 27-7 | 28-7 |
| DEATH              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| MORIBUND SACRIFICE | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HUNCHBACK POSITION | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PARALYTIC GAIT     | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ROTATING           | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| WASTING            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PILOERECTION       | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : MALE

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| Clinical sign      | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|--------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                    |            | 29-7                    | 30-7 | 31-7 | 32-7 | 33-7 | 34-7 | 35-7 | 36-7 | 37-7 | 38-7 | 39-7 | 40-7 | 41-7 | 42-7 |
| DEATH              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| MORIBUND SACRIFICE | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HUNCHBACK POSITION | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PARALYTIC GAIT     | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ROTATING           | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| WASTING            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PILOERECTION       | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |



STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : MALE

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| Clinical sign      | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|--------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                    |            | 43-7                    | 44-7 | 45-7 | 46-7 | 47-7 | 48-7 | 49-7 | 50-7 | 51-7 | 52-7 | 53-7 | 54-7 | 55-7 | 56-7 |
| DEATH              | Control    | 0                       | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 2    | 2    | 2    |
|                    | 32 ppm     | 0                       | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                    | 80 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| MORIBUND SACRIFICE | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HUNCHBACK POSITION | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    | 1    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PARALYTIC GAIT     | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ROTATING           | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| WASTING            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PILOERECTION       | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : MALE

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| Clinical sign      | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|--------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                    |            | 57-7                    | 58-7 | 59-7 | 60-7 | 61-7 | 62-7 | 63-7 | 64-7 | 65-7 | 66-7 | 67-7 | 68-7 | 69-7 | 70-7 |
| DEATH              | Control    | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 3    |
|                    | 32 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                    | 80 ppm     | 1                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 3    | 3    | 3    | 3    | 3    | 3    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| MORIBUND SACRIFICE | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 1                       | 1    | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HUNCHBACK POSITION | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 1                       | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PARALYTIC GAIT     | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ROTATING           | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| WASTING            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 1                       | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PILOERECTION       | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    | 0    | 1    | 1    | 0    |
|                    | 32 ppm     | 1                       | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : MALE

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| Clinical sign      | Group Name | Administration Week-day |      |      |  | 74-7 | 75-7 | 76-7 | 77-7 | 78-7 | 79-7 | 80-7 | 81-7 | 82-7 | 83-7 | 84-7 |
|--------------------|------------|-------------------------|------|------|--|------|------|------|------|------|------|------|------|------|------|------|
|                    |            | 71-7                    | 72-7 | 73-7 |  |      |      |      |      |      |      |      |      |      |      |      |
| DEATH              | Control    | 3                       | 3    | 3    |  | 4    | 4    | 4    | 4    | 4    | 5    | 5    | 6    | 6    | 6    | 6    |
|                    | 32 ppm     | 1                       | 1    | 1    |  | 2    | 2    | 2    | 2    | 3    | 3    | 3    | 3    | 4    | 4    | 4    |
|                    | 80 ppm     | 3                       | 3    | 4    |  | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 5    | 5    | 7    |
|                    | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 3    | 3    | 3    | 3    |
| MORIBUND SACRIFICE | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 2                       | 3    | 3    |  | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    |
|                    | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HUNCHBACK POSITION | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PARALYTIC GAIT     | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ROTATING           | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| WASTING            | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED             | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PILOERECTOR        | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 1    | 1    |  | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 2    | 1    |
|                    | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    |

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : MALE

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| Clinical sign      | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|--------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                    |            | 85-7                    | 86-7 | 87-7 | 88-7 | 89-7 | 90-7 | 91-7 | 92-7 | 93-7 | 94-7 | 95-7 | 96-7 | 97-7 | 98-7 |
| DEATH              | Control    | 6                       | 6    | 7    | 7    | 8    | 8    | 8    | 8    | 8    | 8    | 8    | 9    | 11   | 12   |
|                    | 32 ppm     | 4                       | 4    | 5    | 6    | 7    | 7    | 7    | 7    | 9    | 9    | 10   | 10   | 11   | 11   |
|                    | 80 ppm     | 8                       | 9    | 9    | 9    | 9    | 9    | 9    | 9    | 9    | 10   | 11   | 12   | 12   | 13   |
|                    | 200 ppm    | 3                       | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    |
| MORIBUND SACRIFICE | Control    | 0                       | 1    | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 3    | 3    | 3    |
|                    | 32 ppm     | 3                       | 3    | 3    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 2    | 2    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
| HUNCHBACK POSITION | Control    | 0                       | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PARALYTIC GAIT     | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ROTATING           | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| WASTING            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED             | Control    | 0                       | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                    | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PILORECTION        | Control    | 1                       | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                    | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 200 ppm    | 1                       | 1    | 1    | 1    | 1    | 2    | 2    | 1    | 1    | 1    | 1    | 1    | 1    | 0    |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : MALE

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| Clinical sign      | Group Name | Administration Week-day |       |       |       |       |       |
|--------------------|------------|-------------------------|-------|-------|-------|-------|-------|
|                    |            | 99-7                    | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| DEATH              | Control    | 12                      | 12    | 13    | 13    | 15    | 15    |
|                    | 32 ppm     | 12                      | 12    | 12    | 12    | 12    | 12    |
|                    | 80 ppm     | 13                      | 13    | 13    | 14    | 15    | 15    |
|                    | 200 ppm    | 4                       | 5     | 6     | 7     | 7     | 7     |
| MORIBUND SACRIFICE | Control    | 3                       | 3     | 3     | 3     | 3     | 3     |
|                    | 32 ppm     | 4                       | 4     | 5     | 5     | 5     | 5     |
|                    | 80 ppm     | 2                       | 2     | 2     | 2     | 2     | 2     |
|                    | 200 ppm    | 2                       | 2     | 2     | 2     | 2     | 2     |
| HUNCHBACK POSITION | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                    | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                    | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                    | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 0     |
| PARALYTIC GAIT     | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                    | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                    | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                    | 200 ppm    | 1                       | 0     | 0     | 0     | 0     | 0     |
| ROTATING           | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                    | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                    | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                    | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 0     |
| WASTING            | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                    | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                    | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                    | 200 ppm    | 0                       | 0     | 1     | 0     | 0     | 0     |
| SOILED             | Control    | 1                       | 0     | 0     | 1     | 1     | 1     |
|                    | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                    | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 1     |
|                    | 200 ppm    | 1                       | 0     | 0     | 0     | 0     | 1     |
| PILORECTION        | Control    | 1                       | 0     | 0     | 0     | 0     | 0     |
|                    | 32 ppm     | 0                       | 0     | 1     | 1     | 0     | 0     |
|                    | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                    | 200 ppm    | 0                       | 1     | 2     | 1     | 1     | 1     |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : MALE

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| Clinical sign         | Group Name | Administration Week-day |     |     |     |     |     |     |     |     |      |      |      |      |      |
|-----------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|------|
|                       |            | 1-7                     | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 | 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 | 14-7 |
| TRAUMA                | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| FROG BELLY            | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| SOILED PERI-GENITALIA | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| EXOPHTHALMOS          | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| GUM                   | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 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    | 0    |
|                       | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| EXTERNAL MASS         | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| INTERNAL MASS         | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0   | 0   | 1   | 1   | 1   | 1   | 0   | 0   | 0    | 0    | 1    | 1    | 1    |
|                       | 200 ppm    | 0                       | 0   | 0   | 1   | 1   | 1   | 1   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : MALE

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| Clinical sign         | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-----------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                       |            | 15-7                    | 16-7 | 17-7 | 18-7 | 19-7 | 20-7 | 21-7 | 22-7 | 23-7 | 24-7 | 25-7 | 26-7 | 27-7 | 28-7 |
| TRAUMA                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| FROG BELLY            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED PERI-GENITALIA | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXOPHTHALMOS          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| GUM                   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 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    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXTERNAL MASS         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| INTERNAL MASS         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : MALE

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| Clinical sign         | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-----------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                       |            | 29-7                    | 30-7 | 31-7 | 32-7 | 33-7 | 34-7 | 35-7 | 36-7 | 37-7 | 38-7 | 39-7 | 40-7 | 41-7 | 42-7 |
| TRAUMA                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| FROG BELLY            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED PERI-GENITALIA | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXOPHTHALMOS          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| GUM                   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 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    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXTERNAL MASS         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| INTERNAL MASS         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 1                       | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |



STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : MALE

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| Clinical sign         | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-----------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                       |            | 43-7                    | 44-7 | 45-7 | 46-7 | 47-7 | 48-7 | 49-7 | 50-7 | 51-7 | 52-7 | 53-7 | 54-7 | 55-7 | 56-7 |
| TRAUMA                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| FROG BELLY            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED PERI-GENITALIA | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXOPHTHALMOS          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| GUM                   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 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    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXTERNAL MASS         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| INTERNAL MASS         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 1                       | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/CrJ[Crj:BDF1]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : MALE

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| Clinical sign         | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-----------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                       |            | 57-7                    | 58-7 | 59-7 | 60-7 | 61-7 | 62-7 | 63-7 | 64-7 | 65-7 | 66-7 | 67-7 | 68-7 | 69-7 | 70-7 |
| TRAUMA                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| FROG BELLY            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED PERI-GENITALIA | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXOPHTHALMOS          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| GUM                   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 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    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXTERNAL MASS         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| INTERNAL MASS         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                       | 200 ppm    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : MALE

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| Clinical sign         | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-----------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                       |            | 71-7                    | 72-7 | 73-7 | 74-7 | 75-7 | 76-7 | 77-7 | 78-7 | 79-7 | 80-7 | 81-7 | 82-7 | 83-7 | 84-7 |
| TRAUMA                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| FROG BELLY            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| SOILED PERI-GENITALIA | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXOPHTHALMOS          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| GUM                   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 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    | 1    | 1    | 1    | 1    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXTERNAL MASS         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 1                       | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| INTERNAL MASS         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                       | 80 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 2    | 2    | 2    | 2    | 3    | 3    | 3    | 2    |
|                       | 200 ppm    | 1                       | 1    | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : MALE

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| Clinical sign         | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-----------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                       |            | 85-7                    | 86-7 | 87-7 | 88-7 | 89-7 | 90-7 | 91-7 | 92-7 | 93-7 | 94-7 | 95-7 | 96-7 | 97-7 | 98-7 |
| TRAUMA                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| FROG BELLY            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 1                       | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 1    |
| SOILED PERI-GENITALIA | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXOPHTHALMOS          | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                       | 200 ppm    | 0                       | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 2    |
| GUM                   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    |
| CORNEAL OPACITY       | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
| EXTERNAL MASS         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| INTERNAL MASS         | Control    | 1                       | 1    | 1    | 0    | 2    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 3    |
|                       | 32 ppm     | 2                       | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 5    | 4    | 4    | 3    | 4    |
|                       | 80 ppm     | 1                       | 0    | 0    | 0    | 0    | 0    | 0    | 2    | 2    | 1    | 1    | 0    | 1    | 1    |
|                       | 200 ppm    | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 3    | 4    | 4    | 4    | 4    | 4    | 5    |

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : MALE

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| Clinical sign         | Group Name | Administration Week-day |       |       |       |       |       |
|-----------------------|------------|-------------------------|-------|-------|-------|-------|-------|
|                       |            | 99-7                    | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| TRAUMA                | Control    | 0                       | 1     | 0     | 0     | 0     | 0     |
|                       | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 0     |
| FROG BELLY            | Control    | 0                       | 0     | 3     | 4     | 2     | 2     |
|                       | 32 ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
|                       | 80 ppm     | 0                       | 1     | 1     | 0     | 0     | 0     |
|                       | 200 ppm    | 1                       | 1     | 1     | 1     | 1     | 1     |
| SOILED PERI-GENITALIA | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 0     |
| EXOPHTHALMOS          | Control    | 1                       | 1     | 1     | 1     | 1     | 1     |
|                       | 32 ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
|                       | 80 ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
|                       | 200 ppm    | 2                       | 2     | 2     | 2     | 2     | 2     |
| GUM                   | Control    | 1                       | 1     | 1     | 0     | 0     | 0     |
|                       | 32 ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
|                       | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 200 ppm    | 0                       | 0     | 0     | 1     | 0     | 0     |
| CORNEAL OPACITY       | Control    | 1                       | 1     | 1     | 1     | 1     | 1     |
|                       | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 80 ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
|                       | 200 ppm    | 1                       | 1     | 1     | 1     | 1     | 1     |
| EXTERNAL MASS         | Control    | 0                       | 1     | 0     | 0     | 0     | 0     |
|                       | 32 ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
|                       | 80 ppm     | 0                       | 1     | 1     | 1     | 1     | 1     |
|                       | 200 ppm    | 0                       | 1     | 1     | 1     | 1     | 1     |
| INTERNAL MASS         | Control    | 4                       | 4     | 4     | 4     | 4     | 4     |
|                       | 32 ppm     | 3                       | 2     | 2     | 2     | 3     | 3     |
|                       | 80 ppm     | 1                       | 1     | 1     | 0     | 0     | 2     |
|                       | 200 ppm    | 2                       | 3     | 4     | 5     | 2     | 3     |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day |     |     |     |     |     |     |     |     |      |      |      |      |      |
|---------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|------|
|               |            | 1-7                     | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 | 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 | 14-7 |
| M. EAR        | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. BREAST     | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. ABDOMEN    | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. HINDLIMB   | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. GENITALIA  | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| ULCER         | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| EROSION       | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| CRUSTA        | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|---------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|               |            | 15-7                    | 16-7 | 17-7 | 18-7 | 19-7 | 20-7 | 21-7 | 22-7 | 23-7 | 24-7 | 25-7 | 26-7 | 27-7 | 28-7 |
| M. EAR        | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. BREAST     | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ABDOMEN    | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. HINDLIMB   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. GENITALIA  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ULCER         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EROSION       | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CRUSTA        | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|---------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|               |            | 29-7                    | 30-7 | 31-7 | 32-7 | 33-7 | 34-7 | 35-7 | 36-7 | 37-7 | 38-7 | 39-7 | 40-7 | 41-7 | 42-7 |
| M. EAR        | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. BREAST     | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ABDOMEN    | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. HINDLIMB   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. GENITALIA  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ULCER         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EROSION       | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CRUSTA        | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |



STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1 104

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| Clinical sign | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|---------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|               |            | 43-7                    | 44-7 | 45-7 | 46-7 | 47-7 | 48-7 | 49-7 | 50-7 | 51-7 | 52-7 | 53-7 | 54-7 | 55-7 | 56-7 |
| M. EAR        | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. BREAST     | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ABDOMEN    | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. HINDLIMB   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. GENITALIA  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ULCER         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EROSION       | Control    | 1                       | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CRUSTA        | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1 104

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 ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|---------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|               |            | 57-7                    | 58-7 | 59-7 | 60-7 | 61-7 | 62-7 | 63-7 | 64-7 | 65-7 | 66-7 | 67-7 | 68-7 | 69-7 | 70-7 |
| M. EAR        | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. BREAST     | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ABDOMEN    | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. HINDLIMB   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. GENITALIA  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ULCER         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EROSION       | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CRUSTA        | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1 104

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| Clinical sign | Group Name | Administration Week-day |      |      |  | 74-7 | 75-7 | 76-7 | 77-7 | 78-7 | 79-7 | 80-7 | 81-7 | 82-7 | 83-7 | 84-7 |
|---------------|------------|-------------------------|------|------|--|------|------|------|------|------|------|------|------|------|------|------|
|               |            | 71-7                    | 72-7 | 73-7 |  |      |      |      |      |      |      |      |      |      |      |      |
| M. EAR        | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. BREAST     | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ABDOMEN    | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 1                       | 1    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. HINDLIMB   | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. GENITALIA  | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ULCER         | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EROSION       | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 1                       | 1    | 1    |  | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|               | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CRUSTA        | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
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CLINICAL OBSERVATION (SUMMARY)  
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SEX : MALE

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| Clinical sign | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|---------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|               |            | 85-7                    | 86-7 | 87-7 | 88-7 | 89-7 | 90-7 | 91-7 | 92-7 | 93-7 | 94-7 | 95-7 | 96-7 | 97-7 | 98-7 |
| M. EAR        | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. BREAST     | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ABDOMEN    | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. HINDLIMB   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. GENITALIA  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ULCER         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    | 1    | 1    | 1    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EROSION       | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|               | 32 ppm     | 1                       | 1    | 2    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 1    | 0    | 0    | 2    | 1    | 1    | 1    | 1    | 1    | 1    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    |
| CRUSTA        | Control    | 0                       | 1    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 2    | 1    |
|               | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    |
|               | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|               | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day |       |       |       |       |       |
|---------------|------------|-------------------------|-------|-------|-------|-------|-------|
|               |            | 99-7                    | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| M. EAR        | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|               | 32 ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
|               | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|               | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. BREAST     | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|               | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|               | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|               | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. ABDOMEN    | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|               | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|               | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|               | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. HINDLIMB   | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|               | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|               | 80 ppm     | 0                       | 1     | 1     | 1     | 1     | 1     |
|               | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. GENITALIA  | Control    | 0                       | 1     | 0     | 0     | 0     | 0     |
|               | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|               | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|               | 200 ppm    | 0                       | 1     | 1     | 1     | 1     | 1     |
| ULCER         | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|               | 32 ppm     | 2                       | 2     | 2     | 2     | 2     | 2     |
|               | 80 ppm     | 0                       | 0     | 1     | 1     | 1     | 1     |
|               | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 0     |
| EROSION       | Control    | 1                       | 1     | 2     | 2     | 2     | 2     |
|               | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|               | 80 ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
|               | 200 ppm    | 1                       | 1     | 1     | 1     | 1     | 1     |
| CRUSTA        | Control    | 0                       | 0     | 0     | 0     | 1     | 1     |
|               | 32 ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
|               | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|               | 200 ppm    | 0                       | 0     | 0     | 0     | 1     | 1     |

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : MALE

PAGE : 25

| Clinical sign           | Group Name | Administration Week-day |     |     |     |     |     |     |     |     |      |      |      |      |      |
|-------------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|------|
|                         |            | 1-7                     | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 | 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 | 14-7 |
| TORTICOLLIS             | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| PROLAPSE OF PENIS       | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| IRREGULAR BREATHING     | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |

(HAN190)

BAIS 4

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : MALE

PAGE : 26

| Clinical sign           | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 15-7                    | 16-7 | 17-7 | 18-7 | 19-7 | 20-7 | 21-7 | 22-7 | 23-7 | 24-7 | 25-7 | 26-7 | 27-7 | 28-7 |
| TORTICOLLIS             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PROLAPSE OF PENIS       | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| IRREGULAR BREATHING     | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

(HAN190)

BAIS 4

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : MALE

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| Clinical sign           | Group Name | Administration Week-day |      | 32-7 | 33-7 | 34-7 | 35-7 | 36-7 | 37-7 | 38-7 | 39-7 | 40-7 | 41-7 | 42-7 |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 29-7                    | 30-7 |      |      |      |      |      |      |      |      |      |      |      |
| TORTICOLLIS             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PROLAPSE OF PENIS       | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| IRREGULAR BREATHING     | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

(HAN190)

BAIS 4



STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : MALE

PAGE : 28

| Clinical sign           | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 43-7                    | 44-7 | 45-7 | 46-7 | 47-7 | 48-7 | 49-7 | 50-7 | 51-7 | 52-7 | 53-7 | 54-7 | 55-7 | 56-7 |
| TORTICOLLIS             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PROLAPSE OF PENIS       | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| IRREGULAR BREATHING     | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : MALE

PAGE : 29

| Clinical sign           | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 57-7                    | 58-7 | 59-7 | 60-7 | 61-7 | 62-7 | 63-7 | 64-7 | 65-7 | 66-7 | 67-7 | 68-7 | 69-7 | 70-7 |
| TORTICOLLIS             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PROLAPSE OF PENIS       | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| IRREGULAR BREATHING     | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 1                       | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 1                       | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

(HAN190)

BAIS 4

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : MALE

PAGE : 30

| Clinical sign           | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 71-7                    | 72-7 | 73-7 | 74-7 | 75-7 | 76-7 | 77-7 | 78-7 | 79-7 | 80-7 | 81-7 | 82-7 | 83-7 | 84-7 |
| TORTICOLLIS             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| PROLAPSE OF PENIS       | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| IRREGULAR BREATHING     | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

(HAN190)

BAIS 4

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : MALE

PAGE : 31

| Clinical sign           | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 85-7                    | 86-7 | 87-7 | 88-7 | 89-7 | 90-7 | 91-7 | 92-7 | 93-7 | 94-7 | 95-7 | 96-7 | 97-7 | 98-7 |
| TORTICOLLIS             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PROLAPSE OF PENIS       | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    |
| IRREGULAR BREATHING     | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

(HAN190)

BAIS 4

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : MALE

PAGE : 32

| Clinical sign           | Group Name | Administration Week-day |       |       |       |       |       |
|-------------------------|------------|-------------------------|-------|-------|-------|-------|-------|
|                         |            | 99-7                    | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| TORTICOLLIS             | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 0     |
| PROLAPSE OF PENIS       | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 0     |
| IRREGULAR BREATHING     | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 0     |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 0     |

(HAN190)

BAIS 4

## APPENDIX C 2

### CLINICAL OBSERVATION : FEMALE

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : FEMALE

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| Clinical sign           | Group Name | Administration Week-day |     |     |     |     |     |     |     |     |      |      |      |      |      |
|-------------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|------|
|                         |            | 1-7                     | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 | 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 | 14-7 |
| DEATH                   | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| MORIBUND SACRIFICE      | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| LOCOMOTOR MOVEMENT INCR | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| HUNCHBACK POSITION      | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 1   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| ATAXIC GAIT             | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| PARALYTIC GAIT          | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| ROTATING                | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| WASTING                 | Control    | 1                       | 1   | 0   | 0   | 0   | 0   | 0   | 1   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 2                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : FEMALE

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| Clinical sign           | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 15-7                    | 16-7 | 17-7 | 18-7 | 19-7 | 20-7 | 21-7 | 22-7 | 23-7 | 24-7 | 25-7 | 26-7 | 27-7 | 28-7 |
| DEATH                   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| MORIBUND SACRIFICE      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LOCOMOTOR MOVEMENT INCR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HUNCHBACK POSITION      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ATAXIC GAIT             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PARALYTIC GAIT          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ROTATING                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| WASTING                 | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |



STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
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SEX : FEMALE

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| Clinical sign           | Group Name | Administration Week-day |      |      |  | 32-7 | 33-7 | 34-7 | 35-7 | 36-7 | 37-7 | 38-7 | 39-7 | 40-7 | 41-7 | 42-7 |
|-------------------------|------------|-------------------------|------|------|--|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 29-7                    | 30-7 | 31-7 |  |      |      |      |      |      |      |      |      |      |      |      |
| DEATH                   | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    |
| MORIBUND SACRIFICE      | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LOCOMOTOR MOVEMENT INCR | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HUNCHBACK POSITION      | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ATAXIC GAIT             | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PARALYTIC GAIT          | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ROTATING                | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| WASTING                 | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : FEMALE

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| Clinical sign           | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 43-7                    | 44-7 | 45-7 | 46-7 | 47-7 | 48-7 | 49-7 | 50-7 | 51-7 | 52-7 | 53-7 | 54-7 | 55-7 | 56-7 |
| DEATH                   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 1    | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| MORIBUND SACRIFICE      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LOCOMOTOR MOVEMENT INCR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HUNCHBACK POSITION      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ATAXIC GAIT             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PARALYTIC GAIT          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ROTATING                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| WASTING                 | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : FEMALE

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| Clinical sign           | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 57-7                    | 58-7 | 59-7 | 60-7 | 61-7 | 62-7 | 63-7 | 64-7 | 65-7 | 66-7 | 67-7 | 68-7 | 69-7 | 70-7 |
| DEATH                   | Control    | 0                       | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 2    |
|                         | 32 ppm     | 2                       | 2    | 3    | 3    | 3    | 3    | 4    | 4    | 4    | 4    | 4    | 4    | 5    | 5    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 1    | 2    | 2    | 3    | 3    | 3    | 3    | 4    | 5    | 5    |
|                         | 200 ppm    | 2                       | 3    | 3    | 3    | 3    | 4    | 4    | 4    | 5    | 5    | 5    | 5    | 5    | 5    |
| MORIBUND SACRIFICE      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| LOCOMOTOR MOVEMENT INCR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HUNCHBACK POSITION      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ATAXIC GAIT             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PARALYTIC GAIT          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ROTATING                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 1    | 1    | 1    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| WASTING                 | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 1                       | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1 104

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| Clinical sign           | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 71-7                    | 72-7 | 73-7 | 74-7 | 75-7 | 76-7 | 77-7 | 78-7 | 79-7 | 80-7 | 81-7 | 82-7 | 83-7 | 84-7 |
| DEATH                   | Control    | 2                       | 2    | 2    | 2    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    |
|                         | 32 ppm     | 6                       | 6    | 7    | 7    | 7    | 7    | 7    | 8    | 8    | 8    | 8    | 8    | 8    | 9    |
|                         | 80 ppm     | 5                       | 6    | 6    | 6    | 6    | 6    | 7    | 7    | 7    | 7    | 7    | 7    | 9    | 9    |
|                         | 200 ppm    | 5                       | 5    | 5    | 5    | 5    | 5    | 5    | 6    | 6    | 6    | 6    | 7    | 7    | 8    |
| MORIBUND SACRIFICE      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 1    | 1    | 1    | 1    | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                         | 200 ppm    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| LOCOMOTOR MOVEMENT INCR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HUNCHBACK POSITION      | Control    | 0                       | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ATAXIC GAIT             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PARALYTIC GAIT          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ROTATING                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| WASTING                 | Control    | 0                       | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1 104

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| Clinical sign           | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 85-7                    | 86-7 | 87-7 | 88-7 | 89-7 | 90-7 | 91-7 | 92-7 | 93-7 | 94-7 | 95-7 | 96-7 | 97-7 | 98-7 |
| DEATH                   | Control    | 4                       | 4    | 4    | 4    | 4    | 5    | 5    | 5    | 5    | 6    | 6    | 7    | 9    | 11   |
|                         | 32 ppm     | 9                       | 9    | 9    | 9    | 9    | 10   | 10   | 12   | 13   | 13   | 14   | 15   | 15   | 16   |
|                         | 80 ppm     | 9                       | 9    | 9    | 9    | 10   | 10   | 10   | 11   | 11   | 13   | 14   | 14   | 14   | 15   |
|                         | 200 ppm    | 8                       | 9    | 9    | 9    | 9    | 10   | 11   | 11   | 13   | 13   | 13   | 15   | 15   | 15   |
| MORIBUND SACRIFICE      | Control    | 0                       | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 3    | 3    | 3    | 3    | 3    | 3    |
|                         | 32 ppm     | 0                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                         | 80 ppm     | 3                       | 3    | 3    | 3    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    |
|                         | 200 ppm    | 1                       | 1    | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 3    | 3    | 3    | 4    | 4    |
| LOCOMOTOR MOVEMENT INCR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HUNCHBACK POSITION      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ATAXIC GAIT             | Control    | 0                       | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PARALYTIC GAIT          | Control    | 0                       | 0    | 0    | 0    | 0    | 1    | 2    | 2    | 1    | 1    | 1    | 1    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ROTATING                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| WASTING                 | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                         | 32 ppm     | 0                       | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    |
|                         | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1 104

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| Clinical sign           | Group Name | Administration Week-day |       |       |       |       |       |
|-------------------------|------------|-------------------------|-------|-------|-------|-------|-------|
|                         |            | 99-7                    | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| DEATH                   | Control    | 11                      | 12    | 13    | 15    | 15    | 17    |
|                         | 32 ppm     | 19                      | 20    | 20    | 20    | 21    | 21    |
|                         | 80 ppm     | 15                      | 16    | 16    | 17    | 17    | 19    |
|                         | 200 ppm    | 16                      | 16    | 16    | 16    | 16    | 16    |
| MORIBUND SACRIFICE      | Control    | 3                       | 3     | 3     | 3     | 4     | 4     |
|                         | 32 ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
|                         | 80 ppm     | 5                       | 5     | 5     | 5     | 5     | 5     |
|                         | 200 ppm    | 4                       | 4     | 4     | 4     | 4     | 4     |
| LOCOMOTOR MOVEMENT INCR | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 0     |
| HUNCHBACK POSITION      | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 0     |
| ATAXIC GAIT             | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 0     |
| PARALYTIC GAIT          | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 0     |
| ROTATING                | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 0     |
| WASTING                 | Control    | 1                       | 0     | 0     | 0     | 0     | 0     |
|                         | 32 ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
|                         | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 1     |
|                         | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 1     |

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1 104

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| Clinical sign         | Group Name | Administration Week-day |     |     |     |     |     |     |     |     |      |      |      |      |      |
|-----------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|------|
|                       |            | 1-7                     | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 | 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 | 14-7 |
| PILOERECTION          | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 1   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| FROG BELLY            | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| SOILED PERI-GENITALIA | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| EXOPHTHALMOS          | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 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    | 0    |
|                       | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| EXTERNAL MASS         | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| INTERNAL MASS         | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 1    | 0    |
|                       | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. EYE                | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : FEMALE

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| Clinical sign         | Group Name | Administration |      | Week-day |      |      |      |      |      |      |      |      |      |      |      |
|-----------------------|------------|----------------|------|----------|------|------|------|------|------|------|------|------|------|------|------|
|                       |            | 15-7           | 16-7 | 17-7     | 18-7 | 19-7 | 20-7 | 21-7 | 22-7 | 23-7 | 24-7 | 25-7 | 26-7 | 27-7 | 28-7 |
| PILOERECTION          | Control    | 0              | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0              | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0              | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0              | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| FROG BELLY            | Control    | 0              | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0              | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0              | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0              | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED PERI-GENITALIA | Control    | 0              | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0              | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0              | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0              | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXOPHTHALMOS          | Control    | 0              | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0              | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0              | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0              | 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    | 0    |
|                       | 32 ppm     | 0              | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0              | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0              | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXTERNAL MASS         | Control    | 0              | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0              | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0              | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0              | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| INTERNAL MASS         | Control    | 0              | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0              | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0              | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0              | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. EYE                | Control    | 0              | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0              | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0              | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0              | 0    | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |



STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : FEMALE

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| Clinical sign         | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-----------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                       |            | 29-7                    | 30-7 | 31-7 | 32-7 | 33-7 | 34-7 | 35-7 | 36-7 | 37-7 | 38-7 | 39-7 | 40-7 | 41-7 | 42-7 |
| PILOERECTION          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    |
| FROG BELLY            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED PERI-GENITALIA | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXOPHTHALMOS          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 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    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXTERNAL MASS         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| INTERNAL MASS         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. EYE                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : FEMALE

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| Clinical sign         | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-----------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                       |            | 43-7                    | 44-7 | 45-7 | 46-7 | 47-7 | 48-7 | 49-7 | 50-7 | 51-7 | 52-7 | 53-7 | 54-7 | 55-7 | 56-7 |
| PILOERECTION          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| FROG BELLY            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 1                       | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
| SOILED PERI-GENITALIA | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXOPHTHALMOS          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 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    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXTERNAL MASS         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| INTERNAL MASS         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                       | 32 ppm     | 1                       | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
|                       | 200 ppm    | 0                       | 0    | 0    | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
| M. EYE                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : FEMALE

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| Clinical sign         | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-----------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                       |            | 57-7                    | 58-7 | 59-7 | 60-7 | 61-7 | 62-7 | 63-7 | 64-7 | 65-7 | 66-7 | 67-7 | 68-7 | 69-7 | 70-7 |
| PILOERECTION          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| FROG BELLY            | Control    | 0                       | 0    | 0    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 1    | 1    | 0    | 1    | 1    | 0    | 0    | 1    | 2    | 1    | 1    | 1    |
|                       | 200 ppm    | 1                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED PERI-GENITALIA | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXOPHTHALMOS          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 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    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXTERNAL MASS         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 1                       | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| INTERNAL MASS         | Control    | 1                       | 1    | 1    | 1    | 2    | 1    | 3    | 3    | 3    | 4    | 4    | 4    | 4    | 3    |
|                       | 32 ppm     | 1                       | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    |
|                       | 80 ppm     | 1                       | 1    | 1    | 2    | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 3    |
|                       | 200 ppm    | 1                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. EYE                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1 104

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ALL ANIMALS

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| Clinical sign         | Group Name | Administration Week-day |      |      |  | 74-7 | 75-7 | 76-7 | 77-7 | 78-7 | 79-7 | 80-7 | 81-7 | 82-7 | 83-7 | 84-7 |
|-----------------------|------------|-------------------------|------|------|--|------|------|------|------|------|------|------|------|------|------|------|
|                       |            | 71-7                    | 72-7 | 73-7 |  |      |      |      |      |      |      |      |      |      |      |      |
| PILOERECTION          | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| FROG BELLY            | Control    | 0                       | 1    | 1    |  | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
|                       | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
|                       | 80 ppm     | 2                       | 1    | 0    |  | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 1    |
|                       | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED PERI-GENITALIA | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXOPHTHALMOS          | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    |  | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 2    |
| CORNEAL OPACITY       | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXTERNAL MASS         | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
| INTERNAL MASS         | Control    | 3                       | 3    | 3    |  | 4    | 2    | 3    | 3    | 3    | 3    | 3    | 3    | 4    | 5    | 6    |
|                       | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                       | 80 ppm     | 4                       | 3    | 2    |  | 2    | 2    | 2    | 3    | 2    | 2    | 2    | 2    | 2    | 1    | 1    |
|                       | 200 ppm    | 0                       | 0    | 0    |  | 0    | 1    | 1    | 1    | 1    | 2    | 2    | 2    | 1    | 1    | 3    |
| M. EYE                | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
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| Clinical sign         | Group Name | Administration Week-day |      |      |  | 88-7 | 89-7 | 90-7 | 91-7 | 92-7 | 93-7 | 94-7 | 95-7 | 96-7 | 97-7 | 98-7 |
|-----------------------|------------|-------------------------|------|------|--|------|------|------|------|------|------|------|------|------|------|------|
|                       |            | 85-7                    | 86-7 | 87-7 |  |      |      |      |      |      |      |      |      |      |      |      |
| PILOERECTION          | Control    | 0                       | 0    | 0    |  | 0    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 1    | 0    | 1    |
|                       | 32 ppm     | 0                       | 0    | 0    |  | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 1    |
|                       | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    |
| FROG BELLY            | Control    | 1                       | 1    | 2    |  | 1    | 1    | 1    | 1    | 2    | 2    | 3    | 3    | 2    | 2    | 2    |
|                       | 32 ppm     | 1                       | 0    | 1    |  | 1    | 1    | 1    | 2    | 0    | 1    | 1    | 0    | 0    | 1    | 2    |
|                       | 80 ppm     | 0                       | 0    | 0    |  | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 1    | 2    |  | 1    | 2    | 1    | 0    | 1    | 2    | 1    | 3    | 1    | 1    | 1    |
| SOILED PERI-GENITALIA | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXOPHTHALMOS          | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                       | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 2                       | 2    | 2    |  | 2    | 1    | 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    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 0                       | 0    | 1    |  | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXTERNAL MASS         | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 1    | 1    | 1    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    |  | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 2    | 3    | 3    |
|                       | 200 ppm    | 1                       | 1    | 1    |  | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 1    | 1    | 1    |
| INTERNAL MASS         | Control    | 6                       | 6    | 6    |  | 6    | 6    | 5    | 5    | 5    | 5    | 5    | 4    | 4    | 4    | 5    |
|                       | 32 ppm     | 2                       | 1    | 1    |  | 2    | 2    | 2    | 2    | 0    | 0    | 1    | 1    | 1    | 2    | 4    |
|                       | 80 ppm     | 0                       | 0    | 0    |  | 1    | 0    | 1    | 3    | 3    | 3    | 1    | 0    | 0    | 0    | 1    |
|                       | 200 ppm    | 3                       | 2    | 2    |  | 1    | 1    | 1    | 1    | 2    | 2    | 2    | 2    | 1    | 4    | 4    |
| M. EYE                | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 200 ppm    | 1                       | 1    | 1    |  | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |

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| Clinical sign         | Group Name | Administration Week-day |       |       |       |       |       |
|-----------------------|------------|-------------------------|-------|-------|-------|-------|-------|
|                       |            | 99-7                    | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| PILOERECTION          | Control    | 1                       | 0     | 1     | 0     | 0     | 0     |
|                       | 32 ppm     | 1                       | 1     | 2     | 2     | 0     | 0     |
|                       | 80 ppm     | 0                       | 1     | 1     | 0     | 0     | 0     |
|                       | 200 ppm    | 0                       | 0     | 0     | 0     | 1     | 1     |
| FROG BELLY            | Control    | 2                       | 2     | 4     | 4     | 2     | 2     |
|                       | 32 ppm     | 0                       | 0     | 2     | 2     | 1     | 3     |
|                       | 80 ppm     | 1                       | 1     | 1     | 1     | 3     | 2     |
|                       | 200 ppm    | 0                       | 0     | 1     | 1     | 3     | 4     |
| SOILED PERI-GENITALIA | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 0     |
| EXOPHTHALMOS          | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 0     |
| CORNEAL OPACITY       | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 0     |
| EXTERNAL MASS         | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 80 ppm     | 3                       | 3     | 4     | 4     | 5     | 4     |
|                       | 200 ppm    | 1                       | 1     | 1     | 1     | 2     | 2     |
| INTERNAL MASS         | Control    | 6                       | 7     | 7     | 5     | 3     | 2     |
|                       | 32 ppm     | 2                       | 2     | 2     | 2     | 1     | 1     |
|                       | 80 ppm     | 1                       | 3     | 3     | 3     | 3     | 3     |
|                       | 200 ppm    | 3                       | 4     | 4     | 4     | 5     | 6     |
| M. EYE                | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 200 ppm    | 1                       | 1     | 1     | 1     | 1     | 1     |

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 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1 104

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| Clinical sign    | Group Name | Administration |     | Week-day |     |     |     |     |     |     |     |      |      |      |      |
|------------------|------------|----------------|-----|----------|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|
|                  |            | 1-7            | 2-7 |          | 3-7 | 4-7 | 5-7 | 6-7 | 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 |
| M. NECK          | Control    | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
| M. FORELIMB      | Control    | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
| M. ABDOMEN       | Control    | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
| M. INTERSCAPULUM | Control    | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
| M. GENITALIA     | Control    | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
| EDEMA            | Control    | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
| ANEMIA           | Control    | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
| CICATRIX         | Control    | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0              | 0   | 0        | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    |

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ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
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| Clinical sign    | Group Name | Administration Week-day |      |      |  | 18-7 | 19-7 | 20-7 | 21-7 | 22-7 | 23-7 | 24-7 | 25-7 | 26-7 | 27-7 | 28-7 |
|------------------|------------|-------------------------|------|------|--|------|------|------|------|------|------|------|------|------|------|------|
|                  |            | 15-7                    | 16-7 | 17-7 |  |      |      |      |      |      |      |      |      |      |      |      |
| M. NECK          | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. FORELIMB      | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ABDOMEN       | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. INTERSCAPULUM | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. GENITALIA     | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EDEMA            | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ANEMIA           | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CICATRIX         | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |



STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : FEMALE

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| Clinical sign    | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                  |            | 29-7                    | 30-7 | 31-7 | 32-7 | 33-7 | 34-7 | 35-7 | 36-7 | 37-7 | 38-7 | 39-7 | 40-7 | 41-7 | 42-7 |
| M. NECK          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. FORELIMB      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ABDOMEN       | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. INTERSCAPULUM | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. GENITALIA     | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EDEMA            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ANEMIA           | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CICATRIX         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : FEMALE

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| Clinical sign    | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                  |            | 43-7                    | 44-7 | 45-7 | 46-7 | 47-7 | 48-7 | 49-7 | 50-7 | 51-7 | 52-7 | 53-7 | 54-7 | 55-7 | 56-7 |
| M. NECK          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. FORELIMB      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ABDOMEN       | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. INTERSCAPULUM | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. GENITALIA     | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EDEMA            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ANEMIA           | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CICATRIX         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/CrLj[Crj:BDF1]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : FEMALE

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| Clinical sign    | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                  |            | 57-7                    | 58-7 | 59-7 | 60-7 | 61-7 | 62-7 | 63-7 | 64-7 | 65-7 | 66-7 | 67-7 | 68-7 | 69-7 | 70-7 |
| M. NECK          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. FORELIMB      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ABDOMEN       | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. INTERSCAPULUM | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 1                       | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. GENITALIA     | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EDEMA            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ANEMIA           | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CICATRIX         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : FEMALE

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| Clinical sign    | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                  |            | 71-7                    | 72-7 | 73-7 | 74-7 | 75-7 | 76-7 | 77-7 | 78-7 | 79-7 | 80-7 | 81-7 | 82-7 | 83-7 | 84-7 |
| M. NECK          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. FORELIMB      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ABDOMEN       | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. INTERSCAPULUM | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. GENITALIA     | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EDEMA            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ANEMIA           | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CICATRIX         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : FEMALE

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| Clinical sign    | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                  |            | 85-7                    | 86-7 | 87-7 | 88-7 | 89-7 | 90-7 | 91-7 | 92-7 | 93-7 | 94-7 | 95-7 | 96-7 | 97-7 | 98-7 |
| M. NECK          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    |
| M. FORELIMB      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ABDOMEN       | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. INTERSCAPULUM | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. GENITALIA     | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 1    | 1    | 1    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 2    | 2    | 2    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EDEMA            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 1                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ANEMIA           | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CICATRIX         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    |
|                  | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : FEMALE

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| Clinical sign    | Group Name | Administration Week-day |       |       |       |       |       |
|------------------|------------|-------------------------|-------|-------|-------|-------|-------|
|                  |            | 99-7                    | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| M. NECK          | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                  | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                  | 80 ppm     | 0                       | 0     | 1     | 1     | 1     | 0     |
|                  | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. FORELIMB      | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                  | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                  | 80 ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
|                  | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. ABDOMEN       | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                  | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                  | 80 ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
|                  | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. INTERSCAPULUM | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                  | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                  | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                  | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. GENITALIA     | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                  | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                  | 80 ppm     | 1                       | 1     | 1     | 1     | 2     | 2     |
|                  | 200 ppm    | 0                       | 0     | 0     | 0     | 1     | 1     |
| EDEMA            | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                  | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                  | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                  | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 0     |
| ANEMIA           | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                  | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                  | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                  | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 0     |
| CICATRIX         | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                  | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                  | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                  | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 0     |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : FEMALE

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| Clinical sign       | Group Name | Administration Week-day |     |     |     |     |     |     |     |     |      |      |      |      |      |
|---------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|------|
|                     |            | 1-7                     | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 | 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 | 14-7 |
| ASCITES             | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| TORTICOLLIS         | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| IRREGULAR BREATHING | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| SUBNORMAL TEMP      | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 32 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 80 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 200 ppm    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |

(HAN190)

BAIS 4

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : FEMALE

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| Clinical sign       | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                     |            | 15-7                    | 16-7 | 17-7 | 18-7 | 19-7 | 20-7 | 21-7 | 22-7 | 23-7 | 24-7 | 25-7 | 26-7 | 27-7 | 28-7 |
| ASCITES             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| TORTICOLLIS         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| IRREGULAR BREATHING | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SUBNORMAL TEMP      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

(HAN190)

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STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : FEMALE

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| Clinical sign       | Group Name | Administration Week-day |      |      |  | 32-7 | 33-7 | 34-7 | 35-7 | 36-7 | 37-7 | 38-7 | 39-7 | 40-7 | 41-7 | 42-7 |
|---------------------|------------|-------------------------|------|------|--|------|------|------|------|------|------|------|------|------|------|------|
|                     |            | 29-7                    | 30-7 | 31-7 |  |      |      |      |      |      |      |      |      |      |      |      |
| ASCITES             | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| TORTICOLLIS         | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| IRREGULAR BREATHING | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    |
| SUBNORMAL TEMP      | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 32 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 80 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 200 ppm    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

(HAN190)

BAIS 4

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : FEMALE

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| Clinical sign       | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                     |            | 43-7                    | 44-7 | 45-7 | 46-7 | 47-7 | 48-7 | 49-7 | 50-7 | 51-7 | 52-7 | 53-7 | 54-7 | 55-7 | 56-7 |
| ASCITES             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| TORTICOLLIS         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    |
|                     | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 1    | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
| IRREGULAR BREATHING | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SUBNORMAL TEMP      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

(HAN190)

BAIS 4

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : FEMALE

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| Clinical sign       | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                     |            | 57-7                    | 58-7 | 59-7 | 60-7 | 61-7 | 62-7 | 63-7 | 64-7 | 65-7 | 66-7 | 67-7 | 68-7 | 69-7 | 70-7 |
| ASCITES             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| TORTICOLLIS         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 32 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 200 ppm    | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| IRREGULAR BREATHING | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SUBNORMAL TEMP      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

(HAN190)

BAIS 4

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : FEMALE

PAGE : 62

| Clinical sign       | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                     |            | 71-7                    | 72-7 | 73-7 | 74-7 | 75-7 | 76-7 | 77-7 | 78-7 | 79-7 | 80-7 | 81-7 | 82-7 | 83-7 | 84-7 |
| ASCITES             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| TORTICOLLIS         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 32 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    |
|                     | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 200 ppm    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| IRREGULAR BREATHING | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SUBNORMAL TEMP      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

(HAN190)

BAIS 4

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : FEMALE

PAGE : 63

| Clinical sign       | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                     |            | 85-7                    | 86-7 | 87-7 | 88-7 | 89-7 | 90-7 | 91-7 | 92-7 | 93-7 | 94-7 | 95-7 | 96-7 | 97-7 | 98-7 |
| ASCITES             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    |
| TORTICOLLIS         | Control    | 0                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 200 ppm    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    |
| IRREGULAR BREATHING | Control    | 0                       | 0    | 0    | 0    | 1    | 0    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SUBNORMAL TEMP      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 32 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 80 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 200 ppm    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    |

(HAN190)

BAIS 4

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : FEMALE

PAGE : 64

| Clinical sign       | Group Name | Administration Week-day |       |       |       |       |       |
|---------------------|------------|-------------------------|-------|-------|-------|-------|-------|
|                     |            | 99-7                    | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| ASCITES             | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 0     |
| TORTICOLLIS         | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 0     |
| IRREGULAR BREATHING | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 80 ppm     | 0                       | 0     | 1     | 0     | 0     | 0     |
|                     | 200 ppm    | 0                       | 0     | 0     | 0     | 1     | 2     |
| SUBNORMAL TEMP      | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 32 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 80 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 200 ppm    | 0                       | 0     | 0     | 0     | 0     | 0     |

(HAN190)

BAIS 4

## APPENDIX D 1

### BODY WEIGHT CHANGES : MALE

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 UNIT : g  
 REPORT TYPE : A1 104  
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 1

| Group Name | Administration week-day |           |           |             |           |           |             |
|------------|-------------------------|-----------|-----------|-------------|-----------|-----------|-------------|
|            | 0-0                     | 1-7       | 2-7       | 3-7         | 4-7       | 5-7       | 6-7         |
| Control    | 23.3± 1.0               | 24.5± 1.1 | 25.4± 1.0 | 26.1± 1.2   | 26.6± 1.4 | 27.0± 1.4 | 27.9± 1.4   |
| 32 ppm     | 23.3± 1.0               | 24.2± 1.0 | 25.1± 1.3 | 25.6± 1.2   | 26.3± 1.3 | 26.7± 1.4 | 26.8± 1.4** |
| 80 ppm     | 23.3± 1.0               | 24.5± 1.0 | 25.4± 1.1 | 26.1± 1.2   | 26.8± 1.3 | 27.4± 1.4 | 28.0± 1.8   |
| 200 ppm    | 23.3± 1.0               | 24.4± 1.0 | 25.0± 1.0 | 25.4± 1.0** | 26.2± 1.1 | 26.6± 1.1 | 27.2± 1.1*  |

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

Test of Dunnett



STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 UNIT : g  
 REPORT TYPE : A1 104  
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 2

| Group Name | Administration week-day |             |             |           |            |            |           |
|------------|-------------------------|-------------|-------------|-----------|------------|------------|-----------|
|            | 7-7                     | 8-7         | 9-7         | 10-7      | 11-7       | 12-7       | 13-7      |
| Control    | 28.2± 1.4               | 29.0± 1.6   | 29.4± 2.0   | 30.0± 1.9 | 30.3± 1.8  | 31.2± 2.2  | 31.7± 2.2 |
| 32 ppm     | 27.0± 1.6**             | 28.0± 1.7** | 28.7± 1.8   | 29.6± 1.8 | 30.0± 1.8  | 30.8± 2.1  | 31.7± 2.2 |
| 80 ppm     | 28.5± 1.7               | 29.4± 1.9   | 29.9± 2.0   | 30.4± 2.1 | 30.9± 2.3  | 32.0± 2.4  | 32.6± 2.5 |
| 200 ppm    | 27.6± 1.3               | 28.1± 1.3*  | 28.3± 1.5** | 29.3± 1.6 | 29.4± 1.6* | 30.0± 2.0* | 30.9± 2.0 |

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

Test of Dunnett

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 UNIT : g  
 REPORT TYPE : A1 104  
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 3

| Group Name | Administration week-day |            |            |            |           |           |           |
|------------|-------------------------|------------|------------|------------|-----------|-----------|-----------|
|            | 14-7                    | 18-7       | 22-7       | 26-7       | 30-7      | 34-7      | 38-7      |
| Control    | 32.3± 2.3               | 34.5± 2.5  | 36.6± 2.5  | 38.5± 2.9  | 40.2± 3.2 | 42.0± 3.6 | 43.3± 3.5 |
| 32 ppm     | 32.3± 2.3               | 35.2± 2.6  | 37.2± 3.1  | 39.7± 3.5  | 41.5± 3.8 | 43.2± 4.0 | 44.8± 4.5 |
| 80 ppm     | 33.4± 2.6               | 35.9± 3.0* | 38.2± 3.4* | 40.2± 3.6* | 42.0± 4.1 | 43.7± 4.2 | 44.9± 4.2 |
| 200 ppm    | 31.2± 2.2               | 33.7± 2.7  | 35.3± 3.2  | 37.3± 3.5  | 38.9± 3.9 | 40.6± 4.1 | 41.6± 4.4 |

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

Test of Dunnett

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 UNIT : g  
 REPORT TYPE : A1 104  
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 4

| Group Name | Administration week-day |           |           |           |           |           |           |  |
|------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|--|
|            | 42-7                    | 46-7      | 50-7      | 54-7      | 58-7      | 62-7      | 66-7      |  |
| Control    | 44.4± 4.1               | 45.8± 3.9 | 46.7± 4.2 | 47.1± 4.2 | 47.6± 4.6 | 47.9± 5.0 | 48.5± 5.3 |  |
| 32 ppm     | 45.8± 4.5               | 47.2± 5.3 | 47.8± 5.9 | 48.4± 6.4 | 48.7± 6.4 | 50.2± 4.9 | 50.8± 4.9 |  |
| 80 ppm     | 46.2± 4.3               | 47.7± 4.3 | 48.4± 4.4 | 48.8± 4.3 | 48.8± 4.5 | 49.4± 4.6 | 50.6± 5.0 |  |
| 200 ppm    | 42.9± 4.8               | 44.3± 5.0 | 45.3± 5.3 | 46.0± 5.3 | 46.0± 5.6 | 46.6± 5.9 | 46.9± 5.8 |  |

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

Test of Dunnett

(HAN260)

BAIS 4

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 UNIT : g  
 REPORT TYPE : A1 104  
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 5

| Group Name | Administration |     | week-day |     |       |     |       |     |       |      |       |      |       |      |
|------------|----------------|-----|----------|-----|-------|-----|-------|-----|-------|------|-------|------|-------|------|
|            | 70-7           |     | 74-7     |     | 78-7  |     | 82-7  |     | 86-7  |      | 90-7  |      | 94-7  |      |
| Control    | 49.3±          | 5.0 | 50.1±    | 5.1 | 50.1± | 5.3 | 50.2± | 5.8 | 49.5± | 7.0  | 50.1± | 6.5  | 49.6± | 6.4  |
| 32 ppm     | 51.3±          | 5.4 | 52.1±    | 6.0 | 52.7± | 6.2 | 53.4± | 6.7 | 53.7± | 6.9* | 54.4± | 6.3* | 53.5± | 7.1* |
| 80 ppm     | 50.7±          | 5.2 | 51.0±    | 5.9 | 50.8± | 6.7 | 51.4± | 7.1 | 53.2± | 5.9* | 53.1± | 6.3  | 52.7± | 6.3  |
| 200 ppm    | 47.4±          | 6.0 | 47.9±    | 6.2 | 47.9± | 6.8 | 48.5± | 7.2 | 48.9± | 7.6  | 48.8± | 8.3  | 49.4± | 7.3  |

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

Test of Dunnett

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
UNIT : g  
REPORT TYPE : A1 104  
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)  
ALL ANIMALS

PAGE : 6

| Group Name | Administration week-day |            |           |
|------------|-------------------------|------------|-----------|
|            | 98-7                    | 102-7      | 104-7     |
| Control    | 48.6± 6.5               | 47.2± 7.0  | 46.8± 7.1 |
| 32 ppm     | 53.3± 6.9*              | 52.1± 7.1* | 51.4± 7.1 |
| 80 ppm     | 52.6± 6.1*              | 51.0± 6.9  | 49.9± 7.6 |
| 200 ppm    | 48.9± 7.5               | 48.3± 7.8  | 47.8± 8.0 |

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

## APPENDIX D 2

### BODY WEIGHT CHANGES : FEMALE

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 UNIT : g  
 REPORT TYPE : A1 104  
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 7

| Group Name | Administration week-day |           |           |             |           |             |           |
|------------|-------------------------|-----------|-----------|-------------|-----------|-------------|-----------|
|            | 0-0                     | 1-7       | 2-7       | 3-7         | 4-7       | 5-7         | 6-7       |
| Control    | 19.2± 0.9               | 19.6± 1.0 | 20.5± 1.5 | 20.6± 1.2   | 21.7± 0.9 | 21.8± 1.0   | 22.7± 1.0 |
| 32 ppm     | 19.2± 0.9               | 19.6± 0.8 | 20.4± 0.9 | 21.1± 0.9   | 21.6± 0.9 | 22.0± 0.7   | 22.6± 0.8 |
| 80 ppm     | 19.2± 0.9               | 19.5± 1.9 | 20.4± 0.8 | 21.0± 1.1   | 21.6± 0.9 | 22.1± 1.0   | 22.8± 1.1 |
| 200 ppm    | 19.2± 0.9               | 19.9± 0.9 | 20.7± 0.9 | 21.3± 1.0** | 21.9± 1.2 | 22.6± 1.1** | 23.1± 1.3 |

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

Test of Dunnett

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
UNIT : g  
REPORT TYPE : A1 104  
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)  
ALL ANIMALS

PAGE : 8

| Group Name | Administration week-day |           |           |           |           |           |           |
|------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|
|            | 7-7                     | 8-7       | 9-7       | 10-7      | 11-7      | 12-7      | 13-7      |
| Control    | 23.1± 0.9               | 23.4± 1.8 | 23.8± 1.1 | 24.3± 1.1 | 24.3± 1.2 | 24.8± 1.1 | 25.0± 1.3 |
| 32 ppm     | 22.9± 1.0               | 23.4± 0.9 | 24.0± 1.0 | 24.3± 1.1 | 24.3± 1.1 | 24.8± 1.1 | 25.1± 1.3 |
| 80 ppm     | 23.2± 1.0               | 23.6± 1.1 | 23.7± 0.8 | 24.0± 1.0 | 24.6± 1.1 | 25.0± 1.2 | 25.1± 1.3 |
| 200 ppm    | 23.5± 1.0               | 24.0± 1.2 | 24.0± 1.2 | 24.3± 1.2 | 24.5± 1.2 | 24.9± 1.2 | 25.3± 1.3 |

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

Test of Dunnett



STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 UNIT : g  
 REPORT TYPE : A1 104  
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 9

| Group Name | Administration week-day |           |           |           |           |           |           |
|------------|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|
|            | 14-7                    | 18-7      | 22-7      | 26-7      | 30-7      | 34-7      | 38-7      |
| Control    | 25.2± 1.7               | 26.3± 1.8 | 27.0± 1.9 | 28.0± 2.1 | 28.5± 2.3 | 29.4± 2.9 | 30.2± 3.1 |
| 32 ppm     | 25.2± 1.4               | 26.2± 1.3 | 26.9± 1.8 | 28.0± 2.1 | 28.4± 2.2 | 29.3± 2.5 | 30.0± 2.7 |
| 80 ppm     | 25.1± 1.2               | 26.7± 1.6 | 27.4± 1.8 | 28.1± 1.9 | 29.0± 2.1 | 29.7± 2.3 | 30.4± 2.6 |
| 200 ppm    | 25.3± 1.2               | 26.5± 1.5 | 27.1± 1.6 | 27.7± 1.9 | 28.6± 2.5 | 29.2± 2.4 | 29.3± 2.4 |

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

Test of Dunnett

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 UNIT : g  
 REPORT TYPE : A1 104  
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 10

| Group Name | Administration week-day |           |           |           |           |            |            |
|------------|-------------------------|-----------|-----------|-----------|-----------|------------|------------|
|            | 42-7                    | 46-7      | 50-7      | 54-7      | 58-7      | 62-7       | 66-7       |
| Control    | 30.6± 3.2               | 31.2± 3.3 | 31.4± 3.2 | 32.1± 3.5 | 32.0± 3.3 | 32.0± 3.3  | 32.6± 3.7  |
| 32 ppm     | 30.6± 2.9               | 31.3± 3.5 | 31.1± 3.1 | 31.6± 3.4 | 32.1± 3.7 | 31.8± 3.9  | 32.9± 3.9  |
| 80 ppm     | 30.8± 2.7               | 32.1± 3.1 | 32.6± 3.1 | 32.9± 3.5 | 33.0± 3.2 | 33.7± 3.6* | 34.6± 3.7* |
| 200 ppm    | 29.6± 2.5               | 30.3± 2.8 | 30.3± 2.8 | 30.8± 3.1 | 30.6± 3.0 | 31.3± 3.3  | 31.7± 3.6  |

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

Test of Dunnett

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 UNIT : g  
 REPORT TYPE : A1 104  
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 11

| Group Name | Administration week-day |            |            |           |            |           |           |
|------------|-------------------------|------------|------------|-----------|------------|-----------|-----------|
|            | 70-7                    | 74-7       | 78-7       | 82-7      | 86-7       | 90-7      | 94-7      |
| Control    | 32.5± 3.4               | 33.0± 4.2  | 32.9± 3.7  | 33.9± 4.0 | 34.1± 3.9  | 33.6± 4.4 | 34.4± 4.8 |
| 32 ppm     | 32.9± 3.9               | 33.7± 4.0  | 33.3± 4.1  | 34.2± 4.1 | 34.4± 3.9  | 34.4± 4.4 | 34.2± 5.1 |
| 80 ppm     | 34.8± 4.0**             | 35.0± 3.7* | 35.0± 4.4* | 35.8± 5.0 | 36.2± 4.7* | 35.9± 4.8 | 36.2± 5.0 |
| 200 ppm    | 31.8± 3.0               | 32.3± 3.5  | 32.5± 3.2  | 32.9± 3.0 | 33.2± 3.4  | 33.7± 3.8 | 33.5± 4.1 |

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

Test of Dunnett

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
UNIT : g  
REPORT TYPE : A1 104  
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)  
ALL ANIMALS

PAGE : 12

| Group Name | Administration week-day |           |           |
|------------|-------------------------|-----------|-----------|
|            | 98-7                    | 102-7     | 104-7     |
| Control    | 33.9± 4.8               | 34.1± 4.0 | 33.3± 3.9 |
| 32 ppm     | 35.5± 5.5               | 34.7± 4.6 | 34.5± 4.2 |
| 80 ppm     | 36.6± 4.4               | 35.9± 4.5 | 35.4± 5.5 |
| 200 ppm    | 33.2± 3.8               | 33.3± 4.1 | 33.5± 5.4 |

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

## APPENDIX E 1

### FOOD CONSUMPTION CHANGES : MALE

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 UNIT : g  
 REPORT TYPE : A1 104  
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 1

| Group Name | Administration week-day(effective) |          |          |          |          |            |           |
|------------|------------------------------------|----------|----------|----------|----------|------------|-----------|
|            | 1-7(6)                             | 2-7(7)   | 3-7(7)   | 4-7(7)   | 5-7(7)   | 6-7(7)     | 7-7(7)    |
| Control    | 3.9± 0.4                           | 3.9± 0.3 | 3.9± 0.3 | 4.0± 0.4 | 4.0± 0.3 | 4.3± 0.3   | 4.1± 0.3  |
| 32 ppm     | 3.8± 0.2                           | 3.9± 0.2 | 3.8± 0.2 | 3.9± 0.3 | 4.0± 0.3 | 4.1± 0.3** | 4.2± 0.4  |
| 80 ppm     | 3.9± 0.3                           | 3.9± 0.3 | 3.9± 0.3 | 4.0± 0.3 | 4.1± 0.3 | 4.2± 0.4   | 4.2± 0.3  |
| 200 ppm    | 3.7± 0.2**                         | 3.8± 0.3 | 3.8± 0.3 | 4.0± 0.2 | 4.1± 0.3 | 4.3± 0.3   | 4.3± 0.3* |

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

Test of Dunnett

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
UNIT : g  
REPORT TYPE : A1 104  
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
ALL ANIMALS

PAGE : 2

| Group Name | Administration<br>8-7(7) | week-day(effective)<br>9-7(7) | 10-7(7)    | 11-7(7)  | 12-7(7)  | 13-7(7)  | 14-7(7)  |
|------------|--------------------------|-------------------------------|------------|----------|----------|----------|----------|
| Control    | 4.2± 0.3                 | 4.2± 0.3                      | 4.3± 0.3   | 4.4± 0.3 | 4.4± 0.4 | 4.5± 0.3 | 4.5± 0.3 |
| 32 ppm     | 4.3± 0.4                 | 4.3± 0.3                      | 4.5± 0.3   | 4.4± 0.3 | 4.5± 0.3 | 4.5± 0.3 | 4.4± 0.3 |
| 80 ppm     | 4.2± 0.3                 | 4.3± 0.3                      | 4.3± 0.3   | 4.4± 0.3 | 4.4± 0.3 | 4.4± 0.3 | 4.4± 0.3 |
| 200 ppm    | 4.3± 0.3                 | 4.3± 0.4                      | 4.5± 0.3** | 4.3± 0.3 | 4.4± 0.3 | 4.5± 0.3 | 4.5± 0.3 |

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

\*\* :  $P \leq 0.01$

Test of Dunnett

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
UNIT : g  
REPORT TYPE : A1 104  
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
ALL ANIMALS

PAGE : 3

| Group Name | Administration<br>18-7(7) | week-day(effective)<br>22-7(7) | 26-7(7)  | 30-7(7)  | 34-7(7)  | 38-7(7)  | 42-7(7)  |
|------------|---------------------------|--------------------------------|----------|----------|----------|----------|----------|
| Control    | 4.6± 0.3                  | 4.5± 0.2                       | 4.6± 0.3 | 4.6± 0.3 | 4.7± 0.3 | 4.8± 0.3 | 4.9± 0.3 |
| 32 ppm     | 4.6± 0.2                  | 4.5± 0.2                       | 4.7± 0.3 | 4.7± 0.2 | 4.7± 0.3 | 4.8± 0.3 | 4.9± 0.3 |
| 80 ppm     | 4.5± 0.3                  | 4.5± 0.3                       | 4.6± 0.3 | 4.6± 0.3 | 4.7± 0.3 | 4.9± 0.5 | 4.9± 0.3 |
| 200 ppm    | 4.6± 0.4                  | 4.5± 0.3                       | 4.7± 0.3 | 4.6± 0.3 | 4.7± 0.3 | 4.7± 0.4 | 4.9± 0.4 |

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

\*\* :  $P \leq 0.01$

Test of Dunnett



STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 UNIT : g  
 REPORT TYPE : A1 104  
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 4

| Group Name | Administration week-day(effective) |          |          |          |          |          |          |
|------------|------------------------------------|----------|----------|----------|----------|----------|----------|
|            | 46-7(7)                            | 50-7(7)  | 54-7(7)  | 58-7(7)  | 62-7(7)  | 66-7(7)  | 70-7(7)  |
| Control    | 4.9± 0.3                           | 5.1± 0.3 | 4.9± 0.3 | 4.8± 0.3 | 5.1± 0.4 | 5.1± 0.4 | 5.2± 0.4 |
| 32 ppm     | 4.9± 0.5                           | 5.1± 0.7 | 4.9± 0.5 | 4.8± 0.5 | 5.2± 0.3 | 5.2± 0.3 | 5.1± 0.4 |
| 80 ppm     | 4.9± 0.3                           | 5.0± 0.3 | 4.9± 0.3 | 4.8± 0.3 | 5.2± 0.4 | 5.1± 0.4 | 5.0± 0.5 |
| 200 ppm    | 4.9± 0.4                           | 5.0± 0.4 | 4.9± 0.4 | 4.8± 0.4 | 5.1± 0.4 | 5.0± 0.4 | 5.1± 0.4 |

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

Test of Dunnett

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Crj[Crj:BDF1]  
 UNIT : g  
 REPORT TYPE : A1 104  
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 5

| Group Name | Administration<br>74-7(7) | week-day(effective)<br>78-7(7) | 82-7(7)  | 86-7(7)  | 90-7(7)  | 94-7(7)  | 98-7(7)  |
|------------|---------------------------|--------------------------------|----------|----------|----------|----------|----------|
| Control    | 5.2± 0.4                  | 5.1± 0.4                       | 5.1± 0.5 | 5.2± 0.8 | 5.2± 0.3 | 5.1± 0.3 | 5.0± 0.4 |
| 32 ppm     | 5.3± 0.3                  | 5.3± 0.3                       | 5.4± 0.4 | 5.4± 0.4 | 5.3± 0.5 | 5.1± 0.8 | 5.4± 0.7 |
| 80 ppm     | 5.1± 0.5                  | 5.1± 0.5                       | 5.3± 0.4 | 5.4± 0.4 | 5.4± 0.4 | 5.2± 0.6 | 5.1± 0.7 |
| 200 ppm    | 5.1± 0.4                  | 5.0± 0.5                       | 5.2± 0.4 | 5.3± 0.5 | 5.2± 0.6 | 5.1± 0.5 | 5.2± 0.6 |

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

Test of Dunnett

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
UNIT : g  
REPORT TYPE : A1 104  
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
ALL ANIMALS

PAGE : 6

| Group Name | Administration week-day(effective) |          |
|------------|------------------------------------|----------|
|            | 102-7(7)                           | 104-7(7) |
| Control    | 5.0± 0.6                           | 5.1± 0.5 |
| 32 ppm     | 5.3± 0.5                           | 5.2± 0.7 |
| 80 ppm     | 5.1± 0.6                           | 4.9± 0.9 |
| 200 ppm    | 5.2± 0.6                           | 5.1± 0.6 |

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

Test of Dunnett

## APPENDIX E 2

### FOOD CONSUMPTION CHANGES : FEMALE

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 UNIT : g  
 REPORT TYPE : A1 104  
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 7

| Group Name | Administration<br>1-7(6) | week-day(effective)<br>2-7(7) | 3-7(7)   | 4-7(7)   | 5-7(7)     | 6-7(7)    | 7-7(7)    |
|------------|--------------------------|-------------------------------|----------|----------|------------|-----------|-----------|
| Control    | 3.3± 0.3                 | 3.3± 0.3                      | 3.4± 0.2 | 3.6± 0.2 | 3.7± 0.2   | 4.0± 0.2  | 4.1± 0.4  |
| 32 ppm     | 3.3± 0.2                 | 3.4± 0.2                      | 3.5± 0.2 | 3.7± 0.2 | 3.8± 0.2*  | 4.0± 0.3  | 4.1± 0.2  |
| 80 ppm     | 3.1± 0.5                 | 3.4± 0.3                      | 3.5± 0.3 | 3.7± 0.3 | 3.8± 0.2   | 4.1± 0.4* | 4.1± 0.3  |
| 200 ppm    | 3.0± 0.2**               | 3.4± 0.2                      | 3.5± 0.2 | 3.7± 0.3 | 3.9± 0.3** | 4.1± 0.3* | 4.2± 0.3* |

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

Test of Dunnett

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 UNIT : g  
 REPORT TYPE : A1 104  
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 8

| Group Name | Administration<br>8-7(7) | week-day(effective)<br>9-7(7) | 10-7(7)    | 11-7(7)  | 12-7(7)  | 13-7(7)   | 14-7(7)   |
|------------|--------------------------|-------------------------------|------------|----------|----------|-----------|-----------|
| Control    | 4.0± 0.4                 | 4.1± 0.3                      | 4.2± 0.2   | 4.2± 0.3 | 4.2± 0.3 | 4.2± 0.2  | 4.2± 0.3  |
| 32 ppm     | 4.1± 0.2                 | 4.2± 0.2                      | 4.2± 0.3   | 4.2± 0.3 | 4.2± 0.2 | 4.2± 0.3  | 4.1± 0.3  |
| 80 ppm     | 4.1± 0.2                 | 4.2± 0.3                      | 4.3± 0.3*  | 4.3± 0.3 | 4.2± 0.3 | 4.3± 0.3  | 4.2± 0.4  |
| 200 ppm    | 4.2± 0.3**               | 4.2± 0.3                      | 4.3± 0.3** | 4.2± 0.4 | 4.2± 0.3 | 4.5± 0.5* | 4.4± 0.4* |

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

Test of Dunnett

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 UNIT : g  
 REPORT TYPE : A1 104  
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 9

| Group Name | Administration week-day(effective) |          |          |          |          |          |          |
|------------|------------------------------------|----------|----------|----------|----------|----------|----------|
|            | 18-7(7)                            | 22-7(7)  | 26-7(7)  | 30-7(7)  | 34-7(7)  | 38-7(7)  | 42-7(7)  |
| Control    | 4.3± 0.3                           | 4.2± 0.4 | 4.4± 0.4 | 4.5± 0.4 | 4.5± 0.4 | 4.6± 0.4 | 4.6± 0.4 |
| 32 ppm     | 4.2± 0.3                           | 4.1± 0.3 | 4.3± 0.4 | 4.3± 0.4 | 4.4± 0.4 | 4.4± 0.4 | 4.5± 0.4 |
| 80 ppm     | 4.3± 0.4                           | 4.2± 0.4 | 4.3± 0.4 | 4.4± 0.3 | 4.4± 0.4 | 4.5± 0.4 | 4.5± 0.5 |
| 200 ppm    | 4.4± 0.4                           | 4.2± 0.4 | 4.4± 0.4 | 4.4± 0.4 | 4.5± 0.4 | 4.4± 0.4 | 4.5± 0.5 |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 UNIT : g  
 REPORT TYPE : A1 104  
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 10

| Group Name | Administration<br>46-7(7) | week-day(effective)<br>50-7(7) | 54-7(7)  | 58-7(7)  | 62-7(7)  | 66-7(7)  | 70-7(7)  |
|------------|---------------------------|--------------------------------|----------|----------|----------|----------|----------|
| Control    | 4.6± 0.5                  | 4.7± 0.5                       | 4.6± 0.4 | 4.4± 0.5 | 4.6± 0.5 | 4.7± 0.6 | 4.5± 0.5 |
| 32 ppm     | 4.6± 0.5                  | 4.7± 0.4                       | 4.5± 0.4 | 4.4± 0.5 | 4.4± 0.7 | 4.6± 0.5 | 4.5± 0.5 |
| 80 ppm     | 4.6± 0.5                  | 4.7± 0.4                       | 4.5± 0.5 | 4.4± 0.5 | 4.7± 0.5 | 4.5± 0.5 | 4.6± 0.5 |
| 200 ppm    | 4.6± 1.0                  | 4.6± 0.6                       | 4.4± 0.4 | 4.3± 0.5 | 4.6± 0.5 | 4.5± 0.5 | 4.6± 0.4 |

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

Test of Dunnett



STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 UNIT : g  
 REPORT TYPE : A1 104  
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 11

| Group Name | Administration<br>74-7(7) | week-day(effective)<br>78-7(7) | 82-7(7)  | 86-7(7)  | 90-7(7)   | 94-7(7)  | 98-7(7)  |
|------------|---------------------------|--------------------------------|----------|----------|-----------|----------|----------|
| Control    | 4.6± 0.6                  | 4.5± 0.6                       | 4.7± 0.5 | 4.8± 0.6 | 4.6± 0.7  | 4.8± 0.7 | 4.7± 0.6 |
| 32 ppm     | 4.5± 0.5                  | 4.4± 0.5                       | 4.7± 0.6 | 4.7± 0.6 | 4.6± 0.6  | 4.5± 0.7 | 4.7± 0.7 |
| 80 ppm     | 4.6± 0.5                  | 4.7± 0.5                       | 4.7± 0.8 | 5.0± 0.6 | 4.9± 0.7* | 4.8± 0.5 | 4.8± 0.5 |
| 200 ppm    | 4.5± 0.5                  | 4.6± 0.4                       | 4.7± 0.7 | 4.7± 0.4 | 4.9± 0.6  | 4.7± 0.5 | 4.7± 0.5 |

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

Test of Dunnett

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
UNIT : g  
REPORT TYPE : A1 104  
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
ALL ANIMALS

PAGE : 12

| Group Name | Administration week-day(effective) |          |
|------------|------------------------------------|----------|
|            | 102-7(7)                           | 104-7(7) |
| Control    | 4.9± 0.9                           | 4.7± 1.0 |
| 32 ppm     | 4.8± 0.5                           | 4.7± 0.6 |
| 80 ppm     | 4.9± 0.6                           | 4.7± 0.7 |
| 200 ppm    | 4.8± 0.6                           | 4.6± 0.6 |

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

Test of Dunnett

## APPENDIX F 1

### HEMATOLOGY : MALE

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 MEASURE. TIME : 1  
 SEX : MALE

HEMATOLOGY (SUMMARY)  
 ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 1

| Group Name | NO. of<br>Animals | RED BLOOD CELL<br>10 <sup>6</sup> /μl |      | HEMOGLOBIN<br>g/dl |     | HEMATOCRIT<br>% |     | MCV<br>fl |     | MCH<br>pg |     | MCHC<br>g/dl |       | PLATELET<br>10 <sup>9</sup> /μl |     |
|------------|-------------------|---------------------------------------|------|--------------------|-----|-----------------|-----|-----------|-----|-----------|-----|--------------|-------|---------------------------------|-----|
| Control    | 32                | 9.30±                                 | 1.57 | 13.5±              | 2.1 | 41.4±           | 5.6 | 44.9±     | 3.0 | 14.5±     | 0.7 | 32.4±        | 1.5   | 1805±                           | 423 |
| 32 ppm     | 33                | 9.11±                                 | 1.04 | 13.2±              | 1.7 | 40.7±           | 4.9 | 44.7±     | 2.3 | 14.4±     | 0.7 | 32.3±        | 0.9   | 1826±                           | 424 |
| 80 ppm     | 32                | 8.88±                                 | 1.63 | 12.8±              | 2.4 | 40.0±           | 6.8 | 45.3±     | 2.1 | 14.4±     | 0.5 | 31.9±        | 1.3*  | 1723±                           | 477 |
| 200 ppm    | 40                | 8.97±                                 | 1.12 | 12.8±              | 1.6 | 40.0±           | 4.5 | 44.7±     | 2.1 | 14.3±     | 0.6 | 31.9±        | 0.9** | 1805±                           | 317 |

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

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 4

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 MEASURE. TIME : 1  
 SEX : MALE

HEMATOLOGY (SUMMARY)  
 ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 2

| Group Name | NO. of<br>Animals | WBC<br>10 <sup>9</sup> /μl |      | Differential<br>N-BAND |   | WBC (%)<br>N-SEG |    | EOSINO |   | BASO |   | MONO |   | LYMPHO |    | OTHER |    |
|------------|-------------------|----------------------------|------|------------------------|---|------------------|----|--------|---|------|---|------|---|--------|----|-------|----|
| Control    | 32                | 4.36±                      | 6.91 | 1±                     | 2 | 26±              | 12 | 2±     | 1 | 0±   | 0 | 4±   | 2 | 64±    | 17 | 4±    | 16 |
| 32 ppm     | 33                | 3.55±                      | 1.41 | 1±                     | 1 | 26±              | 11 | 1±     | 1 | 0±   | 0 | 4±   | 2 | 68±    | 12 | 1±    | 1  |
| 80 ppm     | 32                | 3.41±                      | 1.52 | 1±                     | 1 | 26±              | 11 | 1±     | 1 | 0±   | 0 | 3±   | 2 | 67±    | 11 | 1±    | 3  |
| 200 ppm    | 40                | 3.77±                      | 1.71 | 1±                     | 1 | 30±              | 16 | 3±     | 9 | 0±   | 0 | 4±   | 2 | 61±    | 18 | 1±    | 2  |

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

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 4

## APPENDIX F 2

### HEMATOLOGY : FEMALE

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 MEASURE. TIME : 1  
 SEX : FEMALE

HEMATOLOGY (SUMMARY)  
 ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 3

| Group Name | NO. of<br>Animals | RED BLOOD CELL<br>10 <sup>6</sup> /μl |      | HEMOGLOBIN<br>g/dl |     | HEMATOCRIT<br>% |     | MCV<br>fl |       | MCH<br>pg |     | MCHC<br>g/dl |      | PLATELET<br>10 <sup>9</sup> /μl |     |
|------------|-------------------|---------------------------------------|------|--------------------|-----|-----------------|-----|-----------|-------|-----------|-----|--------------|------|---------------------------------|-----|
| Control    | 29                | 9.62±                                 | 0.94 | 14.0±              | 1.3 | 42.5±           | 3.9 | 44.3±     | 2.2   | 14.6±     | 0.7 | 33.0±        | 0.9  | 1175±                           | 243 |
| 32 ppm     | 26                | 9.30±                                 | 0.74 | 13.7±              | 1.1 | 41.4±           | 2.7 | 44.6±     | 1.7   | 14.7±     | 0.4 | 33.0±        | 1.0  | 1087±                           | 283 |
| 80 ppm     | 25                | 9.09±                                 | 1.22 | 13.3±              | 1.6 | 40.8±           | 4.1 | 45.2±     | 2.7   | 14.7±     | 0.6 | 32.5±        | 1.1  | 1021±                           | 357 |
| 200 ppm    | 28                | 8.84±                                 | 1.74 | 13.1±              | 2.4 | 40.6±           | 6.2 | 46.7±     | 4.9** | 14.8±     | 0.5 | 32.0±        | 2.1* | 1028±                           | 330 |

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

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 4

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 MEASURE. TIME : 1  
 SEX : FEMALE

HEMATOLOGY (SUMMARY)  
 ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 4

| Group Name | NO. of<br>Animals | WBC<br>1 O <sup>3</sup> /μℓ |       | Differential<br>N-BAND |   | WBC (%)<br>N-SEG |    | EOSINO |   | BASO |   | MONO |   | LYMPHO |    | OTHER |    |
|------------|-------------------|-----------------------------|-------|------------------------|---|------------------|----|--------|---|------|---|------|---|--------|----|-------|----|
| Control    | 29                | 2.43±                       | 1.95  | 1±                     | 2 | 27±              | 10 | 2±     | 2 | 0±   | 0 | 4±   | 2 | 65±    | 14 | 2±    | 2  |
| 32 ppm     | 26                | 2.84±                       | 3.57  | 1±                     | 1 | 25±              | 8  | 2±     | 2 | 0±   | 0 | 4±   | 2 | 65±    | 10 | 4±    | 6  |
| 80 ppm     | 25                | 3.34±                       | 3.14  | 1±                     | 2 | 26±              | 12 | 2±     | 2 | 0±   | 0 | 3±   | 2 | 58±    | 17 | 10±   | 19 |
| 200 ppm    | 28                | 15.79±                      | 71.36 | 1±                     | 2 | 29±              | 14 | 2±     | 2 | 0±   | 0 | 3±   | 2 | 59±    | 17 | 6±    | 18 |

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

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 4



## APPENDIX G 1

BIOCHEMISTRY : MALE

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 MEASURE. TIME : 1  
 SEX : MALE

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 1

| Group Name | NO. of<br>Animals | TOTAL PROTEIN<br>g/dl |     | ALBUMIN<br>g/dl |     | A/G RATIO |     | T-BILIRUBIN<br>mg/dl |      | GLUCOSE<br>mg/dl |    | T-CHOLESTEROL<br>mg/dl |    | TRIGLYCERIDE<br>mg/dl |    |
|------------|-------------------|-----------------------|-----|-----------------|-----|-----------|-----|----------------------|------|------------------|----|------------------------|----|-----------------------|----|
| Control    | 32                | 5.2±                  | 1.0 | 2.7±            | 0.5 | 1.1±      | 0.2 | 0.14±                | 0.05 | 180±             | 51 | 119±                   | 75 | 29±                   | 12 |
| 32 ppm     | 33                | 5.0±                  | 0.7 | 2.6±            | 0.3 | 1.1±      | 0.2 | 0.14±                | 0.05 | 187±             | 44 | 116±                   | 43 | 34±                   | 15 |
| 80 ppm     | 32                | 5.1±                  | 0.6 | 2.7±            | 0.4 | 1.1±      | 0.2 | 0.19±                | 0.29 | 185±             | 46 | 109±                   | 35 | 35±                   | 21 |
| 200 ppm    | 40                | 5.2±                  | 0.6 | 2.7±            | 0.3 | 1.1±      | 0.2 | 0.13±                | 0.05 | 191±             | 39 | 121±                   | 99 | 36±                   | 20 |

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

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 4

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 MEASURE. TIME : 1  
 SEX : MALE

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 2

| Group Name | NO. of<br>Animals | PHOSPHOLIPID<br>mg/dl |     | AST<br>IU/l |      | ALT<br>IU/dl |      | LDH<br>IU/l |      | ALP<br>IU/l |     | G-GTP<br>IU/l |   | CK<br>IU/l |     |
|------------|-------------------|-----------------------|-----|-------------|------|--------------|------|-------------|------|-------------|-----|---------------|---|------------|-----|
| Control    | 32                | 198±                  | 110 | 166±        | 309  | 110±         | 212  | 428±        | 558  | 159±        | 200 | 1±            | 1 | 70±        | 84  |
| 32 ppm     | 33                | 196±                  | 50  | 134±        | 214  | 69±          | 106  | 450±        | 668  | 129±        | 37  | 1±            | 1 | 71±        | 85  |
| 80 ppm     | 32                | 187±                  | 50  | 598±        | 2780 | 267±         | 1208 | 1945±       | 8364 | 160±        | 146 | 1±            | 1 | 69±        | 128 |
| 200 ppm    | 40                | 211±                  | 128 | 126±        | 265  | 62±          | 118  | 461±        | 730  | 194±        | 477 | 1±            | 1 | 50±        | 20  |

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

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 4

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 MEASURE. TIME : 1  
 SEX : MALE

REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS (105W)

PAGE : 3

| Group Name | NO. of<br>Animals | UREA NITROGEN<br>mg/dl |        | SODIUM<br>mEq/l |   | POTASSIUM<br>mEq/l |      | CHLORIDE<br>mEq/l |   | CALCIUM<br>mg/dl |     | INORGANIC PHOSPHORUS<br>mg/dl |     |
|------------|-------------------|------------------------|--------|-----------------|---|--------------------|------|-------------------|---|------------------|-----|-------------------------------|-----|
| Control    | 32                | 25.9±                  | 12.0   | 153±            | 3 | 4.2±               | 0.4  | 122±              | 5 | 8.8±             | 0.7 | 6.2±                          | 0.8 |
| 32 ppm     | 33                | 22.3±                  | 15.7** | 153±            | 3 | 4.1±               | 0.3  | 122±              | 3 | 8.8±             | 0.4 | 6.4±                          | 1.1 |
| 80 ppm     | 32                | 21.1±                  | 5.5**  | 153±            | 3 | 4.4±               | 0.7* | 122±              | 3 | 8.9±             | 0.5 | 6.5±                          | 1.4 |
| 200 ppm    | 40                | 21.3±                  | 5.2**  | 152±            | 2 | 4.1±               | 0.3  | 121±              | 2 | 8.9±             | 0.6 | 6.2±                          | 0.5 |

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

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 4

## APPENDIX G 2

### BIOCHEMISTRY : FEMALE

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 MEASURE. TIME : 1  
 SEX : FEMALE

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 4

| Group Name | NO. of<br>Animals | TOTAL PROTEIN<br>g/dl |     | ALBUMIN<br>g/dl |     | A/G RATIO |       | T-BILIRUBIN<br>mg/dl |      | GLUCOSE<br>mg/dl |    | T-CHOLESTEROL<br>mg/dl |     | TRIGLYCERIDE<br>mg/dl |    |
|------------|-------------------|-----------------------|-----|-----------------|-----|-----------|-------|----------------------|------|------------------|----|------------------------|-----|-----------------------|----|
| Control    | 29                | 5.2±                  | 0.8 | 2.8±            | 0.4 | 1.1±      | 0.1   | 0.13±                | 0.02 | 137±             | 33 | 103±                   | 119 | 27±                   | 16 |
| 32 ppm     | 27                | 5.1±                  | 0.8 | 2.8±            | 0.4 | 1.3±      | 0.3   | 0.14±                | 0.04 | 148±             | 33 | 86±                    | 67  | 31±                   | 24 |
| 80 ppm     | 25                | 5.1±                  | 0.7 | 2.7±            | 0.2 | 1.2±      | 0.3   | 0.14±                | 0.04 | 135±             | 37 | 73±                    | 18  | 24±                   | 11 |
| 200 ppm    | 28                | 4.9±                  | 0.5 | 2.8±            | 0.3 | 1.4±      | 0.3** | 0.16±                | 0.06 | 133±             | 52 | 71±                    | 15  | 23±                   | 17 |

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

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 4

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]  
 MEASURE. TIME : 1  
 SEX : FEMALE

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 5

| Group Name | NO. of<br>Animals | PHOSPHOLIPID<br>mg/dl |     | AST<br>IU/l |     | ALT<br>IU/l |     | LDH<br>IU/l |      | ALP<br>IU/l |    | G-GTP<br>IU/l |   | CK<br>IU/l |     |
|------------|-------------------|-----------------------|-----|-------------|-----|-------------|-----|-------------|------|-------------|----|---------------|---|------------|-----|
| Control    | 29                | 179±                  | 156 | 96±         | 29  | 51±         | 64  | 317±        | 206  | 198±        | 81 | 1±            | 1 | 66±        | 25  |
| 32 ppm     | 27                | 159±                  | 107 | 92±         | 58  | 37±         | 16  | 344±        | 315  | 182±        | 81 | 1±            | 1 | 102±       | 168 |
| 80 ppm     | 25                | 138±                  | 28  | 109±        | 56  | 44±         | 30  | 776±        | 1943 | 184±        | 65 | 1±            | 1 | 93±        | 95  |
| 200 ppm    | 28                | 131±                  | 34  | 207±        | 395 | 89±         | 201 | 997±        | 2512 | 218±        | 97 | 1±            | 1 | 117±       | 181 |

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

Test of Dunnett

(HCL074)

BAIS 4

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 MEASURE. TIME : 1  
 SEX : FEMALE

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 6

| Group Name | NO. of<br>Animals | UREA NITROGEN<br>mg/dl |      | SODIUM<br>mEq/l |   | POTASSIUM<br>mEq/l |     | CHLORIDE<br>mEq/l |   | CALCIUM<br>mg/dl |     | INORGANIC PHOSPHORUS<br>mg/dl |     |
|------------|-------------------|------------------------|------|-----------------|---|--------------------|-----|-------------------|---|------------------|-----|-------------------------------|-----|
| Control    | 29                | 17.0±                  | 6.9  | 151±            | 2 | 4.0±               | 0.4 | 122±              | 4 | 9.1±             | 0.7 | 6.0±                          | 0.8 |
| 32 ppm     | 27                | 17.8±                  | 10.3 | 151±            | 3 | 4.0±               | 0.5 | 122±              | 4 | 8.9±             | 0.5 | 5.9±                          | 0.9 |
| 80 ppm     | 25                | 15.8±                  | 7.2  | 151±            | 1 | 4.1±               | 0.5 | 122±              | 2 | 9.0±             | 0.6 | 5.8±                          | 0.8 |
| 200 ppm    | 28                | 23.0±                  | 26.6 | 152±            | 4 | 4.2±               | 0.5 | 121±              | 3 | 8.8±             | 0.3 | 6.1±                          | 1.3 |

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

Test of Dunnett

(HCL074)

BAIS 4



## APPENDIX H 1

### URINALYSIS : MALE

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
MEASURE. TIME : 1  
SEX : MALE

# URINALYSIS

REPORT TYPE : A1

PAGE : 1

| Group Name | NO. of<br>Animals | pH  |     |     |     |     |     |     | CHI | Protein |    |    |    |    |    | CHI | Glucose |   |   |    |    |    | CHI | Ketone body |    |    |    |    |    | CHI | Occult blood |   |   |    |    | CHI |
|------------|-------------------|-----|-----|-----|-----|-----|-----|-----|-----|---------|----|----|----|----|----|-----|---------|---|---|----|----|----|-----|-------------|----|----|----|----|----|-----|--------------|---|---|----|----|-----|
|            |                   | 5.0 | 6.0 | 6.5 | 7.0 | 7.5 | 8.0 | 8.5 |     | -       | ±  | +  | 2+ | 3+ | 4+ |     | -       | ± | + | 2+ | 3+ | 4+ |     | -           | ±  | +  | 2+ | 3+ | 4+ |     | -            | ± | + | 2+ | 3+ |     |
| Control    | 32                | 0   | 4   | 2   | 7   | 12  | 7   | 0   |     | 0       | 11 | 18 | 2  | 1  | 0  |     | 32      | 0 | 0 | 0  | 0  | 0  |     | 18          | 8  | 6  | 0  | 0  | 0  |     | 25           | 3 | 0 | 1  | 3  |     |
| 32 ppm     | 33                | 0   | 3   | 7   | 11  | 9   | 3   | 0   |     | 0       | 22 | 8  | 3  | 0  | 0  | *   | 33      | 0 | 0 | 0  | 0  | 0  |     | 23          | 8  | 2  | 0  | 0  | 0  |     | 32           | 0 | 0 | 0  | 1  |     |
| 80 ppm     | 33                | 0   | 1   | 4   | 14  | 7   | 7   | 0   |     | 0       | 14 | 16 | 3  | 0  | 0  |     | 33      | 0 | 0 | 0  | 0  | 0  |     | 16          | 10 | 7  | 0  | 0  | 0  |     | 29           | 1 | 0 | 0  | 3  |     |
| 200 ppm    | 41                | 0   | 3   | 12  | 10  | 13  | 3   | 0   |     | 0       | 16 | 23 | 2  | 0  | 0  |     | 41      | 0 | 0 | 0  | 0  | 0  |     | 15          | 14 | 12 | 0  | 0  | 0  |     | 39           | 0 | 0 | 1  | 1  |     |

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

Test of CHI SQUARE

STUDY NO. : 0458

ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]

MEASURE. TIME : 1

SEX : MALE

REPORT TYPE : A1

URINALYSIS

PAGE : 2

| Group Name | NO. of<br>Animals | Urobilinogen<br>± + 2+ 3+ 4+ CHI |
|------------|-------------------|----------------------------------|
| Control    | 32                | 32 0 0 0 0                       |
| 32 ppm     | 33                | 33 0 0 0 0                       |
| 80 ppm     | 33                | 33 0 0 0 0                       |
| 200 ppm    | 41                | 41 0 0 0 0                       |

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

Test of CHI SQUARE

(HCL101)

BAIS 4

## APPENDIX H 2

### URINALYSIS : FEMALE

STUDY NO. : 0458

ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]

MEASURE. TIME : 1

SEX : FEMALE

REPORT TYPE : A1

## URINALYSIS

PAGE : 3

| Group Name | NO. of<br>Animals | pH_____ |     |     |     |     |     |     | CHI | Protein_____ |    |    |    |    |    |   | CHI | Glucose_____ |   |    |    |    |   |    | CHI | Ketone body |    |    |    |   |    |   | CHI | Occult blood |    |  |  |  | CHI |
|------------|-------------------|---------|-----|-----|-----|-----|-----|-----|-----|--------------|----|----|----|----|----|---|-----|--------------|---|----|----|----|---|----|-----|-------------|----|----|----|---|----|---|-----|--------------|----|--|--|--|-----|
|            |                   | 5.0     | 6.0 | 6.5 | 7.0 | 7.5 | 8.0 | 8.5 |     | -            | ±  | +  | 2+ | 3+ | 4+ | - |     | ±            | + | 2+ | 3+ | 4+ | - | ±  |     | +           | 2+ | 3+ | 4+ | - | ±  | + |     | 2+           | 3+ |  |  |  |     |
| Control    | 30                | 0       | 1   | 2   | 6   | 2   | 16  | 3   |     | 0            | 12 | 10 | 6  | 1  | 1  |   | 30  | 0            | 0 | 0  | 0  | 0  |   | 10 | 13  | 6           | 1  | 0  | 0  |   | 27 | 0 | 0   | 2            | 1  |  |  |  |     |
| 32 ppm     | 28                | 0       | 2   | 0   | 2   | 7   | 17  | 0   |     | 0            | 10 | 11 | 6  | 0  | 1  |   | 28  | 0            | 0 | 0  | 0  | 0  |   | 9  | 14  | 4           | 1  | 0  | 0  |   | 24 | 0 | 1   | 1            | 2  |  |  |  |     |
| 80 ppm     | 27                | 0       | 1   | 1   | 3   | 10  | 12  | 0   |     | 0            | 11 | 10 | 5  | 0  | 1  |   | 27  | 0            | 0 | 0  | 0  | 0  |   | 10 | 13  | 4           | 0  | 0  | 0  |   | 23 | 1 | 2   | 0            | 1  |  |  |  |     |
| 200 ppm    | 30                | 0       | 3   | 3   | 7   | 4   | 12  | 1   |     | 0            | 6  | 13 | 11 | 0  | 0  |   | 30  | 0            | 0 | 0  | 0  | 0  |   | 4  | 19  | 5           | 2  | 0  | 0  |   | 27 | 0 | 0   | 1            | 2  |  |  |  |     |

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

Test of CHI SQUARE

(HCL101)

BAIS 4

STUDY NO. : 0458

ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]

MEASURE. TIME : 1

SEX : FEMALE

REPORT TYPE : A1

URINALYSIS

PAGE : 4

| Group Name | NO. of<br>Animals | Urobilinogen<br>± + 2+ 3+ 4+ CHI |
|------------|-------------------|----------------------------------|
| Control    | 30                | 30 0 0 0 0                       |
| 32 ppm     | 28                | 28 0 0 0 0                       |
| 80 ppm     | 27                | 27 0 0 0 0                       |
| 200 ppm    | 30                | 30 0 0 0 0                       |

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

Test of CHI SQUARE

(HCL101)

BAIS 4

## APPENDIX I 1

GROSS FINDINGS : MALE

ALL ANIMALS

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

GROSS FINDINGS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 1

| Organ       | Findings                   | Group Name<br>NO. of Animals | Control |       | 32 ppm |       | 80 ppm |       | 200 ppm |       |
|-------------|----------------------------|------------------------------|---------|-------|--------|-------|--------|-------|---------|-------|
|             |                            |                              | 50      | (%)   | 50     | (%)   | 50     | (%)   | 50      | (%)   |
| skin/app    | nodule                     |                              | 1       | ( 2)  | 1      | ( 2)  | 0      | ( 0)  | 1       | ( 2)  |
|             | erosion                    |                              | 0       | ( 0)  | 0      | ( 0)  | 2      | ( 4)  | 1       | ( 2)  |
|             | scab                       |                              | 2       | ( 4)  | 1      | ( 2)  | 0      | ( 0)  | 1       | ( 2)  |
| subcutis    | edema                      |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
|             | mass                       |                              | 5       | ( 10) | 3      | ( 6)  | 4      | ( 8)  | 1       | ( 2)  |
| lung        | white zone                 |                              | 1       | ( 2)  | 1      | ( 2)  | 1      | ( 2)  | 0       | ( 0)  |
|             | red zone                   |                              | 1       | ( 2)  | 1      | ( 2)  | 0      | ( 0)  | 0       | ( 0)  |
|             | nodule                     |                              | 6       | ( 12) | 17     | ( 34) | 16     | ( 32) | 16      | ( 32) |
| lymph node  | enlarged                   |                              | 10      | ( 20) | 6      | ( 12) | 7      | ( 14) | 7       | ( 14) |
| spleen      | enlarged                   |                              | 7       | ( 14) | 5      | ( 10) | 3      | ( 6)  | 2       | ( 4)  |
|             | white zone                 |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0       | ( 0)  |
|             | black zone                 |                              | 1       | ( 2)  | 2      | ( 4)  | 1      | ( 2)  | 3       | ( 6)  |
|             | nodule                     |                              | 0       | ( 0)  | 2      | ( 4)  | 4      | ( 8)  | 8       | ( 16) |
|             | deformed                   |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0       | ( 0)  |
|             | adhesion                   |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1       | ( 2)  |
|             | accentuation of white pulp |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 2       | ( 4)  |
| heart       | white zone                 |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1       | ( 2)  |
| gl stomach  | black zone                 |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0       | ( 0)  |
|             | nodule                     |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0       | ( 0)  |
|             | ulcer                      |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
|             | thick                      |                              | 3       | ( 6)  | 2      | ( 4)  | 4      | ( 8)  | 1       | ( 2)  |
| small intes | nodule                     |                              | 1       | ( 2)  | 1      | ( 2)  | 1      | ( 2)  | 1       | ( 2)  |



STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Crj[Crl:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

GROSS FINDINGS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 2

| Organ      | Findings               | Group Name<br>NO. of Animals | Control |       | 32 ppm |       | 80 ppm |       | 200 ppm |       |
|------------|------------------------|------------------------------|---------|-------|--------|-------|--------|-------|---------|-------|
|            |                        |                              | 50      | (%)   | 50     | (%)   | 50     | (%)   | 50      | (%)   |
| liver      | enlarged               |                              | 1       | ( 2)  | 1      | ( 2)  | 2      | ( 4)  | 1       | ( 2)  |
|            | white zone             |                              | 5       | ( 10) | 2      | ( 4)  | 4      | ( 8)  | 2       | ( 4)  |
|            | red zone               |                              | 1       | ( 2)  | 2      | ( 4)  | 9      | ( 18) | 4       | ( 8)  |
|            | nodule                 |                              | 19      | ( 38) | 18     | ( 36) | 23     | ( 46) | 21      | ( 42) |
|            | cyst                   |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0       | ( 0)  |
| pancreas   | red zone               |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0       | ( 0)  |
|            | nodule                 |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0       | ( 0)  |
| kidney     | enlarged               |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0       | ( 0)  |
|            | white zone             |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
|            | nodule                 |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0       | ( 0)  |
|            | cyst                   |                              | 1       | ( 2)  | 1      | ( 2)  | 1      | ( 2)  | 1       | ( 2)  |
|            | hydronephrosis         |                              | 1       | ( 2)  | 0      | ( 0)  | 3      | ( 6)  | 3       | ( 6)  |
|            | dilated pelvis         |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0       | ( 0)  |
| urin bladd | red zone               |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0       | ( 0)  |
|            | urine:marked retention |                              | 4       | ( 8)  | 4      | ( 8)  | 3      | ( 6)  | 2       | ( 4)  |
|            | urine:black            |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
| pituitary  | enlarged               |                              | 1       | ( 2)  | 0      | ( 0)  | 1      | ( 2)  | 0       | ( 0)  |
| thyroid    | enlarged               |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0       | ( 0)  |
| epididymis | nodule                 |                              | 2       | ( 4)  | 1      | ( 2)  | 0      | ( 0)  | 1       | ( 2)  |
| semin ves  | red zone               |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0       | ( 0)  |
|            | brown zone             |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0       | ( 0)  |
| prostate   | cyst                   |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : MALE

GROSS FINDINGS (SUMMARY)  
ALL ANIMALS (0-105W)

PAGE : 3

| Organ       | Findings      | Group Name<br>NO. of Animals | Control |      | 32 ppm |       | 80 ppm |      | 200 ppm |      |
|-------------|---------------|------------------------------|---------|------|--------|-------|--------|------|---------|------|
|             |               |                              | 50      | (%)  | 50     | (%)   | 50     | (%)  | 50      | (%)  |
| prep/cli gl | nodule        |                              | 0       | ( 0) | 5      | ( 10) | 0      | ( 0) | 0       | ( 0) |
|             | cyst          |                              | 1       | ( 2) | 0      | ( 0)  | 0      | ( 0) | 0       | ( 0) |
| brain       | red zone      |                              | 0       | ( 0) | 1      | ( 2)  | 0      | ( 0) | 0       | ( 0) |
|             | hemorrhage    |                              | 0       | ( 0) | 1      | ( 2)  | 1      | ( 2) | 0       | ( 0) |
|             | nodule        |                              | 1       | ( 2) | 0      | ( 0)  | 0      | ( 0) | 0       | ( 0) |
| periph nerv | nodule        |                              | 0       | ( 0) | 2      | ( 4)  | 0      | ( 0) | 0       | ( 0) |
| eye         | turbid        |                              | 1       | ( 2) | 0      | ( 0)  | 1      | ( 2) | 1       | ( 2) |
| Harder gl   | enlarged      |                              | 1       | ( 2) | 1      | ( 2)  | 1      | ( 2) | 2       | ( 4) |
|             | nodule        |                              | 0       | ( 0) | 0      | ( 0)  | 0      | ( 0) | 2       | ( 4) |
| mediastinum | mass          |                              | 1       | ( 2) | 0      | ( 0)  | 2      | ( 4) | 0       | ( 0) |
| peritoneum  | nodule        |                              | 0       | ( 0) | 1      | ( 2)  | 0      | ( 0) | 0       | ( 0) |
| retroperit  | mass          |                              | 0       | ( 0) | 0      | ( 0)  | 0      | ( 0) | 1       | ( 2) |
| abdominal c | hemorrhage    |                              | 0       | ( 0) | 1      | ( 2)  | 3      | ( 6) | 0       | ( 0) |
|             | ascites       |                              | 3       | ( 6) | 1      | ( 2)  | 0      | ( 0) | 2       | ( 4) |
| thoracic ca | hemorrhage    |                              | 0       | ( 0) | 2      | ( 4)  | 1      | ( 2) | 0       | ( 0) |
|             | pleural fluid |                              | 2       | ( 4) | 3      | ( 6)  | 0      | ( 0) | 0       | ( 0) |
| whole body  | anemic        |                              | 1       | ( 2) | 0      | ( 0)  | 1      | ( 2) | 1       | ( 2) |

## APPENDIX I 2

### GROSS FINDINGS : MALE DEAD AND MORIBUND ANIMALS

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

GROSS FINDINGS (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 1

| Organ       | Findings   | Group Name<br>NO. of Animals | Control |       | 32 ppm |       | 80 ppm |       | 200 ppm |       |
|-------------|------------|------------------------------|---------|-------|--------|-------|--------|-------|---------|-------|
|             |            |                              | 18      | (%)   | 17     | (%)   | 17     | (%)   | 9       | (%)   |
| skin/app    | nodule     |                              | 1       | ( 6)  | 0      | ( 0)  | 0      | ( 0)  | 1       | ( 11) |
|             | erosion    |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 6)  | 1       | ( 11) |
|             | scab       |                              | 1       | ( 6)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
| subcutis    | edema      |                              | 1       | ( 6)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
|             | mass       |                              | 4       | ( 22) | 1      | ( 6)  | 2      | ( 12) | 0       | ( 0)  |
| lung        | white zone |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 6)  | 0       | ( 0)  |
|             | red zone   |                              | 1       | ( 6)  | 1      | ( 6)  | 0      | ( 0)  | 0       | ( 0)  |
|             | nodule     |                              | 0       | ( 0)  | 6      | ( 35) | 7      | ( 41) | 2       | ( 22) |
| lymph node  | enlarged   |                              | 5       | ( 28) | 4      | ( 24) | 4      | ( 24) | 1       | ( 11) |
| spleen      | enlarged   |                              | 5       | ( 28) | 4      | ( 24) | 2      | ( 12) | 1       | ( 11) |
|             | white zone |                              | 0       | ( 0)  | 1      | ( 6)  | 0      | ( 0)  | 0       | ( 0)  |
|             | nodule     |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 6)  | 2       | ( 22) |
|             | deformed   |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 6)  | 0       | ( 0)  |
| heart       | white zone |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1       | ( 11) |
| gl stomach  | thick      |                              | 1       | ( 6)  | 1      | ( 6)  | 1      | ( 6)  | 0       | ( 0)  |
| small intes | nodule     |                              | 1       | ( 6)  | 0      | ( 0)  | 1      | ( 6)  | 0       | ( 0)  |
| liver       | enlarged   |                              | 1       | ( 6)  | 1      | ( 6)  | 2      | ( 12) | 1       | ( 11) |
|             | white zone |                              | 4       | ( 22) | 1      | ( 6)  | 3      | ( 18) | 2       | ( 22) |
|             | red zone   |                              | 1       | ( 6)  | 1      | ( 6)  | 2      | ( 12) | 1       | ( 11) |
|             | nodule     |                              | 9       | ( 50) | 8      | ( 47) | 9      | ( 53) | 3       | ( 33) |
| pancreas    | red zone   |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 6)  | 0       | ( 0)  |
|             | nodule     |                              | 0       | ( 0)  | 1      | ( 6)  | 0      | ( 0)  | 0       | ( 0)  |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

GROSS FINDINGS (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 2

| Organ       | Findings               | Group Name<br>NO. of Animals | Control | 32 ppm  | 80 ppm  | 200 ppm |
|-------------|------------------------|------------------------------|---------|---------|---------|---------|
|             |                        |                              | 18 (%)  | 17 (%)  | 17 (%)  | 9 (%)   |
| kidney      | white zone             |                              | 1 ( 6)  | 0 ( 0)  | 0 ( 0)  | 0 ( 0)  |
|             | nodule                 |                              | 0 ( 0)  | 0 ( 0)  | 1 ( 6)  | 0 ( 0)  |
|             | cyst                   |                              | 0 ( 0)  | 0 ( 0)  | 1 ( 6)  | 1 ( 11) |
|             | hydronephrosis         |                              | 0 ( 0)  | 0 ( 0)  | 3 ( 18) | 1 ( 11) |
| urin bladd  | urine:marked retention |                              | 4 ( 22) | 3 ( 18) | 2 ( 12) | 1 ( 11) |
| pituitary   | enlarged               |                              | 1 ( 6)  | 0 ( 0)  | 0 ( 0)  | 0 ( 0)  |
| thyroid     | enlarged               |                              | 0 ( 0)  | 0 ( 0)  | 1 ( 6)  | 0 ( 0)  |
| epididymis  | nodule                 |                              | 2 ( 11) | 0 ( 0)  | 0 ( 0)  | 1 ( 11) |
| prep/cli gl | nodule                 |                              | 0 ( 0)  | 1 ( 6)  | 0 ( 0)  | 0 ( 0)  |
| brain       | red zone               |                              | 0 ( 0)  | 1 ( 6)  | 0 ( 0)  | 0 ( 0)  |
|             | hemorrhage             |                              | 0 ( 0)  | 1 ( 6)  | 1 ( 6)  | 0 ( 0)  |
|             | nodule                 |                              | 1 ( 6)  | 0 ( 0)  | 0 ( 0)  | 0 ( 0)  |
| periph nerv | nodule                 |                              | 0 ( 0)  | 2 ( 12) | 0 ( 0)  | 0 ( 0)  |
| mediastinum | mass                   |                              | 1 ( 6)  | 0 ( 0)  | 2 ( 12) | 0 ( 0)  |
| peritoneum  | nodule                 |                              | 0 ( 0)  | 1 ( 6)  | 0 ( 0)  | 0 ( 0)  |
| retroperit  | mass                   |                              | 0 ( 0)  | 0 ( 0)  | 0 ( 0)  | 1 ( 11) |
| abdominal c | hemorrhage             |                              | 0 ( 0)  | 1 ( 6)  | 2 ( 12) | 0 ( 0)  |
|             | ascites                |                              | 2 ( 11) | 1 ( 6)  | 0 ( 0)  | 1 ( 11) |
| thoracic ca | hemorrhage             |                              | 0 ( 0)  | 2 ( 12) | 0 ( 0)  | 0 ( 0)  |
|             | pleural fluid          |                              | 2 ( 11) | 3 ( 18) | 0 ( 0)  | 0 ( 0)  |
| whole body  | anemic                 |                              | 1 ( 6)  | 0 ( 0)  | 1 ( 6)  | 1 ( 11) |

## APPENDIX I 3

### GROSS FINDINGS : MALE SACRIFICED ANIMALS

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : MALE

GROSS FINDINGS (SUMMARY)  
SACRIFICED ANIMALS (105W)

PAGE : 1

| Organ       | Findings                   | Group Name<br>NO. of Animals | Control |       | 32 ppm |       | 80 ppm |       | 200 ppm |       |
|-------------|----------------------------|------------------------------|---------|-------|--------|-------|--------|-------|---------|-------|
|             |                            |                              | 32      | (%)   | 33     | (%)   | 33     | (%)   | 41      | (%)   |
| skin/app    | nodule                     |                              | 0       | ( 0)  | 1      | ( 3)  | 0      | ( 0)  | 0       | ( 0)  |
|             | erosion                    |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 3)  | 0       | ( 0)  |
|             | scab                       |                              | 1       | ( 3)  | 1      | ( 3)  | 0      | ( 0)  | 1       | ( 2)  |
| subcutis    | mass                       |                              | 1       | ( 3)  | 2      | ( 6)  | 2      | ( 6)  | 1       | ( 2)  |
| lung        | white zone                 |                              | 1       | ( 3)  | 1      | ( 3)  | 0      | ( 0)  | 0       | ( 0)  |
|             | nodule                     |                              | 6       | ( 19) | 11     | ( 33) | 9      | ( 27) | 14      | ( 34) |
| lymph node  | enlarged                   |                              | 5       | ( 16) | 2      | ( 6)  | 3      | ( 9)  | 6       | ( 15) |
| spleen      | enlarged                   |                              | 2       | ( 6)  | 1      | ( 3)  | 1      | ( 3)  | 1       | ( 2)  |
|             | black zone                 |                              | 1       | ( 3)  | 2      | ( 6)  | 1      | ( 3)  | 3       | ( 7)  |
|             | nodule                     |                              | 0       | ( 0)  | 2      | ( 6)  | 3      | ( 9)  | 6       | ( 15) |
|             | adhesion                   |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1       | ( 2)  |
|             | accentuation of white pulp |                              | 1       | ( 3)  | 0      | ( 0)  | 0      | ( 0)  | 2       | ( 5)  |
| gl stomach  | black zone                 |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 3)  | 0       | ( 0)  |
|             | nodule                     |                              | 0       | ( 0)  | 1      | ( 3)  | 0      | ( 0)  | 0       | ( 0)  |
|             | ulcer                      |                              | 1       | ( 3)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
|             | thick                      |                              | 2       | ( 6)  | 1      | ( 3)  | 3      | ( 9)  | 1       | ( 2)  |
| small intes | nodule                     |                              | 0       | ( 0)  | 1      | ( 3)  | 0      | ( 0)  | 1       | ( 2)  |
| liver       | white zone                 |                              | 1       | ( 3)  | 1      | ( 3)  | 1      | ( 3)  | 0       | ( 0)  |
|             | red zone                   |                              | 0       | ( 0)  | 1      | ( 3)  | 7      | ( 21) | 3       | ( 7)  |
|             | nodule                     |                              | 10      | ( 31) | 10     | ( 30) | 14     | ( 42) | 18      | ( 44) |
|             | cyst                       |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 3)  | 0       | ( 0)  |
| kidney      | enlarged                   |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 3)  | 0       | ( 0)  |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

GROSS FINDINGS (SUMMARY)  
 SACRIFICED ANIMALS (105W)

PAGE : 2

| Organ       | Findings               | Group Name<br>NO. of Animals | Control |      | 32 ppm |       | 80 ppm |      | 200 ppm |      |
|-------------|------------------------|------------------------------|---------|------|--------|-------|--------|------|---------|------|
|             |                        |                              | 32      | (%)  | 33     | (%)   | 33     | (%)  | 41      | (%)  |
| kidney      | cyst                   |                              | 1       | ( 3) | 1      | ( 3)  | 0      | ( 0) | 0       | ( 0) |
|             | hydronephrosis         |                              | 1       | ( 3) | 0      | ( 0)  | 0      | ( 0) | 2       | ( 5) |
|             | dilated pelvis         |                              | 0       | ( 0) | 1      | ( 3)  | 0      | ( 0) | 0       | ( 0) |
| urin bladd  | red zone               |                              | 0       | ( 0) | 0      | ( 0)  | 1      | ( 3) | 0       | ( 0) |
|             | urine:marked retention |                              | 0       | ( 0) | 1      | ( 3)  | 1      | ( 3) | 1       | ( 2) |
|             | urine:black            |                              | 1       | ( 3) | 0      | ( 0)  | 0      | ( 0) | 0       | ( 0) |
| pituitary   | enlarged               |                              | 0       | ( 0) | 0      | ( 0)  | 1      | ( 3) | 0       | ( 0) |
| epididymis  | nodule                 |                              | 0       | ( 0) | 1      | ( 3)  | 0      | ( 0) | 0       | ( 0) |
| semin ves   | red zone               |                              | 0       | ( 0) | 1      | ( 3)  | 0      | ( 0) | 0       | ( 0) |
|             | brown zone             |                              | 0       | ( 0) | 1      | ( 3)  | 0      | ( 0) | 0       | ( 0) |
| prostate    | cyst                   |                              | 1       | ( 3) | 0      | ( 0)  | 0      | ( 0) | 0       | ( 0) |
| prep/cli gl | nodule                 |                              | 0       | ( 0) | 4      | ( 12) | 0      | ( 0) | 0       | ( 0) |
|             | cyst                   |                              | 1       | ( 3) | 0      | ( 0)  | 0      | ( 0) | 0       | ( 0) |
| eye         | turbid                 |                              | 1       | ( 3) | 0      | ( 0)  | 1      | ( 3) | 1       | ( 2) |
| Harder gl   | enlarged               |                              | 1       | ( 3) | 1      | ( 3)  | 1      | ( 3) | 2       | ( 5) |
|             | nodule                 |                              | 0       | ( 0) | 0      | ( 0)  | 0      | ( 0) | 2       | ( 5) |
| abdominal c | hemorrhage             |                              | 0       | ( 0) | 0      | ( 0)  | 1      | ( 3) | 0       | ( 0) |
|             | ascites                |                              | 1       | ( 3) | 0      | ( 0)  | 0      | ( 0) | 1       | ( 2) |
| thoracic ca | hemorrhage             |                              | 0       | ( 0) | 0      | ( 0)  | 1      | ( 3) | 0       | ( 0) |



## APPENDIX I 4

GROSS FINDINGS : FEMALE

ALL ANIMALS

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

GROSS FINDINGS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 4

| Organ       | Findings                   | Group Name<br>NO. of Animals | Control |       | 32 ppm |       | 80 ppm |       | 200 ppm |       |
|-------------|----------------------------|------------------------------|---------|-------|--------|-------|--------|-------|---------|-------|
|             |                            |                              | 50      | (%)   | 50     | (%)   | 50     | (%)   | 50      | (%)   |
| skin/app    | nodule                     |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
| subcutis    | edema                      |                              | 5       | ( 10) | 6      | ( 12) | 5      | ( 10) | 7       | ( 14) |
|             | mass                       |                              | 3       | ( 6)  | 2      | ( 4)  | 4      | ( 8)  | 3       | ( 6)  |
|             | cyst                       |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0       | ( 0)  |
| lung        | red                        |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 1       | ( 2)  |
|             | white zone                 |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 1       | ( 2)  |
|             | red zone                   |                              | 1       | ( 2)  | 0      | ( 0)  | 1      | ( 2)  | 0       | ( 0)  |
|             | edema                      |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
|             | nodule                     |                              | 2       | ( 4)  | 4      | ( 8)  | 4      | ( 8)  | 6       | ( 12) |
| lymph node  | enlarged                   |                              | 11      | ( 22) | 15     | ( 30) | 14     | ( 28) | 9       | ( 18) |
|             | nodule                     |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0       | ( 0)  |
| spleen      | enlarged                   |                              | 8       | ( 16) | 11     | ( 22) | 14     | ( 28) | 7       | ( 14) |
|             | white zone                 |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0       | ( 0)  |
|             | black zone                 |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0       | ( 0)  |
|             | nodule                     |                              | 1       | ( 2)  | 3      | ( 6)  | 0      | ( 0)  | 1       | ( 2)  |
|             | accentuation of white pulp |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 3       | ( 6)  |
| heart       | white zone                 |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 2       | ( 4)  |
|             | hypertrophy                |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0       | ( 0)  |
| salivary gl | nodule                     |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
| forestomach | nodule                     |                              | 2       | ( 4)  | 0      | ( 0)  | 2      | ( 4)  | 4       | ( 8)  |
|             | thick                      |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0       | ( 0)  |
| gl stomach  | ulcer                      |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 1       | ( 2)  |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

GROSS FINDINGS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 5

| Organ       | Findings               | Group Name<br>NO. of Animals | Control |       | 32 ppm |       | 80 ppm |       | 200 ppm |       |
|-------------|------------------------|------------------------------|---------|-------|--------|-------|--------|-------|---------|-------|
|             |                        |                              | 50      | (%)   | 50     | (%)   | 50     | (%)   | 50      | (%)   |
| gl stomach  | thick                  |                              | 0       | ( 0)  | 2      | ( 4)  | 2      | ( 4)  | 0       | ( 0)  |
| stomach     | nodule                 |                              | 0       | ( 0)  | 0      | ( 0)  | 2      | ( 4)  | 0       | ( 0)  |
| small intes | nodule                 |                              | 1       | ( 2)  | 1      | ( 2)  | 0      | ( 0)  | 0       | ( 0)  |
| large intes | nodule                 |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
| liver       | enlarged               |                              | 4       | ( 8)  | 3      | ( 6)  | 5      | ( 10) | 1       | ( 2)  |
|             | pale                   |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0       | ( 0)  |
|             | white zone             |                              | 9       | ( 18) | 4      | ( 8)  | 10     | ( 20) | 7       | ( 14) |
|             | red zone               |                              | 3       | ( 6)  | 1      | ( 2)  | 5      | ( 10) | 7       | ( 14) |
|             | nodule                 |                              | 9       | ( 18) | 6      | ( 12) | 8      | ( 16) | 9       | ( 18) |
|             | cyst                   |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0       | ( 0)  |
|             | rough                  |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
|             | nodular                |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0       | ( 0)  |
|             |                        |                              |         |       |        |       |        |       |         |       |
| pancreas    | white zone             |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1       | ( 2)  |
|             | nodule                 |                              | 0       | ( 0)  | 1      | ( 2)  | 1      | ( 2)  | 0       | ( 0)  |
| kidney      | atrophic               |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0       | ( 0)  |
|             | white zone             |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
|             | red zone               |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0       | ( 0)  |
|             | nodule                 |                              | 0       | ( 0)  | 1      | ( 2)  | 1      | ( 2)  | 0       | ( 0)  |
|             | hydronephrosis         |                              | 3       | ( 6)  | 0      | ( 0)  | 0      | ( 0)  | 2       | ( 4)  |
| urin bladd  | urine:marked retention |                              | 1       | ( 2)  | 0      | ( 0)  | 1      | ( 2)  | 1       | ( 2)  |
| pituitary   | enlarged               |                              | 8       | ( 16) | 1      | ( 2)  | 2      | ( 4)  | 2       | ( 4)  |
|             | red zone               |                              | 1       | ( 2)  | 3      | ( 6)  | 2      | ( 4)  | 2       | ( 4)  |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

GROSS FINDINGS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 6

| Organ       | Findings      | Group Name<br>NO. of Animals | Control |       | 32 ppm |       | 80 ppm |       | 200 ppm |       |
|-------------|---------------|------------------------------|---------|-------|--------|-------|--------|-------|---------|-------|
|             |               |                              | 50      | (%)   | 50     | (%)   | 50     | (%)   | 50      | (%)   |
| pituitary   | nodule        |                              | 1       | ( 2)  | 2      | ( 4)  | 5      | ( 10) | 1       | ( 2)  |
|             | cyst          |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
| thyroid     | enlarged      |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0       | ( 0)  |
| adrenal     | enlarged      |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1       | ( 2)  |
| ovary       | enlarged      |                              | 6       | ( 12) | 3      | ( 6)  | 10     | ( 20) | 3       | ( 6)  |
|             | black         |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0       | ( 0)  |
|             | red zone      |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1       | ( 2)  |
|             | cyst          |                              | 9       | ( 18) | 9      | ( 18) | 8      | ( 16) | 8       | ( 16) |
| uterus      | enlarged      |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
|             | red zone      |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
|             | nodule        |                              | 15      | ( 30) | 15     | ( 30) | 15     | ( 30) | 13      | ( 26) |
|             | dilated lumen |                              | 0       | ( 0)  | 2      | ( 4)  | 0      | ( 0)  | 0       | ( 0)  |
| vagina      | nodule        |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1       | ( 2)  |
| prep/cli gl | nodule        |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0       | ( 0)  |
| brain       | red zone      |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0       | ( 0)  |
| spinal cord | red zone      |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0       | ( 0)  |
|             | brown zone    |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
| eye         | turbid        |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1       | ( 2)  |
| Harder gl   | enlarged      |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 2       | ( 4)  |
|             | nodule        |                              | 0       | ( 0)  | 1      | ( 2)  | 1      | ( 2)  | 0       | ( 0)  |
| muscle      | nodule        |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1       | ( 2)  |
| mediastinum | mass          |                              | 1       | ( 2)  | 2      | ( 4)  | 4      | ( 8)  | 1       | ( 2)  |

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : FEMALE

GROSS FINDINGS (SUMMARY)  
ALL ANIMALS (0-105W)

PAGE : 7

| Organ       | Findings        | Group Name<br>NO. of Animals | Control |       | 32 ppm |       | 80 ppm |       | 200 ppm |       |
|-------------|-----------------|------------------------------|---------|-------|--------|-------|--------|-------|---------|-------|
|             |                 |                              | 50      | (%)   | 50     | (%)   | 50     | (%)   | 50      | (%)   |
| peritoneum  | nodule          |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 2       | ( 4)  |
|             | thick           |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0       | ( 0)  |
| retroperit  | mass            |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0       | ( 0)  |
| abdominal c | hemorrhage      |                              | 1       | ( 2)  | 2      | ( 4)  | 2      | ( 4)  | 0       | ( 0)  |
|             | ascites         |                              | 13      | ( 26) | 12     | ( 24) | 15     | ( 30) | 14      | ( 28) |
| thoracic ca | pleural fluid   |                              | 13      | ( 26) | 8      | ( 16) | 14     | ( 28) | 12      | ( 24) |
| other       | hindlimb:nodule |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1       | ( 2)  |
|             | tail:scab       |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
| whole body  | anemic          |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0       | ( 0)  |

(HPT080)

BAIS 4

## APPENDIX I 5

### GROSS FINDINGS : FEMALE DEAD AND MORIBUND ANIMALS

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

GROSS FINDINGS (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 3

| Organ       | Findings    | Group Name<br>NO. of Animals | Control |       | 32 ppm |       | 80 ppm |       | 200 ppm |       |
|-------------|-------------|------------------------------|---------|-------|--------|-------|--------|-------|---------|-------|
|             |             |                              | 21      | (%)   | 22     | (%)   | 24     | (%)   | 20      | (%)   |
| skin/app    | nodule      |                              | 1       | ( 5)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
| subcutis    | edema       |                              | 5       | ( 24) | 6      | ( 27) | 5      | ( 21) | 6       | ( 30) |
|             | mass        |                              | 1       | ( 5)  | 1      | ( 5)  | 2      | ( 8)  | 1       | ( 5)  |
| lung        | red         |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 4)  | 1       | ( 5)  |
|             | white zone  |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 4)  | 0       | ( 0)  |
|             | red zone    |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 4)  | 0       | ( 0)  |
|             | edema       |                              | 1       | ( 5)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
|             | nodule      |                              | 1       | ( 5)  | 0      | ( 0)  | 2      | ( 8)  | 3       | ( 15) |
| lymph node  | enlarged    |                              | 4       | ( 19) | 10     | ( 45) | 7      | ( 29) | 5       | ( 25) |
| spleen      | enlarged    |                              | 5       | ( 24) | 8      | ( 36) | 9      | ( 38) | 5       | ( 25) |
|             | black zone  |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 4)  | 0       | ( 0)  |
|             | nodule      |                              | 0       | ( 0)  | 3      | ( 14) | 0      | ( 0)  | 1       | ( 5)  |
| heart       | white zone  |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 2       | ( 10) |
|             | hypertrophy |                              | 0       | ( 0)  | 1      | ( 5)  | 0      | ( 0)  | 0       | ( 0)  |
| forestomach | nodule      |                              | 1       | ( 5)  | 0      | ( 0)  | 1      | ( 4)  | 1       | ( 5)  |
|             | thick       |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 4)  | 0       | ( 0)  |
| gl stomach  | ulcer       |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1       | ( 5)  |
|             | thick       |                              | 0       | ( 0)  | 1      | ( 5)  | 1      | ( 4)  | 0       | ( 0)  |
| stomach     | nodule      |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 4)  | 0       | ( 0)  |
| liver       | enlarged    |                              | 4       | ( 19) | 2      | ( 9)  | 5      | ( 21) | 1       | ( 5)  |
|             | pale        |                              | 0       | ( 0)  | 1      | ( 5)  | 0      | ( 0)  | 0       | ( 0)  |
|             | white zone  |                              | 9       | ( 43) | 3      | ( 14) | 9      | ( 38) | 4       | ( 20) |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

GROSS FINDINGS (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 4

| Organ      | Findings               | Group Name<br>NO. of Animals | Control |       | 32 ppm |       | 80 ppm |       | 200 ppm |       |
|------------|------------------------|------------------------------|---------|-------|--------|-------|--------|-------|---------|-------|
|            |                        |                              | 21      | (%)   | 22     | (%)   | 24     | (%)   | 20      | (%)   |
| liver      | red zone               |                              | 0       | ( 0)  | 1      | ( 5)  | 1      | ( 4)  | 1       | ( 5)  |
|            | nodule                 |                              | 3       | ( 14) | 4      | ( 18) | 2      | ( 8)  | 2       | ( 10) |
|            | rough                  |                              | 1       | ( 5)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
|            | nodular                |                              | 0       | ( 0)  | 1      | ( 5)  | 0      | ( 0)  | 0       | ( 0)  |
| pancreas   | white zone             |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1       | ( 5)  |
|            | nodule                 |                              | 0       | ( 0)  | 1      | ( 5)  | 1      | ( 4)  | 0       | ( 0)  |
| kidney     | atrophic               |                              | 0       | ( 0)  | 1      | ( 5)  | 0      | ( 0)  | 0       | ( 0)  |
|            | white zone             |                              | 1       | ( 5)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
|            | red zone               |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 4)  | 0       | ( 0)  |
|            | nodule                 |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 4)  | 0       | ( 0)  |
|            | hydronephrosis         |                              | 2       | ( 10) | 0      | ( 0)  | 0      | ( 0)  | 1       | ( 5)  |
| urin bladd | urine:marked retention |                              | 1       | ( 5)  | 0      | ( 0)  | 1      | ( 4)  | 1       | ( 5)  |
| pituitary  | enlarged               |                              | 2       | ( 10) | 0      | ( 0)  | 1      | ( 4)  | 1       | ( 5)  |
|            | red zone               |                              | 1       | ( 5)  | 1      | ( 5)  | 1      | ( 4)  | 1       | ( 5)  |
|            | nodule                 |                              | 0       | ( 0)  | 0      | ( 0)  | 3      | ( 13) | 0       | ( 0)  |
| thyroid    | enlarged               |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 4)  | 0       | ( 0)  |
| adrenal    | enlarged               |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1       | ( 5)  |
| ovary      | enlarged               |                              | 6       | ( 29) | 2      | ( 9)  | 8      | ( 33) | 3       | ( 15) |
|            | cyst                   |                              | 2       | ( 10) | 5      | ( 23) | 2      | ( 8)  | 1       | ( 5)  |
| uterus     | enlarged               |                              | 1       | ( 5)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
|            | nodule                 |                              | 9       | ( 43) | 7      | ( 32) | 11     | ( 46) | 6       | ( 30) |
|            | dilated lumen          |                              | 0       | ( 0)  | 1      | ( 5)  | 0      | ( 0)  | 0       | ( 0)  |



STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

GROSS FINDINGS (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 5

| Organ       | Findings        | Group Name<br>NO. of Animals | Control |       | 32 ppm |       | 80 ppm |       | 200 ppm |       |
|-------------|-----------------|------------------------------|---------|-------|--------|-------|--------|-------|---------|-------|
|             |                 |                              | 21      | (%)   | 22     | (%)   | 24     | (%)   | 20      | (%)   |
| brain       | red zone        |                              | 0       | ( 0)  | 1      | ( 5)  | 0      | ( 0)  | 0       | ( 0)  |
| spinal cord | red zone        |                              | 0       | ( 0)  | 1      | ( 5)  | 0      | ( 0)  | 0       | ( 0)  |
|             | brown zone      |                              | 1       | ( 5)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
| eye         | turbid          |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1       | ( 5)  |
| Harder gl   | enlarged        |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1       | ( 5)  |
|             | nodule          |                              | 0       | ( 0)  | 1      | ( 5)  | 1      | ( 4)  | 0       | ( 0)  |
| muscle      | nodule          |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1       | ( 5)  |
| mediastinum | mass            |                              | 1       | ( 5)  | 2      | ( 9)  | 4      | ( 17) | 1       | ( 5)  |
| peritoneum  | nodule          |                              | 0       | ( 0)  | 1      | ( 5)  | 0      | ( 0)  | 2       | ( 10) |
|             | thick           |                              | 0       | ( 0)  | 1      | ( 5)  | 0      | ( 0)  | 0       | ( 0)  |
| retroperit  | mass            |                              | 0       | ( 0)  | 1      | ( 5)  | 0      | ( 0)  | 0       | ( 0)  |
| abdominal c | hemorrhage      |                              | 1       | ( 5)  | 2      | ( 9)  | 2      | ( 8)  | 0       | ( 0)  |
|             | ascites         |                              | 12      | ( 57) | 9      | ( 41) | 12     | ( 50) | 9       | ( 45) |
| thoracic ca | pleural fluid   |                              | 9       | ( 43) | 5      | ( 23) | 13     | ( 54) | 8       | ( 40) |
| other       | hindlimb:nodule |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1       | ( 5)  |
|             | tail:scab       |                              | 1       | ( 5)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
| whole body  | anemic          |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 4)  | 0       | ( 0)  |

## APPENDIX I 6

### GROSS FINDINGS : FEMALE SACRIFICED ANIMALS

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

GROSS FINDINGS (SUMMARY)  
 SACRIFICED ANIMALS (105W)

PAGE : 3

| Organ       | Findings                   | Group Name<br>NO. of Animals | Control |       | 32 ppm |       | 80 ppm |       | 200 ppm |       |
|-------------|----------------------------|------------------------------|---------|-------|--------|-------|--------|-------|---------|-------|
|             |                            |                              | 29      | (%)   | 28     | (%)   | 26     | (%)   | 30      | (%)   |
| subcutis    | edema                      |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1       | ( 3)  |
|             | mass                       |                              | 2       | ( 7)  | 1      | ( 4)  | 2      | ( 8)  | 2       | ( 7)  |
|             | cyst                       |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 4)  | 0       | ( 0)  |
| lung        | white zone                 |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1       | ( 3)  |
|             | red zone                   |                              | 1       | ( 3)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
|             | nodule                     |                              | 1       | ( 3)  | 4      | ( 14) | 2      | ( 8)  | 3       | ( 10) |
| lymph node  | enlarged                   |                              | 7       | ( 24) | 5      | ( 18) | 7      | ( 27) | 4       | ( 13) |
|             | nodule                     |                              | 0       | ( 0)  | 1      | ( 4)  | 0      | ( 0)  | 0       | ( 0)  |
| spleen      | enlarged                   |                              | 3       | ( 10) | 3      | ( 11) | 5      | ( 19) | 2       | ( 7)  |
|             | white zone                 |                              | 0       | ( 0)  | 1      | ( 4)  | 0      | ( 0)  | 0       | ( 0)  |
|             | nodule                     |                              | 1       | ( 3)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
|             | accentuation of white pulp |                              | 1       | ( 3)  | 0      | ( 0)  | 0      | ( 0)  | 3       | ( 10) |
| salivary gl | nodule                     |                              | 1       | ( 3)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
| forestomach | nodule                     |                              | 1       | ( 3)  | 0      | ( 0)  | 1      | ( 4)  | 3       | ( 10) |
| gl stomach  | ulcer                      |                              | 1       | ( 3)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
|             | thick                      |                              | 0       | ( 0)  | 1      | ( 4)  | 1      | ( 4)  | 0       | ( 0)  |
| stomach     | nodule                     |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 4)  | 0       | ( 0)  |
| small intes | nodule                     |                              | 1       | ( 3)  | 1      | ( 4)  | 0      | ( 0)  | 0       | ( 0)  |
| large intes | nodule                     |                              | 1       | ( 3)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
| liver       | enlarged                   |                              | 0       | ( 0)  | 1      | ( 4)  | 0      | ( 0)  | 0       | ( 0)  |
|             | white zone                 |                              | 0       | ( 0)  | 1      | ( 4)  | 1      | ( 4)  | 3       | ( 10) |
|             | red zone                   |                              | 3       | ( 10) | 0      | ( 0)  | 4      | ( 15) | 6       | ( 20) |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

GROSS FINDINGS (SUMMARY)  
 SACRIFICED ANIMALS (105W)

PAGE : 4

| Organ       | Findings       | Group Name<br>NO. of Animals | Control |       | 32 ppm |       | 80 ppm |       | 200 ppm |       |
|-------------|----------------|------------------------------|---------|-------|--------|-------|--------|-------|---------|-------|
|             |                |                              | 29      | (%)   | 28     | (%)   | 26     | (%)   | 30      | (%)   |
| liver       | nodule         |                              | 6       | ( 21) | 2      | ( 7)  | 6      | ( 23) | 7       | ( 23) |
|             | cyst           |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 4)  | 0       | ( 0)  |
| kidney      | nodule         |                              | 0       | ( 0)  | 1      | ( 4)  | 0      | ( 0)  | 0       | ( 0)  |
|             | hydronephrosis |                              | 1       | ( 3)  | 0      | ( 0)  | 0      | ( 0)  | 1       | ( 3)  |
| pituitary   | enlarged       |                              | 6       | ( 21) | 1      | ( 4)  | 1      | ( 4)  | 1       | ( 3)  |
|             | red zone       |                              | 0       | ( 0)  | 2      | ( 7)  | 1      | ( 4)  | 1       | ( 3)  |
|             | nodule         |                              | 1       | ( 3)  | 2      | ( 7)  | 2      | ( 8)  | 1       | ( 3)  |
|             | cyst           |                              | 1       | ( 3)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
| ovary       | enlarged       |                              | 0       | ( 0)  | 1      | ( 4)  | 2      | ( 8)  | 0       | ( 0)  |
|             | black          |                              | 0       | ( 0)  | 1      | ( 4)  | 0      | ( 0)  | 0       | ( 0)  |
|             | red zone       |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1       | ( 3)  |
|             | cyst           |                              | 7       | ( 24) | 4      | ( 14) | 6      | ( 23) | 7       | ( 23) |
| uterus      | red zone       |                              | 1       | ( 3)  | 0      | ( 0)  | 0      | ( 0)  | 0       | ( 0)  |
|             | nodule         |                              | 6       | ( 21) | 8      | ( 29) | 4      | ( 15) | 7       | ( 23) |
|             | dilated lumen  |                              | 0       | ( 0)  | 1      | ( 4)  | 0      | ( 0)  | 0       | ( 0)  |
| vagina      | nodule         |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1       | ( 3)  |
| prep/cli gl | nodule         |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 4)  | 0       | ( 0)  |
| Harder gl   | enlarged       |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 4)  | 1       | ( 3)  |
| abdominal c | ascites        |                              | 1       | ( 3)  | 3      | ( 11) | 3      | ( 12) | 5       | ( 17) |
| thoracic ca | pleural fluid  |                              | 4       | ( 14) | 3      | ( 11) | 1      | ( 4)  | 4       | ( 13) |

## APPENDIX J 1

ORGAN WEIGHT, ABSOLUTE : MALE

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : MALE  
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)  
SURVIVAL ANIMALS (105W)

PAGE : 1

| Group Name | NO. of<br>Animals | Body Weight | ADRENALS |       | TESTES |       | HEART  |       | LUNGS  |       | KIDNEYS |         |
|------------|-------------------|-------------|----------|-------|--------|-------|--------|-------|--------|-------|---------|---------|
| Control    | 32                | 41.9± 7.5   | 0.011±   | 0.002 | 0.230± | 0.027 | 0.224± | 0.018 | 0.225± | 0.079 | 0.634±  | 0.048   |
| 32 ppm     | 33                | 46.8± 7.4   | 0.011±   | 0.002 | 0.230± | 0.041 | 0.235± | 0.025 | 0.226± | 0.079 | 0.705±  | 0.048** |
| 80 ppm     | 33                | 45.5± 8.0   | 0.012±   | 0.003 | 0.215± | 0.038 | 0.237± | 0.019 | 0.234± | 0.098 | 0.764±  | 0.212** |
| 200 ppm    | 41                | 44.0± 8.1   | 0.011±   | 0.002 | 0.224± | 0.038 | 0.238± | 0.035 | 0.230± | 0.082 | 0.989±  | 1.690** |

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

Test of Dunnett

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : MALE  
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)  
SURVIVAL ANIMALS (105W)

PAGE : 2

| Group Name | NO. of<br>Animals | SPLEEN |        | LIVER  |       | BRAIN  |       |
|------------|-------------------|--------|--------|--------|-------|--------|-------|
| Control    | 32                | 0.192± | 0.556  | 1.712± | 0.723 | 0.453± | 0.020 |
| 32 ppm     | 33                | 0.163± | 0.350  | 1.929± | 1.122 | 0.445± | 0.017 |
| 80 ppm     | 33                | 0.117± | 0.105  | 1.775± | 0.579 | 0.451± | 0.014 |
| 200 ppm    | 41                | 0.145± | 0.107* | 1.873± | 0.823 | 0.456± | 0.013 |

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

Test of Dunnett

(HCL040)

BAIS 4

## APPENDIX J 2

ORGAN WEIGHT, ABSOLUTE : FEMALE



STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : FEMALE  
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)  
SURVIVAL ANIMALS (105W)

PAGE : 3

| Group Name | NO. of<br>Animals | Body Weight | ADRENALS     | OVARIES      | HEART        | LUNGS        | KIDNEYS      |
|------------|-------------------|-------------|--------------|--------------|--------------|--------------|--------------|
| Control    | 29                | 29.2± 3.7   | 0.015± 0.002 | 0.059± 0.038 | 0.186± 0.033 | 0.190± 0.014 | 0.484± 0.262 |
| 32 ppm     | 28                | 30.6± 4.1   | 0.015± 0.003 | 0.059± 0.030 | 0.183± 0.024 | 0.213± 0.060 | 0.483± 0.127 |
| 80 ppm     | 26                | 31.2± 5.0   | 0.015± 0.002 | 0.108± 0.158 | 0.180± 0.019 | 0.197± 0.036 | 0.458± 0.057 |
| 200 ppm    | 30                | 29.9± 5.4   | 0.014± 0.002 | 0.060± 0.042 | 0.183± 0.029 | 0.216± 0.071 | 0.487± 0.118 |

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

Test of Dunnett

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : FEMALE  
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)  
SURVIVAL ANIMALS (105W)

PAGE : 4

| Group Name | NO. of<br>Animals | SPLEEN |       | LIVER  |       | BRAIN  |       |
|------------|-------------------|--------|-------|--------|-------|--------|-------|
| Control    | 29                | 0.219± | 0.310 | 1.532± | 0.600 | 0.474± | 0.016 |
| 32 ppm     | 28                | 0.211± | 0.178 | 1.610± | 0.644 | 0.474± | 0.020 |
| 80 ppm     | 26                | 0.331± | 0.439 | 1.638± | 0.643 | 0.475± | 0.025 |
| 200 ppm    | 30                | 0.162± | 0.137 | 1.850± | 1.586 | 0.462± | 0.018 |

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

Test of Dunnett

(HCL040)

BAIS 4

## APPENDIX K 1

ORGAN WEIGHT, RELATIVE : MALE

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : MALE  
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)  
SURVIVAL ANIMALS (105W)

PAGE : 1

| Group Name | NO. of<br>Animals | Body Weight<br>(g) | ADRENALS     | TESTES        | HEART        | LUNGS        | KIDNEYS       |
|------------|-------------------|--------------------|--------------|---------------|--------------|--------------|---------------|
| Control    | 32                | 41.9± 7.5          | 0.027± 0.007 | 0.562± 0.101  | 0.551± 0.112 | 0.556± 0.225 | 1.551± 0.269  |
| 32 ppm     | 33                | 46.8± 7.4          | 0.025± 0.008 | 0.496± 0.080* | 0.517± 0.115 | 0.492± 0.168 | 1.540± 0.251  |
| 80 ppm     | 33                | 45.5± 8.0          | 0.027± 0.008 | 0.487± 0.127* | 0.539± 0.120 | 0.537± 0.270 | 1.732± 0.560  |
| 200 ppm    | 41                | 44.0± 8.1          | 0.026± 0.009 | 0.519± 0.096  | 0.562± 0.183 | 0.545± 0.243 | 2.290± 3.833* |

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

Test of Dunnett

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : MALE  
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)  
SURVIVAL ANIMALS (105W)

PAGE : 2

| Group Name | NO. of<br>Animals | SPLEEN       | LIVER        | BRAIN         |
|------------|-------------------|--------------|--------------|---------------|
| Control    | 32                | 0.496± 1.456 | 4.281± 2.348 | 1.115± 0.211  |
| 32 ppm     | 33                | 0.424± 1.085 | 4.263± 2.596 | 0.976± 0.169* |
| 80 ppm     | 33                | 0.276± 0.292 | 3.967± 1.357 | 1.028± 0.226  |
| 200 ppm    | 41                | 0.343± 0.262 | 4.503± 2.718 | 1.074± 0.206  |

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

Test of Dunnett

(HCL042)

BAIS 4

## APPENDIX K 2

ORGAN WEIGHT, RELATIVE : FEMALE

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE  
 UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)  
 SURVIVAL ANIMALS (105W)

PAGE : 3

| Group Name | NO. of<br>Animals | Body Weight<br>(g) | ADRENALS     | OVARIES      | HEART        | LUNGS        | KIDNEYS      |
|------------|-------------------|--------------------|--------------|--------------|--------------|--------------|--------------|
| Control    | 29                | 29.2± 3.7          | 0.053± 0.010 | 0.203± 0.123 | 0.645± 0.115 | 0.660± 0.071 | 1.668± 0.876 |
| 32 ppm     | 28                | 30.6± 4.1          | 0.049± 0.010 | 0.195± 0.099 | 0.611± 0.119 | 0.706± 0.211 | 1.595± 0.380 |
| 80 ppm     | 26                | 31.2± 5.0          | 0.049± 0.011 | 0.322± 0.408 | 0.592± 0.127 | 0.644± 0.135 | 1.501± 0.308 |
| 200 ppm    | 30                | 29.9± 5.4          | 0.048± 0.009 | 0.212± 0.187 | 0.620± 0.100 | 0.740± 0.256 | 1.673± 0.545 |

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

Test of Dunnett

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : FEMALE  
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)  
SURVIVAL ANIMALS (105W)

PAGE : 4

| Group Name | NO. of<br>Animals | SPLEEN       | LIVER        | BRAIN        |
|------------|-------------------|--------------|--------------|--------------|
| Control    | 29                | 0.719± 0.926 | 5.301± 2.313 | 1.649± 0.187 |
| 32 ppm     | 28                | 0.685± 0.565 | 5.347± 2.407 | 1.574± 0.188 |
| 80 ppm     | 26                | 0.979± 1.137 | 5.249± 1.697 | 1.568± 0.322 |
| 200 ppm    | 30                | 0.536± 0.446 | 5.835± 3.308 | 1.588± 0.240 |

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

Test of Dunnett

(HCL042)

BATS 4



## APPENDIX L 1

HISTOPATHOLOGICAL FINDINGS :  
NON-NEOPLASTIC LESIONS : MALE  
ALL ANIMALS

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 1

|                                  |  | Group Name              | Control |       |       |       | 32 ppm |       |       |       | 80 ppm |       |       |       | 200 ppm |       |       |       |
|----------------------------------|--|-------------------------|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|---------|-------|-------|-------|
|                                  |  | No. of Animals on Study | 50      |       |       |       | 50     |       |       |       | 50     |       |       |       | 50      |       |       |       |
|                                  |  | Grade                   | 1       | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1       | 2     | 3     | 4     |
| Organ                            | Findings                                 |                         | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)     | (%)   | (%)   | (%)   |
| <hr/>                            |  |                         |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
| {Integumentary system/appandage} |  |                         |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
| skin/app                         |  |                         | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>    |       |       |       |
|                                  | inflammation                             |                         | 0       | 1     | 2     | 0     | 0      | 1     | 0     | 0     | 0      | 0     | 2     | 0     | 0       | 1     | 1     | 0     |
|                                  |  |                         | ( 0 )   | ( 2 ) | ( 4 ) | ( 0 ) | ( 0 )  | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 4 ) | ( 0 ) | ( 0 )   | ( 2 ) | ( 2 ) | ( 0 ) |
| subcutis                         |  |                         | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>    |       |       |       |
|                                  | inflammation                             |                         | 0       | 0     | 3     | 0     | 0      | 0     | 1     | 0     | 0      | 0     | 1     | 0     | 0       | 0     | 0     | 0     |
|                                  |  |                         | ( 0 )   | ( 0 ) | ( 6 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 2 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 2 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
| {Respiratory system}             |  |                         |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
| nasal cavit                      |  |                         | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>    |       |       |       |
|                                  | exudate                                  |                         | 0       | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                                  |  |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                                  | mineralization                           |                         | 1       | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                                  |  |                         | ( 2 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                                  | inflammation                             |                         | 0       | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                                  |  |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                                  | eosinophilic change:olfactory epithelium |                         | 7       | 0     | 0     | 0     | 21     | 0     | 0     | 0 **  | 9      | 0     | 0     | 0     | 14      | 1     | 0     | 0     |
|                                  |  |                         | ( 14 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 42 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 18 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 28 )  | ( 2 ) | ( 0 ) | ( 0 ) |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/CrIj[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 2

| Organ                | Findings                                    | Group Name<br>No. of Animals on Study<br>Grade | Control |      |      |      | 32 ppm |      |      |      | 80 ppm |      |      |      | 200 ppm |      |      |      |
|----------------------|---|--|---------|------|------|------|--------|------|------|------|--------|------|------|------|---------|------|------|------|
|                      |   |  | 50      |      |      |      | 50     |      |      |      | 50     |      |      |      | 50      |      |      |      |
|                      |   |  | 1       | 2    | 3    | 4    | 1      | 2    | 3    | 4    | 1      | 2    | 3    | 4    | 1       | 2    | 3    | 4    |
|                      |   |  | (%)     | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  | (%)     | (%)  | (%)  | (%)  |
| (Respiratory system) |   |  |         |      |      |      |        |      |      |      |        |      |      |      |         |      |      |      |
| nasal cavit          | eosinophilic change:respiratory epithelium  |  | 8       | 0    | 1    | 0    | 2      | 0    | 0    | 0    | 8      | 0    | 0    | 0    | 3       | 0    | 0    | 0    |
|                      |   |  | ( 16)   | ( 0) | ( 2) | ( 0) | ( 4)   | ( 0) | ( 0) | ( 0) | ( 16)  | ( 0) | ( 0) | ( 0) | ( 6)    | ( 0) | ( 0) | ( 0) |
|                      | respiratory metaplasia:olfactory epithelium |  | 19      | 0    | 0    | 0    | 27     | 0    | 0    | 0    | 23     | 0    | 0    | 0    | 21      | 0    | 0    | 0    |
|                      |   |  | ( 38)   | ( 0) | ( 0) | ( 0) | ( 54)  | ( 0) | ( 0) | ( 0) | ( 46)  | ( 0) | ( 0) | ( 0) | ( 42)   | ( 0) | ( 0) | ( 0) |
|                      | respiratory metaplasia:gland                |  | 9       | 0    | 0    | 0    | 13     | 0    | 0    | 0    | 12     | 0    | 0    | 0    | 18      | 0    | 0    | 0    |
|                      |   |  | ( 18)   | ( 0) | ( 0) | ( 0) | ( 26)  | ( 0) | ( 0) | ( 0) | ( 24)  | ( 0) | ( 0) | ( 0) | ( 36)   | ( 0) | ( 0) | ( 0) |
|                      | atrophy:olfactory epithelium                |  | 1       | 0    | 0    | 0    | 0      | 1    | 0    | 0    | 19     | 0    | 0    | 0 ** | 20      | 0    | 0    | 0 ** |
|                      |   |  | ( 2)    | ( 0) | ( 0) | ( 0) | ( 0)   | ( 2) | ( 0) | ( 0) | ( 38)  | ( 0) | ( 0) | ( 0) | ( 40)   | ( 0) | ( 0) | ( 0) |
| nasopharynx          | eosinophilic change                         |  | 0       | 0    | 1    | 0    | 0      | 0    | 0    | 0    | 0      | 1    | 0    | 0    | 1       | 0    | 0    | 0    |
|                      |   |  | ( 0)    | ( 0) | ( 2) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 2) | ( 0) | ( 0) | ( 2)    | ( 0) | ( 0) | ( 0) |
| lung                 | congestion                                  |  | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 1       | 0    | 0    | 0    |
|                      |   |  | ( 0)    | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 2)    | ( 0) | ( 0) | ( 0) |
|                      | hemorrhage                                  |  | 1       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0       | 0    | 0    | 0    |
|                      |   |  | ( 2)    | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 3

| Organ                  | Findings                              | Group Name<br>No. of Animals on Study |      |      |      | Control |      |      |      | 32 ppm |      |      |      | 80 ppm |      |      |      | 200 ppm |      |      |      |
|------------------------|---------------------------------------|---------------------------------------|------|------|------|---------|------|------|------|--------|------|------|------|--------|------|------|------|---------|------|------|------|
|                        |                                       | Grade                                 |      |      |      | 50      |      |      |      | 50     |      |      |      | 50     |      |      |      | 50      |      |      |      |
|                        |                                       | 1                                     | 2    | 3    | 4    | 1       | 2    | 3    | 4    | 1      | 2    | 3    | 4    | 1      | 2    | 3    | 4    | 1       | 2    | 3    | 4    |
|                        |                                       | (%)                                   | (%)  | (%)  | (%)  | (%)     | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  | (%)     | (%)  | (%)  | (%)  |
| {Respiratory system}   |                                       |                                       |      |      |      |         |      |      |      |        |      |      |      |        |      |      |      |         |      |      |      |
| lung                   |                                       | <50>                                  |      |      |      | <50>    |      |      |      | <50>   |      |      |      | <50>   |      |      |      | <50>    |      |      |      |
|                        | inflammatory infiltration             | 2                                     | 0    | 0    | 0    | 1       | 0    | 0    | 0    | 1      | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0       | 0    | 0    | 0    |
|                        |                                       | ( 4)                                  | ( 0) | ( 0) | ( 0) | ( 2)    | ( 0) | ( 0) | ( 0) | ( 2)   | ( 0) | ( 0) | ( 0) | ( 2)   | ( 0) | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) |
|                        | inflammatory cell nest                | 0                                     | 0    | 0    | 0    | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 1       | 0    | 0    | 0    |
|                        |                                       | ( 0)                                  | ( 0) | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 2)    | ( 0) | ( 0) | ( 0) |
|                        | bronchiolar-alveolar cell hyperplasia | 2                                     | 0    | 0    | 0    | 5       | 0    | 0    | 0    | 5      | 0    | 0    | 0    | 5      | 0    | 0    | 0    | 1       | 0    | 0    | 0    |
|                        |                                       | ( 4)                                  | ( 0) | ( 0) | ( 0) | ( 10)   | ( 0) | ( 0) | ( 0) | ( 10)  | ( 0) | ( 0) | ( 0) | ( 10)  | ( 0) | ( 0) | ( 0) | ( 2)    | ( 0) | ( 0) | ( 0) |
| {Hematopoietic system} |                                       |                                       |      |      |      |         |      |      |      |        |      |      |      |        |      |      |      |         |      |      |      |
| bone marrow            |                                       | <50>                                  |      |      |      | <50>    |      |      |      | <50>   |      |      |      | <50>   |      |      |      | <50>    |      |      |      |
|                        | granulation                           | 1                                     | 0    | 0    | 0    | 0       | 0    | 0    | 0    | 1      | 0    | 0    | 0    | 1      | 0    | 0    | 0    | 0       | 0    | 0    | 0    |
|                        |                                       | ( 2)                                  | ( 0) | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) | ( 2)   | ( 0) | ( 0) | ( 0) | ( 2)   | ( 0) | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) |
|                        | increased hematopoiesis               | 2                                     | 0    | 0    | 0    | 4       | 0    | 0    | 0    | 3      | 0    | 0    | 0    | 3      | 0    | 0    | 0    | 3       | 0    | 0    | 0    |
|                        |                                       | ( 4)                                  | ( 0) | ( 0) | ( 0) | ( 8)    | ( 0) | ( 0) | ( 0) | ( 6)   | ( 0) | ( 0) | ( 0) | ( 6)   | ( 0) | ( 0) | ( 0) | ( 6)    | ( 0) | ( 0) | ( 0) |
|                        | decreased hematopoiesis               | 0                                     | 0    | 0    | 0    | 1       | 0    | 0    | 0    | 1      | 0    | 0    | 0    | 1      | 0    | 0    | 0    | 1       | 0    | 0    | 0    |
|                        |                                       | ( 0)                                  | ( 0) | ( 0) | ( 0) | ( 2)    | ( 0) | ( 0) | ( 0) | ( 2)   | ( 0) | ( 0) | ( 0) | ( 2)   | ( 0) | ( 0) | ( 0) | ( 2)    | ( 0) | ( 0) | ( 0) |
|                        | granulopoiesis:increased              | 2                                     | 0    | 0    | 0    | 1       | 0    | 0    | 0    | 2      | 0    | 0    | 0    | 4      | 0    | 0    | 0    | 4       | 0    | 0    | 0    |
|                        |                                       | ( 4)                                  | ( 0) | ( 0) | ( 0) | ( 2)    | ( 0) | ( 0) | ( 0) | ( 4)   | ( 0) | ( 0) | ( 0) | ( 8)   | ( 0) | ( 0) | ( 0) | ( 8)    | ( 0) | ( 0) | ( 0) |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 4

| Organ                  | Findings                | Group Name<br>No. of Animals on Study<br>Grade | Control |       |       |       | 32 ppm |       |       |       | 80 ppm |       |       |       | 200 ppm |       |       |       |
|------------------------|-------------------------|--|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|---------|-------|-------|-------|
|                        |                         |  | 50      |       |       |       | 50     |       |       |       | 50     |       |       |       | 50      |       |       |       |
|                        |                         |  | 1       | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1       | 2     | 3     | 4     |
|                        |                         |  | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)     | (%)   | (%)   | (%)   |
| {Hematopoietic system} |                         |  |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
| bone marrow            | xanthogranuloma         |  | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>    |       |       |       |
|                        |                         |  | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 1     | 0     | 0     | 0       | 0     | 0     | 0     |
|                        |                         |  | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
| lymph node             | plasma cell hyperplasia |  | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>    |       |       |       |
|                        |                         |  | 1       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                        |                         |  | ( 2 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                        | lymphadenitis           |  | 0       | 1     | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                        |                         |  | ( 0 )   | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
| spleen                 | angiectasis             |  | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>    |       |       |       |
|                        |                         |  | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 2      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                        |                         |  | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                        | deposit of amyloid      |  | 0       | 0     | 0     | 0     | 0      | 0     | 1     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                        |                         |  | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 2 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                        | deposit of hemosiderin  |  | 1       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                        |                         |  | ( 2 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                        | deposit of melanin      |  | 2       | 1     | 0     | 0     | 0      | 2     | 0     | 0     | 1      | 0     | 0     | 0     | 1       | 1     | 0     | 0     |
|                        |                         |  | ( 4 )   | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 4 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )   | ( 2 ) | ( 0 ) | ( 0 ) |

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

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
ALL ANIMALS (0-105W)

PAGE : 5

| Organ                  | Findings                     | Group Name<br>No. of Animals on Study |        |       |       | Control<br>50 |        |       |       | 32 ppm<br>50 |        |        |       | 80 ppm<br>50 |        |       |       | 200 ppm<br>50 |       |       |       |
|------------------------|------------------------------|---------------------------------------|--------|-------|-------|---------------|--------|-------|-------|--------------|--------|--------|-------|--------------|--------|-------|-------|---------------|-------|-------|-------|
|                        |                              | Grade                                 |        |       |       |               |        |       |       |              |        |        |       |              |        |       |       |               |       |       |       |
|                        |                              | 1                                     | 2      | 3     | 4     | 1             | 2      | 3     | 4     | 1            | 2      | 3      | 4     | 1            | 2      | 3     | 4     | 1             | 2     | 3     | 4     |
|                        |                              | (%)                                   | (%)    | (%)   | (%)   | (%)           | (%)    | (%)   | (%)   | (%)          | (%)    | (%)    | (%)   | (%)          | (%)    | (%)   | (%)   | (%)           | (%)   | (%)   | (%)   |
| {Hematopoietic system} |                              |                                       |        |       |       |               |        |       |       |              |        |        |       |              |        |       |       |               |       |       |       |
| spleen                 |                              | <50>                                  |        |       |       | <50>          |        |       |       | <50>         |        |        |       | <50>         |        |       |       | <50>          |       |       |       |
|                        | fibrosis                     | 0                                     | 0      | 0     | 0     | 0             | 0      | 0     | 0     | 1            | 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 ) | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) |
|                        | extramedullary hematopoiesis | 6                                     | 5      | 4     | 0     | 10            | 6      | 3     | 0     | 5            | 7      | 5      | 0     | 10           | 7      | 1     | 0     | 0             | 0     | 0     | 0     |
|                        |                              | ( 12 )                                | ( 10 ) | ( 8 ) | ( 0 ) | ( 20 )        | ( 12 ) | ( 6 ) | ( 0 ) | ( 10 )       | ( 14 ) | ( 10 ) | ( 0 ) | ( 20 )       | ( 14 ) | ( 2 ) | ( 0 ) | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) |
|                        | follicular hyperplasia       | 2                                     | 1      | 0     | 0     | 0             | 4      | 0     | 0     | 1            | 1      | 0      | 0     | 6            | 1      | 1     | 0     | 0             | 0     | 0     | 0     |
|                        |                              | ( 4 )                                 | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 )         | ( 8 )  | ( 0 ) | ( 0 ) | ( 2 )        | ( 2 )  | ( 0 )  | ( 0 ) | ( 12 )       | ( 2 )  | ( 2 ) | ( 0 ) | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) |
| {Circulatory system}   |                              |                                       |        |       |       |               |        |       |       |              |        |        |       |              |        |       |       |               |       |       |       |
| heart                  |                              | <50>                                  |        |       |       | <50>          |        |       |       | <50>         |        |        |       | <50>         |        |       |       | <50>          |       |       |       |
|                        | congestion                   | 0                                     | 0      | 0     | 0     | 0             | 0      | 0     | 0     | 0            | 0      | 0      | 0     | 1            | 0      | 0     | 0     | 0             | 0     | 0     | 0     |
|                        |                              | ( 0 )                                 | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )         | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 )  | ( 0 )  | ( 0 ) | ( 2 )        | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) |
|                        | mineralization               | 0                                     | 0      | 0     | 0     | 3             | 0      | 0     | 0     | 0            | 0      | 0      | 0     | 0            | 1      | 0     | 0     | 0             | 0     | 0     | 0     |
|                        |                              | ( 0 )                                 | ( 0 )  | ( 0 ) | ( 0 ) | ( 6 )         | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )        | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) |
|                        | arteritis                    | 0                                     | 0      | 1     | 0     | 0             | 0      | 0     | 0     | 0            | 0      | 0      | 0     | 0            | 1      | 0     | 0     | 0             | 0     | 0     | 0     |
|                        |                              | ( 0 )                                 | ( 0 )  | ( 2 ) | ( 0 ) | ( 0 )         | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )        | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) |
| {Digestive system}     |                              |                                       |        |       |       |               |        |       |       |              |        |        |       |              |        |       |       |               |       |       |       |
| tooth                  |                              | <50>                                  |        |       |       | <50>          |        |       |       | <50>         |        |        |       | <50>         |        |       |       | <50>          |       |       |       |
|                        | dysplasia                    | 7                                     | 2      | 0     | 0     | 8             | 3      | 0     | 0     | 9            | 2      | 0      | 0     | 9            | 3      | 0     | 0     | 0             | 0     | 0     | 0     |
|                        |                              | ( 14 )                                | ( 4 )  | ( 0 ) | ( 0 ) | ( 16 )        | ( 6 )  | ( 0 ) | ( 0 ) | ( 18 )       | ( 4 )  | ( 0 )  | ( 0 ) | ( 18 )       | ( 6 )  | ( 0 ) | ( 0 ) | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) |

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

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

b b : Number of animals with lesion

( c ) c : b / a \* 100

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 6

| Organ              | Findings                   | Group Name<br>No. of Animals on Study<br>Grade | Control      |              |            |             | 32 ppm       |              |            |             | 80 ppm       |              |            |             | 200 ppm      |              |            |            |
|--------------------|----------------------------|--|--------------|--------------|------------|-------------|--------------|--------------|------------|-------------|--------------|--------------|------------|-------------|--------------|--------------|------------|------------|
|                    |                            |  | 50           |              |            |             | 50           |              |            |             | 50           |              |            |             | 50           |              |            |            |
|                    |                            |  | 1<br>(%)     | 2<br>(%)     | 3<br>(%)   | 4<br>(%)    | 1<br>(%)     | 2<br>(%)     | 3<br>(%)   | 4<br>(%)    | 1<br>(%)     | 2<br>(%)     | 3<br>(%)   | 4<br>(%)    | 1<br>(%)     | 2<br>(%)     | 3<br>(%)   | 4<br>(%)   |
| {Digestive system} |                            |  |              |              |            |             |              |              |            |             |              |              |            |             |              |              |            |            |
| tongue             | arteritis                  |  | <49>         |              |            |             | <50>         |              |            |             | <50>         |              |            |             | <50>         |              |            |            |
|                    |                            | 0<br>( 0 )                                     | 1<br>( 2 )   | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 )   | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 )   | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 )   | 0<br>( 0 )   | 0<br>( 0 ) |            |
| stomach            | hyperplasia:gland          |  | <50>         |              |            |             | <50>         |              |            |             | <50>         |              |            |             | <50>         |              |            |            |
|                    |                            | 7<br>( 14 )                                    | 29<br>( 58 ) | 13<br>( 26 ) | 0<br>( 0 ) | 6<br>( 12 ) | 32<br>( 64 ) | 11<br>( 22 ) | 0<br>( 0 ) | 6<br>( 12 ) | 27<br>( 54 ) | 12<br>( 24 ) | 0<br>( 0 ) | 8<br>( 16 ) | 28<br>( 56 ) | 14<br>( 28 ) | 0<br>( 0 ) |            |
|                    | hyperkeratosis:forestomach |  | 0<br>( 0 )   | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 )   | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 )   | 0<br>( 0 )   | 0<br>( 0 ) | 1<br>( 2 )  | 0<br>( 0 )   | 0<br>( 0 )   | 0<br>( 0 ) |            |
|                    |                            | erosion:glandular stomach                      |              | 1<br>( 2 )   | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 )   | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 )   | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 )   | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) |
|                    | small intes                | inflammatory infiltration                      |              | <50>         |            |             |              | <50>         |            |             |              | <50>         |            |             |              | <50>         |            |            |
| 0<br>( 0 )         |                            |  | 0<br>( 0 )   | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 )  | 1<br>( 2 )   | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 )   | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 )   | 0<br>( 0 )   | 0<br>( 0 ) |            |
| liver              | angiectasis                |  | <50>         |              |            |             | <50>         |              |            |             | <50>         |              |            |             | <50>         |              |            |            |
|                    |                            | 0<br>( 0 )                                     | 0<br>( 0 )   | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 )  | 1<br>( 2 )   | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 )   | 0<br>( 0 )   | 0<br>( 0 ) | 1<br>( 2 )  | 1<br>( 2 )   | 0<br>( 0 )   | 0<br>( 0 ) |            |
|                    | necrosis                   |  | 0<br>( 0 )   | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 )   | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 )  | 1<br>( 2 )   | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 )   | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 7

| Organ                  | Findings                  | Group Name<br>No. of Animals on Study<br>Grade | Control   |           |           |           | 32 ppm     |           |           |           | 80 ppm    |           |           |           | 200 ppm   |           |           |           |
|------------------------|---------------------------|--|-----------|-----------|-----------|-----------|------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
|                        |                           |  | 50        |           |           |           | 50         |           |           |           | 50        |           |           |           | 50        |           |           |           |
|                        |                           |  | 1<br>(%)  | 2<br>(%)  | 3<br>(%)  | 4<br>(%)  | 1<br>(%)   | 2<br>(%)  | 3<br>(%)  | 4<br>(%)  | 1<br>(%)  | 2<br>(%)  | 3<br>(%)  | 4<br>(%)  | 1<br>(%)  | 2<br>(%)  | 3<br>(%)  | 4<br>(%)  |
| {Digestive system}     |                           |  |           |           |           |           |            |           |           |           |           |           |           |           |           |           |           |           |
| liver                  |                           |  | <50>      |           |           |           | <50>       |           |           |           | <50>      |           |           |           | <50>      |           |           |           |
|                        | necrosis:focal            |  | 1<br>( 2) | 1<br>( 2) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)  | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
|                        | deposit of amyloid        |  | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)  | 1<br>( 2) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
|                        | hydropic change:central   |  | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)  | 1<br>( 2) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
|                        | inflammatory infiltration |  | 1<br>( 2) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)  | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 2) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 2) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
|                        | granulation               |  | 1<br>( 2) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 2<br>( 4)  | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 3<br>( 6) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 2) | 1<br>( 2) | 0<br>( 0) | 0<br>( 0) |
|                        | hyperplasia:vascular      |  | 1<br>( 2) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)  | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
|                        | clear cell focus          |  | 3<br>( 6) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 5<br>( 10) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 3<br>( 6) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 4<br>( 8) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
| acidophilic cell focus |                           | 0<br>( 0)                                      | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 2) | 0<br>( 0)  | 0<br>( 0) | 0<br>( 0) | 1<br>( 2) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |           |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe  
 < a > a : Number of animals examined at the site  
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 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 8

| Organ              | Findings              | Group Name<br>No. of Animals on Study<br>Grade | Control |       |       |       | 32 ppm |       |       |       | 80 ppm |       |       |       | 200 ppm |        |       |       |
|--------------------|-----------------------|--|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|---------|--------|-------|-------|
|                    |                       |  | 50      |       |       |       | 50     |       |       |       | 50     |       |       |       | 50      |        |       |       |
|                    |                       |  | 1       | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1       | 2      | 3     | 4     |
|                    |                       |  | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)     | (%)    | (%)   | (%)   |
| {Digestive system} |                       |  |         |       |       |       |        |       |       |       |        |       |       |       |         |        |       |       |
| liver              | basophilic cell focus |  | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>    |        |       |       |
|                    |                       |  | 2       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 2      | 0     | 0     | 0     | 2       | 0      | 0     | 0     |
|                    |                       |  | ( 4 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )   | ( 0 )  | ( 0 ) | ( 0 ) |
|                    | biliary cyst          |  | 1       | 0     | 0     | 0     | 3      | 0     | 0     | 0     | 1      | 0     | 1     | 0     | 1       | 1      | 0     | 0     |
|                    |                       |  | ( 2 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 6 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 2 ) | ( 0 ) | ( 2 )   | ( 2 )  | ( 0 ) | ( 0 ) |
| pancreas           | atrophy               |  | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>    |        |       |       |
|                    |                       |  | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 1     | 0     | 0     | 0       | 0      | 0     | 0     |
|                    |                       |  | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) |
| {Urinary system}   |                       |  |         |       |       |       |        |       |       |       |        |       |       |       |         |        |       |       |
| kidney             | hyaline droplet       |  | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>    |        |       |       |
|                    |                       |  | 0       | 2     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 2     | 0     | 0       | 0      | 0     | 0     |
|                    |                       |  | ( 0 )   | ( 4 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 4 ) | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) |
|                    | basophilic change     |  | 8       | 2     | 1     | 0     | 30     | 0     | 0     | 0 **  | 26     | 2     | 0     | 0 **  | 22      | 9      | 2     | 0 **  |
|                    |                       |  | ( 16 )  | ( 4 ) | ( 2 ) | ( 0 ) | ( 60 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 52 ) | ( 4 ) | ( 0 ) | ( 0 ) | ( 44 )  | ( 18 ) | ( 4 ) | ( 0 ) |
|                    | deposit of amyloid    |  | 0       | 0     | 0     | 0     | 0      | 0     | 1     | 0     | 0      | 0     | 0     | 0     | 0       | 0      | 0     | 0     |
|                    |                       |  | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 2 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) |

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

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

b : Number of animals with lesion

( c ) c : b / a \* 100

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

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 ALL ANIMALS (0-105W)

PAGE : 9

| Organ            | Findings                  | Group Name<br>No. of Animals on Study |            |            |            | Control      |            |            |            | 32 ppm     |            |            |            | 80 ppm       |            |            |            | 200 ppm      |            |            |            |
|------------------|---------------------------|---------------------------------------|------------|------------|------------|--------------|------------|------------|------------|------------|------------|------------|------------|--------------|------------|------------|------------|--------------|------------|------------|------------|
|                  |                           | Grade                                 |            |            |            | 50           |            |            |            | 50         |            |            |            | 50           |            |            |            | 50           |            |            |            |
|                  |                           | 1                                     | 2          | 3          | 4          | 1            | 2          | 3          | 4          | 1          | 2          | 3          | 4          | 1            | 2          | 3          | 4          | 1            | 2          | 3          | 4          |
|                  |                           | (%)                                   | (%)        | (%)        | (%)        | (%)          | (%)        | (%)        | (%)        | (%)        | (%)        | (%)        | (%)        | (%)          | (%)        | (%)        | (%)        | (%)          | (%)        | (%)        | (%)        |
| {Urinary system} |                           |                                       |            |            |            |              |            |            |            |            |            |            |            |              |            |            |            |              |            |            |            |
| kidney           |                           | <50>                                  |            |            |            | <50>         |            |            |            | <50>       |            |            |            | <50>         |            |            |            | <50>         |            |            |            |
|                  | hyaline cast              | 1<br>( 2 )                            | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 )   | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |
|                  | inflammatory infiltration | 0<br>( 0 )                            | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )   | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) |
|                  | lymphocytic infiltration  | 0<br>( 0 )                            | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )   | 1<br>( 2 ) | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |
|                  | scar                      | 0<br>( 0 )                            | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )   | 2<br>( 4 ) | 0<br>( 0 ) | 0<br>( 0 ) |
|                  | inflammatory polyp        | 0<br>( 0 )                            | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 ) | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 )   | 1<br>( 2 ) | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 )   | 0<br>( 0 ) | 1<br>( 2 ) | 0<br>( 0 ) |
|                  | hydronephrosis            | 0<br>( 0 )                            | 0<br>( 0 ) | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 )   | 0<br>( 0 ) | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 ) | 3<br>( 6 ) | 0<br>( 0 ) | 0<br>( 0 )   | 1<br>( 2 ) | 3<br>( 6 ) | 0<br>( 0 ) | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 2<br>( 4 ) |
|                  | retention cyst            | 0<br>( 0 )                            | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )   | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |
|                  | mineralization:cortex     | 7<br>( 14 )                           | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 20<br>( 40 ) | 3<br>( 6 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 3<br>( 6 ) | 0<br>( 0 ) | 0<br>( 0 ) | 26<br>( 52 ) | 4<br>( 8 ) | 0<br>( 0 ) | 0<br>( 0 ) | 15<br>( 30 ) | 3<br>( 6 ) | 0<br>( 0 ) | 0<br>( 0 ) |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 10

| Organ              | Findings                 | Group Name<br>No. of Animals on Study |        |       |       | Control |        |       |       | 32 ppm |        |       |       | 80 ppm |        |       |       | 200 ppm |        |       |       |
|--------------------|--------------------------|---------------------------------------|--------|-------|-------|---------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|---------|--------|-------|-------|
|                    |                          | Grade                                 |        |       |       | 50      |        |       |       | 50     |        |       |       | 50     |        |       |       | 50      |        |       |       |
|                    |                          | 1                                     | 2      | 3     | 4     | 1       | 2      | 3     | 4     | 1      | 2      | 3     | 4     | 1      | 2      | 3     | 4     | 1       | 2      | 3     | 4     |
|                    |                          | (%)                                   | (%)    | (%)   | (%)   | (%)     | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)     | (%)    | (%)   | (%)   |
| {Urinary system}   |                          |                                       |        |       |       |         |        |       |       |        |        |       |       |        |        |       |       |         |        |       |       |
| urin bladd         |                          | <50>                                  |        |       |       | <50>    |        |       |       | <50>   |        |       |       | <50>   |        |       |       | <50>    |        |       |       |
|                    | inflammation             | 0                                     | 0      | 0     | 0     | 0       | 0      | 0     | 0     | 0      | 1      | 0     | 0     | 0      | 0      | 1     | 0     | 0       | 1      | 0     | 0     |
|                    |                          | ( 0 )                                 | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 2 ) | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) |
|                    | lymphocytic infiltration | 0                                     | 0      | 0     | 0     | 1       | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 1       | 0      | 0     | 0     |
|                    |                          | ( 0 )                                 | ( 0 )  | ( 0 ) | ( 0 ) | ( 2 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 2 )   | ( 0 )  | ( 0 ) | ( 0 ) |
| {Endocrine system} |                          |                                       |        |       |       |         |        |       |       |        |        |       |       |        |        |       |       |         |        |       |       |
| pituitary          |                          | <49>                                  |        |       |       | <50>    |        |       |       | <50>   |        |       |       | <50>   |        |       |       | <50>    |        |       |       |
|                    | cyst                     | 0                                     | 0      | 0     | 0     | 0       | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 1       | 0      | 0     | 0     |
|                    |                          | ( 0 )                                 | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 2 )   | ( 0 )  | ( 0 ) | ( 0 ) |
|                    | hyperplasia              | 3                                     | 0      | 0     | 0     | 0       | 0      | 0     | 0     | 4      | 0      | 0     | 0     | 1      | 0      | 0     | 0     | 1       | 0      | 0     | 0     |
|                    |                          | ( 6 )                                 | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 8 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 2 )   | ( 0 )  | ( 0 ) | ( 0 ) |
|                    | Rathke pouch             | 1                                     | 0      | 0     | 0     | 0       | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 1       | 0      | 0     | 0     |
|                    |                          | ( 2 )                                 | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 2 )   | ( 0 )  | ( 0 ) | ( 0 ) |
|                    | focal hypertrophy        | 2                                     | 0      | 0     | 0     | 1       | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 0       | 0      | 0     | 0     |
|                    |                          | ( 4 )                                 | ( 0 )  | ( 0 ) | ( 0 ) | ( 2 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) |
| adrenal            |                          | <50>                                  |        |       |       | <50>    |        |       |       | <50>   |        |       |       | <50>   |        |       |       | <50>    |        |       |       |
|                    | spindle-cell hyperplasia | 24                                    | 8      | 0     | 0     | 27      | 5      | 0     | 0     | 26     | 6      | 0     | 0     | 28     | 6      | 0     | 0     | 28      | 6      | 0     | 0     |
|                    |                          | ( 48 )                                | ( 16 ) | ( 0 ) | ( 0 ) | ( 54 )  | ( 10 ) | ( 0 ) | ( 0 ) | ( 52 ) | ( 12 ) | ( 0 ) | ( 0 ) | ( 56 ) | ( 12 ) | ( 0 ) | ( 0 ) | ( 56 )  | ( 12 ) | ( 0 ) | ( 0 ) |

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

STUDY NO. : 0458  
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REPORT TYPE : A1  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
ALL ANIMALS (0-105W)

PAGE : 11

| Organ                 | Findings                  | Group Name<br>No. of Animals on Study |      |      |      | Control |      |      |      | 32 ppm |      |      |      | 80 ppm |      |      |      | 200 ppm |      |      |      |
|-----------------------|---------------------------|---------------------------------------|------|------|------|---------|------|------|------|--------|------|------|------|--------|------|------|------|---------|------|------|------|
|                       |                           | Grade                                 |      |      |      | 50      |      |      |      | 50     |      |      |      | 50     |      |      |      | 50      |      |      |      |
|                       |                           | 1                                     | 2    | 3    | 4    | 1       | 2    | 3    | 4    | 1      | 2    | 3    | 4    | 1      | 2    | 3    | 4    | 1       | 2    | 3    | 4    |
|                       |                           | (%)                                   | (%)  | (%)  | (%)  | (%)     | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  | (%)     | (%)  | (%)  | (%)  |
| {Endocrine system}    |                           |                                       |      |      |      |         |      |      |      |        |      |      |      |        |      |      |      |         |      |      |      |
| adrenal               |                           | <50>                                  |      |      |      | <50>    |      |      |      | <50>   |      |      |      | <50>   |      |      |      | <50>    |      |      |      |
|                       | hyperplasia:cortical cell | 3                                     | 0    | 0    | 0    | 1       | 0    | 0    | 0    | 1      | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0       | 1    | 0    | 0    |
|                       |                           | ( 6)                                  | ( 0) | ( 0) | ( 0) | ( 2)    | ( 0) | ( 0) | ( 0) | ( 2)   | ( 0) | ( 0) | ( 0) | ( 2)   | ( 0) | ( 0) | ( 0) | ( 0)    | ( 2) | ( 0) | ( 0) |
|                       | hyperplasia:medulla       | 0                                     | 0    | 0    | 0    | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 1       | 0    | 0    | 0    |
|                       |                           | ( 0)                                  | ( 0) | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 2)    | ( 0) | ( 0) | ( 0) |
|                       | focal hypertrophy:cortex  | 2                                     | 0    | 0    | 0    | 2       | 1    | 0    | 0    | 2      | 0    | 0    | 0    | 2      | 0    | 0    | 0    | 0       | 1    | 0    | 0    |
|                       |                           | ( 4)                                  | ( 0) | ( 0) | ( 0) | ( 4)    | ( 2) | ( 0) | ( 0) | ( 4)   | ( 0) | ( 0) | ( 0) | ( 4)   | ( 0) | ( 0) | ( 0) | ( 0)    | ( 2) | ( 0) | ( 0) |
| {Reproductive system} |                           |                                       |      |      |      |         |      |      |      |        |      |      |      |        |      |      |      |         |      |      |      |
| testis                |                           | <50>                                  |      |      |      | <50>    |      |      |      | <50>   |      |      |      | <50>   |      |      |      | <50>    |      |      |      |
|                       | mineralization            | 32                                    | 2    | 3    | 0    | 41      | 1    | 0    | 0    | 40     | 2    | 2    | 0    | 35     | 2    | 2    | 0    | 35      | 2    | 0    | 0    |
|                       |                           | ( 64)                                 | ( 4) | ( 6) | ( 0) | ( 82)   | ( 2) | ( 0) | ( 0) | ( 80)  | ( 4) | ( 4) | ( 0) | ( 70)  | ( 4) | ( 4) | ( 0) | ( 70)   | ( 4) | ( 0) | ( 0) |
| epididymis            |                           | <50>                                  |      |      |      | <50>    |      |      |      | <50>   |      |      |      | <50>   |      |      |      | <50>    |      |      |      |
|                       | inflammation              | 0                                     | 0    | 0    | 0    | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 1       | 0    | 0    | 0    |
|                       |                           | ( 0)                                  | ( 0) | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 2)    | ( 0) | ( 0) | ( 0) |
|                       | xanthogranuloma           | 1                                     | 0    | 0    | 0    | 0       | 1    | 0    | 0    | 2      | 0    | 0    | 0    | 1      | 0    | 0    | 0    | 1       | 0    | 0    | 0    |
|                       |                           | ( 2)                                  | ( 0) | ( 0) | ( 0) | ( 0)    | ( 2) | ( 0) | ( 0) | ( 4)   | ( 0) | ( 0) | ( 0) | ( 2)   | ( 0) | ( 0) | ( 0) | ( 2)    | ( 0) | ( 0) | ( 0) |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

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| Organ_____            | Findings_____   | Group Name              | Control |       |       |       | 32 ppm |       |       |       | 80 ppm |       |       |       | 200 ppm |       |       |       |
|-----------------------|-----------------|-------------------------|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|---------|-------|-------|-------|
|                       |                 | No. of Animals on Study | 50      |       |       |       | 50     |       |       |       | 50     |       |       |       | 50      |       |       |       |
|                       |                 | Grade                   | 1       | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1       | 2     | 3     | 4     |
|                       |                 |                         | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)     | (%)   | (%)   | (%)   |
| <hr/>                 |                 |                         |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
| {Reproductive system} |                 |                         |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
| semin ves             |                 | <50>                    |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
|                       | congestion      | 0                       | 0       | 0     | 0     | 1     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                       |                 | ( 0 )                   | ( 0 )   | ( 0 ) | ( 0 ) | ( 2 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                       | inflammation    | 0                       | 0       | 0     | 0     | 1     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                       |                 | ( 0 )                   | ( 0 )   | ( 0 ) | ( 0 ) | ( 2 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
| prostate              |                 | <50>                    |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
|                       | cyst            | 0                       | 0       | 1     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                       |                 | ( 0 )                   | ( 0 )   | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                       | inflammation    | 0                       | 0       | 1     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                       |                 | ( 0 )                   | ( 0 )   | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
| prep/cli gl           |                 | <50>                    |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
|                       | duct ectasia    | 0                       | 1       | 0     | 0     | 0     | 3      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                       |                 | ( 0 )                   | ( 2 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 6 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                       | xanthogranuloma | 0                       | 0       | 0     | 0     | 1     | 1      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                       |                 | ( 0 )                   | ( 0 )   | ( 0 ) | ( 0 ) | ( 2 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
| <hr/>                 |                 |                         |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
| {Nervous system}      |                 |                         |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
| brain                 |                 | <50>                    |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
|                       | hemorrhage      | 0                       | 0       | 0     | 0     | 0     | 1      | 0     | 0     | 1     | 0      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                       |                 | ( 0 )                   | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 2 ) | ( 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  
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 ( c ) c : b / a \* 100  
 Significant difference ; \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0458  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 13

| Organ                            | Findings              | Group Name              | Control |      |      |      | 32 ppm |      |      |      | 80 ppm |      |      |      | 200 ppm |      |      |      |
|----------------------------------|-----------------------|-------------------------|---------|------|------|------|--------|------|------|------|--------|------|------|------|---------|------|------|------|
|                                  |                       | No. of Animals on Study | 50      |      |      |      | 50     |      |      |      | 50     |      |      |      | 50      |      |      |      |
|                                  |                       | Grade                   | 1       | 2    | 3    | 4    | 1      | 2    | 3    | 4    | 1      | 2    | 3    | 4    | 1       | 2    | 3    | 4    |
|                                  |                       |                         | (%)     | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  | (%)     | (%)  | (%)  | (%)  |
| {Nervous system}                 |                       |                         |         |      |      |      |        |      |      |      |        |      |      |      |         |      |      |      |
| brain                            |                       |                         | <50>    |      |      |      | <50>   |      |      |      | <50>   |      |      |      | <50>    |      |      |      |
|                                  | mineralization        |                         | 26      | 0    | 0    | 0    | 24     | 0    | 0    | 0    | 25     | 0    | 0    | 0    | 28      | 0    | 0    | 0    |
|                                  |                       |                         | ( 52)   | ( 0) | ( 0) | ( 0) | ( 48)  | ( 0) | ( 0) | ( 0) | ( 50)  | ( 0) | ( 0) | ( 0) | ( 56)   | ( 0) | ( 0) | ( 0) |
| {Special sense organs/appendage} |                       |                         |         |      |      |      |        |      |      |      |        |      |      |      |         |      |      |      |
| eye                              |                       |                         | <50>    |      |      |      | <50>   |      |      |      | <49>   |      |      |      | <50>    |      |      |      |
|                                  | keratitis             |                         | 0       | 1    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0    | 1    | 0    | 0       | 1    | 0    | 0    |
|                                  |                       |                         | ( 0)    | ( 2) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 2) | ( 0) | ( 0)    | ( 2) | ( 0) | ( 0) |
|                                  | mineralization:cornea |                         | 0       | 0    | 0    | 0    | 1      | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0       | 0    | 0    | 0    |
|                                  |                       |                         | ( 0)    | ( 0) | ( 0) | ( 0) | ( 2)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) |
| Harder gl                        |                       |                         | <50>    |      |      |      | <50>   |      |      |      | <49>   |      |      |      | <50>    |      |      |      |
|                                  | degeneration          |                         | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 1       | 1    | 0    | 0    |
|                                  |                       |                         | ( 0)    | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 2) | ( 2)    | ( 0) | ( 0) |      |
|                                  | inflammation          |                         | 0       | 1    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0       | 0    | 0    | 0    |
|                                  |                       |                         | ( 0)    | ( 2) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) |
|                                  | hyperplasia           |                         | 0       | 0    | 0    | 0    | 1      | 1    | 0    | 0    | 0      | 1    | 0    | 0    | 1       | 1    | 0    | 0    |
|                                  |                       |                         | ( 0)    | ( 0) | ( 0) | ( 0) | ( 2)   | ( 2) | ( 0) | ( 0) | ( 0)   | ( 2) | ( 0) | ( 0) | ( 2)    | ( 2) | ( 0) | ( 0) |

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 ALL ANIMALS (0-105W)

PAGE : 14

| Organ                    | Findings    | Group Name<br>No. of Animals on Study<br>Grade | Control |       |       |       | 32 ppm |       |       |       | 80 ppm |       |       |       | 200 ppm |       |       |       |
|--------------------------|-------------|--|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|---------|-------|-------|-------|
|                          |             |  | 50      |       |       |       | 50     |       |       |       | 50     |       |       |       | 50      |       |       |       |
|                          |             |  | 1       | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1       | 2     | 3     | 4     |
|                          |             |  | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)     | (%)   | (%)   | (%)   |
| {Musculoskeletal system} |             |  |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
| muscle                   | arteritis   |  | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>    |       |       |       |
|                          |             |  | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 1     | 0     | 0     |
|                          |             |  | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 2 ) | ( 0 ) | ( 0 ) |
| {Body cavities}          |             |  |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
| mediastinum              | granulation |  | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>    |       |       |       |
|                          |             |  | 0       | 1     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                          |             |  | ( 0 )   | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |

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

(HPT150)

BAIS4

## APPENDIX L 2

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



STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 1

| Organ                            | Findings                                    | Group Name<br>No. of Animals on Study<br>Grade | Control<br>18 |       |        |       | 32 ppm<br>17 |       |       |       | 80 ppm<br>17 |       |       |       | 200 ppm<br>9 |       |        |       |
|----------------------------------|---|--|---------------|-------|--------|-------|--------------|-------|-------|-------|--------------|-------|-------|-------|--------------|-------|--------|-------|
|                                  |   |  | 1             | 2     | 3      | 4     | 1            | 2     | 3     | 4     | 1            | 2     | 3     | 4     | 1            | 2     | 3      | 4     |
|                                  |   |  | (%)           | (%)   | (%)    | (%)   | (%)          | (%)   | (%)   | (%)   | (%)          | (%)   | (%)   | (%)   | (%)          | (%)   | (%)    | (%)   |
| {Integumentary system/appandage} |   |  |               |       |        |       |              |       |       |       |              |       |       |       |              |       |        |       |
| skin/app                         |   |  | <18>          |       |        |       | <17>         |       |       |       | <17>         |       |       |       | < 9>         |       |        |       |
|                                  | inflammation                                |  | 0             | 0     | 2      | 0     | 0            | 0     | 0     | 0     | 0            | 0     | 1     | 0     | 0            | 0     | 1      | 0     |
|                                  |   |  | ( 0 )         | ( 0 ) | ( 11 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 6 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 11 ) | ( 0 ) |
| subcutis                         |   |  | <18>          |       |        |       | <17>         |       |       |       | <17>         |       |       |       | < 9>         |       |        |       |
|                                  | inflammation                                |  | 0             | 0     | 2      | 0     | 0            | 0     | 1     | 0     | 0            | 0     | 1     | 0     | 0            | 0     | 0      | 0     |
|                                  |   |  | ( 0 )         | ( 0 ) | ( 11 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 6 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 6 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 )  | ( 0 ) |
| {Respiratory system}             |   |  |               |       |        |       |              |       |       |       |              |       |       |       |              |       |        |       |
| nasal cavit                      |   |  | <18>          |       |        |       | <17>         |       |       |       | <17>         |       |       |       | < 9>         |       |        |       |
|                                  | exudate                                     |  | 0             | 0     | 0      | 0     | 1            | 0     | 0     | 0     | 0            | 0     | 0     | 0     | 0            | 0     | 0      | 0     |
|                                  |   |  | ( 0 )         | ( 0 ) | ( 0 )  | ( 0 ) | ( 6 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 )  | ( 0 ) |
|                                  | eosinophilic change:olfactory epithelium    |  | 2             | 0     | 0      | 0     | 3            | 0     | 0     | 0     | 3            | 0     | 0     | 0     | 0            | 0     | 0      | 0     |
|                                  |   |  | ( 11 )        | ( 0 ) | ( 0 )  | ( 0 ) | ( 18 )       | ( 0 ) | ( 0 ) | ( 0 ) | ( 18 )       | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 )  | ( 0 ) |
|                                  | eosinophilic change:respiratory epithelium  |  | 1             | 0     | 0      | 0     | 0            | 0     | 0     | 0     | 4            | 0     | 0     | 0     | 0            | 0     | 0      | 0     |
|                                  |   |  | ( 6 )         | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 24 )       | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 )  | ( 0 ) |
|                                  | respiratory metaplasia:olfactory epithelium |  | 7             | 0     | 0      | 0     | 3            | 0     | 0     | 0     | 9            | 0     | 0     | 0     | 3            | 0     | 0      | 0     |
|                                  |   |  | ( 39 )        | ( 0 ) | ( 0 )  | ( 0 ) | ( 18 )       | ( 0 ) | ( 0 ) | ( 0 ) | ( 53 )       | ( 0 ) | ( 0 ) | ( 0 ) | ( 33 )       | ( 0 ) | ( 0 )  | ( 0 ) |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 2

|                        |                              | Group Name              | Control |      |      |      | 32 ppm |      |      |      | 80 ppm |      |      |      | 200 ppm |      |      |      |
|------------------------|------------------------------|-------------------------|---------|------|------|------|--------|------|------|------|--------|------|------|------|---------|------|------|------|
|                        |                              | No. of Animals on Study | 18      |      |      |      | 17     |      |      |      | 17     |      |      |      | 9       |      |      |      |
| Organ                  | Findings                     | Grade                   | 1       | 2    | 3    | 4    | 1      | 2    | 3    | 4    | 1      | 2    | 3    | 4    | 1       | 2    | 3    | 4    |
|                        |                              |                         | (%)     | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  | (%)     | (%)  | (%)  | (%)  |
| {Respiratory system}   |                              |                         |         |      |      |      |        |      |      |      |        |      |      |      |         |      |      |      |
| nasal cavit            |                              |                         | <18>    |      |      |      | <17>   |      |      |      | <17>   |      |      |      | < 9>    |      |      |      |
|                        | respiratory metaplasia:gland |                         | 1       | 0    | 0    | 0    | 5      | 0    | 0    | 0    | 3      | 0    | 0    | 0    | 3       | 0    | 0    | 0    |
|                        |                              |                         | ( 6)    | ( 0) | ( 0) | ( 0) | ( 29)  | ( 0) | ( 0) | ( 0) | ( 18)  | ( 0) | ( 0) | ( 0) | ( 33)   | ( 0) | ( 0) | ( 0) |
|                        |                              |                         | <18>    |      |      |      | <17>   |      |      |      | <17>   |      |      |      | < 9>    |      |      |      |
|                        | atrophy:olfactory epithelium |                         | 1       | 0    | 0    | 0    | 0      | 1    | 0    | 0    | 10     | 0    | 0    | 0 ** | 4       | 0    | 0    | 0    |
|                        |                              |                         | ( 6)    | ( 0) | ( 0) | ( 0) | ( 0)   | ( 6) | ( 0) | ( 0) | ( 59)  | ( 0) | ( 0) | ( 0) | ( 44)   | ( 0) | ( 0) | ( 0) |
| nasopharynx            |                              |                         | <18>    |      |      |      | <17>   |      |      |      | <17>   |      |      |      | < 9>    |      |      |      |
|                        | eosinophilic change          |                         | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 1    | 0    | 0    | 0       | 0    | 0    | 0    |
|                        |                              |                         | ( 0)    | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 6) | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) |
| lung                   |                              |                         | <18>    |      |      |      | <17>   |      |      |      | <17>   |      |      |      | < 9>    |      |      |      |
|                        | congestion                   |                         | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 1       | 0    | 0    | 0    |
|                        |                              |                         | ( 0)    | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 11)   | ( 0) | ( 0) | ( 0) |
|                        | hemorrhage                   |                         | 1       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0       | 0    | 0    | 0    |
|                        |                              |                         | ( 6)    | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) |
|                        |                              |                         | <18>    |      |      |      | <17>   |      |      |      | <17>   |      |      |      | < 9>    |      |      |      |
|                        | inflammatory infiltration    |                         | 2       | 0    | 0    | 0    | 1      | 0    | 0    | 0    | 1      | 0    | 0    | 0    | 0       | 0    | 0    | 0    |
|                        |                              |                         | ( 11)   | ( 0) | ( 0) | ( 0) | ( 6)   | ( 0) | ( 0) | ( 0) | ( 6)   | ( 0) | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) |
| {Hematopoietic system} |                              |                         |         |      |      |      |        |      |      |      |        |      |      |      |         |      |      |      |
| bone marrow            |                              |                         | <18>    |      |      |      | <17>   |      |      |      | <17>   |      |      |      | < 9>    |      |      |      |
|                        | granulation                  |                         | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 1      | 0    | 0    | 0    | 0       | 0    | 0    | 0    |
|                        |                              |                         | ( 0)    | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 6) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 3

| Organ                  | Findings                 | Group Name<br>No. of Animals on Study<br>Grade | Control<br>18 |      |      |      | 32 ppm<br>17 |      |      |      | 80 ppm<br>17 |      |      |       | 200 ppm<br>9 |      |      |      |
|------------------------|--------------------------|--|---------------|------|------|------|--------------|------|------|------|--------------|------|------|-------|--------------|------|------|------|
|                        |                          |  | 1             | 2    | 3    | 4    | 1            | 2    | 3    | 4    | 1            | 2    | 3    | 4     | 1            | 2    | 3    | 4    |
|                        |                          |  | (%)           | (%)  | (%)  | (%)  | (%)          | (%)  | (%)  | (%)  | (%)          | (%)  | (%)  | (%)   | (%)          | (%)  | (%)  | (%)  |
| {Hematopoietic system} |                          |  |               |      |      |      |              |      |      |      |              |      |      |       |              |      |      |      |
| bone marrow            |                          |  | <18>          |      |      |      | <17>         |      |      |      | <17>         |      |      |       | < 9>         |      |      |      |
|                        | increased hematopoiesis  |  | 2             | 0    | 0    | 0    | 2            | 0    | 0    | 0    | 2            | 0    | 0    | 0     | 3            | 0    | 0    | 0    |
|                        |                          |  | ( 11)         | ( 0) | ( 0) | ( 0) | ( 12)        | ( 0) | ( 0) | ( 0) | ( 12)        | ( 0) | ( 0) | ( 0)  | ( 33)        | ( 0) | ( 0) | ( 0) |
|                        | decreased hematopoiesis  |  | 0             | 0    | 0    | 0    | 0            | 0    | 0    | 0    | 0            | 0    | 0    | 0     | 1            | 0    | 0    | 0    |
|                        |                          |  | ( 0)          | ( 0) | ( 0) | ( 0) | ( 0)         | ( 0) | ( 0) | ( 0) | ( 0)         | ( 0) | ( 0) | ( 11) | ( 0)         | ( 0) | ( 0) |      |
|                        | granulopoiesis:increased |  | 0             | 0    | 0    | 0    | 0            | 0    | 0    | 0    | 1            | 0    | 0    | 0     | 1            | 0    | 0    | 0    |
|                        |                          |  | ( 0)          | ( 0) | ( 0) | ( 0) | ( 0)         | ( 0) | ( 0) | ( 0) | ( 6)         | ( 0) | ( 0) | ( 0)  | ( 11)        | ( 0) | ( 0) | ( 0) |
|                        | xanthogranuloma          |  | 0             | 0    | 0    | 0    | 0            | 0    | 0    | 0    | 0            | 1    | 0    | 0     | 0            | 0    | 0    | 0    |
|                        |                          |  | ( 0)          | ( 0) | ( 0) | ( 0) | ( 0)         | ( 0) | ( 0) | ( 0) | ( 0)         | ( 6) | ( 0) | ( 0)  | ( 0)         | ( 0) | ( 0) | ( 0) |
| lymph node             |                          |  | <18>          |      |      |      | <17>         |      |      |      | <17>         |      |      |       | < 9>         |      |      |      |
|                        | plasma cell hyperplasia  |  | 1             | 0    | 0    | 0    | 0            | 0    | 0    | 0    | 0            | 0    | 0    | 0     | 0            | 0    | 0    | 0    |
|                        |                          |  | ( 6)          | ( 0) | ( 0) | ( 0) | ( 0)         | ( 0) | ( 0) | ( 0) | ( 0)         | ( 0) | ( 0) | ( 0)  | ( 0)         | ( 0) | ( 0) | ( 0) |
|                        | lymphadenitis            |  | 0             | 0    | 0    | 0    | 0            | 0    | 0    | 0    | 1            | 0    | 0    | 0     | 0            | 0    | 0    | 0    |
|                        |                          |  | ( 0)          | ( 0) | ( 0) | ( 0) | ( 0)         | ( 0) | ( 0) | ( 0) | ( 6)         | ( 0) | ( 0) | ( 0)  | ( 0)         | ( 0) | ( 0) | ( 0) |
| spleen                 |                          |  | <18>          |      |      |      | <17>         |      |      |      | <17>         |      |      |       | < 9>         |      |      |      |
|                        | angiectasis              |  | 0             | 0    | 0    | 0    | 0            | 0    | 0    | 0    | 1            | 0    | 0    | 0     | 0            | 0    | 0    | 0    |
|                        |                          |  | ( 0)          | ( 0) | ( 0) | ( 0) | ( 0)         | ( 0) | ( 0) | ( 0) | ( 6)         | ( 0) | ( 0) | ( 0)  | ( 0)         | ( 0) | ( 0) | ( 0) |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 4

| Organ                  | Findings                     | Group Name<br>No. of Animals on Study<br>Grade | Control<br>18 |        |        |       | 32 ppm<br>17 |        |        |       | 80 ppm<br>17 |        |        |       | 200 ppm<br>9 |        |        |       |
|------------------------|------------------------------|--|---------------|--------|--------|-------|--------------|--------|--------|-------|--------------|--------|--------|-------|--------------|--------|--------|-------|
|                        |                              |  | 1             | 2      | 3      | 4     | 1            | 2      | 3      | 4     | 1            | 2      | 3      | 4     | 1            | 2      | 3      | 4     |
|                        |                              |  | (%)           | (%)    | (%)    | (%)   | (%)          | (%)    | (%)    | (%)   | (%)          | (%)    | (%)    | (%)   | (%)          | (%)    | (%)    | (%)   |
| {Hematopoietic system} |                              |  |               |        |        |       |              |        |        |       |              |        |        |       |              |        |        |       |
| spleen                 |                              |  | <18>          |        |        |       | <17>         |        |        |       | <17>         |        |        |       | < 9>         |        |        |       |
|                        | deposit of hemosiderin       |  | 1             | 0      | 0      | 0     | 0            | 0      | 0      | 0     | 0            | 0      | 0      | 0     | 0            | 0      | 0      | 0     |
|                        |                              |  | ( 6 )         | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )        | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )        | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )        | ( 0 )  | ( 0 )  | ( 0 ) |
|                        | fibrosis                     |  | 0             | 0      | 0      | 0     | 0            | 0      | 0      | 0     | 1            | 0      | 0      | 0     | 0            | 0      | 0      | 0     |
|                        |                              |  | ( 0 )         | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )        | ( 0 )  | ( 0 )  | ( 0 ) | ( 6 )        | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )        | ( 0 )  | ( 0 )  | ( 0 ) |
|                        | extramedullary hematopoiesis |  | 3             | 4      | 4      | 0     | 2            | 4      | 3      | 0     | 2            | 4      | 4      | 0     | 0            | 4      | 1      | 0     |
|                        |                              |  | ( 17 )        | ( 22 ) | ( 22 ) | ( 0 ) | ( 12 )       | ( 24 ) | ( 18 ) | ( 0 ) | ( 12 )       | ( 24 ) | ( 24 ) | ( 0 ) | ( 0 )        | ( 44 ) | ( 11 ) | ( 0 ) |
| {Circulatory system}   |                              |  |               |        |        |       |              |        |        |       |              |        |        |       |              |        |        |       |
| heart                  |                              |  | <18>          |        |        |       | <17>         |        |        |       | <17>         |        |        |       | < 9>         |        |        |       |
|                        | congestion                   |  | 0             | 0      | 0      | 0     | 0            | 0      | 0      | 0     | 0            | 0      | 0      | 0     | 1            | 0      | 0      | 0     |
|                        |                              |  | ( 0 )         | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )        | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )        | ( 0 )  | ( 0 )  | ( 0 ) | ( 11 )       | ( 0 )  | ( 0 )  | ( 0 ) |
|                        | mineralization               |  | 0             | 0      | 0      | 0     | 3            | 0      | 0      | 0     | 0            | 0      | 0      | 0     | 0            | 1      | 0      | 0     |
|                        |                              |  | ( 0 )         | ( 0 )  | ( 0 )  | ( 0 ) | ( 18 )       | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )        | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )        | ( 11 ) | ( 0 )  | ( 0 ) |
|                        | arteritis                    |  | 0             | 0      | 1      | 0     | 0            | 0      | 0      | 0     | 0            | 0      | 0      | 0     | 0            | 1      | 0      | 0     |
|                        |                              |  | ( 0 )         | ( 0 )  | ( 6 )  | ( 0 ) | ( 0 )        | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )        | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )        | ( 11 ) | ( 0 )  | ( 0 ) |
| {Digestive system}     |                              |  |               |        |        |       |              |        |        |       |              |        |        |       |              |        |        |       |
| tooth                  |                              |  | <18>          |        |        |       | <17>         |        |        |       | <17>         |        |        |       | < 9>         |        |        |       |
|                        | dysplasia                    |  | 0             | 1      | 0      | 0     | 0            | 0      | 0      | 0     | 1            | 0      | 0      | 0     | 0            | 0      | 0      | 0     |
|                        |                              |  | ( 0 )         | ( 8 )  | ( 0 )  | ( 0 ) | ( 0 )        | ( 0 )  | ( 0 )  | ( 0 ) | ( 6 )        | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )        | ( 0 )  | ( 0 )  | ( 0 ) |

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

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

b : Number of animals with lesion

( c ) c : b / a \* 100

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crl:BDF1]  
 REPORT TYPE : A1  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 5

|                    |                         | Group Name              | Control |        |        |       | 32 ppm |        |        |       | 80 ppm |        |       |       | 200 ppm |        |       |       |
|--------------------|-------------------------|-------------------------|---------|--------|--------|-------|--------|--------|--------|-------|--------|--------|-------|-------|---------|--------|-------|-------|
|                    |                         | No. of Animals on Study | 18      |        |        |       | 17     |        |        |       | 17     |        |       |       | 9       |        |       |       |
| Organ              | Findings                | Grade                   | 1       | 2      | 3      | 4     | 1      | 2      | 3      | 4     | 1      | 2      | 3     | 4     | 1       | 2      | 3     | 4     |
|                    |                         |                         | (%)     | (%)    | (%)    | (%)   | (%)    | (%)    | (%)    | (%)   | (%)    | (%)    | (%)   | (%)   | (%)     | (%)    | (%)   | (%)   |
| {Digestive system} |                         |                         |         |        |        |       |        |        |        |       |        |        |       |       |         |        |       |       |
| tongue             |                         |                         | <17>    |        |        |       | <17>   |        |        |       | <17>   |        |       |       | < 9>    |        |       |       |
|                    | arteritis               |                         | 0       | 1      | 0      | 0     | 0      | 0      | 0      | 0     | 0      | 0      | 0     | 0     | 0       | 0      | 0     | 0     |
|                    |                         |                         | ( 0 )   | ( 6 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) |
| stomach            |                         |                         | <18>    |        |        |       | <17>   |        |        |       | <17>   |        |       |       | < 9>    |        |       |       |
|                    | hyperplasia:gland       |                         | 2       | 13     | 2      | 0     | 3      | 11     | 2      | 0     | 4      | 8      | 0     | 0     | 2       | 7      | 0     | 0     |
|                    |                         |                         | ( 11 )  | ( 72 ) | ( 11 ) | ( 0 ) | ( 18 ) | ( 65 ) | ( 12 ) | ( 0 ) | ( 24 ) | ( 47 ) | ( 0 ) | ( 0 ) | ( 22 )  | ( 78 ) | ( 0 ) | ( 0 ) |
| liver              |                         |                         | <18>    |        |        |       | <17>   |        |        |       | <17>   |        |       |       | < 9>    |        |       |       |
|                    | necrosis                |                         | 0       | 0      | 0      | 0     | 0      | 0      | 0      | 0     | 0      | 1      | 0     | 0     | 0       | 0      | 0     | 0     |
|                    |                         |                         | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 6 )  | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) |
|                    | hydropic change:central |                         | 0       | 0      | 0      | 0     | 0      | 1      | 0      | 0     | 0      | 0      | 0     | 0     | 0       | 0      | 0     | 0     |
|                    |                         |                         | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 6 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) |
|                    | clear cell focus        |                         | 0       | 0      | 0      | 0     | 1      | 0      | 0      | 0     | 0      | 0      | 0     | 0     | 0       | 0      | 0     | 0     |
|                    |                         |                         | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 6 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) |
|                    | acidophilic cell focus  |                         | 0       | 0      | 0      | 0     | 1      | 0      | 0      | 0     | 0      | 0      | 0     | 0     | 0       | 0      | 0     | 0     |
|                    |                         |                         | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 6 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) |
|                    | basophilic cell focus   |                         | 0       | 0      | 0      | 0     | 0      | 0      | 0      | 0     | 1      | 0      | 0     | 0     | 1       | 0      | 0     | 0     |
|                    |                         |                         | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 6 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 11 )  | ( 0 )  | ( 0 ) | ( 0 ) |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 6

| Organ              | Findings              | Group Name<br>No. of Animals on Study<br>Grade | Control<br>18 |       |       |       | 32 ppm<br>17 |       |       |       | 80 ppm<br>17 |       |        |       | 200 ppm<br>9 |        |        |        |
|--------------------|-----------------------|--|---------------|-------|-------|-------|--------------|-------|-------|-------|--------------|-------|--------|-------|--------------|--------|--------|--------|
|                    |                       |  | 1             | 2     | 3     | 4     | 1            | 2     | 3     | 4     | 1            | 2     | 3      | 4     | 1            | 2      | 3      | 4      |
|                    |                       |  | (%)           | (%)   | (%)   | (%)   | (%)          | (%)   | (%)   | (%)   | (%)          | (%)   | (%)    | (%)   | (%)          | (%)    | (%)    | (%)    |
| {Urinary system}   |                       |  |               |       |       |       |              |       |       |       |              |       |        |       |              |        |        |        |
| kidney             |                       |  | <18>          |       |       |       | <17>         |       |       |       | <17>         |       |        |       | < 9>         |        |        |        |
|                    | hyaline droplet       |  | 0             | 1     | 0     | 0     | 0            | 0     | 0     | 0     | 0            | 0     | 2      | 0     | 0            | 0      | 0      | 0      |
|                    |                       |  | ( 0 )         | ( 6 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 12 ) | ( 0 ) | ( 0 )        | ( 0 )  | ( 0 )  | ( 0 )  |
|                    | basophilic change     |  | 1             | 0     | 1     | 0     | 4            | 0     | 0     | 0     | 2            | 0     | 0      | 0     | 1            | 0      | 1      | 0      |
|                    |                       |  | ( 6 )         | ( 0 ) | ( 6 ) | ( 0 ) | ( 24 )       | ( 0 ) | ( 0 ) | ( 0 ) | ( 12 )       | ( 0 ) | ( 0 )  | ( 0 ) | ( 11 )       | ( 0 )  | ( 11 ) | ( 0 )  |
|                    | scar                  |  | 0             | 0     | 0     | 0     | 0            | 0     | 0     | 0     | 0            | 0     | 0      | 0     | 0            | 1      | 0      | 0      |
|                    |                       |  | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 )        | ( 11 ) | ( 0 )  | ( 0 )  |
|                    | inflammatory polyp    |  | 0             | 0     | 0     | 0     | 0            | 0     | 0     | 0     | 0            | 1     | 1      | 0     | 0            | 0      | 0      | 0      |
|                    |                       |  | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 6 ) | ( 6 )  | ( 0 ) | ( 0 )        | ( 0 )  | ( 0 )  | ( 0 )  |
|                    | hydronephrosis        |  | 0             | 0     | 0     | 0     | 0            | 0     | 0     | 0     | 0            | 1     | 3      | 0     | 0            | 0      | 0      | 1      |
|                    |                       |  | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 6 ) | ( 18 ) | ( 0 ) | ( 0 )        | ( 0 )  | ( 0 )  | ( 11 ) |
|                    | mineralization:cortex |  | 1             | 0     | 0     | 0     | 3            | 1     | 0     | 0     | 5            | 0     | 0      | 0     | 1            | 0      | 0      | 0      |
|                    |                       |  | ( 6 )         | ( 0 ) | ( 0 ) | ( 0 ) | ( 18 )       | ( 6 ) | ( 0 ) | ( 0 ) | ( 29 )       | ( 0 ) | ( 0 )  | ( 0 ) | ( 11 )       | ( 0 )  | ( 0 )  | ( 0 )  |
| urin bladd         |                       |  | <18>          |       |       |       | <17>         |       |       |       | <17>         |       |        |       | < 9>         |        |        |        |
|                    | inflammation          |  | 0             | 0     | 0     | 0     | 0            | 0     | 0     | 0     | 0            | 1     | 0      | 0     | 0            | 0      | 0      | 0      |
|                    |                       |  | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 6 ) | ( 0 )  | ( 0 ) | ( 0 )        | ( 0 )  | ( 0 )  | ( 0 )  |
| {Endocrine system} |                       |  |               |       |       |       |              |       |       |       |              |       |        |       |              |        |        |        |
| pituitary          |                       |  | <17>          |       |       |       | <17>         |       |       |       | <17>         |       |        |       | < 9>         |        |        |        |
|                    | cyst                  |  | 0             | 0     | 0     | 0     | 0            | 0     | 0     | 0     | 0            | 0     | 0      | 0     | 1            | 0      | 0      | 0      |
|                    |                       |  | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 )  | ( 0 ) | ( 11 )       | ( 0 )  | ( 0 )  | ( 0 )  |

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

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

b : Number of animals with lesion

( c ) c : b / a \* 100

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 7

|                       |                           | Group Name              | Control |       |      |      | 32 ppm |      |      |      | 80 ppm |       |      |      | 200 ppm |      |      |      |
|-----------------------|---------------------------|-------------------------|---------|-------|------|------|--------|------|------|------|--------|-------|------|------|---------|------|------|------|
|                       |                           | No. of Animals on Study | 18      |       |      |      | 17     |      |      |      | 17     |       |      |      | 9       |      |      |      |
|                       |                           | Grade                   | 1       | 2     | 3    | 4    | 1      | 2    | 3    | 4    | 1      | 2     | 3    | 4    | 1       | 2    | 3    | 4    |
| Organ                 | Findings                  |                         | (%)     | (%)   | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  | (%)    | (%)   | (%)  | (%)  | (%)     | (%)  | (%)  | (%)  |
|                       |                           |                         |         |       |      |      |        |      |      |      |        |       |      |      |         |      |      |      |
| {Endocrine system}    |                           |                         |         |       |      |      |        |      |      |      |        |       |      |      |         |      |      |      |
| pituitary             |                           |                         | <17>    |       |      |      | <17>   |      |      |      | <17>   |       |      |      | < 9>    |      |      |      |
|                       | hyperplasia               |                         | 1       | 0     | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0     | 0    | 0    | 0       | 0    | 0    | 0    |
|                       |                           |                         | ( 6)    | ( 0)  | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0)  | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) |
| adrenal               |                           |                         | <18>    |       |      |      | <17>   |      |      |      | <17>   |       |      |      | < 9>    |      |      |      |
|                       | spindle-cell hyperplasia  |                         | 6       | 3     | 0    | 0    | 9      | 0    | 0    | 0    | 6      | 2     | 0    | 0    | 5       | 0    | 0    | 0    |
|                       |                           |                         | ( 33)   | ( 17) | ( 0) | ( 0) | ( 53)  | ( 0) | ( 0) | ( 0) | ( 35)  | ( 12) | ( 0) | ( 0) | ( 56)   | ( 0) | ( 0) | ( 0) |
|                       | hyperplasia:cortical cell |                         | 1       | 0     | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0     | 0    | 0    | 0       | 0    | 0    | 0    |
|                       |                           |                         | ( 6)    | ( 0)  | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0)  | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) |
|                       |                           |                         |         |       |      |      |        |      |      |      |        |       |      |      |         |      |      |      |
| {Reproductive system} |                           |                         |         |       |      |      |        |      |      |      |        |       |      |      |         |      |      |      |
| testis                |                           |                         | <18>    |       |      |      | <17>   |      |      |      | <17>   |       |      |      | < 9>    |      |      |      |
|                       | mineralization            |                         | 9       | 1     | 1    | 0    | 10     | 1    | 0    | 0    | 11     | 0     | 0    | 0    | 5       | 0    | 0    | 0    |
|                       |                           |                         | ( 50)   | ( 6)  | ( 6) | ( 0) | ( 59)  | ( 6) | ( 0) | ( 0) | ( 65)  | ( 0)  | ( 0) | ( 0) | ( 56)   | ( 0) | ( 0) | ( 0) |
| prostate              |                           |                         | <18>    |       |      |      | <17>   |      |      |      | <17>   |       |      |      | < 9>    |      |      |      |
|                       | inflammation              |                         | 0       | 0     | 1    | 0    | 0      | 0    | 0    | 0    | 0      | 0     | 0    | 0    | 0       | 0    | 0    | 0    |
|                       |                           |                         | ( 0)    | ( 0)  | ( 6) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0)  | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) |
| prep/cli gl           |                           |                         | <18>    |       |      |      | <17>   |      |      |      | <17>   |       |      |      | < 9>    |      |      |      |
|                       | xanthogranuloma           |                         | 0       | 0     | 0    | 0    | 1      | 0    | 0    | 0    | 0      | 0     | 0    | 0    | 0       | 0    | 0    | 0    |
|                       |                           |                         | ( 0)    | ( 0)  | ( 0) | ( 0) | ( 6)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0)  | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 8

|                                  |                       | Group Name              | Control |       |       |       | 32 ppm |       |       |       | 80 ppm |       |       |       | 200 ppm |        |       |       |
|----------------------------------|-----------------------|-------------------------|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|---------|--------|-------|-------|
|                                  |                       | No. of Animals on Study | 18      |       |       |       | 17     |       |       |       | 17     |       |       |       | 9       |        |       |       |
| Organ                            | Findings              | Grade                   | 1       | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1       | 2      | 3     | 4     |
|                                  |                       |                         | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)     | (%)    | (%)   | (%)   |
| {Nervous system}                 |                       |                         |         |       |       |       |        |       |       |       |        |       |       |       |         |        |       |       |
| brain                            |                       |                         | <18>    |       |       |       | <17>   |       |       |       | <17>   |       |       |       | < 9>    |        |       |       |
|                                  | hemorrhage            |                         | 0       | 0     | 0     | 0     | 0      | 1     | 0     | 0     | 1      | 0     | 0     | 0     | 0       | 0      | 0     | 0     |
|                                  |                       |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 6 ) | ( 0 ) | ( 0 ) | ( 6 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) |
|                                  | mineralization        |                         | 9       | 0     | 0     | 0     | 7      | 0     | 0     | 0     | 7      | 0     | 0     | 0     | 3       | 0      | 0     | 0     |
|                                  |                       |                         | ( 50 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 41 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 41 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 33 )  | ( 0 )  | ( 0 ) | ( 0 ) |
| {Special sense organs/appendage} |                       |                         |         |       |       |       |        |       |       |       |        |       |       |       |         |        |       |       |
| eye                              |                       |                         | <18>    |       |       |       | <17>   |       |       |       | <16>   |       |       |       | < 9>    |        |       |       |
|                                  | mineralization:cornea |                         | 0       | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 0      | 0     | 0     |
|                                  |                       |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 6 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) |
| Harder gl                        |                       |                         | <18>    |       |       |       | <17>   |       |       |       | <16>   |       |       |       | < 9>    |        |       |       |
|                                  | degeneration          |                         | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 1       | 0      | 0     | 0     |
|                                  |                       |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 11 )  | ( 0 )  | ( 0 ) | ( 0 ) |
| {Musculoskeletal system}         |                       |                         |         |       |       |       |        |       |       |       |        |       |       |       |         |        |       |       |
| muscle                           |                       |                         | <18>    |       |       |       | <17>   |       |       |       | <17>   |       |       |       | < 9>    |        |       |       |
|                                  | arteritis             |                         | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 1      | 0     | 0     |
|                                  |                       |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 11 ) | ( 0 ) | ( 0 ) |

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



STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 9

| Organ | Findings | Group Name              |  |  |  | Control |     |     |     | 32 ppm |     |     |     | 80 ppm |     |     |     | 200 ppm |     |     |     |
|-------|----------|-------------------------|--|--|--|---------|-----|-----|-----|--------|-----|-----|-----|--------|-----|-----|-----|---------|-----|-----|-----|
|       |          | No. of Animals on Study |  |  |  | 18      |     |     |     | 17     |     |     |     | 17     |     |     |     | 9       |     |     |     |
|       |          | Grade                   |  |  |  | 1       | 2   | 3   | 4   | 1      | 2   | 3   | 4   | 1      | 2   | 3   | 4   | 1       | 2   | 3   | 4   |
|       |          |                         |  |  |  | (%)     | (%) | (%) | (%) | (%)    | (%) | (%) | (%) | (%)    | (%) | (%) | (%) | (%)     | (%) | (%) | (%) |

{Body cavities}

|             |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
|-------------|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| mediastinum | granulation | <18>  |       |       |       | <17>  |       |       |       | <17>  |       |       |       | < 9>  |       |       |       |
|             |             | 0     | 1     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     |
|             |             | ( 0 ) | ( 6 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) |

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

(HPT150)

BAIS4

## APPENDIX L 3

HISTOPATHOLOGICAL FINDINGS :  
NON-NEOPLASTIC LESIONS : MALE  
SACRIFICED ANIMALS

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS (105W)

PAGE : 1

|                                  |  | Group Name              | Control |       |       |       | 32 ppm |       |       |       | 80 ppm |       |       |       | 200 ppm |       |       |       |
|----------------------------------|--|-------------------------|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|---------|-------|-------|-------|
|                                  |  | No. of Animals on Study | 32      |       |       |       | 33     |       |       |       | 33     |       |       |       | 41      |       |       |       |
| Organ                            | Findings                                   | Grade                   | 1       | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1       | 2     | 3     | 4     |
|                                  |  |                         | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)     | (%)   | (%)   | (%)   |
| {Integumentary system/appandage} |  |                         |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
| skin/app                         |  |                         | <32>    |       |       |       | <33>   |       |       |       | <33>   |       |       |       | <41>    |       |       |       |
|                                  | inflammation                               |                         | 0       | 1     | 0     | 0     | 0      | 1     | 0     | 0     | 0      | 0     | 1     | 0     | 0       | 1     | 0     | 0     |
|                                  |  |                         | ( 0 )   | ( 3 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 3 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 3 ) | ( 0 ) | ( 0 )   | ( 2 ) | ( 0 ) | ( 0 ) |
| subcutis                         |  |                         | <32>    |       |       |       | <33>   |       |       |       | <33>   |       |       |       | <41>    |       |       |       |
|                                  | inflammation                               |                         | 0       | 0     | 1     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                                  |  |                         | ( 0 )   | ( 0 ) | ( 3 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
| {Respiratory system}             |  |                         |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
| nasal cavit                      |  |                         | <32>    |       |       |       | <33>   |       |       |       | <33>   |       |       |       | <41>    |       |       |       |
|                                  | mineralization                             |                         | 1       | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                                  |  |                         | ( 3 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 3 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                                  | inflammation                               |                         | 0       | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                                  |  |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 3 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                                  | eosinophilic change:olfactory epithelium   |                         | 5       | 0     | 0     | 0     | 18     | 0     | 0     | 0 **  | 6      | 0     | 0     | 0     | 14      | 1     | 0     | 0     |
|                                  |  |                         | ( 16 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 55 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 18 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 34 )  | ( 2 ) | ( 0 ) | ( 0 ) |
|                                  | eosinophilic change:respiratory epithelium |                         | 7       | 0     | 1     | 0     | 2      | 0     | 0     | 0     | 4      | 0     | 0     | 0     | 3       | 0     | 0     | 0     |
|                                  |  |                         | ( 22 )  | ( 0 ) | ( 3 ) | ( 0 ) | ( 6 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 12 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 7 )   | ( 0 ) | ( 0 ) | ( 0 ) |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS (105#)

PAGE : 2

| Organ                  | Findings                                    | Group Name<br>No. of Animals on Study<br>Grade | Control<br>32 |      |      |      | 32 ppm<br>33 |      |      |      | 80 ppm<br>33 |      |      |      | 200 ppm<br>41 |      |      |      |
|------------------------|---|--|---------------|------|------|------|--------------|------|------|------|--------------|------|------|------|---------------|------|------|------|
|                        |   |  | 1             | 2    | 3    | 4    | 1            | 2    | 3    | 4    | 1            | 2    | 3    | 4    | 1             | 2    | 3    | 4    |
|                        |   |  | (%)           | (%)  | (%)  | (%)  | (%)          | (%)  | (%)  | (%)  | (%)          | (%)  | (%)  | (%)  | (%)           | (%)  | (%)  | (%)  |
| {Respiratory system}   |   |  |               |      |      |      |              |      |      |      |              |      |      |      |               |      |      |      |
| nasal cavit            |   |  | <32>          |      |      |      | <33>         |      |      |      | <33>         |      |      |      | <41>          |      |      |      |
|                        | respiratory metaplasia:olfactory epithelium |  | 12            | 0    | 0    | 0    | 24           | 0    | 0    | 0 ** | 14           | 0    | 0    | 0    | 18            | 0    | 0    | 0    |
|                        |   |  | ( 38)         | ( 0) | ( 0) | ( 0) | ( 73)        | ( 0) | ( 0) | ( 0) | ( 42)        | ( 0) | ( 0) | ( 0) | ( 44)         | ( 0) | ( 0) | ( 0) |
|                        | respiratory metaplasia:gland                |  | 8             | 0    | 0    | 0    | 8            | 0    | 0    | 0    | 9            | 0    | 0    | 0    | 15            | 0    | 0    | 0    |
|                        |   |  | ( 25)         | ( 0) | ( 0) | ( 0) | ( 24)        | ( 0) | ( 0) | ( 0) | ( 27)        | ( 0) | ( 0) | ( 0) | ( 37)         | ( 0) | ( 0) | ( 0) |
|                        | atrophy:olfactory epithelium                |  | 0             | 0    | 0    | 0    | 0            | 0    | 0    | 0    | 9            | 0    | 0    | 0 ** | 16            | 0    | 0    | 0 ** |
|                        |   |  | ( 0)          | ( 0) | ( 0) | ( 0) | ( 0)         | ( 0) | ( 0) | ( 0) | ( 27)        | ( 0) | ( 0) | ( 0) | ( 39)         | ( 0) | ( 0) | ( 0) |
| nasopharynx            |   |  |               |      |      |      |              |      |      |      |              |      |      |      |               |      |      |      |
|                        | eosinophilic change                         |  | <32>          |      |      |      | <33>         |      |      |      | <33>         |      |      |      | <41>          |      |      |      |
|                        |   |  | 0             | 0    | 1    | 0    | 0            | 0    | 0    | 0    | 0            | 0    | 0    | 0    | 1             | 0    | 0    | 0    |
|                        |   |  | ( 0)          | ( 0) | ( 3) | ( 0) | ( 0)         | ( 0) | ( 0) | ( 0) | ( 0)         | ( 0) | ( 0) | ( 0) | ( 2)          | ( 0) | ( 0) | ( 0) |
| lung                   |   |  |               |      |      |      |              |      |      |      |              |      |      |      |               |      |      |      |
|                        | inflammatory cell nest                      |  | <32>          |      |      |      | <33>         |      |      |      | <33>         |      |      |      | <41>          |      |      |      |
|                        |   |  | 0             | 0    | 0    | 0    | 0            | 0    | 0    | 0    | 0            | 0    | 0    | 0    | 1             | 0    | 0    | 0    |
|                        |   |  | ( 0)          | ( 0) | ( 0) | ( 0) | ( 0)         | ( 0) | ( 0) | ( 0) | ( 0)         | ( 0) | ( 0) | ( 0) | ( 2)          | ( 0) | ( 0) | ( 0) |
|                        | bronchiolar-alveolar cell hyperplasia       |  | 2             | 0    | 0    | 0    | 5            | 0    | 0    | 0    | 5            | 0    | 0    | 0    | 1             | 0    | 0    | 0    |
|                        |   |  | ( 6)          | ( 0) | ( 0) | ( 0) | ( 15)        | ( 0) | ( 0) | ( 0) | ( 15)        | ( 0) | ( 0) | ( 0) | ( 2)          | ( 0) | ( 0) | ( 0) |
| {Hematopoietic system} |   |  |               |      |      |      |              |      |      |      |              |      |      |      |               |      |      |      |
| bone marrow            |   |  |               |      |      |      |              |      |      |      |              |      |      |      |               |      |      |      |
|                        | granulation                                 |  | <32>          |      |      |      | <33>         |      |      |      | <33>         |      |      |      | <41>          |      |      |      |
|                        |   |  | 1             | 0    | 0    | 0    | 0            | 0    | 0    | 0    | 0            | 0    | 0    | 0    | 0             | 0    | 0    | 0    |
|                        |   |  | ( 3)          | ( 0) | ( 0) | ( 0) | ( 0)         | ( 0) | ( 0) | ( 0) | ( 0)         | ( 0) | ( 0) | ( 0) | ( 0)          | ( 0) | ( 0) | ( 0) |

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

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

b : Number of animals with lesion

( c ) c : b / a \* 100

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS (105W)

PAGE : 3

|                        |                          | Group Name              | Control |       |       |       | 32 ppm |       |       |       | 80 ppm |       |       |       | 200 ppm |       |       |       |
|------------------------|--------------------------|-------------------------|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|---------|-------|-------|-------|
|                        |                          | No. of Animals on Study | 32      |       |       |       | 33     |       |       |       | 33     |       |       |       | 41      |       |       |       |
| Organ                  | Findings                 | Grade                   | 1       | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1       | 2     | 3     | 4     |
|                        |                          |                         | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)     | (%)   | (%)   | (%)   |
| {Hematopoietic system} |                          |                         |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
| bone marrow            |                          |                         | <32>    |       |       |       | <33>   |       |       |       | <33>   |       |       |       | <41>    |       |       |       |
|                        | increased hematopoiesis  |                         | 0       | 0     | 0     | 0     | 2      | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                        |                          |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 6 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 3 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                        | decreased hematopoiesis  |                         | 0       | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                        |                          |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 3 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 3 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                        | granulopoiesis:increased |                         | 2       | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 3       | 0     | 0     | 0     |
|                        |                          |                         | ( 6 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 3 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 3 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 7 )   | ( 0 ) | ( 0 ) | ( 0 ) |
| lymph node             |                          |                         | <32>    |       |       |       | <33>   |       |       |       | <33>   |       |       |       | <41>    |       |       |       |
|                        | lymphadenitis            |                         | 0       | 1     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                        |                          |                         | ( 0 )   | ( 3 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
| spleen                 |                          |                         | <32>    |       |       |       | <33>   |       |       |       | <33>   |       |       |       | <41>    |       |       |       |
|                        | angiectasis              |                         | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                        |                          |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 3 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                        | deposit of amyloid       |                         | 0       | 0     | 0     | 0     | 0      | 0     | 1     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                        |                          |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 3 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                        | deposit of melanin       |                         | 2       | 1     | 0     | 0     | 0      | 2     | 0     | 0     | 1      | 0     | 0     | 0     | 1       | 1     | 0     | 0     |
|                        |                          |                         | ( 6 )   | ( 3 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 6 ) | ( 0 ) | ( 0 ) | ( 3 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )   | ( 2 ) | ( 0 ) | ( 0 ) |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS (105W)

PAGE : 4

| Organ                  | Findings                     | Group Name              | Control |        |        |       | 32 ppm |        |        |       | 80 ppm |        |        |       | 200 ppm |        |        |       |
|------------------------|------------------------------|-------------------------|---------|--------|--------|-------|--------|--------|--------|-------|--------|--------|--------|-------|---------|--------|--------|-------|
|                        |                              | No. of Animals on Study | 32      |        |        |       | 33     |        |        |       | 33     |        |        |       | 41      |        |        |       |
|                        |                              | Grade                   | 1       | 2      | 3      | 4     | 1      | 2      | 3      | 4     | 1      | 2      | 3      | 4     | 1       | 2      | 3      | 4     |
|                        |                              |                         | (%)     | (%)    | (%)    | (%)   | (%)    | (%)    | (%)    | (%)   | (%)    | (%)    | (%)    | (%)   | (%)     | (%)    | (%)    | (%)   |
| {Hematopoietic system} |                              |                         |         |        |        |       |        |        |        |       |        |        |        |       |         |        |        |       |
| spleen                 |                              |                         | <32>    |        |        |       | <33>   |        |        |       | <33>   |        |        |       | <41>    |        |        |       |
|                        | extramedullary hematopoiesis |                         | 3       | 1      | 0      | 0     | 8      | 2      | 0      | 0     | 3      | 3      | 1      | 0     | 10      | 3      | 0      | 0     |
|                        |                              |                         | ( 9 )   | ( 3 )  | ( 0 )  | ( 0 ) | ( 24 ) | ( 6 )  | ( 0 )  | ( 0 ) | ( 9 )  | ( 9 )  | ( 3 )  | ( 0 ) | ( 24 )  | ( 7 )  | ( 0 )  | ( 0 ) |
|                        | follicular hyperplasia       |                         | 2       | 1      | 0      | 0     | 0      | 4      | 0      | 0     | 1      | 1      | 0      | 0     | 6       | 1      | 1      | 0     |
|                        |                              |                         | ( 6 )   | ( 3 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 12 ) | ( 0 )  | ( 0 ) | ( 3 )  | ( 3 )  | ( 0 )  | ( 0 ) | ( 15 )  | ( 2 )  | ( 2 )  | ( 0 ) |
| {Digestive system}     |                              |                         |         |        |        |       |        |        |        |       |        |        |        |       |         |        |        |       |
| tooth                  |                              |                         | <32>    |        |        |       | <33>   |        |        |       | <33>   |        |        |       | <41>    |        |        |       |
|                        | dysplasia                    |                         | 7       | 1      | 0      | 0     | 8      | 3      | 0      | 0     | 8      | 2      | 0      | 0     | 9       | 3      | 0      | 0     |
|                        |                              |                         | ( 22 )  | ( 3 )  | ( 0 )  | ( 0 ) | ( 24 ) | ( 9 )  | ( 0 )  | ( 0 ) | ( 24 ) | ( 6 )  | ( 0 )  | ( 0 ) | ( 22 )  | ( 7 )  | ( 0 )  | ( 0 ) |
| stomach                |                              |                         | <32>    |        |        |       | <33>   |        |        |       | <33>   |        |        |       | <41>    |        |        |       |
|                        | hyperplasia:gland            |                         | 5       | 16     | 11     | 0     | 3      | 21     | 9      | 0     | 2      | 19     | 12     | 0     | 6       | 21     | 14     | 0     |
|                        |                              |                         | ( 16 )  | ( 50 ) | ( 34 ) | ( 0 ) | ( 9 )  | ( 64 ) | ( 27 ) | ( 0 ) | ( 6 )  | ( 58 ) | ( 36 ) | ( 0 ) | ( 15 )  | ( 51 ) | ( 34 ) | ( 0 ) |
|                        | hyperkeratosis:forestomach   |                         | 0       | 0      | 0      | 0     | 0      | 0      | 0      | 0     | 0      | 0      | 0      | 1     | 0       | 0      | 0      |       |
|                        |                              |                         | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 2 ) | ( 0 )   | ( 0 )  | ( 0 )  |       |
|                        | erosion:glandular stomach    |                         | 1       | 0      | 0      | 0     | 0      | 0      | 0      | 0     | 0      | 0      | 0      | 0     | 0       | 0      | 0      | 0     |
|                        |                              |                         | ( 3 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) |

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

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

b : Number of animals with lesion

( c ) c : b / a \* 100

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS (105W)

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|                    |                           | Group Name              | Control |       |       |       | 32 ppm |       |       |       | 80 ppm |       |       |       | 200 ppm |       |       |       |
|--------------------|---------------------------|-------------------------|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|---------|-------|-------|-------|
|                    |                           | No. of Animals on Study | 32      |       |       |       | 33     |       |       |       | 33     |       |       |       | 41      |       |       |       |
| Organ              | Findings                  | Grade                   | 1       | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1       | 2     | 3     | 4     |
|                    |                           |                         | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)     | (%)   | (%)   | (%)   |
| {Digestive system} |                           |                         |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
| small intes        |                           |                         | <32>    |       |       |       | <33>   |       |       |       | <33>   |       |       |       | <41>    |       |       |       |
|                    | inflammatory infiltration |                         | 0       | 0     | 0     | 0     | 0      | 1     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                    |                           |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 3 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
| liver              |                           |                         | <32>    |       |       |       | <33>   |       |       |       | <33>   |       |       |       | <41>    |       |       |       |
|                    | angiectasis               |                         | 0       | 0     | 0     | 0     | 0      | 1     | 0     | 0     | 0      | 0     | 0     | 0     | 1       | 1     | 0     | 0     |
|                    |                           |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 3 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )   | ( 2 ) | ( 0 ) | ( 0 ) |
|                    | necrosis:focal            |                         | 1       | 1     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                    |                           |                         | ( 3 )   | ( 3 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                    | deposit of amyloid        |                         | 0       | 0     | 0     | 0     | 0      | 1     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                    |                           |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 3 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                    | inflammatory infiltration |                         | 1       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 1       | 0     | 0     | 0     |
|                    |                           |                         | ( 3 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 3 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                    | granulation               |                         | 1       | 0     | 0     | 0     | 2      | 0     | 0     | 0     | 3      | 0     | 0     | 0     | 1       | 1     | 0     | 0     |
|                    |                           |                         | ( 3 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 6 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 9 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )   | ( 2 ) | ( 0 ) | ( 0 ) |
|                    | hyperplasia:vascular      |                         | 1       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                    |                           |                         | ( 3 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                    | clear cell focus          |                         | 3       | 0     | 0     | 0     | 4      | 0     | 0     | 0     | 3      | 0     | 0     | 0     | 4       | 0     | 0     | 0     |
|                    |                           |                         | ( 9 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 12 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 9 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 10 )  | ( 0 ) | ( 0 ) | ( 0 ) |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS (105W)

PAGE : 6

|                    |                        | Group Name              | Control |       |       |       | 32 ppm |       |       |       | 80 ppm |       |       |       | 200 ppm |        |       |       |
|--------------------|------------------------|-------------------------|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|---------|--------|-------|-------|
|                    |                        | No. of Animals on Study | 32      |       |       |       | 33     |       |       |       | 33     |       |       |       | 41      |        |       |       |
| Organ              | Findings               | Grade                   | 1       | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1       | 2      | 3     | 4     |
|                    |                        |                         | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)     | (%)    | (%)   | (%)   |
| {Digestive system} |                        |                         |         |       |       |       |        |       |       |       |        |       |       |       |         |        |       |       |
| liver              |                        |                         | <32>    |       |       |       | <33>   |       |       |       | <33>   |       |       |       | <41>    |        |       |       |
|                    | acidophilic cell focus |                         | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0       | 0      | 0     | 0     |
|                    |                        |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 3 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) |
|                    | basophilic cell focus  |                         | 2       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 1       | 0      | 0     | 0     |
|                    |                        |                         | ( 6 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 3 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )   | ( 0 )  | ( 0 ) | ( 0 ) |
|                    | biliary cyst           |                         | 1       | 0     | 0     | 0     | 3      | 0     | 0     | 0     | 1      | 0     | 1     | 0     | 1       | 1      | 0     | 0     |
|                    |                        |                         | ( 3 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 9 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 3 )  | ( 0 ) | ( 3 ) | ( 0 ) | ( 2 )   | ( 2 )  | ( 0 ) | ( 0 ) |
| pancreas           |                        |                         | <32>    |       |       |       | <33>   |       |       |       | <33>   |       |       |       | <41>    |        |       |       |
|                    | atrophy                |                         | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 1     | 0     | 0     | 0       | 0      | 0     | 0     |
|                    |                        |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 3 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) |
| {Urinary system}   |                        |                         |         |       |       |       |        |       |       |       |        |       |       |       |         |        |       |       |
| kidney             |                        |                         | <32>    |       |       |       | <33>   |       |       |       | <33>   |       |       |       | <41>    |        |       |       |
|                    | hyaline droplet        |                         | 0       | 1     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 0      | 0     | 0     |
|                    |                        |                         | ( 0 )   | ( 3 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) |
|                    | basophilic change      |                         | 7       | 2     | 0     | 0     | 26     | 0     | 0     | 0 **  | 24     | 2     | 0     | 0 **  | 21      | 9      | 1     | 0 **  |
|                    |                        |                         | ( 22 )  | ( 6 ) | ( 0 ) | ( 0 ) | ( 79 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 73 ) | ( 6 ) | ( 0 ) | ( 0 ) | ( 51 )  | ( 22 ) | ( 2 ) | ( 0 ) |

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

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

b : Number of animals with lesion

( c ) c : b / a \* 100

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



STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS (105W)

PAGE : 7

| Organ              | Findings                  | Group Name              | Control |       |       |       | 32 ppm |       |       |       | 80 ppm |       |       |       | 200 ppm |       |       |       |
|--------------------|---------------------------|-------------------------|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|---------|-------|-------|-------|
|                    |                           | No. of Animals on Study | 32      |       |       |       | 33     |       |       |       | 33     |       |       |       | 41      |       |       |       |
|                    |                           | Grade                   | 1       | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1       | 2     | 3     | 4     |
|                    |                           |                         | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)     | (%)   | (%)   | (%)   |
| {Urinary system}   |                           |                         |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
| kidney             |                           |                         | <32>    |       |       |       | <33>   |       |       |       | <33>   |       |       |       | <41>    |       |       |       |
|                    | deposit of amyloid        |                         | 0       | 0     | 0     | 0     | 0      | 0     | 1     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                    |                           |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 3 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                    | hyaline cast              |                         | 1       | 1     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 1       | 0     | 0     | 0     |
|                    |                           |                         | ( 3 )   | ( 3 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                    | inflammatory infiltration |                         | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 1     | 0     | 0     |
|                    |                           |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 2 ) | ( 0 ) | ( 0 ) |
|                    | lymphocytic infiltration  |                         | 0       | 0     | 0     | 0     | 0      | 1     | 1     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                    |                           | ( 0 )                   | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 3 )  | ( 3 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) |       |
| scar               |                           | 0                       | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 1       | 0     | 0     |       |
|                    |                           | ( 0 )                   | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )   | ( 0 ) | ( 0 ) |       |
| inflammatory polyp |                           | 0                       | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 1     | 0     |       |
|                    |                           | ( 0 )                   | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 2 ) | ( 0 ) |       |
| hydronephrosis     |                           | 0                       | 0       | 1     | 0     | 0     | 0      | 1     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 1     |       |
|                    |                           | ( 0 )                   | ( 0 )   | ( 3 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 3 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 2 ) |       |
| retention cyst     |                           | 0                       | 1       | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 0     |       |
|                    |                           | ( 0 )                   | ( 3 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 3 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) |       |

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

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

b b : Number of animals with lesion

( c ) c : b / a \* 100

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS (105W)

PAGE : 8

| Organ              | Findings                 | Group Name<br>No. of Animals on Study<br>Grade | Control<br>32 |      |      |      | 32 ppm<br>33 |      |      |      | 80 ppm<br>33 |       |      |      | 200 ppm<br>41 |      |      |      |
|--------------------|--------------------------|--|---------------|------|------|------|--------------|------|------|------|--------------|-------|------|------|---------------|------|------|------|
|                    |                          |  | 1             | 2    | 3    | 4    | 1            | 2    | 3    | 4    | 1            | 2     | 3    | 4    | 1             | 2    | 3    | 4    |
|                    |                          |  | (%)           | (%)  | (%)  | (%)  | (%)          | (%)  | (%)  | (%)  | (%)          | (%)   | (%)  | (%)  | (%)           | (%)  | (%)  | (%)  |
| {Urinary system}   |                          |  |               |      |      |      |              |      |      |      |              |       |      |      |               |      |      |      |
| kidney             | mineralization:cortex    |  | <32>          |      |      |      | <33>         |      |      |      | <33>         |       |      |      | <41>          |      |      |      |
|                    |                          |  | 6             | 0    | 0    | 0    | 17           | 2    | 0    | 0 ** | 21           | 4     | 0    | 0 ** | 14            | 3    | 0    | 0    |
|                    |                          |  | ( 19)         | ( 0) | ( 0) | ( 0) | ( 52)        | ( 6) | ( 0) | ( 0) | ( 64)        | ( 12) | ( 0) | ( 0) | ( 34)         | ( 7) | ( 0) | ( 0) |
| urin bladd         | inflammation             |  | <32>          |      |      |      | <33>         |      |      |      | <33>         |       |      |      | <41>          |      |      |      |
|                    |                          |  | 0             | 0    | 0    | 0    | 0            | 0    | 0    | 0    | 0            | 0     | 0    | 0    | 0             | 1    | 0    | 0    |
|                    |                          |  | ( 0)          | ( 0) | ( 0) | ( 0) | ( 0)         | ( 0) | ( 0) | ( 0) | ( 0)         | ( 0)  | ( 0) | ( 0) | ( 0)          | ( 2) | ( 0) | ( 0) |
|                    | lymphocytic infiltration |  | 0             | 0    | 0    | 0    | 1            | 0    | 0    | 0    | 0            | 0     | 0    | 0    | 1             | 0    | 0    | 0    |
|                    |                          |  | ( 0)          | ( 0) | ( 0) | ( 0) | ( 3)         | ( 0) | ( 0) | ( 0) | ( 0)         | ( 0)  | ( 0) | ( 0) | ( 2)          | ( 0) | ( 0) | ( 0) |
| {Endocrine system} |                          |  |               |      |      |      |              |      |      |      |              |       |      |      |               |      |      |      |
| pituitary          | hyperplasia              |  | <32>          |      |      |      | <33>         |      |      |      | <33>         |       |      |      | <41>          |      |      |      |
|                    |                          |  | 2             | 0    | 0    | 0    | 0            | 0    | 0    | 0    | 4            | 0     | 0    | 0    | 1             | 0    | 0    | 0    |
|                    |                          |  | ( 6)          | ( 0) | ( 0) | ( 0) | ( 0)         | ( 0) | ( 0) | ( 0) | ( 12)        | ( 0)  | ( 0) | ( 0) | ( 2)          | ( 0) | ( 0) | ( 0) |
|                    | Rathke pouch             |  | 1             | 0    | 0    | 0    | 0            | 0    | 0    | 0    | 0            | 0     | 0    | 0    | 1             | 0    | 0    | 0    |
|                    |                          |  | ( 3)          | ( 0) | ( 0) | ( 0) | ( 0)         | ( 0) | ( 0) | ( 0) | ( 0)         | ( 0)  | ( 0) | ( 0) | ( 2)          | ( 0) | ( 0) | ( 0) |
|                    | focal hypertrophy        |  | 2             | 0    | 0    | 0    | 1            | 0    | 0    | 0    | 0            | 0     | 0    | 0    | 0             | 0    | 0    | 0    |
|                    |                          |  | ( 6)          | ( 0) | ( 0) | ( 0) | ( 3)         | ( 0) | ( 0) | ( 0) | ( 0)         | ( 0)  | ( 0) | ( 0) | ( 0)          | ( 0) | ( 0) | ( 0) |

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

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

b : Number of animals with lesion

( c ) c : b / a \* 100

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS (105W)

PAGE : 9

| Organ                 | Findings                  | Group Name<br>No. of Animals on Study<br>Grade | Control<br>32 |       |      |      | 32 ppm<br>33 |       |      |      | 80 ppm<br>33 |       |      |      | 200 ppm<br>41 |       |      |      |
|-----------------------|---------------------------|--|---------------|-------|------|------|--------------|-------|------|------|--------------|-------|------|------|---------------|-------|------|------|
|                       |                           |  | 1             | 2     | 3    | 4    | 1            | 2     | 3    | 4    | 1            | 2     | 3    | 4    | 1             | 2     | 3    | 4    |
|                       |                           |  | (%)           | (%)   | (%)  | (%)  | (%)          | (%)   | (%)  | (%)  | (%)          | (%)   | (%)  | (%)  | (%)           | (%)   | (%)  | (%)  |
| {Endocrine system}    |                           |  |               |       |      |      |              |       |      |      |              |       |      |      |               |       |      |      |
| adrenal               |                           |  | <32>          |       |      |      | <33>         |       |      |      | <33>         |       |      |      | <41>          |       |      |      |
|                       | spindle-cell hyperplasia  |  | 18            | 5     | 0    | 0    | 18           | 5     | 0    | 0    | 20           | 4     | 0    | 0    | 23            | 6     | 0    | 0    |
|                       |                           |  | ( 56)         | ( 16) | ( 0) | ( 0) | ( 55)        | ( 15) | ( 0) | ( 0) | ( 61)        | ( 12) | ( 0) | ( 0) | ( 56)         | ( 15) | ( 0) | ( 0) |
|                       |                           |  |               |       |      |      |              |       |      |      |              |       |      |      |               |       |      |      |
|                       | hyperplasia:cortical cell |  | 2             | 0     | 0    | 0    | 1            | 0     | 0    | 0    | 1            | 0     | 0    | 0    | 0             | 1     | 0    | 0    |
|                       |                           |  | ( 6)          | ( 0)  | ( 0) | ( 0) | ( 3)         | ( 0)  | ( 0) | ( 0) | ( 3)         | ( 0)  | ( 0) | ( 0) | ( 0)          | ( 2)  | ( 0) | ( 0) |
|                       | hyperplasia:medulla       |  | 0             | 0     | 0    | 0    | 0            | 0     | 0    | 0    | 0            | 0     | 0    | 0    | 1             | 0     | 0    | 0    |
|                       |                           |  | ( 0)          | ( 0)  | ( 0) | ( 0) | ( 0)         | ( 0)  | ( 0) | ( 0) | ( 0)         | ( 0)  | ( 0) | ( 0) | ( 2)          | ( 0)  | ( 0) | ( 0) |
|                       | focal hypertrophy:cortex  |  | 2             | 0     | 0    | 0    | 2            | 1     | 0    | 0    | 2            | 0     | 0    | 0    | 0             | 1     | 0    | 0    |
|                       |                           |  | ( 6)          | ( 0)  | ( 0) | ( 0) | ( 6)         | ( 3)  | ( 0) | ( 0) | ( 6)         | ( 0)  | ( 0) | ( 0) | ( 0)          | ( 2)  | ( 0) | ( 0) |
| {Reproductive system} |                           |  |               |       |      |      |              |       |      |      |              |       |      |      |               |       |      |      |
| testis                |                           |  | <32>          |       |      |      | <33>         |       |      |      | <33>         |       |      |      | <41>          |       |      |      |
|                       | mineralization            |  | 23            | 1     | 2    | 0    | 31           | 0     | 0    | 0    | 29           | 2     | 2    | 0    | 30            | 2     | 0    | 0    |
|                       |                           |  | ( 72)         | ( 3)  | ( 6) | ( 0) | ( 94)        | ( 0)  | ( 0) | ( 0) | ( 88)        | ( 6)  | ( 6) | ( 0) | ( 73)         | ( 5)  | ( 0) | ( 0) |
| epididymis            |                           |  | <32>          |       |      |      | <33>         |       |      |      | <33>         |       |      |      | <41>          |       |      |      |
|                       | inflammation              |  | 0             | 0     | 0    | 0    | 0            | 0     | 0    | 0    | 0            | 0     | 0    | 0    | 1             | 0     | 0    | 0    |
|                       |                           |  | ( 0)          | ( 0)  | ( 0) | ( 0) | ( 0)         | ( 0)  | ( 0) | ( 0) | ( 0)         | ( 0)  | ( 0) | ( 0) | ( 2)          | ( 0)  | ( 0) | ( 0) |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS (105W)

PAGE : 10

| Organ                 | Findings        | Group Name<br>No. of Animals on Study<br>Grade | Control<br>32 |       |       |       | 32 ppm<br>33 |       |       |       | 80 ppm<br>33 |       |       |       | 200 ppm<br>41 |       |       |       |
|-----------------------|-----------------|--|---------------|-------|-------|-------|--------------|-------|-------|-------|--------------|-------|-------|-------|---------------|-------|-------|-------|
|                       |                 |  | 1             | 2     | 3     | 4     | 1            | 2     | 3     | 4     | 1            | 2     | 3     | 4     | 1             | 2     | 3     | 4     |
|                       |                 |  | (%)           | (%)   | (%)   | (%)   | (%)          | (%)   | (%)   | (%)   | (%)          | (%)   | (%)   | (%)   | (%)           | (%)   | (%)   | (%)   |
| {Reproductive system} |                 |  |               |       |       |       |              |       |       |       |              |       |       |       |               |       |       |       |
| epididymis            | xanthogranuloma |  | <32>          |       |       |       | <33>         |       |       |       | <33>         |       |       |       | <41>          |       |       |       |
|                       |                 |  | 1             | 0     | 0     | 0     | 0            | 1     | 0     | 0     | 2            | 0     | 0     | 0     | 1             | 0     | 0     | 0     |
|                       |                 |  | ( 3 )         | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 3 ) | ( 0 ) | ( 0 ) | ( 6 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )         | ( 0 ) | ( 0 ) | ( 0 ) |
| semin ves             | congestion      |  | <32>          |       |       |       | <33>         |       |       |       | <33>         |       |       |       | <41>          |       |       |       |
|                       |                 |  | 0             | 0     | 0     | 0     | 1            | 0     | 0     | 0     | 0            | 0     | 0     | 0     | 0             | 0     | 0     | 0     |
|                       |                 |  | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) | ( 3 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) |
|                       | inflammation    |  | 0             | 0     | 0     | 0     | 1            | 0     | 0     | 0     | 0            | 0     | 0     | 0     | 0             | 0     | 0     | 0     |
|                       |                 |  | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) | ( 3 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) |
| prostate              | cyst            |  | <32>          |       |       |       | <33>         |       |       |       | <33>         |       |       |       | <41>          |       |       |       |
|                       |                 |  | 0             | 0     | 1     | 0     | 0            | 0     | 0     | 0     | 0            | 0     | 0     | 0     | 0             | 0     | 0     | 0     |
|                       |                 |  | ( 0 )         | ( 0 ) | ( 3 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) |
| prep/cli gl           | duct ectasia    |  | <32>          |       |       |       | <33>         |       |       |       | <33>         |       |       |       | <41>          |       |       |       |
|                       |                 |  | 0             | 1     | 0     | 0     | 0            | 3     | 0     | 0     | 0            | 0     | 0     | 0     | 0             | 0     | 0     | 0     |
|                       |                 |  | ( 0 )         | ( 3 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 9 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) |
|                       | xanthogranuloma |  | 0             | 0     | 0     | 0     | 0            | 1     | 0     | 0     | 0            | 0     | 0     | 0     | 0             | 0     | 0     | 0     |
|                       |                 |  | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 3 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) |
| {Nervous system}      |                 |  |               |       |       |       |              |       |       |       |              |       |       |       |               |       |       |       |
| brain                 | mineralization  |  | <32>          |       |       |       | <33>         |       |       |       | <33>         |       |       |       | <41>          |       |       |       |
|                       |                 |  | 17            | 0     | 0     | 0     | 17           | 0     | 0     | 0     | 18           | 0     | 0     | 0     | 25            | 0     | 0     | 0     |
|                       |                 |  | ( 53 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 52 )       | ( 0 ) | ( 0 ) | ( 0 ) | ( 55 )       | ( 0 ) | ( 0 ) | ( 0 ) | ( 61 )        | ( 0 ) | ( 0 ) | ( 0 ) |

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

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

b b : Number of animals with lesion

( c ) c : b / a \* 100

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS (105W)

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| Organ | Findings | Group Name              |     |     |     | Control |     |     |     | 32 ppm |     |     |     | 80 ppm |     |     |     | 200 ppm |     |     |     |     |     |     |     |     |     |  |  |   |  |
|-------|----------|-------------------------|-----|-----|-----|---------|-----|-----|-----|--------|-----|-----|-----|--------|-----|-----|-----|---------|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|--|---|--|
|       |          | No. of Animals on Study |     |     |     | 32      |     |     |     | 33     |     |     |     | 33     |     |     |     | 41      |     |     |     |     |     |     |     |     |     |  |  |   |  |
|       |          | Grade                   |     |     |     | 1       |     |     |     | 2      |     |     |     | 3      |     |     |     | 4       |     |     |     |     |     |     |     |     |     |  |  |   |  |
|       |          | 1                       |     |     |     | 2       |     |     |     | 3      |     |     |     | 4      |     |     |     | 1       |     |     |     | 2   |     |     |     | 3   |     |  |  | 4 |  |
|       |          | (%)                     | (%) | (%) | (%) | (%)     | (%) | (%) | (%) | (%)    | (%) | (%) | (%) | (%)    | (%) | (%) | (%) | (%)     | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |  |  |   |  |

{Special sense organs/appendage}

|           |              |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
|-----------|--------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| eye       | keratitis    | <32>  |       |       |       | <33>  |       |       |       | <33>  |       |       |       | <41>  |       |       |       |
|           |              | 0     | 1     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 1     | 0     | 0     | 1     | 0     | 0     |
|           |              | ( 0 ) | ( 3 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 3 ) | ( 0 ) | ( 0 ) | ( 2 ) | ( 0 ) | ( 0 ) |
| Harder gl | degeneration | <32>  |       |       |       | <33>  |       |       |       | <33>  |       |       |       | <41>  |       |       |       |
|           |              | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 1     | 0     | 0     |
|           |              | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 ) | ( 0 ) | ( 0 ) |
|           | inflammation | 0     | 1     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     |
|           |              | ( 0 ) | ( 3 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) |
|           | hyperplasia  | 0     | 0     | 0     | 0     | 1     | 1     | 0     | 0     | 0     | 1     | 0     | 0     | 1     | 1     | 0     | 0     |
|           |              | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 3 ) | ( 3 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 3 ) | ( 0 ) | ( 0 ) | ( 2 ) | ( 2 ) | ( 0 ) | ( 0 ) |

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

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

b b : Number of animals with lesion

( c ) c : b / a \* 100

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

(HPT150)

BAIS4

## APPENDIX L 4

HISTOPATHOLOGICAL FINDINGS :  
NON-NEOPLASTIC LESIONS : FEMALE  
ALL ANIMALS

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 15

| Organ                            | Findings                                   | Group Name              | Control |        |       |       | 32 ppm |        |       |       | 80 ppm |        |       |       | 200 ppm |        |       |       |
|----------------------------------|--|-------------------------|---------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|---------|--------|-------|-------|
|                                  |  | No. of Animals on Study | 50      |        |       |       | 50     |        |       |       | 50     |        |       |       | 50      |        |       |       |
|                                  |  | Grade                   | 1       | 2      | 3     | 4     | 1      | 2      | 3     | 4     | 1      | 2      | 3     | 4     | 1       | 2      | 3     | 4     |
|                                  |  |                         | (%)     | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)     | (%)    | (%)   | (%)   |
| {Integumentary system/appandage} |  |                         |         |        |       |       |        |        |       |       |        |        |       |       |         |        |       |       |
| skin/app                         |  |                         | <50>    |        |       |       | <50>   |        |       |       | <50>   |        |       |       | <50>    |        |       |       |
|                                  | inflammation                               |                         | 0       | 0      | 1     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 0       | 0      | 0     | 0     |
|                                  |  |                         | ( 0 )   | ( 0 )  | ( 2 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) |
| {Respiratory system}             |  |                         |         |        |       |       |        |        |       |       |        |        |       |       |         |        |       |       |
| nasal cavit                      |  |                         | <50>    |        |       |       | <50>   |        |       |       | <50>   |        |       |       | <50>    |        |       |       |
|                                  | exudate                                    |                         | 0       | 0      | 0     | 0     | 1      | 0      | 0     | 0     | 0      | 2      | 0     | 0     | 1       | 0      | 0     | 0     |
|                                  |  |                         | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 4 )  | ( 0 ) | ( 0 ) | ( 2 )   | ( 0 )  | ( 0 ) | ( 0 ) |
|                                  | mineralization                             |                         | 3       | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 0       | 0      | 0     | 0     |
|                                  |  |                         | ( 6 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) |
|                                  | inflammation                               |                         | 2       | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 0       | 0      | 0     | 0     |
|                                  |  |                         | ( 4 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) |
|                                  | fibrosis                                   |                         | 1       | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 0       | 0      | 0     | 0     |
|                                  |  |                         | ( 2 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) |
|                                  | eosinophilic change:olfactory epithelium   |                         | 23      | 3      | 0     | 0     | 11     | 0      | 0     | 0     | 12     | 2      | 0     | 0 *   | 19      | 2      | 0     | 0     |
|                                  |  |                         | ( 46 )  | ( 6 )  | ( 0 ) | ( 0 ) | ( 22 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 24 ) | ( 4 )  | ( 0 ) | ( 0 ) | ( 38 )  | ( 4 )  | ( 0 ) | ( 0 ) |
|                                  | eosinophilic change:respiratory epithelium |                         | 31      | 14     | 2     | 0     | 34     | 5      | 2     | 0     | 29     | 6      | 0     | 0 **  | 35      | 8      | 2     | 0     |
|                                  |  |                         | ( 62 )  | ( 28 ) | ( 4 ) | ( 0 ) | ( 68 ) | ( 10 ) | ( 4 ) | ( 0 ) | ( 58 ) | ( 12 ) | ( 0 ) | ( 0 ) | ( 70 )  | ( 16 ) | ( 4 ) | ( 0 ) |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 16

| Organ                | Findings                                    | Group Name<br>No. of Animals on Study<br>Grade | Control     |           |           |           | 32 ppm      |           |           |           | 80 ppm      |           |           |           | 200 ppm     |           |           |           |
|----------------------|---|--|-------------|-----------|-----------|-----------|-------------|-----------|-----------|-----------|-------------|-----------|-----------|-----------|-------------|-----------|-----------|-----------|
|                      |   |  | 50          |           |           |           | 50          |           |           |           | 50          |           |           |           | 50          |           |           |           |
|                      |   |  | 1           | 2         | 3         | 4         | 1           | 2         | 3         | 4         | 1           | 2         | 3         | 4         | 1           | 2         | 3         | 4         |
|                      |   |  | (%)         | (%)       | (%)       | (%)       | (%)         | (%)       | (%)       | (%)       | (%)         | (%)       | (%)       | (%)       | (%)         | (%)       | (%)       | (%)       |
| {Respiratory system} |   |  |             |           |           |           |             |           |           |           |             |           |           |           |             |           |           |           |
| nasal cavit          | respiratory metaplasia:olfactory epithelium |  | 32<br>( 64) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 14<br>( 28) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 34<br>( 68) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 43<br>( 86) | 1<br>( 2) | 0<br>( 0) | 0<br>( 0) |
|                      |   |  | <50>        |           |           |           | <50>        |           |           |           | <50>        |           |           |           | <50>        |           |           |           |
|                      | respiratory metaplasia:gland                |  | 16<br>( 32) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 11<br>( 22) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 13<br>( 26) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 40<br>( 80) | 3<br>( 6) | 0<br>( 0) | 0<br>( 0) |
|                      | hyperplasia:transitional epithelium         |  | 1<br>( 2)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
|                      | atrophy:olfactory epithelium                |  | 8<br>( 16)  | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 7<br>( 14)  | 1<br>( 2) | 0<br>( 0) | 0<br>( 0) | 19<br>( 38) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 16<br>( 32) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
| nasopharynx          | necrosis:olfactory epithelium               |  | 0<br>( 0)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 2)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
|                      | eosinophilic change                         |  | 8<br>( 16)  | 4<br>( 8) | 1<br>( 2) | 0<br>( 0) | 3<br>( 6)   | 1<br>( 2) | 2<br>( 4) | 0<br>( 0) | 2<br>( 4)   | 0<br>( 0) | 1<br>( 2) | 0<br>( 0) | 4<br>( 8)   | 1<br>( 2) | 1<br>( 2) | 0<br>( 0) |
| lung                 | congestion                                  |  | 0<br>( 0)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 2)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
|                      |   |  | <50>        |           |           |           | <50>        |           |           |           | <50>        |           |           |           | <50>        |           |           |           |

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



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 REPORT TYPE : A1  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 17

| Organ                  | Findings                              | Group Name<br>No. of Animals on Study |           |           |           | Control<br>50 |           |           |           | 32 ppm<br>50 |           |           |           | 80 ppm<br>50 |           |           |           | 200 ppm<br>50 |           |           |           |
|------------------------|---------------------------------------|---------------------------------------|-----------|-----------|-----------|---------------|-----------|-----------|-----------|--------------|-----------|-----------|-----------|--------------|-----------|-----------|-----------|---------------|-----------|-----------|-----------|
|                        |                                       | Grade                                 |           |           |           |               |           |           |           |              |           |           |           |              |           |           |           |               |           |           |           |
|                        |                                       | 1                                     | 2         | 3         | 4         | 1             | 2         | 3         | 4         | 1            | 2         | 3         | 4         | 1            | 2         | 3         | 4         | 1             | 2         | 3         | 4         |
|                        |                                       | (%)                                   | (%)       | (%)       | (%)       | (%)           | (%)       | (%)       | (%)       | (%)          | (%)       | (%)       | (%)       | (%)          | (%)       | (%)       | (%)       | (%)           | (%)       | (%)       | (%)       |
| {Respiratory system}   |                                       |                                       |           |           |           |               |           |           |           |              |           |           |           |              |           |           |           |               |           |           |           |
| lung                   |                                       | <50>                                  |           |           |           | <50>          |           |           |           | <50>         |           |           |           | <50>         |           |           |           | <50>          |           |           |           |
|                        | hemorrhage                            | 1<br>( 2)                             | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)    | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)    | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
|                        | inflammatory infiltration             | 0<br>( 0)                             | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 3<br>( 6)    | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 2)    | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 2)     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
|                        | bronchiolar-alveolar cell hyperplasia | 3<br>( 6)                             | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 2)     | 1<br>( 2) | 0<br>( 0) | 0<br>( 0) | 3<br>( 6)    | 1<br>( 2) | 0<br>( 0) | 0<br>( 0) | 2<br>( 4)    | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 2<br>( 4)     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
| {Hematopoietic system} |                                       |                                       |           |           |           |               |           |           |           |              |           |           |           |              |           |           |           |               |           |           |           |
| bone marrow            |                                       | <50>                                  |           |           |           | <50>          |           |           |           | <50>         |           |           |           | <50>         |           |           |           | <50>          |           |           |           |
|                        | granulation                           | 0<br>( 0)                             | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 2)    | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)    | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
|                        | increased hematopoiesis               | 8<br>( 16)                            | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 6<br>( 12)    | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 9<br>( 18)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 6<br>( 12)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 6<br>( 12)    | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
|                        | myelofibrosis                         | 1<br>( 2)                             | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)    | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)    | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
|                        | granulopoiesis:increased              | 0<br>( 0)                             | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 2)     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 2<br>( 4)    | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)    | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 18

| Organ                  | Findings                     | Group Name<br>No. of Animals on Study<br>Grade | Control |       |        |       | 32 ppm |        |       |       | 80 ppm |       |        |       | 200 ppm |        |        |       |
|------------------------|------------------------------|--|---------|-------|--------|-------|--------|--------|-------|-------|--------|-------|--------|-------|---------|--------|--------|-------|
|                        |                              |  | 50      |       |        |       | 50     |        |       |       | 50     |       |        |       | 50      |        |        |       |
|                        |                              |  | 1       | 2     | 3      | 4     | 1      | 2      | 3     | 4     | 1      | 2     | 3      | 4     | 1       | 2      | 3      | 4     |
|                        |                              |  | (%)     | (%)   | (%)    | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)   | (%)    | (%)   | (%)     | (%)    | (%)    | (%)   |
| {Hematopoietic system} |                              |  |         |       |        |       |        |        |       |       |        |       |        |       |         |        |        |       |
| lymph node             |                              |  | <50>    |       |        |       | <50>   |        |       |       | <50>   |       |        |       | <50>    |        |        |       |
|                        | lymphadenitis                |  | 0       | 0     | 1      | 0     | 0      | 0      | 0     | 0     | 0      | 0     | 0      | 0     | 0       | 0      | 0      | 0     |
|                        |                              |  | ( 0 )   | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) |
| spleen                 |                              |  | <50>    |       |        |       | <50>   |        |       |       | <50>   |       |        |       | <50>    |        |        |       |
|                        | atrophy                      |  | 1       | 0     | 0      | 0     | 0      | 0      | 0     | 0     | 0      | 0     | 0      | 0     | 1       | 0      | 0      | 0     |
|                        |                              |  | ( 2 )   | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 2 )   | ( 0 )  | ( 0 )  | ( 0 ) |
|                        | deposit of amyloid           |  | 1       | 0     | 0      | 0     | 0      | 0      | 0     | 0     | 0      | 0     | 0      | 0     | 0       | 0      | 0      | 0     |
|                        |                              |  | ( 2 )   | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) |
|                        | deposit of hemosiderin       |  | 6       | 0     | 0      | 0     | 3      | 0      | 0     | 0     | 3      | 1     | 0      | 0     | 6       | 1      | 0      | 0     |
|                        |                              |  | ( 12 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 6 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 6 )  | ( 2 ) | ( 0 )  | ( 0 ) | ( 12 )  | ( 2 )  | ( 0 )  | ( 0 ) |
|                        | deposit of melanin           |  | 2       | 1     | 0      | 0     | 0      | 0      | 0     | 0     | 0      | 0     | 0      | 0     | 1       | 0      | 0      | 0     |
|                        |                              |  | ( 4 )   | ( 2 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 2 )   | ( 0 )  | ( 0 )  | ( 0 ) |
|                        | mastcell hyperplasia         |  | 0       | 0     | 0      | 0     | 0      | 0      | 0     | 0     | 2      | 0     | 0      | 0     | 0       | 0      | 0      | 0     |
|                        |                              |  | ( 0 )   | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 4 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) |
|                        | extramedullary hematopoiesis |  | 3       | 3     | 10     | 0     | 3      | 7      | 4     | 0     | 5      | 4     | 12     | 0     | 2       | 7      | 5      | 0     |
|                        |                              |  | ( 6 )   | ( 6 ) | ( 20 ) | ( 0 ) | ( 6 )  | ( 14 ) | ( 8 ) | ( 0 ) | ( 10 ) | ( 8 ) | ( 24 ) | ( 0 ) | ( 4 )   | ( 14 ) | ( 10 ) | ( 0 ) |
|                        | hyperplasia:vascular         |  | 0       | 0     | 0      | 0     | 0      | 0      | 0     | 0     | 0      | 0     | 0      | 0     | 1       | 0      | 0      | 0     |
|                        |                              |  | ( 0 )   | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 2 )   | ( 0 )  | ( 0 )  | ( 0 ) |

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

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

b : Number of animals with lesion

( c ) c : b / a \* 100

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 19

| Organ                  | Findings               | Group Name<br>No. of Animals on Study<br>Grade | Control |       |       |       | 32 ppm |       |       |       | 80 ppm |       |       |       | 200 ppm |       |       |       |
|------------------------|------------------------|--|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|---------|-------|-------|-------|
|                        |                        |  | 50      |       |       |       | 50     |       |       |       | 50     |       |       |       | 50      |       |       |       |
|                        |                        |  | 1       | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1       | 2     | 3     | 4     |
|                        |                        |  | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)     | (%)   | (%)   | (%)   |
| {Hematopoietic system} |                        |  |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
| spleen                 |                        |  | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>    |       |       |       |
|                        | follicular hyperplasia |  | 2       | 0     | 0     | 0     | 2      | 3     | 1     | 0     | 4      | 2     | 0     | 0     | 2       | 1     | 0     | 0     |
|                        |                        |  | ( 4 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )  | ( 6 ) | ( 2 ) | ( 0 ) | ( 8 )  | ( 4 ) | ( 0 ) | ( 0 ) | ( 4 )   | ( 2 ) | ( 0 ) | ( 0 ) |
| {Circulatory system}   |                        |  |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
| heart                  |                        |  | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>    |       |       |       |
|                        | thrombus               |  | 0       | 0     | 0     | 0     | 0      | 0     | 1     | 0     | 0      | 0     | 0     | 0     | 1       | 0     | 1     | 0     |
|                        |                        |  | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 2 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )   | ( 0 ) | ( 2 ) | ( 0 ) |
|                        | mineralization         |  | 3       | 0     | 0     | 0     | 3      | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 1       | 0     | 0     | 0     |
|                        |                        |  | ( 6 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 6 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                        | arteritis              |  | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 1     | 0     | 0     |
|                        |                        |  | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 2 ) | ( 0 ) | ( 0 ) |
| {Digestive system}     |                        |  |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
| tooth                  |                        |  | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>    |       |       |       |
|                        | dysplasia              |  | 3       | 1     | 0     | 0     | 3      | 0     | 0     | 0     | 5      | 1     | 0     | 0     | 5       | 1     | 0     | 0     |
|                        |                        |  | ( 6 )   | ( 2 ) | ( 0 ) | ( 0 ) | ( 6 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 10 ) | ( 2 ) | ( 0 ) | ( 0 ) | ( 10 )  | ( 2 ) | ( 0 ) | ( 0 ) |

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

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

b : Number of animals with lesion

( c ) c : b / a \* 100

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 20

| Organ              | Findings                  | Group Name<br>No. of Animals on Study |        |        |       | Control |        |        |       | 32 ppm |        |        |       | 80 ppm |        |        |       | 200 ppm |        |        |       |
|--------------------|---------------------------|---------------------------------------|--------|--------|-------|---------|--------|--------|-------|--------|--------|--------|-------|--------|--------|--------|-------|---------|--------|--------|-------|
|                    |                           | Grade                                 |        |        |       | 50      |        |        |       | 50     |        |        |       | 50     |        |        |       | 50      |        |        |       |
|                    |                           | 1                                     | 2      | 3      | 4     | 1       | 2      | 3      | 4     | 1      | 2      | 3      | 4     | 1      | 2      | 3      | 4     | 1       | 2      | 3      | 4     |
|                    |                           | (%)                                   | (%)    | (%)    | (%)   | (%)     | (%)    | (%)    | (%)   | (%)    | (%)    | (%)    | (%)   | (%)    | (%)    | (%)    | (%)   | (%)     | (%)    | (%)    | (%)   |
| {Digestive system} |                           |                                       |        |        |       |         |        |        |       |        |        |        |       |        |        |        |       |         |        |        |       |
| tongue             | arteritis                 | <50>                                  |        |        |       | <50>    |        |        |       | <50>   |        |        |       | <50>   |        |        |       | <50>    |        |        |       |
|                    |                           | 0                                     | 1      | 0      | 0     | 0       | 0      | 0      | 0     | 1      | 0      | 0      | 0     | 0      | 0      | 0      | 0     | 0       | 1      | 0      | 0     |
|                    |                           | ( 0 )                                 | ( 2 )  | ( 0 )  | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 2 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )   | ( 2 )  | ( 0 )  | ( 0 ) |
| stomach            | erosion                   | <50>                                  |        |        |       | <50>    |        |        |       | <50>   |        |        |       | <50>   |        |        |       | <50>    |        |        |       |
|                    |                           | 1                                     | 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 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) |
|                    | hyperplasia:gland         | 7                                     | 29     | 11     | 0     | 12      | 24     | 12     | 0     | 8      | 32     | 10     | 0     | 8      | 29     | 12     | 0     | 8       | 29     | 12     | 0     |
|                    |                           | ( 14 )                                | ( 58 ) | ( 22 ) | ( 0 ) | ( 24 )  | ( 48 ) | ( 24 ) | ( 0 ) | ( 16 ) | ( 64 ) | ( 20 ) | ( 0 ) | ( 16 ) | ( 58 ) | ( 24 ) | ( 0 ) | ( 16 )  | ( 58 ) | ( 24 ) | ( 0 ) |
|                    | ulcer:forestomach         | 0                                     | 0      | 0      | 0     | 0       | 0      | 0      | 0     | 1      | 0      | 0      | 0     | 1      | 0      | 0      | 0     | 1       | 0      | 0      | 0     |
|                    |                           | ( 0 )                                 | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 2 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 2 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 2 )   | ( 0 )  | ( 0 )  | ( 0 ) |
| liver              | erosion:glandular stomach | 0                                     | 0      | 0      | 0     | 0       | 0      | 0      | 0     | 0      | 0      | 0      | 0     | 0      | 0      | 0      | 0     | 1       | 1      | 0      | 0     |
|                    |                           | ( 0 )                                 | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 2 )   | ( 2 )  | ( 0 )  | ( 0 ) |
|                    | ulcer:glandular stomach   | 0                                     | 0      | 0      | 0     | 0       | 0      | 0      | 0     | 0      | 0      | 0      | 0     | 1      | 0      | 0      | 0     | 1       | 0      | 0      | 0     |
|                    |                           | ( 0 )                                 | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 2 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 2 )   | ( 0 )  | ( 0 )  | ( 0 ) |
| liver              | angiectasis               | <50>                                  |        |        |       | <50>    |        |        |       | <50>   |        |        |       | <50>   |        |        |       | <50>    |        |        |       |
|                    |                           | 1                                     | 3      | 0      | 0     | 0       | 1      | 0      | 0     | 1      | 3      | 0      | 0     | 0      | 2      | 0      | 0     | 0       | 2      | 0      | 0     |
|                    |                           | ( 2 )                                 | ( 6 )  | ( 0 )  | ( 0 ) | ( 0 )   | ( 2 )  | ( 0 )  | ( 0 ) | ( 2 )  | ( 6 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 4 )  | ( 0 )  | ( 0 ) | ( 0 )   | ( 4 )  | ( 0 )  | ( 0 ) |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 21

| Organ              | Findings                    | Group Name<br>No. of Animals on Study |      |      |      | Control |      |      |      | 32 ppm |      |      |      | 80 ppm |      |      |      | 200 ppm |      |      |      |
|--------------------|-----------------------------|---------------------------------------|------|------|------|---------|------|------|------|--------|------|------|------|--------|------|------|------|---------|------|------|------|
|                    |                             | Grade                                 |      |      |      | 50      |      |      |      | 50     |      |      |      | 50     |      |      |      | 50      |      |      |      |
|                    |                             | 1                                     | 2    | 3    | 4    | 1       | 2    | 3    | 4    | 1      | 2    | 3    | 4    | 1      | 2    | 3    | 4    | 1       | 2    | 3    | 4    |
|                    |                             | (%)                                   | (%)  | (%)  | (%)  | (%)     | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  | (%)     | (%)  | (%)  | (%)  |
| {Digestive system} |                             |                                       |      |      |      |         |      |      |      |        |      |      |      |        |      |      |      |         |      |      |      |
| liver              | necrosis:focal              | <50>                                  |      |      |      | <50>    |      |      |      | <50>   |      |      |      | <50>   |      |      |      | <50>    |      |      |      |
|                    |                             | 1                                     | 0    | 0    | 0    | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 1       | 1    | 0    | 0    |
|                    |                             | ( 2)                                  | ( 0) | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 2)    | ( 2) | ( 0) | ( 0) |
|                    | inflammatory infiltration   | 0                                     | 0    | 0    | 0    | 1       | 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) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) |
|                    | lymphocytic infiltration    | 0                                     | 0    | 0    | 0    | 1       | 1    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0       | 0    | 0    | 0    |
|                    |                             | ( 0)                                  | ( 0) | ( 0) | ( 0) | ( 2)    | ( 2) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) |
|                    | granulation                 | 2                                     | 0    | 0    | 0    | 5       | 0    | 0    | 0    | 1      | 0    | 0    | 0    | 4      | 0    | 0    | 0    | 8       | 0    | 0    | 0    |
|                    |                             | ( 4)                                  | ( 0) | ( 0) | ( 0) | ( 10)   | ( 0) | ( 0) | ( 0) | ( 2)   | ( 0) | ( 0) | ( 0) | ( 8)   | ( 0) | ( 0) | ( 0) | ( 8)    | ( 0) | ( 0) | ( 0) |
|                    | fibrosis                    | 0                                     | 0    | 0    | 0    | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0       | 1    | 0    | 0    |
|                    |                             | ( 0)                                  | ( 0) | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)    | ( 2) | ( 0) | ( 0) |
|                    | clear cell focus            | 2                                     | 1    | 0    | 0    | 3       | 0    | 0    | 0    | 2      | 0    | 0    | 0    | 1      | 0    | 0    | 0    | 2       | 0    | 0    | 0    |
|                    |                             | ( 4)                                  | ( 2) | ( 0) | ( 0) | ( 6)    | ( 0) | ( 0) | ( 0) | ( 4)   | ( 0) | ( 0) | ( 0) | ( 2)   | ( 0) | ( 0) | ( 0) | ( 2)    | ( 0) | ( 0) | ( 0) |
|                    | basophilic cell focus       | 2                                     | 0    | 0    | 0    | 0       | 0    | 0    | 0    | 1      | 0    | 0    | 0    | 3      | 1    | 0    | 0    | 6       | 2    | 0    | 0    |
|                    |                             | ( 4)                                  | ( 0) | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) | ( 2)   | ( 0) | ( 0) | ( 0) | ( 6)   | ( 2) | ( 0) | ( 0) | ( 6)    | ( 2) | ( 0) | ( 0) |
|                    | bile ductular proliferation | 0                                     | 0    | 0    | 0    | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 1      | 0    | 0    | 0    | 2       | 0    | 0    | 0    |
|                    |                             | ( 0)                                  | ( 0) | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 2)    | ( 0) | ( 0) | ( 0) |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 22

| Organ              | Findings                  | Group Name<br>No. of Animals on Study<br>Grade | Control |       |        |       | 32 ppm |       |        |       | 80 ppm |       |        |       | 200 ppm |       |        |       |
|--------------------|---------------------------|--|---------|-------|--------|-------|--------|-------|--------|-------|--------|-------|--------|-------|---------|-------|--------|-------|
|                    |                           |  | 50      |       |        |       | 50     |       |        |       | 50     |       |        |       | 50      |       |        |       |
|                    |                           |  | 1       | 2     | 3      | 4     | 1      | 2     | 3      | 4     | 1      | 2     | 3      | 4     | 1       | 2     | 3      | 4     |
|                    |                           |  | (%)     | (%)   | (%)    | (%)   | (%)    | (%)   | (%)    | (%)   | (%)    | (%)   | (%)    | (%)   | (%)     | (%)   | (%)    | (%)   |
| {Digestive system} |                           |  |         |       |        |       |        |       |        |       |        |       |        |       |         |       |        |       |
| liver              | biliary cyst              |  | <50>    |       |        |       | <50>   |       |        |       | <50>   |       |        |       | <50>    |       |        |       |
|                    |                           |  | 0       | 0     | 0      | 0     | 2      | 0     | 0      | 0     | 2      | 0     | 0      | 0     | 2       | 0     | 0      | 0     |
|                    |                           |  | ( 0 )   | ( 0 ) | ( 0 )  | ( 0 ) | ( 4 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 4 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 4 )   | ( 0 ) | ( 0 )  | ( 0 ) |
| gall bladd         | lymphocytic infiltration  |  | <50>    |       |        |       | <50>   |       |        |       | <50>   |       |        |       | <50>    |       |        |       |
|                    |                           |  | 0       | 0     | 0      | 0     | 1      | 0     | 0      | 0     | 0      | 0     | 0      | 0     | 0       | 0     | 0      | 0     |
|                    |                           |  | ( 0 )   | ( 0 ) | ( 0 )  | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 )  | ( 0 ) |
| pancreas           | atrophy                   |  | <50>    |       |        |       | <50>   |       |        |       | <50>   |       |        |       | <50>    |       |        |       |
|                    |                           |  | 0       | 0     | 0      | 0     | 0      | 0     | 0      | 0     | 0      | 0     | 0      | 0     | 1       | 0     | 0      | 0     |
|                    |                           |  | ( 0 )   | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 2 )   | ( 0 ) | ( 0 )  | ( 0 ) |
| {Urinary system}   |                           |  |         |       |        |       |        |       |        |       |        |       |        |       |         |       |        |       |
| kidney             | hyaline droplet           |  | <50>    |       |        |       | <50>   |       |        |       | <50>   |       |        |       | <50>    |       |        |       |
|                    |                           |  | 0       | 1     | 10     | 0     | 0      | 3     | 5      | 0     | 0      | 3     | 9      | 0     | 1       | 2     | 5      | 0     |
|                    |                           |  | ( 0 )   | ( 2 ) | ( 20 ) | ( 0 ) | ( 0 )  | ( 6 ) | ( 10 ) | ( 0 ) | ( 0 )  | ( 6 ) | ( 18 ) | ( 0 ) | ( 2 )   | ( 4 ) | ( 10 ) | ( 0 ) |
|                    | hyaline cast              |  | 5       | 0     | 0      | 0     | 3      | 0     | 0      | 0     | 3      | 0     | 0      | 0     | 3       | 0     | 0      | 0     |
|                    |                           |  | ( 10 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 6 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 6 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 6 )   | ( 0 ) | ( 0 )  | ( 0 ) |
|                    | inflammatory infiltration |  | 0       | 0     | 0      | 0     | 0      | 0     | 1      | 0     | 0      | 0     | 0      | 0     | 0       | 0     | 0      | 0     |
|                    |                           |  | ( 0 )   | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 2 )  | ( 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  
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 ( c ) c : b / a \* 100  
 Significant difference ; \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
ALL ANIMALS (0-105W)

PAGE : 23

| Organ              | Findings                 | Group Name<br>No. of Animals on Study<br>Grade | Control |       |       |       | 32 ppm |       |       |       | 80 ppm |       |       |       | 200 ppm |       |       |       |
|--------------------|--------------------------|--|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|---------|-------|-------|-------|
|                    |                          |  | 50      |       |       |       | 50     |       |       |       | 50     |       |       |       | 50      |       |       |       |
|                    |                          |  | 1       | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1       | 2     | 3     | 4     |
|                    |                          |  | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)     | (%)   | (%)   | (%)   |
| {Urinary system}   |                          |  |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
| kidney             |                          |  | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>    |       |       |       |
|                    | lymphocytic infiltration |  | 0       | 1     | 0     | 0     | 1      | 1     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                    |                          |  | ( 0 )   | ( 2 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                    |                          |  |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
|                    | inflammatory polyp       |  | 0       | 1     | 1     | 0     | 0      | 1     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                    |                          |  | ( 0 )   | ( 2 ) | ( 2 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 2 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                    |                          |  |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
|                    |                          |  |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
|                    | hydronephrosis           |  | 0       | 0     | 3     | 0     | 0      | 0     | 1     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 1     | 1     |
|                    |                          |  | ( 0 )   | ( 0 ) | ( 6 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 2 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 2 ) | ( 2 ) | ( 2 ) |
|                    |                          |  |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
|                    |                          |  |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
|                    | retention cyst           |  | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 1     | 0     | 0     |
|                    |                          |  | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 2 ) | ( 0 ) | ( 0 ) |
|                    |                          |  |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
|                    |                          |  |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
| urin bladd         |                          |  | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>    |       |       |       |
|                    | lymphocytic infiltration |  | 0       | 0     | 0     | 0     | 4      | 0     | 0     | 0     | 5      | 0     | 0     | 0     | 4       | 0     | 0     | 0     |
|                    |                          |  | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 10 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 8 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                    |                          |  |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
| {Endocrine system} |                          |  |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
| pituitary          |                          |  | <49>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>    |       |       |       |
|                    | congestion               |  | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 1       | 0     | 0     | 0     |
|                    |                          |  | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                    |                          |  |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |

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

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

b : Number of animals with lesion

( c ) c : b / a \* 100

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 24

|                       |                          | Group Name              | Control |        |        |       | 32 ppm |        |        |       | 80 ppm |        |        |       | 200 ppm |        |        |       |
|-----------------------|--------------------------|-------------------------|---------|--------|--------|-------|--------|--------|--------|-------|--------|--------|--------|-------|---------|--------|--------|-------|
|                       |                          | No. of Animals on Study | 50      |        |        |       | 50     |        |        |       | 50     |        |        |       | 50      |        |        |       |
|                       |                          | Grade                   | 1       | 2      | 3      | 4     | 1      | 2      | 3      | 4     | 1      | 2      | 3      | 4     | 1       | 2      | 3      | 4     |
| Organ                 | Findings                 |                         | (%)     | (%)    | (%)    | (%)   | (%)    | (%)    | (%)    | (%)   | (%)    | (%)    | (%)    | (%)   | (%)     | (%)    | (%)    | (%)   |
| {Endocrine system}    |                          |                         |         |        |        |       |        |        |        |       |        |        |        |       |         |        |        |       |
| pituitary             |                          |                         | <49>    |        |        |       | <50>   |        |        |       | <50>   |        |        |       | <50>    |        |        |       |
|                       | cyst                     |                         | 0       | 0      | 1      | 0     | 1      | 0      | 0      | 0     | 0      | 0      | 0      | 0     | 0       | 0      | 0      | 0     |
|                       |                          |                         | ( 0 )   | ( 0 )  | ( 2 )  | ( 0 ) | ( 2 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) |
|                       | hyperplasia              |                         | 6       | 1      | 0      | 0     | 5      | 2      | 0      | 0     | 3      | 6      | 0      | 0     | 2       | 1      | 0      | 0     |
|                       |                          |                         | ( 12 )  | ( 2 )  | ( 0 )  | ( 0 ) | ( 10 ) | ( 4 )  | ( 0 )  | ( 0 ) | ( 6 )  | ( 12 ) | ( 0 )  | ( 0 ) | ( 4 )   | ( 2 )  | ( 0 )  | ( 0 ) |
|                       | focal hypertrophy        |                         | 5       | 1      | 0      | 0     | 6      | 1      | 0      | 0     | 4      | 1      | 0      | 0     | 5       | 0      | 0      | 0     |
|                       |                          |                         | ( 10 )  | ( 2 )  | ( 0 )  | ( 0 ) | ( 12 ) | ( 2 )  | ( 0 )  | ( 0 ) | ( 8 )  | ( 2 )  | ( 0 )  | ( 0 ) | ( 10 )  | ( 0 )  | ( 0 )  | ( 0 ) |
| adrenal               |                          |                         | <50>    |        |        |       | <50>   |        |        |       | <50>   |        |        |       | <50>    |        |        |       |
|                       | spindle-cell hyperplasia |                         | 2       | 22     | 26     | 0     | 5      | 25     | 20     | 0     | 4      | 29     | 16     | 0     | 7       | 32     | 10     | 0 **  |
|                       |                          |                         | ( 4 )   | ( 44 ) | ( 52 ) | ( 0 ) | ( 10 ) | ( 50 ) | ( 40 ) | ( 0 ) | ( 8 )  | ( 58 ) | ( 32 ) | ( 0 ) | ( 14 )  | ( 64 ) | ( 20 ) | ( 0 ) |
|                       | hyperplasia:medulla      |                         | 0       | 0      | 0      | 0     | 0      | 0      | 0      | 0     | 0      | 1      | 0      | 0     | 0       | 0      | 0      | 0     |
|                       |                          |                         | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 2 )  | ( 0 )  | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) |
| {Reproductive system} |                          |                         |         |        |        |       |        |        |        |       |        |        |        |       |         |        |        |       |
| ovary                 |                          |                         | <50>    |        |        |       | <50>   |        |        |       | <50>   |        |        |       | <50>    |        |        |       |
|                       | thrombus                 |                         | 0       | 0      | 0      | 0     | 0      | 0      | 0      | 0     | 0      | 0      | 3      | 0     | 0       | 0      | 1      | 0     |
|                       |                          |                         | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 6 )  | ( 0 ) | ( 0 )   | ( 0 )  | ( 2 )  | ( 0 ) |

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

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

b : Number of animals with lesion

( c ) c : b / a \* 100

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



STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

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|                       |                                | Group Name              | Control |        |        |        | 32 ppm |        |        |        | 80 ppm |        |        |        | 200 ppm |        |        |       |
|-----------------------|--------------------------------|-------------------------|---------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|---------|--------|--------|-------|
|                       |                                | No. of Animals on Study | 50      |        |        |        | 50     |        |        |        | 50     |        |        |        | 50      |        |        |       |
|                       |                                | Grade                   | 1       | 2      | 3      | 4      | 1      | 2      | 3      | 4      | 1      | 2      | 3      | 4      | 1       | 2      | 3      | 4     |
| Organ                 | Findings                       |                         | (%)     | (%)    | (%)    | (%)    | (%)    | (%)    | (%)    | (%)    | (%)    | (%)    | (%)    | (%)    | (%)     | (%)    | (%)    | (%)   |
| {Reproductive system} |                                |                         |         |        |        |        |        |        |        |        |        |        |        |        |         |        |        |       |
| ovary                 |                                |                         | <50>    |        |        |        | <50>   |        |        |        | <50>   |        |        |        | <50>    |        |        |       |
|                       | cyst                           |                         | 1       | 0      | 8      | 0      | 0      | 0      | 6      | 0      | 0      | 0      | 6      | 0      | 0       | 0      | 9      | 0     |
|                       |                                |                         | ( 2 )   | ( 0 )  | ( 16 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 12 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 12 ) | ( 0 )  | ( 0 )   | ( 0 )  | ( 18 ) | ( 0 ) |
|                       | lymphocytic infiltration       |                         | 0       | 0      | 0      | 0      | 1      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0       | 0      | 0      | 0     |
|                       |                                |                         | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 )  | ( 2 )  | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) |
| uterus                |                                |                         | <50>    |        |        |        | <50>   |        |        |        | <50>   |        |        |        | <50>    |        |        |       |
|                       | cystic endometrial hyperplasia |                         | 15      | 9      | 3      | 0      | 20     | 6      | 2      | 0      | 20     | 9      | 4      | 0      | 15      | 13     | 5      | 0     |
|                       |                                |                         | ( 30 )  | ( 18 ) | ( 6 )  | ( 0 )  | ( 40 ) | ( 12 ) | ( 4 )  | ( 0 )  | ( 40 ) | ( 18 ) | ( 8 )  | ( 0 )  | ( 30 )  | ( 26 ) | ( 10 ) | ( 0 ) |
| mammary gl            |                                |                         | <50>    |        |        |        | <50>   |        |        |        | <50>   |        |        |        | <50>    |        |        |       |
|                       | hyperplasia                    |                         | 2       | 0      | 0      | 0      | 1      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0       | 0      | 0      | 0     |
|                       |                                |                         | ( 4 )   | ( 0 )  | ( 0 )  | ( 0 )  | ( 2 )  | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) |
|                       | galactoceles                   |                         | 0       | 0      | 0      | 0      | 0      | 0      | 1      | 0      | 0      | 0      | 0      | 0      | 0       | 0      | 0      | 0     |
|                       |                                |                         | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 )  | ( 2 )  | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) |
| {Nervous system}      |                                |                         |         |        |        |        |        |        |        |        |        |        |        |        |         |        |        |       |
| brain                 |                                |                         | <50>    |        |        |        | <50>   |        |        |        | <50>   |        |        |        | <50>    |        |        |       |
|                       | mineralization                 |                         | 16      | 0      | 0      | 0      | 19     | 0      | 0      | 0      | 16     | 0      | 0      | 0      | 12      | 0      | 0      | 0     |
|                       |                                | ( 32 )                  | ( 0 )   | ( 0 )  | ( 0 )  | ( 38 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 32 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 24 ) | ( 0 )   | ( 0 )  | ( 0 )  |       |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 26

| Organ                            | Findings            | Group Name<br>No. of Animals on Study<br>Grade | Control |       |       |       | 32 ppm |       |       |       | 80 ppm |       |       |       | 200 ppm |       |       |       |
|----------------------------------|---------------------|--|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|---------|-------|-------|-------|
|                                  |                     |  | 50      |       |       |       | 50     |       |       |       | 50     |       |       |       | 50      |       |       |       |
|                                  |                     |  | 1       | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1       | 2     | 3     | 4     |
|                                  |                     |  | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)     | (%)   | (%)   | (%)   |
| {Nervous system}                 |                     |  |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
| spinal cord                      | deposit of melanin  |  | <49>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <49>    |       |       |       |
|                                  |                     |  | 1       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                                  |                     |  | ( 2 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
| {Special sense organs/appendage} |                     |  |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
| eye                              | keratitis           |  | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>    |       |       |       |
|                                  |                     |  | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 1     | 0     |
|                                  |                     |  | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 2 ) | ( 0 ) |
|                                  | phthisis bulbi      |  | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 1     | 0     |
|                                  |                     |  | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 2 ) | ( 0 ) |
|                                  | degeneration:cornea |  | 1       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 1       | 0     | 0     | 0     |
|                                  |                     |  | ( 2 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )   | ( 0 ) | ( 0 ) | ( 0 ) |
| Harder gl                        | thrombus            |  | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>    |       |       |       |
|                                  |                     |  | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 1     | 0     |
|                                  |                     |  | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 2 ) | ( 0 ) |
|                                  | hyperplasia         |  | 0       | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 2       | 1     | 0     | 0     |
|                                  |                     |  | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )   | ( 2 ) | ( 0 ) | ( 0 ) |

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

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

b b : Number of animals with lesion

( c ) c : b / a \* 100

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 27

| Organ | Findings | Group Name              |     | Control |     |     |     | 32 ppm |     |     |     | 80 ppm |     |     |     | 200 ppm |     |     |     |
|-------|----------|-------------------------|-----|---------|-----|-----|-----|--------|-----|-----|-----|--------|-----|-----|-----|---------|-----|-----|-----|
|       |          | No. of Animals on Study |     | 50      |     |     |     | 50     |     |     |     | 50     |     |     |     | 50      |     |     |     |
|       |          | Grade                   |     | 1       | 2   | 3   | 4   | 1      | 2   | 3   | 4   | 1      | 2   | 3   | 4   | 1       | 2   | 3   | 4   |
|       |          | (%)                     | (%) | (%)     | (%) | (%) | (%) | (%)    | (%) | (%) | (%) | (%)    | (%) | (%) | (%) | (%)     | (%) | (%) | (%) |

{Musculoskeletal system}

|      |                |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
|------|----------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| bone | osteosclerosis | <50>  |       |       |       | <50>  |       |       |       | <50>  |       |       |       | <50>  |       |       |       |
|      |                | 0     | 0     | 0     | 0     | 0     | 1     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     |
|      |                | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) |

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

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

b b : Number of animals with lesion

( c ) c : b / a \* 100

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

(HPT150)

BAIS4

## APPENDIX L 5

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 10

| Organ                            | Findings                                   | Group Name<br>No. of Animals on Study |        |       |       | Control |       |       |       | 32 ppm |        |       |       | 80 ppm |        |        |       | 200 ppm |       |       |       |
|----------------------------------|--|---------------------------------------|--------|-------|-------|---------|-------|-------|-------|--------|--------|-------|-------|--------|--------|--------|-------|---------|-------|-------|-------|
|                                  |  | Grade                                 |        |       |       | 21      |       |       |       | 22     |        |       |       | 24     |        |        |       | 20      |       |       |       |
|                                  |  | 1                                     | 2      | 3     | 4     | 1       | 2     | 3     | 4     | 1      | 2      | 3     | 4     | 1      | 2      | 3      | 4     | 1       | 2     | 3     | 4     |
|                                  |  | (%)                                   | (%)    | (%)   | (%)   | (%)     | (%)   | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)    | (%)    | (%)   | (%)     | (%)   | (%)   | (%)   |
| {Integumentary system/appandage} |  |                                       |        |       |       |         |       |       |       |        |        |       |       |        |        |        |       |         |       |       |       |
| skin/app                         |  | <21>                                  |        |       |       | <22>    |       |       |       | <24>   |        |       |       | <20>   |        |        |       |         |       |       |       |
|                                  | inflammation                               | 0                                     | 0      | 1     | 0     | 0       | 0     | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0      | 0     | 0       | 0     | 0     | 0     |
|                                  |  | ( 0 )                                 | ( 0 )  | ( 5 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
| {Respiratory system}             |  |                                       |        |       |       |         |       |       |       |        |        |       |       |        |        |        |       |         |       |       |       |
| nasal cavit                      |  | <21>                                  |        |       |       | <22>    |       |       |       | <24>   |        |       |       | <20>   |        |        |       |         |       |       |       |
|                                  | exudate                                    | 0                                     | 0      | 0     | 0     | 0       | 0     | 0     | 0     | 0      | 1      | 0     | 0     | 0      | 0      | 0      | 0     | 0       | 0     | 0     | 0     |
|                                  |  | ( 0 )                                 | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 4 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                                  | mineralization                             | 2                                     | 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 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                                  | inflammation                               | 1                                     | 0      | 0     | 0     | 0       | 0     | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0      | 0     | 0       | 0     | 0     | 0     |
|                                  |  | ( 5 )                                 | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                                  | fibrosis                                   | 1                                     | 0      | 0     | 0     | 0       | 0     | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0      | 0     | 0       | 0     | 0     | 0     |
|                                  |  | ( 5 )                                 | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                                  | eosinophilic change:olfactory epithelium   | 8                                     | 0      | 0     | 0     | 5       | 0     | 0     | 0     | 8      | 0      | 0     | 0     | 5      | 1      | 0      | 0     | 0       | 0     | 0     | 0     |
|                                  |  | ( 38 )                                | ( 0 )  | ( 0 ) | ( 0 ) | ( 23 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 33 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 25 ) | ( 5 )  | ( 0 )  | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                                  | eosinophilic change:respiratory epithelium | 14                                    | 3      | 1     | 0     | 13      | 1     | 2     | 0     | 13     | 3      | 0     | 0     | 12     | 2      | 2      | 0     | 0       | 0     | 0     | 0     |
|                                  |  | ( 67 )                                | ( 14 ) | ( 5 ) | ( 0 ) | ( 59 )  | ( 5 ) | ( 9 ) | ( 0 ) | ( 54 ) | ( 13 ) | ( 0 ) | ( 0 ) | ( 60 ) | ( 10 ) | ( 10 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 11

| Organ                | Findings                                    | Group Name<br>No. of Animals on Study<br>Grade | Control<br>21 |           |           |           | 32 ppm<br>22 |           |           |           | 80 ppm<br>24 |           |           |           | 200 ppm<br>20 |           |           |           |     |
|----------------------|---|--|---------------|-----------|-----------|-----------|--------------|-----------|-----------|-----------|--------------|-----------|-----------|-----------|---------------|-----------|-----------|-----------|-----|
|                      |   |  | 1             | 2         | 3         | 4         | 1            | 2         | 3         | 4         | 1            | 2         | 3         | 4         | 1             | 2         | 3         | 4         |     |
|                      |   |  | (%)           | (%)       | (%)       | (%)       | (%)          | (%)       | (%)       | (%)       | (%)          | (%)       | (%)       | (%)       | (%)           | (%)       | (%)       | (%)       | (%) |
| {Respiratory system} |   |  |               |           |           |           |              |           |           |           |              |           |           |           |               |           |           |           |     |
| nasal cavit          |   |  | <21>          |           |           |           | <22>         |           |           |           | <24>         |           |           |           | <20>          |           |           |           |     |
|                      | respiratory metaplasia:olfactory epithelium |  | 9<br>( 43)    | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 3<br>( 14)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 14<br>( 58)  | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 16<br>( 80)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0 * |
|                      | respiratory metaplasia:gland                |  | 9<br>( 43)    | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 3<br>( 14)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 3<br>( 13)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 14<br>( 70)   | 1<br>( 5) | 0<br>( 0) | 0<br>( 0) | 0   |
|                      | atrophy:olfactory epithelium                |  | 5<br>( 24)    | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 3<br>( 14)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 11<br>( 46)  | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 7<br>( 35)    | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0   |
|                      | necrosis:olfactory epithelium               |  | 0<br>( 0)     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)    | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 4)    | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0   |
| nasopharynx          |   |  | <21>          |           |           |           | <22>         |           |           |           | <24>         |           |           |           | <20>          |           |           |           |     |
|                      | eosinophilic change                         |  | 2<br>( 10)    | 1<br>( 5) | 0<br>( 0) | 0<br>( 0) | 1<br>( 5)    | 1<br>( 5) | 1<br>( 5) | 0<br>( 0) | 1<br>( 4)    | 0<br>( 0) | 1<br>( 4) | 0<br>( 0) | 1<br>( 5)     | 0<br>( 0) | 1<br>( 5) | 0<br>( 0) | 0   |
| lung                 |   |  | <21>          |           |           |           | <22>         |           |           |           | <24>         |           |           |           | <20>          |           |           |           |     |
|                      | congestion                                  |  | 0<br>( 0)     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)    | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)    | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 5)     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0   |
|                      | hemorrhage                                  |  | 1<br>( 5)     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)    | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)    | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)     | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0   |

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

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

b b : Number of animals with lesion

( c ) c : b / a \* 100

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 12

|                        |                                       | Group Name              | Control |       |       |       | 32 ppm |       |       |       | 80 ppm |       |       |       | 200 ppm |       |       |       |
|------------------------|---------------------------------------|-------------------------|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|---------|-------|-------|-------|
|                        |                                       | No. of Animals on Study | 21      |       |       |       | 22     |       |       |       | 24     |       |       |       | 20      |       |       |       |
| Organ                  | Findings                              | Grade                   | 1       | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1       | 2     | 3     | 4     |
|                        |                                       |                         | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)     | (%)   | (%)   | (%)   |
| {Respiratory system}   |                                       |                         |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
| lung                   |                                       |                         | <21>    |       |       |       | <22>   |       |       |       | <24>   |       |       |       | <20>    |       |       |       |
|                        | inflammatory infiltration             |                         | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 3      | 0     | 0     | 0     | 1       | 0     | 0     | 0     |
|                        |                                       |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 13 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 5 )   | ( 0 ) | ( 0 ) | ( 0 ) |
|                        | bronchiolar-alveolar cell hyperplasia |                         | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 2      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                        |                                       |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
| {Hematopoietic system} |                                       |                         |         |       |       |       |        |       |       |       |        |       |       |       |         |       |       |       |
| bone marrow            |                                       |                         | <21>    |       |       |       | <22>   |       |       |       | <24>   |       |       |       | <20>    |       |       |       |
|                        | increased hematopoiesis               |                         | 7       | 0     | 0     | 0     | 4      | 0     | 0     | 0     | 9      | 0     | 0     | 0     | 4       | 0     | 0     | 0     |
|                        |                                       |                         | ( 33 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 18 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 38 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 20 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                        | granulopoiesis:increased              |                         | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                        |                                       |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
| lymph node             |                                       |                         | <21>    |       |       |       | <22>   |       |       |       | <24>   |       |       |       | <20>    |       |       |       |
|                        | lymphadenitis                         |                         | 0       | 0     | 1     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0       | 0     | 0     | 0     |
|                        |                                       |                         | ( 0 )   | ( 0 ) | ( 5 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) |
| spleen                 |                                       |                         | <21>    |       |       |       | <22>   |       |       |       | <24>   |       |       |       | <20>    |       |       |       |
|                        | atrophy                               |                         | 1       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 1       | 0     | 0     | 0     |
|                        |                                       |                         | ( 5 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 5 )   | ( 0 ) | ( 0 ) | ( 0 ) |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 13

| Organ | Findings | Group Name<br>No. of Animals on Study<br>Grade | Control |     |     |     | 32 ppm |     |     |     | 80 ppm |     |     |     | 200 ppm |     |     |     |
|-------|----------|--|---------|-----|-----|-----|--------|-----|-----|-----|--------|-----|-----|-----|---------|-----|-----|-----|
|       |          |  | 21      |     |     |     | 22     |     |     |     | 24     |     |     |     | 20      |     |     |     |
|       |          |  | 1       | 2   | 3   | 4   | 1      | 2   | 3   | 4   | 1      | 2   | 3   | 4   | 1       | 2   | 3   | 4   |
|       |          |  | (%)     | (%) | (%) | (%) | (%)    | (%) | (%) | (%) | (%)    | (%) | (%) | (%) | (%)     | (%) | (%) | (%) |

{Hematopoietic system}

|        |                              |  |      |       |       |      |      |       |       |      |      |       |       |      |       |       |       |      |
|--------|------------------------------|--|------|-------|-------|------|------|-------|-------|------|------|-------|-------|------|-------|-------|-------|------|
| spleen |                              |  | <21> |       |       |      | <22> |       |       |      | <24> |       |       |      | <20>  |       |       |      |
|        | deposit of hemosiderin       |  | 1    | 0     | 0     | 0    | 0    | 0     | 0     | 0    | 1    | 1     | 0     | 0    | 2     | 1     | 0     | 0    |
|        |                              |  | ( 5) | ( 0)  | ( 0)  | ( 0) | ( 0) | ( 0)  | ( 0)  | ( 0) | ( 4) | ( 4)  | ( 0)  | ( 0) | ( 10) | ( 5)  | ( 0)  | ( 0) |
|        | deposit of melanin           |  | 1    | 1     | 0     | 0    | 0    | 0     | 0     | 0    | 0    | 0     | 0     | 0    | 0     | 0     | 0     | 0    |
|        |                              |  | ( 5) | ( 5)  | ( 0)  | ( 0) | ( 0) | ( 0)  | ( 0)  | ( 0) | ( 0) | ( 0)  | ( 0)  | ( 0) | ( 0)  | ( 0)  | ( 0)  | ( 0) |
|        | mastcell hyperplasia         |  | 0    | 0     | 0     | 0    | 0    | 0     | 0     | 0    | 1    | 0     | 0     | 0    | 0     | 0     | 0     | 0    |
|        |                              |  | ( 0) | ( 0)  | ( 0)  | ( 0) | ( 0) | ( 0)  | ( 0)  | ( 0) | ( 4) | ( 0)  | ( 0)  | ( 0) | ( 0)  | ( 0)  | ( 0)  | ( 0) |
|        | extramedullary hematopoiesis |  | 1    | 2     | 10    | 0    | 2    | 5     | 4     | 0    | 1    | 3     | 12    | 0    | 2     | 3     | 5     | 0    |
|        |                              |  | ( 5) | ( 10) | ( 48) | ( 0) | ( 9) | ( 23) | ( 18) | ( 0) | ( 4) | ( 13) | ( 50) | ( 0) | ( 10) | ( 15) | ( 25) | ( 0) |
|        |                              |  |      |       |       |      |      |       |       |      |      |       |       |      |       |       |       |      |

{Circulatory system}

|       |                |  |       |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-------|----------------|--|-------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| heart |                |  | <21>  |      |      |      | <22> |      |      |      | <24> |      |      |      | <20> |      |      |      |
|       | thrombus       |  | 0     | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 1    | 0    |
|       |                |  | ( 0)  | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 5) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 5) | ( 0) | ( 5) | ( 0) |
|       | mineralization |  | 3     | 0    | 0    | 0    | 2    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 1    | 0    | 0    | 0    |
|       |                |  | ( 14) | ( 0) | ( 0) | ( 0) | ( 9) | ( 0) | ( 0) | ( 0) | ( 4) | ( 0) | ( 0) | ( 0) | ( 5) | ( 0) | ( 0) | ( 0) |
|       | arteritis      |  | 0     | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    |
|       |                |  | ( 0)  | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 5) | ( 0) | ( 0) |
|       |                |  |       |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |
|       |                |  |       |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |
|       |                |  |       |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |

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

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

b : Number of animals with lesion

( c ) c : b / a \* 100

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



STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/CrLj[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 14

| Organ              | Findings                  | Group Name<br>No. of Animals on Study<br>Grade | Control      |            |            |             | 32 ppm       |             |            |             | 80 ppm       |             |            |             | 200 ppm      |            |            |          |
|--------------------|---------------------------|--|--------------|------------|------------|-------------|--------------|-------------|------------|-------------|--------------|-------------|------------|-------------|--------------|------------|------------|----------|
|                    |                           |  | 21           |            |            |             | 22           |             |            |             | 24           |             |            |             | 20           |            |            |          |
|                    |                           |  | 1<br>(%)     | 2<br>(%)   | 3<br>(%)   | 4<br>(%)    | 1<br>(%)     | 2<br>(%)    | 3<br>(%)   | 4<br>(%)    | 1<br>(%)     | 2<br>(%)    | 3<br>(%)   | 4<br>(%)    | 1<br>(%)     | 2<br>(%)   | 3<br>(%)   | 4<br>(%) |
| {Digestive system} |                           |  |              |            |            |             |              |             |            |             |              |             |            |             |              |            |            |          |
| tooth              | dysplasia                 |  | <21>         |            |            |             | <22>         |             |            |             | <24>         |             |            |             | <20>         |            |            |          |
|                    |                           | 0<br>( 0 )                                     | 1<br>( 5 )   | 0<br>( 0 ) | 0<br>( 0 ) | 2<br>( 9 )  | 0<br>( 0 )   | 0<br>( 0 )  | 0<br>( 0 ) | 1<br>( 4 )  | 0<br>( 0 )   | 0<br>( 0 )  | 0<br>( 0 ) | 2<br>( 10 ) | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) |          |
| tongue             | arteritis                 |  | <21>         |            |            |             | <22>         |             |            |             | <24>         |             |            |             | <20>         |            |            |          |
|                    |                           | 0<br>( 0 )                                     | 1<br>( 5 )   | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 )   | 0<br>( 0 )  | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 )   | 0<br>( 0 )  | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 )   | 1<br>( 5 ) | 0<br>( 0 ) |          |
| stomach            | hyperplasia:gland         |  | <21>         |            |            |             | <22>         |             |            |             | <24>         |             |            |             | <20>         |            |            |          |
|                    |                           | 5<br>( 24 )                                    | 12<br>( 57 ) | 1<br>( 5 ) | 0<br>( 0 ) | 6<br>( 27 ) | 12<br>( 55 ) | 3<br>( 14 ) | 0<br>( 0 ) | 8<br>( 33 ) | 13<br>( 54 ) | 3<br>( 13 ) | 0<br>( 0 ) | 5<br>( 25 ) | 14<br>( 70 ) | 0<br>( 0 ) | 0<br>( 0 ) |          |
|                    | erosion:glandular stomach |  | <21>         |            |            |             | <22>         |             |            |             | <24>         |             |            |             | <20>         |            |            |          |
|                    |                           |  | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 )   | 0<br>( 0 )  | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 )   | 0<br>( 0 )  | 0<br>( 0 ) | 0<br>( 0 )  | 1<br>( 5 )   | 0<br>( 0 ) | 0<br>( 0 ) |          |
| liver              | angiectasis               |  | <21>         |            |            |             | <22>         |             |            |             | <24>         |             |            |             | <20>         |            |            |          |
|                    |                           | 0<br>( 0 )                                     | 1<br>( 5 )   | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 )   | 0<br>( 0 )  | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 )   | 0<br>( 0 )  | 0<br>( 0 ) | 0<br>( 0 )  | 1<br>( 5 )   | 0<br>( 0 ) | 0<br>( 0 ) |          |
|                    | necrosis:focal            |  | <21>         |            |            |             | <22>         |             |            |             | <24>         |             |            |             | <20>         |            |            |          |
|                    |                           |  | 1<br>( 5 )   | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 )   | 0<br>( 0 )  | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 )   | 0<br>( 0 )  | 0<br>( 0 ) | 1<br>( 5 )  | 1<br>( 5 )   | 0<br>( 0 ) | 0<br>( 0 ) |          |
|                    | basophilic cell focus     |  | <21>         |            |            |             | <22>         |             |            |             | <24>         |             |            |             | <20>         |            |            |          |
|                    |                           |  | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 )   | 0<br>( 0 )  | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 )   | 0<br>( 0 )  | 0<br>( 0 ) | 1<br>( 5 )  | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) |          |

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

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 15

| Organ              | Findings           | Group Name<br>No. of Animals on Study<br>Grade | Control |       |        |       | 32 ppm |       |        |       | 80 ppm |        |        |       | 200 ppm |       |        |       |
|--------------------|--------------------|--|---------|-------|--------|-------|--------|-------|--------|-------|--------|--------|--------|-------|---------|-------|--------|-------|
|                    |                    |  | 21      |       |        |       | 22     |       |        |       | 24     |        |        |       | 20      |       |        |       |
|                    |                    |  | 1       | 2     | 3      | 4     | 1      | 2     | 3      | 4     | 1      | 2      | 3      | 4     | 1       | 2     | 3      | 4     |
|                    |                    |  | (%)     | (%)   | (%)    | (%)   | (%)    | (%)   | (%)    | (%)   | (%)    | (%)    | (%)    | (%)   | (%)     | (%)   | (%)    | (%)   |
| {Digestive system} |                    |  |         |       |        |       |        |       |        |       |        |        |        |       |         |       |        |       |
| pancreas           |                    |  | <21>    |       |        |       | <22>   |       |        |       | <24>   |        |        |       | <20>    |       |        |       |
|                    | atrophy            |  | 0       | 0     | 0      | 0     | 0      | 0     | 0      | 0     | 0      | 0      | 0      | 0     | 1       | 0     | 0      | 0     |
|                    |                    |  | ( 0 )   | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 5 )   | ( 0 ) | ( 0 )  | ( 0 ) |
| {Urinary system}   |                    |  |         |       |        |       |        |       |        |       |        |        |        |       |         |       |        |       |
| kidney             |                    |  | <21>    |       |        |       | <22>   |       |        |       | <24>   |        |        |       | <20>    |       |        |       |
|                    | hyaline droplet    |  | 0       | 1     | 10     | 0     | 0      | 2     | 5      | 0     | 0      | 3      | 8      | 0     | 1       | 1     | 2      | 0     |
|                    |                    |  | ( 0 )   | ( 5 ) | ( 48 ) | ( 0 ) | ( 0 )  | ( 9 ) | ( 23 ) | ( 0 ) | ( 0 )  | ( 13 ) | ( 33 ) | ( 0 ) | ( 5 )   | ( 5 ) | ( 10 ) | ( 0 ) |
|                    | hyaline cast       |  | 0       | 0     | 0      | 0     | 1      | 0     | 0      | 0     | 1      | 0      | 0      | 0     | 0       | 0     | 0      | 0     |
|                    |                    |  | ( 0 )   | ( 0 ) | ( 0 )  | ( 0 ) | ( 5 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 4 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 )  | ( 0 ) |
|                    | inflammatory polyp |  | 0       | 1     | 1      | 0     | 0      | 1     | 0      | 0     | 0      | 0      | 0      | 0     | 0       | 0     | 0      | 0     |
|                    |                    |  | ( 0 )   | ( 5 ) | ( 5 )  | ( 0 ) | ( 0 )  | ( 5 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 )  | ( 0 ) |
|                    | hydronephrosis     |  | 0       | 0     | 2      | 0     | 0      | 0     | 1      | 0     | 0      | 0      | 0      | 0     | 0       | 0     | 0      | 1     |
|                    |                    |  | ( 0 )   | ( 0 ) | ( 10 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 5 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 )  | ( 5 ) |
| {Endocrine system} |                    |  |         |       |        |       |        |       |        |       |        |        |        |       |         |       |        |       |
| pituitary          |                    |  | <20>    |       |        |       | <22>   |       |        |       | <24>   |        |        |       | <20>    |       |        |       |
|                    | congestion         |  | 0       | 0     | 0      | 0     | 0      | 0     | 0      | 0     | 0      | 0      | 0      | 0     | 1       | 0     | 0      | 0     |
|                    |                    |  | ( 0 )   | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 5 )   | ( 0 ) | ( 0 )  | ( 0 ) |

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< a > a : Number of animals examined at the site  
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( c ) c : b / a \* 100  
Significant difference : \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 16

| Organ                 | Findings                       | Group Name<br>No. of Animals on Study<br>Grade | Control |        |        |       | 32 ppm |        |        |       | 80 ppm |        |        |       | 200 ppm |        |        |       |
|-----------------------|--------------------------------|--|---------|--------|--------|-------|--------|--------|--------|-------|--------|--------|--------|-------|---------|--------|--------|-------|
|                       |                                |  | 21      |        |        |       | 22     |        |        |       | 24     |        |        |       | 20      |        |        |       |
|                       |                                |  | 1       | 2      | 3      | 4     | 1      | 2      | 3      | 4     | 1      | 2      | 3      | 4     | 1       | 2      | 3      | 4     |
|                       |                                |  | (%)     | (%)    | (%)    | (%)   | (%)    | (%)    | (%)    | (%)   | (%)    | (%)    | (%)    | (%)   | (%)     | (%)    | (%)    | (%)   |
| {Endocrine system}    |                                |  |         |        |        |       |        |        |        |       |        |        |        |       |         |        |        |       |
| pituitary             | hyperplasia                    |  | <20>    |        |        |       | <22>   |        |        |       | <24>   |        |        |       | <20>    |        |        |       |
|                       |                                |  | 0       | 0      | 0      | 0     | 0      | 1      | 0      | 0     | 0      | 2      | 0      | 0     | 0       | 0      | 0      | 0     |
|                       |                                |  | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 5 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 8 )  | ( 0 )  | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) |
|                       | focal hypertrophy              |  | 1       | 0      | 0      | 0     | 0      | 0      | 0      | 0     | 2      | 0      | 0      | 0     | 1       | 0      | 0      | 0     |
|                       |                                |  | ( 5 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 8 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 5 )   | ( 0 )  | ( 0 )  | ( 0 ) |
| adrenal               | spindle-cell hyperplasia       |  | <21>    |        |        |       | <22>   |        |        |       | <24>   |        |        |       | <20>    |        |        |       |
|                       |                                |  | 1       | 10     | 10     | 0     | 4      | 11     | 7      | 0     | 3      | 16     | 5      | 0     | 7       | 11     | 1      | 0 **  |
|                       |                                |  | ( 5 )   | ( 48 ) | ( 48 ) | ( 0 ) | ( 18 ) | ( 50 ) | ( 32 ) | ( 0 ) | ( 13 ) | ( 67 ) | ( 21 ) | ( 0 ) | ( 35 )  | ( 55 ) | ( 5 )  | ( 0 ) |
| {Reproductive system} |                                |  |         |        |        |       |        |        |        |       |        |        |        |       |         |        |        |       |
| ovary                 | thrombus                       |  | <21>    |        |        |       | <22>   |        |        |       | <24>   |        |        |       | <20>    |        |        |       |
|                       |                                |  | 0       | 0      | 0      | 0     | 0      | 0      | 0      | 0     | 0      | 0      | 1      | 0     | 0       | 0      | 1      | 0     |
|                       |                                |  | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 4 )  | ( 0 ) | ( 0 )   | ( 0 )  | ( 5 )  | ( 0 ) |
|                       | cyst                           |  | 0       | 0      | 2      | 0     | 0      | 0      | 2      | 0     | 0      | 0      | 1      | 0     | 0       | 0      | 2      | 0     |
|                       |                                |  | ( 0 )   | ( 0 )  | ( 10 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 9 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 4 )  | ( 0 ) | ( 0 )   | ( 0 )  | ( 10 ) | ( 0 ) |
| uterus                | cystic endometrial hyperplasia |  | <21>    |        |        |       | <22>   |        |        |       | <24>   |        |        |       | <20>    |        |        |       |
|                       |                                |  | 5       | 1      | 0      | 0     | 7      | 2      | 0      | 0     | 9      | 2      | 0      | 0     | 4       | 4      | 1      | 0     |
|                       |                                |  | ( 24 )  | ( 5 )  | ( 0 )  | ( 0 ) | ( 32 ) | ( 9 )  | ( 0 )  | ( 0 ) | ( 38 ) | ( 8 )  | ( 0 )  | ( 0 ) | ( 20 )  | ( 20 ) | ( 5 )  | ( 0 ) |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 17

|                                  |                    | Group Name              | Control |      |      |      | 32 ppm |      |      |      | 80 ppm |      |      |      | 200 ppm |      |      |      |
|----------------------------------|--------------------|-------------------------|---------|------|------|------|--------|------|------|------|--------|------|------|------|---------|------|------|------|
|                                  |                    | No. of Animals on Study | 21      |      |      |      | 22     |      |      |      | 24     |      |      |      | 20      |      |      |      |
| Organ                            | Findings           | Grade                   | 1       | 2    | 3    | 4    | 1      | 2    | 3    | 4    | 1      | 2    | 3    | 4    | 1       | 2    | 3    | 4    |
|                                  |                    |                         | (%)     | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  | (%)     | (%)  | (%)  | (%)  |
| {Reproductive system}            |                    |                         |         |      |      |      |        |      |      |      |        |      |      |      |         |      |      |      |
| mammary gl                       |                    |                         | <21>    |      |      |      | <22>   |      |      |      | <24>   |      |      |      | <20>    |      |      |      |
|                                  | hyperplasia        |                         | 1       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0       | 0    | 0    | 0    |
|                                  |                    |                         | ( 5)    | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) |
|                                  | galactoceles       |                         | 0       | 0    | 0    | 0    | 0      | 0    | 1    | 0    | 0      | 0    | 0    | 0    | 0       | 0    | 0    | 0    |
|                                  |                    |                         | ( 0)    | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 5) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) |
| {Nervous system}                 |                    |                         |         |      |      |      |        |      |      |      |        |      |      |      |         |      |      |      |
| brain                            |                    |                         | <21>    |      |      |      | <22>   |      |      |      | <24>   |      |      |      | <20>    |      |      |      |
|                                  | mineralization     |                         | 5       | 0    | 0    | 0    | 5      | 0    | 0    | 0    | 7      | 0    | 0    | 0    | 1       | 0    | 0    | 0    |
|                                  |                    |                         | ( 24)   | ( 0) | ( 0) | ( 0) | ( 23)  | ( 0) | ( 0) | ( 0) | ( 29)  | ( 0) | ( 0) | ( 0) | ( 5)    | ( 0) | ( 0) | ( 0) |
| spinal cord                      |                    |                         | <21>    |      |      |      | <22>   |      |      |      | <24>   |      |      |      | <19>    |      |      |      |
|                                  | deposit of melanin |                         | 1       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0       | 0    | 0    | 0    |
|                                  |                    |                         | ( 5)    | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) |
| {Special sense organs/appendage} |                    |                         |         |      |      |      |        |      |      |      |        |      |      |      |         |      |      |      |
| eye                              |                    |                         | <21>    |      |      |      | <22>   |      |      |      | <24>   |      |      |      | <20>    |      |      |      |
|                                  | keratitis          |                         | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0       | 0    | 1    | 0    |
|                                  |                    |                         | ( 0)    | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)    | ( 0) | ( 5) | ( 0) |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 18

| Organ | Findings | Group Name              |     |     |     | Control |     |     |     | 32 ppm |     |     |     | 80 ppm |     |     |     | 200 ppm |  |  |  |
|-------|----------|-------------------------|-----|-----|-----|---------|-----|-----|-----|--------|-----|-----|-----|--------|-----|-----|-----|---------|--|--|--|
|       |          | No. of Animals on Study |     |     |     | 21      |     |     |     | 22     |     |     |     | 24     |     |     |     | 20      |  |  |  |
|       |          | Grade                   |     |     |     |         |     |     |     |        |     |     |     |        |     |     |     |         |  |  |  |
|       |          | 1                       | 2   | 3   | 4   | 1       | 2   | 3   | 4   | 1      | 2   | 3   | 4   | 1      | 2   | 3   | 4   |         |  |  |  |
|       |          | (%)                     | (%) | (%) | (%) | (%)     | (%) | (%) | (%) | (%)    | (%) | (%) | (%) | (%)    | (%) | (%) | (%) | (%)     |  |  |  |

{Special sense organs/appendage}

|     |                     |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
|-----|---------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| eye | degeneration:cornea | <21>  |       |       |       | <22>  |       |       |       | <24>  |       |       |       | <20>  |       |       |       |
|     |                     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 1     | 0     | 0     | 0     | 1     | 0     | 0     | 0     |
|     |                     | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 5 ) | ( 0 ) | ( 0 ) | ( 0 ) |

|           |          |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
|-----------|----------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Harder gl | thrombus | <21>  |       |       |       | <22>  |       |       |       | <24>  |       |       |       | <20>  |       |       |       |
|           |          | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 1     | 0     |
|           |          | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 5 ) | ( 0 ) |

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

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

b b : Number of animals with lesion

( c ) c : b / a \* 100

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

(HPT150)

BAIS4

## APPENDIX L 6

HISTOPATHOLOGICAL FINDINGS :  
NON-NEOPLASTIC LESIONS : FEMALE  
SACRIFICED ANIMALS

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
SACRIFICED ANIMALS (105W)

PAGE : 12

|   |  | Group Name              | Control |        |       |        | 32 ppm |       |       |       | 80 ppm |        |       |       | 200 ppm |        |       |       |       |
|---|--|-------------------------|---------|--------|-------|--------|--------|-------|-------|-------|--------|--------|-------|-------|---------|--------|-------|-------|-------|
|   |  | No. of Animals on Study | 29      |        |       |        | 28     |       |       |       | 26     |        |       |       | 30      |        |       |       |       |
| Organ                                       | Findings                                   | Grade                   | 1       | 2      | 3     | 4      | 1      | 2     | 3     | 4     | 1      | 2      | 3     | 4     | 1       | 2      | 3     | 4     |       |
|   |  |                         | (%)     | (%)    | (%)   | (%)    | (%)    | (%)   | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)     | (%)    | (%)   | (%)   |       |
| {Respiratory system}                        |  |                         |         |        |       |        |        |       |       |       |        |        |       |       |         |        |       |       |       |
| nasal cavit                                 | exudate                                    |                         | <29>    |        |       |        | <28>   |       |       |       | <26>   |        |       |       | <30>    |        |       |       |       |
|   |  |                         | 0       | 0      | 0     | 0      | 1      | 0     | 0     | 0     | 0      | 1      | 0     | 0     | 1       | 0      | 0     | 0     |       |
|   |  |                         | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 )  | ( 4 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 4 )  | ( 0 ) | ( 0 ) | ( 3 )   | ( 0 )  | ( 0 ) | ( 0 ) |       |
|   | mineralization                             |                         | 1       | 0      | 0     | 0      | 0      | 0     | 0     | 0     | 0      | 0      | 0     | 0     | 0       | 0      | 0     | 0     |       |
|   |  |                         | ( 3 )   | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) |       |
|   | inflammation                               |                         | 1       | 0      | 0     | 0      | 0      | 0     | 0     | 0     | 0      | 0      | 0     | 0     | 0       | 0      | 0     | 0     |       |
|   |  |                         | ( 3 )   | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) |       |
|   | eosinophilic change:olfactory epithelium   |                         | 15      | 3      | 0     | 0      | 6      | 0     | 0     | 0     | 0 **   | 4      | 2     | 0     | 0 *     | 14     | 1     | 0     | 0     |
|   |  |                         | ( 52 )  | ( 10 ) | ( 0 ) | ( 0 )  | ( 21 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 15 ) | ( 8 ) | ( 0 ) | ( 0 )   | ( 47 ) | ( 3 ) | ( 0 ) | ( 0 ) |
|   | eosinophilic change:respiratory epithelium |                         | 17      | 11     | 1     | 0      | 21     | 4     | 0     | 0     | 0      | 16     | 3     | 0     | 0 **    | 23     | 6     | 0     | 0     |
|   |  | ( 59 )                  | ( 38 )  | ( 3 )  | ( 0 ) | ( 75 ) | ( 14 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 62 ) | ( 12 ) | ( 0 ) | ( 0 ) | ( 77 )  | ( 20 ) | ( 0 ) | ( 0 ) |       |
| respiratory metaplasia:olfactory epithelium |  | 23                      | 0       | 0      | 0     | 11     | 0      | 0     | 0     | 0 **  | 20     | 0      | 0     | 0     | 27      | 1      | 0     | 0     |       |
|   |  | ( 79 )                  | ( 0 )   | ( 0 )  | ( 0 ) | ( 39 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 77 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 90 )  | ( 3 )  | ( 0 ) | ( 0 ) |       |
| respiratory metaplasia:gland                |  | 7                       | 0       | 0      | 0     | 8      | 0      | 0     | 0     | 0     | 10     | 0      | 0     | 0     | 26      | 2      | 0     | 0 **  |       |
|   |  | ( 24 )                  | ( 0 )   | ( 0 )  | ( 0 ) | ( 29 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 38 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 87 )  | ( 7 )  | ( 0 ) | ( 0 ) |       |
| hyperplasia:transitional epithelium         |  | 1                       | 0       | 0      | 0     | 0      | 0      | 0     | 0     | 0     | 0      | 0      | 0     | 0     | 0       | 0      | 0     | 0     |       |
|   |  | ( 3 )                   | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) |       |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS (105W)

PAGE : 13

| Organ                  | Findings                              | Group Name<br>No. of Animals on Study<br>Grade | Control<br>29 |        |       |       | 32 ppm<br>28 |       |       |       | 80 ppm<br>26 |       |       |       | 200 ppm<br>30 |       |       |       |
|------------------------|---------------------------------------|--|---------------|--------|-------|-------|--------------|-------|-------|-------|--------------|-------|-------|-------|---------------|-------|-------|-------|
|                        |                                       |  | 1             | 2      | 3     | 4     | 1            | 2     | 3     | 4     | 1            | 2     | 3     | 4     | 1             | 2     | 3     | 4     |
|                        |                                       |  | (%)           | (%)    | (%)   | (%)   | (%)          | (%)   | (%)   | (%)   | (%)          | (%)   | (%)   | (%)   | (%)           | (%)   | (%)   | (%)   |
| {Respiratory system}   |                                       |  |               |        |       |       |              |       |       |       |              |       |       |       |               |       |       |       |
| nasal cavit            | atrophy:olfactory epithelium          |  | <29>          |        |       |       | <28>         |       |       |       | <26>         |       |       |       | <30>          |       |       |       |
|                        |                                       |  | 3             | 0      | 0     | 0     | 4            | 1     | 0     | 0     | 8            | 0     | 0     | 0     | 9             | 0     | 0     | 0     |
|                        |                                       |  | ( 10 )        | ( 0 )  | ( 0 ) | ( 0 ) | ( 14 )       | ( 4 ) | ( 0 ) | ( 0 ) | ( 31 )       | ( 0 ) | ( 0 ) | ( 0 ) | ( 30 )        | ( 0 ) | ( 0 ) | ( 0 ) |
| nasopharynx            | eosinophilic change                   |  | <29>          |        |       |       | <28>         |       |       |       | <26>         |       |       |       | <30>          |       |       |       |
|                        |                                       |  | 6             | 3      | 1     | 0     | 2            | 0     | 1     | 0     | 1            | 0     | 0     | 0 *   | 3             | 1     | 0     | 0     |
|                        |                                       |  | ( 21 )        | ( 10 ) | ( 3 ) | ( 0 ) | ( 7 )        | ( 0 ) | ( 4 ) | ( 0 ) | ( 4 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 10 )        | ( 3 ) | ( 0 ) | ( 0 ) |
| lung                   | bronchiolar-alveolar cell hyperplasia |  | <29>          |        |       |       | <28>         |       |       |       | <26>         |       |       |       | <30>          |       |       |       |
|                        |                                       |  | 3             | 0      | 0     | 0     | 1            | 1     | 0     | 0     | 1            | 1     | 0     | 0     | 2             | 0     | 0     | 0     |
|                        |                                       |  | ( 10 )        | ( 0 )  | ( 0 ) | ( 0 ) | ( 4 )        | ( 4 ) | ( 0 ) | ( 0 ) | ( 4 )        | ( 4 ) | ( 0 ) | ( 0 ) | ( 7 )         | ( 0 ) | ( 0 ) | ( 0 ) |
| {Hematopoietic system} |                                       |  |               |        |       |       |              |       |       |       |              |       |       |       |               |       |       |       |
| bone marrow            | granulation                           |  | <29>          |        |       |       | <28>         |       |       |       | <26>         |       |       |       | <30>          |       |       |       |
|                        |                                       |  | 0             | 0      | 0     | 0     | 0            | 0     | 0     | 0     | 1            | 0     | 0     | 0     | 0             | 0     | 0     | 0     |
|                        |                                       |  | ( 0 )         | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) |
|                        | increased hematopoiesis               |  | <29>          |        |       |       | <28>         |       |       |       | <26>         |       |       |       | <30>          |       |       |       |
|                        |                                       |  | 1             | 0      | 0     | 0     | 2            | 0     | 0     | 0     | 0            | 0     | 0     | 0     | 2             | 0     | 0     | 0     |
|                        |                                       |  | ( 3 )         | ( 0 )  | ( 0 ) | ( 0 ) | ( 7 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 7 )         | ( 0 ) | ( 0 ) | ( 0 ) |
|                        | myelofibrosis                         |  | <29>          |        |       |       | <28>         |       |       |       | <26>         |       |       |       | <30>          |       |       |       |
|                        |                                       |  | 1             | 0      | 0     | 0     | 0            | 0     | 0     | 0     | 0            | 0     | 0     | 0     | 0             | 0     | 0     | 0     |
|                        |                                       |  | ( 3 )         | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) |

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



STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS (105W)

PAGE : 14

| Organ                  | Findings                     | Group Name<br>No. of Animals on Study<br>Grade |       |       |       | Control<br>29 |        |       |       | 32 ppm<br>28 |       |       |       | 80 ppm<br>26 |        |       |       | 200 ppm<br>30 |       |       |       |
|------------------------|------------------------------|--|-------|-------|-------|---------------|--------|-------|-------|--------------|-------|-------|-------|--------------|--------|-------|-------|---------------|-------|-------|-------|
|                        |                              | 1  | 2     | 3     | 4     | 1             | 2      | 3     | 4     | 1            | 2     | 3     | 4     | 1            | 2      | 3     | 4     | 1             | 2     | 3     | 4     |
|                        |                              | (%)  | (%)   | (%)   | (%)   | (%)           | (%)    | (%)   | (%)   | (%)          | (%)   | (%)   | (%)   | (%)          | (%)    | (%)   | (%)   | (%)           | (%)   | (%)   | (%)   |
| {Hematopoietic system} |                              |  |       |       |       |               |        |       |       |              |       |       |       |              |        |       |       |               |       |       |       |
| bone marrow            |                              | <29>   |       |       |       | <28>          |        |       |       | <26>         |       |       |       | <30>         |        |       |       |               |       |       |       |
|                        | granulopoiesis:increased     | 0  | 0     | 0     | 0     | 1             | 0      | 0     | 0     | 1            | 0     | 0     | 0     | 0            | 0      | 0     | 0     | 0             | 0     | 0     | 0     |
|                        |                              | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )         | ( 0 )  | ( 0 ) | ( 0 ) | ( 4 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) |
| spleen                 |                              | <29>   |       |       |       | <28>          |        |       |       | <26>         |       |       |       | <30>         |        |       |       |               |       |       |       |
|                        | deposit of amyloid           | 1  | 0     | 0     | 0     | 0             | 0      | 0     | 0     | 0            | 0     | 0     | 0     | 0            | 0      | 0     | 0     | 0             | 0     | 0     | 0     |
|                        |                              | ( 3 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )         | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) |
|                        | deposit of hemosiderin       | 5  | 0     | 0     | 0     | 3             | 0      | 0     | 0     | 2            | 0     | 0     | 0     | 4            | 0      | 0     | 0     | 0             | 0     | 0     | 0     |
|                        |                              | ( 17 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 11 )        | ( 0 )  | ( 0 ) | ( 0 ) | ( 8 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 13 )       | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) |
|                        | deposit of melanin           | 1  | 0     | 0     | 0     | 0             | 0      | 0     | 0     | 0            | 0     | 0     | 0     | 1            | 0      | 0     | 0     | 0             | 0     | 0     | 0     |
|                        |                              | ( 3 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )         | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 3 )        | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) |
|                        | mastcell hyperplasia         | 0  | 0     | 0     | 0     | 0             | 0      | 0     | 0     | 1            | 0     | 0     | 0     | 0            | 0      | 0     | 0     | 0             | 0     | 0     | 0     |
|                        |                              | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )         | ( 0 )  | ( 0 ) | ( 0 ) | ( 4 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) |
|                        | extramedullary hematopoiesis | 2  | 1     | 0     | 0     | 1             | 2      | 0     | 0     | 4            | 1     | 0     | 0     | 0            | 4      | 0     | 0     | 0             | 0     | 0     | 0     |
|                        |                              | ( 7 )  | ( 3 ) | ( 0 ) | ( 0 ) | ( 4 )         | ( 7 )  | ( 0 ) | ( 0 ) | ( 15 )       | ( 4 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 13 ) | ( 0 ) | ( 0 ) | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) |
|                        | hyperplasia:vascular         | 0  | 0     | 0     | 0     | 0             | 0      | 0     | 0     | 0            | 0     | 0     | 0     | 1            | 0      | 0     | 0     | 0             | 0     | 0     | 0     |
|                        |                              | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )         | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 3 )        | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) |
|                        | follicular hyperplasia       | 2  | 0     | 0     | 0     | 2             | 3      | 1     | 0     | 4            | 2     | 0     | 0     | 2            | 1      | 0     | 0     | 0             | 0     | 0     | 0     |
|                        |                              | ( 7 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 7 )         | ( 11 ) | ( 4 ) | ( 0 ) | ( 15 )       | ( 8 ) | ( 0 ) | ( 0 ) | ( 7 )        | ( 3 )  | ( 0 ) | ( 0 ) | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS (105W)

PAGE : 15

| Organ | Findings | Group Name              | Control |     |     |     | 32 ppm |     |     |     | 80 ppm |     |     |     | 200 ppm |     |     |     |
|-------|----------|-------------------------|---------|-----|-----|-----|--------|-----|-----|-----|--------|-----|-----|-----|---------|-----|-----|-----|
|       |          | No. of Animals on Study | 29      |     |     |     | 28     |     |     |     | 26     |     |     |     | 30      |     |     |     |
|       |          | Grade                   | 1       | 2   | 3   | 4   | 1      | 2   | 3   | 4   | 1      | 2   | 3   | 4   | 1       | 2   | 3   | 4   |
|       |          |                         | (%)     | (%) | (%) | (%) | (%)    | (%) | (%) | (%) | (%)    | (%) | (%) | (%) | (%)     | (%) | (%) | (%) |

|                      |                |   |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
|----------------------|----------------|---|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| {Circulatory system} |                |   |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
| heart                | mineralization |   | <29>  |       |       |       | <28>  |       |       |       | <26>  |       |       |       | <30>  |       |       |       |
|                      |                | 0 | 0     | 0     | 0     | 1     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     |       |
|                      |                |   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) |

|                    |                   |   |        |        |        |       |        |        |        |       |        |        |        |       |        |        |        |       |
|--------------------|-------------------|---|--------|--------|--------|-------|--------|--------|--------|-------|--------|--------|--------|-------|--------|--------|--------|-------|
| {Digestive system} |                   |   |        |        |        |       |        |        |        |       |        |        |        |       |        |        |        |       |
| tooth              | dysplasia         |   | <29>   |        |        |       | <28>   |        |        |       | <26>   |        |        |       | <30>   |        |        |       |
|                    |                   | 3 | 0      | 0      | 0      | 1     | 0      | 0      | 0      | 4     | 1      | 0      | 0      | 3     | 1      | 0      | 0      |       |
|                    |                   |   | ( 10 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 4 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 15 ) | ( 4 )  | ( 0 )  | ( 0 ) | ( 10 ) | ( 3 )  | ( 0 )  | ( 0 ) |
| tongue             | arteritis         |   | <29>   |        |        |       | <28>   |        |        |       | <26>   |        |        |       | <30>   |        |        |       |
|                    |                   | 0 | 0      | 0      | 0      | 0     | 0      | 0      | 0      | 1     | 0      | 0      | 0      | 0     | 0      | 0      | 0      |       |
|                    |                   |   | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 4 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) |
| stomach            | erosion           |   | <29>   |        |        |       | <28>   |        |        |       | <26>   |        |        |       | <30>   |        |        |       |
|                    |                   | 1 | 0      | 0      | 0      | 0     | 0      | 0      | 0      | 0     | 0      | 0      | 0      | 0     | 0      | 0      | 0      |       |
|                    |                   |   |        | ( 3 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) |
|                    | hyperplasia:gland |   | 2      | 17     | 10     | 0     | 6      | 12     | 9      | 0     | 0      | 19     | 7      | 0     | 3      | 15     | 12     | 0     |
|                    |                   |   | ( 7 )  | ( 59 ) | ( 34 ) | ( 0 ) | ( 21 ) | ( 43 ) | ( 32 ) | ( 0 ) | ( 0 )  | ( 73 ) | ( 27 ) | ( 0 ) | ( 10 ) | ( 50 ) | ( 40 ) | ( 0 ) |
|                    |                   |   | <29>   |        |        |       | <28>   |        |        |       | <26>   |        |        |       | <30>   |        |        |       |
|                    |                   |   | 0      | 0      | 0      | 0     | 0      | 0      | 0      | 0     | 1      | 0      | 0      | 0     | 1      | 0      | 0      | 0     |
|                    |                   |   | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 4 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 3 )  | ( 0 )  | ( 0 )  | ( 0 ) |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS (105W)

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| Organ              | Findings                  | Group Name              | Control    |            |            |            | 32 ppm      |            |            |            | 80 ppm     |            |             |             | 200 ppm    |            |            |            |
|--------------------|---------------------------|-------------------------|------------|------------|------------|------------|-------------|------------|------------|------------|------------|------------|-------------|-------------|------------|------------|------------|------------|
|                    |                           | No. of Animals on Study | 29         |            |            |            | 28          |            |            |            | 26         |            |             |             | 30         |            |            |            |
|                    |                           | Grade                   | 1          | 2          | 3          | 4          | 1           | 2          | 3          | 4          | 1          | 2          | 3           | 4           | 1          | 2          | 3          | 4          |
|                    |                           |                         | (%)        | (%)        | (%)        | (%)        | (%)         | (%)        | (%)        | (%)        | (%)        | (%)        | (%)         | (%)         | (%)        | (%)        | (%)        | (%)        |
| {Digestive system} |                           |                         |            |            |            |            |             |            |            |            |            |            |             |             |            |            |            |            |
| stomach            |                           |                         | <29>       |            |            |            | <28>        |            |            |            | <26>       |            |             |             | <30>       |            |            |            |
|                    | erosion:glandular stomach |                         | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 )  | 1<br>( 3 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |
|                    | ulcer:glandular stomach   |                         | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )  | 1<br>( 3 )  | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |            |
| liver              |                           |                         | <29>       |            |            |            | <28>        |            |            |            | <26>       |            |             |             | <30>       |            |            |            |
|                    | angiectasis               |                         | 1<br>( 3 ) | 2<br>( 7 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )  | 1<br>( 4 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 4 ) | 3<br>( 12 ) | 0<br>( 0 )  | 0<br>( 0 ) | 1<br>( 3 ) | 0<br>( 0 ) | 0<br>( 0 ) |
|                    | inflammatory infiltration |                         | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 4 )  | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 )  | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |            |
|                    | lymphocytic infiltration  |                         | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 4 )  | 1<br>( 4 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 )  | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |            |
|                    | granulation               |                         | 2<br>( 7 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 5<br>( 18 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 4 ) | 0<br>( 0 ) | 0<br>( 0 )  | 4<br>( 13 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |            |
|                    | fibrosis                  |                         | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 )  | 1<br>( 3 ) | 0<br>( 0 ) | 0<br>( 0 ) |            |
|                    | clear cell focus          |                         | 2<br>( 7 ) | 1<br>( 3 ) | 0<br>( 0 ) | 0<br>( 0 ) | 3<br>( 11 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 2<br>( 8 ) | 0<br>( 0 ) | 0<br>( 0 )  | 1<br>( 3 )  | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |            |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS (105W)

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| Organ              | Findings                    | Group Name              | Control |       |       |       | 32 ppm |       |       |       | 80 ppm |       |       |        | 200 ppm |       |        |       |
|--------------------|-----------------------------|-------------------------|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|--------|---------|-------|--------|-------|
|                    |                             | No. of Animals on Study | 29      |       |       |       | 28     |       |       |       | 26     |       |       |        | 30      |       |        |       |
|                    |                             | Grade                   | 1       | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4      | 1       | 2     | 3      | 4     |
|                    |                             |                         | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)    | (%)     | (%)   | (%)    | (%)   |
| {Digestive system} |                             |                         |         |       |       |       |        |       |       |       |        |       |       |        |         |       |        |       |
| liver              |                             |                         | <29>    |       |       |       | <28>   |       |       |       | <26>   |       |       |        | <30>    |       |        |       |
|                    | basophilic cell focus       | 2                       | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 0     | 0     | 0      | 2       | 1     | 0      | 0     |
|                    |                             | ( 7 )                   | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 7 )   | ( 3 ) | ( 0 )  | ( 0 ) |
|                    | bile ductular proliferation | 0                       | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 1      | 0       | 0     | 0      |       |
|                    |                             | ( 0 )                   | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 3 )  | ( 0 )   | ( 0 ) | ( 0 )  |       |
|                    | biliary cyst                | 0                       | 0       | 0     | 0     | 2     | 0      | 0     | 0     | 2     | 0      | 0     | 0     | 2      | 0       | 0     | 0      |       |
|                    |                             | ( 0 )                   | ( 0 )   | ( 0 ) | ( 0 ) | ( 7 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 8 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 7 )  | ( 0 )   | ( 0 ) | ( 0 )  |       |
| gall bladd         |                             |                         | <29>    |       |       |       | <28>   |       |       |       | <26>   |       |       |        | <30>    |       |        |       |
|                    | lymphocytic infiltration    | 0                       | 0       | 0     | 0     | 1     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0      | 0       | 0     | 0      |       |
|                    |                             | ( 0 )                   | ( 0 )   | ( 0 ) | ( 0 ) | ( 4 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )   | ( 0 ) | ( 0 )  |       |
| {Urinary system}   |                             |                         |         |       |       |       |        |       |       |       |        |       |       |        |         |       |        |       |
| kidney             |                             |                         | <29>    |       |       |       | <28>   |       |       |       | <26>   |       |       |        | <30>    |       |        |       |
|                    | hyaline droplet             | 0                       | 0       | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 0     | 1     | 0      | 0       | 1     | 3      | 0     |
|                    |                             | ( 0 )                   | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 4 ) | ( 0 )  | ( 0 )   | ( 3 ) | ( 10 ) | ( 0 ) |
|                    | hyaline cast                | 5                       | 0       | 0     | 0     | 2     | 0      | 0     | 0     | 2     | 0      | 0     | 0     | 3      | 0       | 0     | 0      |       |
|                    |                             | ( 17 )                  | ( 0 )   | ( 0 ) | ( 0 ) | ( 7 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 8 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 10 ) | ( 0 )   | ( 0 ) | ( 0 )  |       |

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

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

b : Number of animals with lesion

( c ) c : b / a \* 100

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS (105W)

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| Organ              | Findings                  | Group Name<br>No. of Animals on Study<br>Grade | Control<br>29 |       |       |       | 32 ppm<br>28 |       |       |       | 80 ppm<br>26 |       |       |       | 200 ppm<br>30 |       |       |       |
|--------------------|---------------------------|--|---------------|-------|-------|-------|--------------|-------|-------|-------|--------------|-------|-------|-------|---------------|-------|-------|-------|
|                    |                           |  | 1             | 2     | 3     | 4     | 1            | 2     | 3     | 4     | 1            | 2     | 3     | 4     | 1             | 2     | 3     | 4     |
|                    |                           |  | (%)           | (%)   | (%)   | (%)   | (%)          | (%)   | (%)   | (%)   | (%)          | (%)   | (%)   | (%)   | (%)           | (%)   | (%)   | (%)   |
| {Urinary system}   |                           |  |               |       |       |       |              |       |       |       |              |       |       |       |               |       |       |       |
| kidney             |                           |  | <29>          |       |       |       | <28>         |       |       |       | <26>         |       |       |       | <30>          |       |       |       |
|                    | inflammatory infiltration |  | 0             | 0     | 0     | 0     | 0            | 0     | 1     | 0     | 0            | 0     | 0     | 0     | 0             | 0     | 0     | 0     |
|                    |                           |  | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 4 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) |
|                    | lymphocytic infiltration  |  | 0             | 1     | 0     | 0     | 1            | 1     | 0     | 0     | 0            | 0     | 0     | 0     | 0             | 0     | 0     | 0     |
|                    |                           |  | ( 0 )         | ( 3 ) | ( 0 ) | ( 0 ) | ( 4 )        | ( 4 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) |
|                    | hydronephrosis            |  | 0             | 0     | 1     | 0     | 0            | 0     | 0     | 0     | 0            | 0     | 0     | 0     | 0             | 0     | 1     | 0     |
|                    |                           |  | ( 0 )         | ( 0 ) | ( 3 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )         | ( 0 ) | ( 3 ) | ( 0 ) |
|                    | retention cyst            |  | 0             | 0     | 0     | 0     | 0            | 0     | 0     | 0     | 0            | 0     | 0     | 0     | 0             | 1     | 0     | 0     |
|                    |                           |  | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )         | ( 3 ) | ( 0 ) | ( 0 ) |
| urin bladd         |                           |  | <29>          |       |       |       | <28>         |       |       |       | <26>         |       |       |       | <30>          |       |       |       |
|                    | lymphocytic infiltration  |  | 0             | 0     | 0     | 0     | 4            | 0     | 0     | 0     | 5            | 0     | 0     | 0 *   | 4             | 0     | 0     | 0     |
|                    |                           |  | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) | ( 14 )       | ( 0 ) | ( 0 ) | ( 0 ) | ( 19 )       | ( 0 ) | ( 0 ) | ( 0 ) | ( 13 )        | ( 0 ) | ( 0 ) | ( 0 ) |
| {Endocrine system} |                           |  |               |       |       |       |              |       |       |       |              |       |       |       |               |       |       |       |
| pituitary          |                           |  | <29>          |       |       |       | <28>         |       |       |       | <26>         |       |       |       | <30>          |       |       |       |
|                    | cyst                      |  | 0             | 0     | 1     | 0     | 1            | 0     | 0     | 0     | 0            | 0     | 0     | 0     | 0             | 0     | 0     | 0     |
|                    |                           |  | ( 0 )         | ( 0 ) | ( 3 ) | ( 0 ) | ( 4 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )        | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )         | ( 0 ) | ( 0 ) | ( 0 ) |

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 < a > a : Number of animals examined at the site  
 b : Number of animals with lesion  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS (105W)

PAGE : 19

| Organ_____            | Findings_____            | Group Name<br>No. of Animals on Study<br>Grade | Control |       |       |      | 32 ppm |       |       |      | 80 ppm |       |       |      | 200 ppm |       |       |      |
|-----------------------|--------------------------|--|---------|-------|-------|------|--------|-------|-------|------|--------|-------|-------|------|---------|-------|-------|------|
|                       |                          |  | 29      |       |       |      | 28     |       |       |      | 26     |       |       |      | 30      |       |       |      |
|                       |                          |  | 1       | 2     | 3     | 4    | 1      | 2     | 3     | 4    | 1      | 2     | 3     | 4    | 1       | 2     | 3     | 4    |
|                       |                          |  | (%)     | (%)   | (%)   | (%)  | (%)    | (%)   | (%)   | (%)  | (%)    | (%)   | (%)   | (%)  | (%)     | (%)   | (%)   |      |
| {Endocrine system}    |                          |  |         |       |       |      |        |       |       |      |        |       |       |      |         |       |       |      |
| pituitary             |                          |  | <29>    |       |       |      | <28>   |       |       |      | <26>   |       |       |      | <30>    |       |       |      |
|                       | hyperplasia              |  | 6       | 1     | 0     | 0    | 5      | 1     | 0     | 0    | 3      | 4     | 0     | 0    | 2       | 1     | 0     | 0    |
|                       |                          |  | ( 21)   | ( 3)  | ( 0)  | ( 0) | ( 18)  | ( 4)  | ( 0)  | ( 0) | ( 12)  | ( 15) | ( 0)  | ( 0) | ( 7)    | ( 3)  | ( 0)  | ( 0) |
|                       |                          |  |         |       |       |      |        |       |       |      |        |       |       |      |         |       |       |      |
|                       | focal hypertrophy        |  | 4       | 1     | 0     | 0    | 6      | 1     | 0     | 0    | 2      | 1     | 0     | 0    | 4       | 0     | 0     | 0    |
|                       |                          |  | ( 14)   | ( 3)  | ( 0)  | ( 0) | ( 21)  | ( 4)  | ( 0)  | ( 0) | ( 8)   | ( 4)  | ( 0)  | ( 0) | ( 13)   | ( 0)  | ( 0)  | ( 0) |
| adrenal               |                          |  | <29>    |       |       |      | <28>   |       |       |      | <26>   |       |       |      | <30>    |       |       |      |
|                       | spindle-cell hyperplasia |  | 1       | 12    | 16    | 0    | 1      | 14    | 13    | 0    | 1      | 13    | 11    | 0    | 0       | 21    | 9     | 0    |
|                       |                          |  | ( 3)    | ( 41) | ( 55) | ( 0) | ( 4)   | ( 50) | ( 46) | ( 0) | ( 4)   | ( 50) | ( 42) | ( 0) | ( 0)    | ( 70) | ( 30) | ( 0) |
|                       |                          |  |         |       |       |      |        |       |       |      |        |       |       |      |         |       |       |      |
|                       | hyperplasia:medulla      |  | 0       | 0     | 0     | 0    | 0      | 0     | 0     | 0    | 1      | 0     | 0     | 0    | 0       | 0     | 0     | 0    |
|                       |                          |  | ( 0)    | ( 0)  | ( 0)  | ( 0) | ( 0)   | ( 0)  | ( 0)  | ( 0) | ( 4)   | ( 0)  | ( 0)  | ( 0) | ( 0)    | ( 0)  | ( 0)  | ( 0) |
| {Reproductive system} |                          |  |         |       |       |      |        |       |       |      |        |       |       |      |         |       |       |      |
| ovary                 |                          |  | <29>    |       |       |      | <28>   |       |       |      | <26>   |       |       |      | <30>    |       |       |      |
|                       | thrombus                 |  | 0       | 0     | 0     | 0    | 0      | 0     | 0     | 0    | 0      | 0     | 2     | 0    | 0       | 0     | 0     | 0    |
|                       |                          |  | ( 0)    | ( 0)  | ( 0)  | ( 0) | ( 0)   | ( 0)  | ( 0)  | ( 0) | ( 0)   | ( 0)  | ( 8)  | ( 0) | ( 0)    | ( 0)  | ( 0)  | ( 0) |
|                       |                          |  |         |       |       |      |        |       |       |      |        |       |       |      |         |       |       |      |
|                       | cyst                     |  | 1       | 0     | 6     | 0    | 0      | 0     | 4     | 0    | 0      | 0     | 5     | 0    | 0       | 0     | 7     | 0    |
|                       |                          |  | ( 3)    | ( 0)  | ( 21) | ( 0) | ( 0)   | ( 0)  | ( 14) | ( 0) | ( 0)   | ( 0)  | ( 19) | ( 0) | ( 0)    | ( 0)  | ( 23) | ( 0) |

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

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

b : Number of animals with lesion

( c ) c : b / a \* 100

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS (105W)

PAGE : 20

|                                  |                                | Group Name              | Control |        |        |        | 32 ppm |       |        |        | 80 ppm |        |        |        | 200 ppm |        |       |       |
|----------------------------------|--------------------------------|-------------------------|---------|--------|--------|--------|--------|-------|--------|--------|--------|--------|--------|--------|---------|--------|-------|-------|
|                                  |                                | No. of Animals on Study | 29      |        |        |        | 28     |       |        |        | 26     |        |        |        | 30      |        |       |       |
| Organ                            | Findings                       | Grade                   | 1       | 2      | 3      | 4      | 1      | 2     | 3      | 4      | 1      | 2      | 3      | 4      | 1       | 2      | 3     | 4     |
|                                  |                                |                         | (%)     | (%)    | (%)    | (%)    | (%)    | (%)   | (%)    | (%)    | (%)    | (%)    | (%)    | (%)    | (%)     | (%)    | (%)   | (%)   |
| {Reproductive system}            |                                |                         |         |        |        |        |        |       |        |        |        |        |        |        |         |        |       |       |
| ovary                            | lymphocytic infiltration       |                         | <29>    |        |        |        | <28>   |       |        |        | <26>   |        |        |        | <30>    |        |       |       |
|                                  |                                | 0                       | 0       | 0      | 0      | 1      | 0      | 0     | 0      | 0      | 0      | 0      | 0      | 0      | 0       | 0      | 0     | 0     |
|                                  |                                | ( 0 )                   | ( 0 )   | ( 0 )  | ( 0 )  | ( 4 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) |
| uterus                           | cystic endometrial hyperplasia |                         | <29>    |        |        |        | <28>   |       |        |        | <26>   |        |        |        | <30>    |        |       |       |
|                                  |                                | 10                      | 8       | 3      | 0      | 13     | 4      | 2     | 0      | 11     | 7      | 4      | 0      | 11     | 9       | 4      | 0     |       |
|                                  |                                | ( 34 )                  | ( 28 )  | ( 10 ) | ( 0 )  | ( 46 ) | ( 14 ) | ( 7 ) | ( 0 )  | ( 42 ) | ( 27 ) | ( 15 ) | ( 0 )  | ( 37 ) | ( 30 )  | ( 13 ) | ( 0 ) |       |
| mammary gl                       | hyperplasia                    |                         | <29>    |        |        |        | <28>   |       |        |        | <26>   |        |        |        | <30>    |        |       |       |
|                                  |                                | 1                       | 0       | 0      | 0      | 1      | 0      | 0     | 0      | 0      | 0      | 0      | 0      | 0      | 0       | 0      | 0     | 0     |
|                                  |                                | ( 3 )                   | ( 0 )   | ( 0 )  | ( 0 )  | ( 4 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) |
| {Nervous system}                 |                                |                         |         |        |        |        |        |       |        |        |        |        |        |        |         |        |       |       |
| brain                            | mineralization                 |                         | <29>    |        |        |        | <28>   |       |        |        | <26>   |        |        |        | <30>    |        |       |       |
|                                  |                                | 11                      | 0       | 0      | 0      | 14     | 0      | 0     | 0      | 9      | 0      | 0      | 0      | 11     | 0       | 0      | 0     |       |
|                                  | ( 38 )                         | ( 0 )                   | ( 0 )   | ( 0 )  | ( 50 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 35 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 37 ) | ( 0 )  | ( 0 )   | ( 0 )  |       |       |
| {Special sense organs/appendage} |                                |                         |         |        |        |        |        |       |        |        |        |        |        |        |         |        |       |       |
| eye                              | phthisis bulbi                 |                         | <29>    |        |        |        | <28>   |       |        |        | <26>   |        |        |        | <30>    |        |       |       |
|                                  |                                | 0                       | 0       | 0      | 0      | 0      | 0      | 0     | 0      | 0      | 0      | 0      | 0      | 0      | 0       | 1      | 0     |       |
|                                  | ( 0 )                          | ( 0 )                   | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 )  | ( 3 )   | ( 0 )  |       |       |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS (105W)

PAGE : 21

| Organ | Findings | Group Name              |     |     |     | Control |     |     |     | 32 ppm |     |     |     | 80 ppm |     |     |     | 200 ppm |     |     |     |     |     |     |     |     |     |     |     |   |  |
|-------|----------|-------------------------|-----|-----|-----|---------|-----|-----|-----|--------|-----|-----|-----|--------|-----|-----|-----|---------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|---|--|
|       |          | No. of Animals on Study |     |     |     | 29      |     |     |     | 28     |     |     |     | 26     |     |     |     | 30      |     |     |     |     |     |     |     |     |     |     |     |   |  |
|       |          | Grade                   |     |     |     | 1       |     |     |     | 2      |     |     |     | 3      |     |     |     | 4       |     |     |     |     |     |     |     |     |     |     |     |   |  |
|       |          | 1                       |     |     |     | 2       |     |     |     | 3      |     |     |     | 4      |     |     |     | 1       |     |     |     | 2   |     |     |     | 3   |     |     |     | 4 |  |
|       |          |                         | (%) | (%) | (%) | (%)     | (%) | (%) | (%) | (%)    | (%) | (%) | (%) | (%)    | (%) | (%) | (%) | (%)     | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |   |  |

{Special sense organs/appendage}

|     |                     |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
|-----|---------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| eye | degeneration:cornea | <29>  |       |       |       | <28>  |       |       |       | <26>  |       |       |       | <30>  |       |       |       |
|     |                     | 1     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     |
|     |                     | ( 3 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) |

|           |             |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
|-----------|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Harder gl | hyperplasia | <29>  |       |       |       | <28>  |       |       |       | <26>  |       |       |       | <30>  |       |       |       |
|           |             | 0     | 0     | 0     | 0     | 1     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 2     | 1     | 0     | 0     |
|           |             | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 7 ) | ( 3 ) | ( 0 ) | ( 0 ) |

{Musculoskeletal system}

|      |                |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
|------|----------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| bone | osteosclerosis | <29>  |       |       |       | <28>  |       |       |       | <26>  |       |       |       | <30>  |       |       |       |
|      |                | 0     | 0     | 0     | 0     | 0     | 1     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     |
|      |                | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) |

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

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

b b : Number of animals with lesion

( c ) c : b / a \* 100

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



## APPENDIX M 1

NUMBER OF ANIMALS WITH TUMORS  
AND NUMBER OF TUMORS-TIME RELATED : MALE

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS - TIME RELATED

PAGE : 1

| Time-related<br>Weeks | Items                               | Group Name | Control | 32 ppm | 80 ppm | 200 ppm |
|-----------------------|-------------------------------------|------------|---------|--------|--------|---------|
| 0 - 52                | NO. OF EXAMINED ANIMALS             |            | 1       | 2      | 1      | 0       |
|                       | NO. OF ANIMALS WITH TUMORS          |            | 0       | 1      | 0      | 0       |
|                       | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 0       | 1      | 0      | 0       |
|                       | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 0       | 0      | 0      | 0       |
|                       | NO. OF BENIGN TUMORS                |            | 0       | 0      | 0      | 0       |
|                       | NO. OF MALIGNANT TUMORS             |            | 0       | 1      | 0      | 0       |
|                       | NO. OF TOTAL TUMORS                 |            | 0       | 1      | 0      | 0       |
| 53 - 78               | NO. OF EXAMINED ANIMALS             |            | 3       | 4      | 3      | 0       |
|                       | NO. OF ANIMALS WITH TUMORS          |            | 2       | 2      | 2      | 0       |
|                       | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 2       | 2      | 2      | 0       |
|                       | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 0       | 0      | 0      | 0       |
|                       | NO. OF BENIGN TUMORS                |            | 1       | 0      | 0      | 0       |
|                       | NO. OF MALIGNANT TUMORS             |            | 1       | 2      | 2      | 0       |
|                       | NO. OF TOTAL TUMORS                 |            | 2       | 2      | 2      | 0       |
| 79 - 104              | NO. OF EXAMINED ANIMALS             |            | 14      | 11     | 13     | 9       |
|                       | NO. OF ANIMALS WITH TUMORS          |            | 12      | 11     | 13     | 8       |
|                       | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 10      | 2      | 6      | 5       |
|                       | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 2       | 9      | 7      | 3       |
|                       | NO. OF BENIGN TUMORS                |            | 4       | 10     | 7      | 4       |
|                       | NO. OF MALIGNANT TUMORS             |            | 11      | 15     | 14     | 7       |
|                       | NO. OF TOTAL TUMORS                 |            | 15      | 25     | 21     | 11      |
| 105 - 105             | NO. OF EXAMINED ANIMALS             |            | 32      | 33     | 33     | 41      |
|                       | NO. OF ANIMALS WITH TUMORS          |            | 20      | 21     | 26     | 35      |
|                       | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 10      | 7      | 13     | 18      |
|                       | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 10      | 14     | 13     | 17      |
|                       | NO. OF BENIGN TUMORS                |            | 18      | 22     | 29     | 32      |
|                       | NO. OF MALIGNANT TUMORS             |            | 13      | 18     | 20     | 27      |
|                       | NO. OF TOTAL TUMORS                 |            | 31      | 40     | 49     | 59      |

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : MALE

NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS - TIME RELATED

PAGE : 2

| Time-related<br>Weeks | Items                               | Group Name | Control | 32 ppm | 80 ppm | 200 ppm |
|-----------------------|-------------------------------------|------------|---------|--------|--------|---------|
| 0 - 105               | NO. OF EXAMINED ANIMALS             |            | 50      | 50     | 50     | 50      |
|                       | NO. OF ANIMALS WITH TUMORS          |            | 34      | 35     | 41     | 43      |
|                       | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 22      | 12     | 21     | 23      |
|                       | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 12      | 23     | 20     | 20      |
|                       | NO. OF BENIGN TUMORS                |            | 23      | 32     | 36     | 36      |
|                       | NO. OF MALIGNANT TUMORS             |            | 25      | 36     | 36     | 34      |
|                       | NO. OF TOTAL TUMORS                 |            | 48      | 68     | 72     | 70      |

(HPT070)

BAIS4

## APPENDIX M 2

NUMBER OF ANIMALS WITH TUMORS  
AND NUMBER OF TUMORS-TIME RELATED : FEMALE

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : FEMALE

NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS - TIME RELATED

PAGE : 3

| Time-related<br>Weeks | Items_____                          | Group Name | Control | 32 ppm | 80 ppm | 200 ppm |
|-----------------------|-------------------------------------|------------|---------|--------|--------|---------|
| 0 - 52                | NO. OF EXAMINED ANIMALS             |            | 0       | 2      | 0      | 1       |
|                       | NO. OF ANIMALS WITH TUMORS          |            | 0       | 2      | 0      | 0       |
|                       | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 0       | 2      | 0      | 0       |
|                       | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 0       | 0      | 0      | 0       |
|                       | NO. OF BENIGN TUMORS                |            | 0       | 0      | 0      | 0       |
|                       | NO. OF MALIGNANT TUMORS             |            | 0       | 2      | 0      | 0       |
|                       | NO. OF TOTAL TUMORS                 |            | 0       | 2      | 0      | 0       |
| 53 - 78               | NO. OF EXAMINED ANIMALS             |            | 4       | 6      | 9      | 6       |
|                       | NO. OF ANIMALS WITH TUMORS          |            | 4       | 6      | 8      | 4       |
|                       | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 4       | 3      | 8      | 4       |
|                       | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 0       | 3      | 0      | 0       |
|                       | NO. OF BENIGN TUMORS                |            | 1       | 2      | 0      | 1       |
|                       | NO. OF MALIGNANT TUMORS             |            | 3       | 7      | 8      | 3       |
|                       | NO. OF TOTAL TUMORS                 |            | 4       | 9      | 8      | 4       |
| 79 - 104              | NO. OF EXAMINED ANIMALS             |            | 17      | 14     | 15     | 13      |
|                       | NO. OF ANIMALS WITH TUMORS          |            | 15      | 13     | 15     | 13      |
|                       | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 7       | 9      | 8      | 7       |
|                       | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 8       | 4      | 7      | 6       |
|                       | NO. OF BENIGN TUMORS                |            | 10      | 3      | 9      | 5       |
|                       | NO. OF MALIGNANT TUMORS             |            | 15      | 14     | 15     | 14      |
|                       | NO. OF TOTAL TUMORS                 |            | 25      | 17     | 24     | 19      |
| 105 - 105             | NO. OF EXAMINED ANIMALS             |            | 29      | 28     | 26     | 30      |
|                       | NO. OF ANIMALS WITH TUMORS          |            | 25      | 23     | 21     | 25      |
|                       | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 9       | 10     | 6      | 12      |
|                       | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 16      | 13     | 15     | 13      |
|                       | NO. OF BENIGN TUMORS                |            | 27      | 23     | 29     | 30      |
|                       | NO. OF MALIGNANT TUMORS             |            | 22      | 19     | 17     | 18      |
|                       | NO. OF TOTAL TUMORS                 |            | 49      | 42     | 46     | 48      |

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : FEMALE

NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS - TIME RELATED

PAGE : 4

| Time-related<br>Weeks | Items_____                          | Group Name | Control | 32 ppm | 80 ppm | 200 ppm |
|-----------------------|-------------------------------------|------------|---------|--------|--------|---------|
| 0 - 105               | NO. OF EXAMINED ANIMALS             |            | 50      | 50     | 50     | 50      |
|                       | NO. OF ANIMALS WITH TUMORS          |            | 44      | 44     | 44     | 42      |
|                       | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 20      | 24     | 22     | 23      |
|                       | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 24      | 20     | 22     | 19      |
|                       | NO. OF BENIGN TUMORS                |            | 38      | 28     | 38     | 36      |
|                       | NO. OF MALIGNANT TUMORS             |            | 40      | 42     | 40     | 35      |
|                       | NO. OF TOTAL TUMORS                 |            | 78      | 70     | 78     | 71      |

(HPT070)

BAIS4

## APPENDIX N 1

HISTOPATHOLOGICAL FINDINGS :

NEOPLASTIC LESIONS : MALE

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 1

| Organ                            | Findings                       | Group Name<br>No. of animals on Study | Control<br>50 | 32 ppm<br>50 | 80 ppm<br>50 | 200 ppm<br>50 |
|----------------------------------|--------------------------------|---------------------------------------|---------------|--------------|--------------|---------------|
| {Integumentary system/appandage} |                                |                                       |               |              |              |               |
| skin/app                         |                                |                                       | <50>          | <50>         | <50>         | <50>          |
|                                  | schwannoma                     |                                       | 0 ( 0%)       | 1 ( 2%)      | 0 ( 0%)      | 0 ( 0%)       |
| subcutis                         |                                |                                       | <50>          | <50>         | <50>         | <50>          |
|                                  | hemangioma                     |                                       | 0 ( 0%)       | 1 ( 2%)      | 0 ( 0%)      | 0 ( 0%)       |
|                                  | fibrosarcoma                   |                                       | 0 ( 0%)       | 0 ( 0%)      | 1 ( 2%)      | 0 ( 0%)       |
|                                  | schwannoma:malignant           |                                       | 0 ( 0%)       | 0 ( 0%)      | 1 ( 2%)      | 0 ( 0%)       |
|                                  | histiocytic sarcoma            |                                       | 1 ( 2%)       | 1 ( 2%)      | 1 ( 2%)      | 1 ( 2%)       |
|                                  | hemangiosarcoma                |                                       | 0 ( 0%)       | 1 ( 2%)      | 1 ( 2%)      | 0 ( 0%)       |
| {Respiratory system}             |                                |                                       |               |              |              |               |
| nasal cavit                      |                                |                                       | <50>          | <50>         | <50>         | <50>          |
|                                  | histiocytic sarcoma            |                                       | 1 ( 2%)       | 0 ( 0%)      | 1 ( 2%)      | 0 ( 0%)       |
| lung                             |                                |                                       | <50>          | <50>         | <50>         | <50>          |
|                                  | bronchiolar-alveolar adenoma   |                                       | 5 ( 10%)      | 14 ( 28%)    | 9 ( 18%)     | 12 ( 24%)     |
|                                  | bronchiolar-alveolar carcinoma |                                       | 4 ( 8%)       | 6 ( 12%)     | 6 ( 12%)     | 8 ( 16%)      |
| {Hematopoietic system}           |                                |                                       |               |              |              |               |
| lymph node                       |                                |                                       | <50>          | <50>         | <50>         | <50>          |
|                                  | malignant lymphoma             |                                       | 9 ( 18%)      | 6 ( 12%)     | 4 ( 8%)      | 9 ( 18%)      |
| spleen                           |                                |                                       | <50>          | <50>         | <50>         | <50>          |
|                                  | hemangioma                     |                                       | 0 ( 0%)       | 1 ( 2%)      | 0 ( 0%)      | 1 ( 2%)       |

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



STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 2

| Organ                  | Findings                 | Group Name<br>No. of animals on Study | Control<br>50 | 32 ppm<br>50 | 80 ppm<br>50 | 200 ppm<br>50 |
|------------------------|--------------------------|---------------------------------------|---------------|--------------|--------------|---------------|
| {Hematopoietic system} |                          |                                       |               |              |              |               |
| spleen                 |                          |                                       | <50>          | <50>         | <50>         | <50>          |
|                        | malignant lymphoma       |                                       | 0 ( 0%)       | 0 ( 0%)      | 1 ( 2%)      | 1 ( 2%)       |
|                        | mastcytoma:malignant     |                                       | 0 ( 0%)       | 0 ( 0%)      | 1 ( 2%)      | 0 ( 0%)       |
|                        | hemangiosarcoma          |                                       | 0 ( 0%)       | 3 ( 6%)      | 3 ( 6%)      | 5 ( 10%)      |
| {Digestive system}     |                          |                                       |               |              |              |               |
| stomach                |                          |                                       | <50>          | <50>         | <50>         | <50>          |
|                        | adenocarcinoma           |                                       | 0 ( 0%)       | 1 ( 2%)      | 0 ( 0%)      | 0 ( 0%)       |
| small intes            |                          |                                       | <50>          | <50>         | <50>         | <50>          |
|                        | adenoma                  |                                       | 0 ( 0%)       | 0 ( 0%)      | 1 ( 2%)      | 0 ( 0%)       |
| liver                  |                          |                                       | <50>          | <50>         | <50>         | <50>          |
|                        | hemangioma               |                                       | 1 ( 2%)       | 2 ( 4%)      | 4 ( 8%)      | 5 ( 10%)      |
|                        | hepatocellular adenoma   |                                       | 13 ( 26%)     | 10 ( 20%)    | 16 ( 32%)    | 12 ( 24%)     |
|                        | histiocytic sarcoma      |                                       | 1 ( 2%)       | 4 ( 8%)      | 7 ( 14%)     | 0 ( 0%)       |
|                        | mastcytoma:malignant     |                                       | 0 ( 0%)       | 0 ( 0%)      | 1 ( 2%)      | 0 ( 0%)       |
|                        | hemangiosarcoma          |                                       | 2 ( 4%)       | 3 ( 6%)      | 4 ( 8%)      | 2 ( 4%)       |
|                        | hepatocellular carcinoma |                                       | 5 ( 10%)      | 5 ( 10%)     | 3 ( 6%)      | 6 ( 12%)      |
| {Urinary system}       |                          |                                       |               |              |              |               |
| kidney                 |                          |                                       | <50>          | <50>         | <50>         | <50>          |
|                        | renal cell adenoma       |                                       | 0 ( 0%)       | 0 ( 0%)      | 1 ( 2%)      | 0 ( 0%)       |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 3

| Organ                            | Findings            | Group Name<br>No. of animals on Study | Control<br>50 | 32 ppm<br>50 | 80 ppm<br>50 | 200 ppm<br>50 |
|----------------------------------|---------------------|---------------------------------------|---------------|--------------|--------------|---------------|
| {Urinary system}                 |                     |                                       |               |              |              |               |
| kidney                           |                     |                                       | <50>          | <50>         | <50>         | <50>          |
|                                  | hemangiosarcoma     |                                       | 0 ( 0%)       | 0 ( 0%)      | 1 ( 2%)      | 0 ( 0%)       |
| urin bladd                       |                     |                                       | <50>          | <50>         | <50>         | <50>          |
|                                  | hemangioma          |                                       | 0 ( 0%)       | 0 ( 0%)      | 1 ( 2%)      | 0 ( 0%)       |
|                                  | histiocytic sarcoma |                                       | 1 ( 2%)       | 2 ( 4%)      | 0 ( 0%)      | 0 ( 0%)       |
| {Endocrine system}               |                     |                                       |               |              |              |               |
| pituitary                        |                     |                                       | <49>          | <50>         | <50>         | <50>          |
|                                  | adenoma             |                                       | 1 ( 2%)       | 1 ( 2%)      | 1 ( 2%)      | 0 ( 0%)       |
| adrenal                          |                     |                                       | <50>          | <50>         | <50>         | <50>          |
|                                  | cortical adenoma    |                                       | 1 ( 2%)       | 0 ( 0%)      | 0 ( 0%)      | 0 ( 0%)       |
| {Reproductive system}            |                     |                                       |               |              |              |               |
| epididymis                       |                     |                                       | <50>          | <50>         | <50>         | <50>          |
|                                  | histiocytic sarcoma |                                       | 1 ( 2%)       | 1 ( 2%)      | 0 ( 0%)      | 1 ( 2%)       |
| mammary gl                       |                     |                                       | <50>          | <50>         | <50>         | <50>          |
|                                  | adenocarcinoma      |                                       | 0 ( 0%)       | 0 ( 0%)      | 0 ( 0%)      | 1 ( 2%)       |
| {Nervous system}                 |                     |                                       |               |              |              |               |
| periph nerv                      |                     |                                       | <50>          | <50>         | <50>         | <50>          |
|                                  | histiocytic sarcoma |                                       | 0 ( 0%)       | 2 ( 4%)      | 0 ( 0%)      | 0 ( 0%)       |
| {Special sense organs/appendage} |                     |                                       |               |              |              |               |
| Harder gl                        |                     |                                       | <50>          | <50>         | <49>         | <50>          |
|                                  | adenoma             |                                       | 1 ( 2%)       | 2 ( 4%)      | 3 ( 6%)      | 6 ( 12%)      |

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 b ( c ) b : Number of animals with neoplasm c : b / a \* 100

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : MALE

HISTOPATHOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)  
ALL ANIMALS (0-105W)

PAGE : 4

| Organ           | Findings        | Group Name<br>No. of animals on Study | Control<br>50   | 32 ppm<br>50    | 80 ppm<br>50    | 200 ppm<br>50   |
|-----------------|-----------------|---------------------------------------|-----------------|-----------------|-----------------|-----------------|
| {Body cavities} |                 |                                       |                 |                 |                 |                 |
| peritoneum      | hemangioma      |                                       | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) |
|                 | hemangiosarcoma |                                       | 0 ( 0%)         | 1 ( 2%)         | 0 ( 0%)         | 0 ( 0%)         |

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

(HPT085)

BAIS4

## APPENDIX N 2

HISTOPATHOLOGICAL FINDINGS :

NEOPLASTIC LESIONS : FEMALE

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)  
ALL ANIMALS (0-105W)

PAGE : 5

| Organ                            | Findings                       | Group Name<br>No. of animals on Study | Control<br>50 | 32 ppm<br>50 | 80 ppm<br>50 | 200 ppm<br>50 |
|----------------------------------|--------------------------------|---------------------------------------|---------------|--------------|--------------|---------------|
| {Integumentary system/appandage} |                                |                                       |               |              |              |               |
| skin/app                         |                                |                                       | <50>          | <50>         | <50>         | <50>          |
|                                  | squamous cell papilloma        |                                       | 2 ( 4%)       | 0 ( 0%)      | 0 ( 0%)      | 0 ( 0%)       |
| subcutis                         |                                |                                       | <50>          | <50>         | <50>         | <50>          |
|                                  | hemangioma                     |                                       | 1 ( 2%)       | 0 ( 0%)      | 0 ( 0%)      | 0 ( 0%)       |
|                                  | histiocytic sarcoma            |                                       | 0 ( 0%)       | 0 ( 0%)      | 1 ( 2%)      | 0 ( 0%)       |
|                                  | mastcytoma:malignant           |                                       | 0 ( 0%)       | 0 ( 0%)      | 1 ( 2%)      | 0 ( 0%)       |
|                                  | hemangiosarcoma                |                                       | 2 ( 4%)       | 0 ( 0%)      | 0 ( 0%)      | 0 ( 0%)       |
| {Respiratory system}             |                                |                                       |               |              |              |               |
| lung                             |                                |                                       | <50>          | <50>         | <50>         | <50>          |
|                                  | bronchiolar-alveolar adenoma   |                                       | 1 ( 2%)       | 4 ( 8%)      | 4 ( 8%)      | 4 ( 8%)       |
|                                  | bronchiolar-alveolar carcinoma |                                       | 1 ( 2%)       | 1 ( 2%)      | 1 ( 2%)      | 4 ( 8%)       |
| {Hematopoietic system}           |                                |                                       |               |              |              |               |
| lymph node                       |                                |                                       | <50>          | <50>         | <50>         | <50>          |
|                                  | mastcytoma:benign              |                                       | 1 ( 2%)       | 0 ( 0%)      | 0 ( 0%)      | 0 ( 0%)       |
|                                  | hemangioma                     |                                       | 0 ( 0%)       | 1 ( 2%)      | 0 ( 0%)      | 0 ( 0%)       |
|                                  | malignant lymphoma             |                                       | 14 ( 28%)     | 21 ( 42%)    | 16 ( 32%)    | 11 ( 22%)     |
|                                  | mastcytoma:malignant           |                                       | 0 ( 0%)       | 0 ( 0%)      | 1 ( 2%)      | 0 ( 0%)       |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 6

| Organ                  | Findings                 | Group Name<br>No. of animals on Study | Control<br>50 | 32 ppm<br>50 | 80 ppm<br>50 | 200 ppm<br>50 |
|------------------------|--------------------------|---------------------------------------|---------------|--------------|--------------|---------------|
| {Hematopoietic system} |                          |                                       |               |              |              |               |
| spleen                 |                          |                                       | <50>          | <50>         | <50>         | <50>          |
|                        | hemangioma               |                                       | 0 ( 0%)       | 0 ( 0%)      | 1 ( 2%)      | 0 ( 0%)       |
|                        | malignant lymphoma       |                                       | 1 ( 2%)       | 2 ( 4%)      | 0 ( 0%)      | 2 ( 4%)       |
|                        | hemangiosarcoma          |                                       | 2 ( 4%)       | 0 ( 0%)      | 0 ( 0%)      | 0 ( 0%)       |
| {Digestive system}     |                          |                                       |               |              |              |               |
| stomach                |                          |                                       | <50>          | <50>         | <50>         | <50>          |
|                        | squamous cell papilloma  |                                       | 3 ( 6%)       | 0 ( 0%)      | 1 ( 2%)      | 3 ( 6%)       |
| large intes            |                          |                                       | <50>          | <50>         | <50>         | <50>          |
|                        | fibrosarcoma             |                                       | 1 ( 2%)       | 0 ( 0%)      | 0 ( 0%)      | 0 ( 0%)       |
| liver                  |                          |                                       | <50>          | <50>         | <50>         | <50>          |
|                        | hemangioma               |                                       | 1 ( 2%)       | 1 ( 2%)      | 1 ( 2%)      | 3 ( 6%)       |
|                        | hepatocellular adenoma   |                                       | 6 ( 12%)      | 7 ( 14%)     | 9 ( 18%)     | 8 ( 16%)      |
|                        | histiocytic sarcoma      |                                       | 0 ( 0%)       | 1 ( 2%)      | 0 ( 0%)      | 1 ( 2%)       |
|                        | hemangiosarcoma          |                                       | 2 ( 4%)       | 0 ( 0%)      | 0 ( 0%)      | 1 ( 2%)       |
|                        | hepatocellular carcinoma |                                       | 1 ( 2%)       | 1 ( 2%)      | 0 ( 0%)      | 0 ( 0%)       |
| {Endocrine system}     |                          |                                       |               |              |              |               |
| pituitary              |                          |                                       | <49>          | <50>         | <50>         | <50>          |
|                        | adenoma                  |                                       | 16 ( 33%)     | 9 ( 18%)     | 16 ( 32%)    | 14 ( 28%)     |

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

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 7

| Organ                 | Findings                   | Group Name<br>No. of animals on Study | Control<br>50   | 32 ppm<br>50    | 80 ppm<br>50    | 200 ppm<br>50   |
|-----------------------|----------------------------|---------------------------------------|-----------------|-----------------|-----------------|-----------------|
| {Endocrine system}    |                            |                                       |                 |                 |                 |                 |
| thyroid               | follicular adenoma         |                                       | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) |
| {Reproductive system} |                            |                                       |                 |                 |                 |                 |
| ovary                 | cystadenoma                |                                       | <50><br>1 ( 2%) | <50><br>1 ( 2%) | <50><br>2 ( 4%) | <50><br>0 ( 0%) |
|                       | granulosa-theca cell tumor |                                       | 1 ( 2%)         | 0 ( 0%)         | 0 ( 0%)         | 0 ( 0%)         |
| uterus                | hemangioma                 |                                       | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) |
|                       | endometrial stromal polyp  |                                       | 2 ( 4%)         | 2 ( 4%)         | 2 ( 4%)         | 1 ( 2%)         |
|                       | histiocytic sarcoma        |                                       | 16 ( 32%)       | 15 ( 30%)       | 15 ( 30%)       | 11 ( 22%)       |
|                       | hemangiosarcoma            |                                       | 0 ( 0%)         | 0 ( 0%)         | 0 ( 0%)         | 1 ( 2%)         |
| vagina                | histiocytic sarcoma        |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) |
| mammary gl            | adenocarcinoma             |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>3 ( 6%) | <50><br>1 ( 2%) |
| prep/cli gl           | squamous cell carcinoma    |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) |
| {Nervous system}      |                            |                                       |                 |                 |                 |                 |
| periph nerv           | histiocytic sarcoma        |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) |

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

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)  
ALL ANIMALS (0-105W)

PAGE : 8

| Organ                            | Findings            | Group Name<br>No. of animals on Study | Control<br>50   | 32 ppm<br>50    | 80 ppm<br>50    | 200 ppm<br>50   |
|----------------------------------|---------------------|---------------------------------------|-----------------|-----------------|-----------------|-----------------|
| {Special sense organs/appendage} |                     |                                       |                 |                 |                 |                 |
| Harder gl                        | adenoma             |                                       | <50><br>2 ( 4%) | <50><br>2 ( 4%) | <50><br>2 ( 4%) | <50><br>2 ( 4%) |
| {Musculoskeletal system}         |                     |                                       |                 |                 |                 |                 |
| muscle                           | hemangiosarcoma     |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) |
| {Body cavities}                  |                     |                                       |                 |                 |                 |                 |
| peritoneum                       | hemangiosarcoma     |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) |
| retroperit                       | histiocytic sarcoma |                                       | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) |

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

(HP1085)

BAIS4



## APPENDIX O 1

### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS : MALE

STUDY No. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 1

| Group Name  | Control     | 32 ppm       | 80 ppm       | 200 ppm      |
|---|-------------|--------------|--------------|--------------|
| SITE : lung<br>TUMOR : bronchiolar-alveolar adenoma                                 |             |              |              |              |
| Tumor rate  |             |              |              |              |
| Overall rates(a)  | 5/50( 10.0) | 14/50( 28.0) | 9/50( 18.0)  | 12/50( 24.0) |
| Adjusted rates(b)   | 15.63       | 35.90        | 25.00        | 25.58        |
| Terminal rates(c)   | 5/32( 15.6) | 9/33( 27.3)  | 8/33( 24.2)  | 10/41( 24.4) |
| Statistical analysis  |             |              |              |              |
| Peto test   |             |              |              |              |
| Standard method(d)  | P = -----   |              |              |              |
| Prevalence method(d)  | P = 0.2431  |              |              |              |
| Combined analysis(d)  | P = -----   |              |              |              |
| Cochran-Armitage test(e)  | P = 0.2972  |              |              |              |
| Fisher Exact test(e)  |             | P = 0.0198*  | P = 0.1940   | P = 0.0542   |
| SITE : lung<br>TUMOR : bronchiolar-alveolar carcinoma                               |             |              |              |              |
| Tumor rate  |             |              |              |              |
| Overall rates(a)  | 4/50( 8.0)  | 6/50( 12.0)  | 6/50( 12.0)  | 8/50( 16.0)  |
| Adjusted rates(b)   | 12.50       | 16.22        | 12.50        | 19.51        |
| Terminal rates(c)   | 4/32( 12.5) | 4/33( 12.1)  | 3/33( 9.1)   | 8/41( 19.5)  |
| Statistical analysis  |             |              |              |              |
| Peto test   |             |              |              |              |
| Standard method(d)  | P = 0.4281  |              |              |              |
| Prevalence method(d)  | P = 0.1952  |              |              |              |
| Combined analysis(d)  | P = 0.2051  |              |              |              |
| Cochran-Armitage test(e)  | P = 0.2519  |              |              |              |
| Fisher Exact test(e)  |             | P = 0.3703   | P = 0.3703   | P = 0.1783   |
| SITE : lung<br>TUMOR : bronchiolar-alveolar adenoma, bronchiolar-alveolar carcinoma |             |              |              |              |
| Tumor rate  |             |              |              |              |
| Overall rates(a)  | 9/50( 18.0) | 18/50( 36.0) | 14/50( 28.0) | 18/50( 36.0) |
| Adjusted rates(b)   | 28.13       | 46.15        | 32.50        | 39.53        |
| Terminal rates(c)   | 9/32( 28.1) | 13/33( 39.4) | 10/33( 30.3) | 16/41( 39.0) |
| Statistical analysis  |             |              |              |              |
| Peto test   |             |              |              |              |
| Standard method(d)  | P = 0.4281  |              |              |              |
| Prevalence method(d)  | P = 0.1648  |              |              |              |
| Combined analysis(d)  | P = 0.1707  |              |              |              |
| Cochran-Armitage test(e)  | P = 0.1567  |              |              |              |
| Fisher Exact test(e)  |             | P = 0.0352*  | P = 0.1710   | P = 0.0352*  |

STUDY No. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 2

| Group Name   | Control     | 32 ppm      | 80 ppm     | 200 ppm     |
|--|-------------|-------------|------------|-------------|
| SITE : lymph node<br>TUMOR : malignant lymphoma      |             |             |            |             |
| Tumor rate   |             |             |            |             |
| Overall rates(a)                                     | 9/50( 18.0) | 6/50( 12.0) | 4/50( 8.0) | 9/50( 18.0) |
| Adjusted rates(b)                                    | 15.63       | 3.03        | 3.03       | 17.07       |
| Terminal rates(c)                                    | 5/32( 15.6) | 1/33( 3.0)  | 1/33( 3.0) | 7/41( 17.1) |
| Statistical analysis                                 |             |             |            |             |
| Peto test  |             |             |            |             |
| Standard method(d)                                   | P = 0.8914  |             |            |             |
| Prevalence method(d)                                 | P = 0.1352  |             |            |             |
| Combined analysis(d)                                 | P = 0.5371  |             |            |             |
| Cochran-Armitage test(e)                             | P = 0.7313  |             |            |             |
| Fisher Exact test(e)                                 |             | P = 0.2883  | P = 0.1168 | P = 0.6024  |
| SITE : spleen<br>TUMOR : hemangiosarcoma             |             |             |            |             |
| Tumor rate   |             |             |            |             |
| Overall rates(a)                                     | 0/50( 0.0)  | 3/50( 6.0)  | 3/50( 6.0) | 5/50( 10.0) |
| Adjusted rates(b)                                    | 0.0         | 6.06        | 8.33       | 9.76        |
| Terminal rates(c)                                    | 0/32( 0.0)  | 2/33( 6.1)  | 2/33( 6.1) | 4/41( 9.8)  |
| Statistical analysis                                 |             |             |            |             |
| Peto test  |             |             |            |             |
| Standard method(d)                                   | P = 0.2949  |             |            |             |
| Prevalence method(d)                                 | P = 0.0780  |             |            |             |
| Combined analysis(d)                                 | P = 0.0652  |             |            |             |
| Cochran-Armitage test(e)                             | P = 0.0510  |             |            |             |
| Fisher Exact test(e)                                 |             | P = 0.1212  | P = 0.1212 | P = 0.0281* |
| SITE : spleen<br>TUMOR : hemangioma, hemangiosarcoma |             |             |            |             |
| Tumor rate   |             |             |            |             |
| Overall rates(a)                                     | 0/50( 0.0)  | 4/50( 8.0)  | 3/50( 6.0) | 6/50( 12.0) |
| Adjusted rates(b)                                    | 0.0         | 9.09        | 8.33       | 12.20       |
| Terminal rates(c)                                    | 0/32( 0.0)  | 3/33( 9.1)  | 2/33( 6.1) | 5/41( 12.2) |
| Statistical analysis                                 |             |             |            |             |
| Peto test  |             |             |            |             |
| Standard method(d)                                   | P = 0.2949  |             |            |             |
| Prevalence method(d)                                 | P = 0.0628  |             |            |             |
| Combined analysis(d)                                 | P = 0.0527  |             |            |             |
| Cochran-Armitage test(e)                             | P = 0.0365* |             |            |             |
| Fisher Exact test(e)                                 |             | P = 0.0587  | P = 0.1212 | P = 0.0133* |

STUDY No. : 0458  
 ANIMAL : MOUSE B6D2F1/CrJ[Crj:BDF1]  
 SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 3

| Group Name                                     | Control      | 32 ppm       | 80 ppm       | 200 ppm      |
|--|--------------|--------------|--------------|--------------|
| SITE : liver<br>TUMOR : hemangioma             |              |              |              |              |
| Tumor rate                                     |              |              |              |              |
| Overall rates(a)                               | 1/50( 2.0)   | 2/50( 4.0)   | 4/50( 8.0)   | 5/50( 10.0)  |
| Adjusted rates(b)                              | 2.70         | 5.56         | 6.06         | 9.30         |
| Terminal rates(c)                              | 0/32( 0.0)   | 1/33( 3.0)   | 2/33( 6.1)   | 3/41( 7.3)   |
| Statistical analysis                           |              |              |              |              |
| Peto test                                      |              |              |              |              |
| Standard method(d)                             | P = 0.2124   |              |              |              |
| Prevalence method(d)                           | P = 0.1254   |              |              |              |
| Combined analysis(d)                           | P = 0.0811   |              |              |              |
| Cochran-Armitage test(e)                       | P = 0.0791   |              |              |              |
| Fisher Exact test(e)                           |              | P = 0.5000   | P = 0.1811   | P = 0.1022   |
| SITE : liver<br>TUMOR : hepatocellular adenoma |              |              |              |              |
| Tumor rate                                     |              |              |              |              |
| Overall rates(a)                               | 13/50( 26.0) | 10/50( 20.0) | 16/50( 32.0) | 12/50( 24.0) |
| Adjusted rates(b)                              | 31.58        | 22.73        | 39.39        | 29.27        |
| Terminal rates(c)                              | 10/32( 31.3) | 6/33( 18.2)  | 13/33( 39.4) | 12/41( 29.3) |
| Statistical analysis                           |              |              |              |              |
| Peto test                                      |              |              |              |              |
| Standard method(d)                             | P = 0.7324   |              |              |              |
| Prevalence method(d)                           | P = 0.5872   |              |              |              |
| Combined analysis(d)                           | P = 0.6520   |              |              |              |
| Cochran-Armitage test(e)                       | P = 0.9625   |              |              |              |
| Fisher Exact test(e)                           |              | P = 0.3176   | P = 0.3299   | P = 0.5000   |
| SITE : liver<br>TUMOR : histiocytic sarcoma    |              |              |              |              |
| Tumor rate                                     |              |              |              |              |
| Overall rates(a)                               | 1/50( 2.0)   | 4/50( 8.0)   | 7/50( 14.0)  | 0/50( 0.0)   |
| Adjusted rates(b)                              | 3.13         | 6.06         | 6.06         | 0.0          |
| Terminal rates(c)                              | 1/32( 3.1)   | 2/33( 6.1)   | 2/33( 6.1)   | 0/41( 0.0)   |
| Statistical analysis                           |              |              |              |              |
| Peto test                                      |              |              |              |              |
| Standard method(d)                             | P = 0.6883   |              |              |              |
| Prevalence method(d)                           | P = 0.8778   |              |              |              |
| Combined analysis(d)                           | P = 0.8786   |              |              |              |
| Cochran-Armitage test(e)                       | P = 0.3311   |              |              |              |
| Fisher Exact test(e)                           |              | P = 0.1811   | P = 0.0297*  | P = 0.5000   |

STUDY No. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 4

| Group Name  | Control     | 32 ppm      | 80 ppm      | 200 ppm     |
|---|-------------|-------------|-------------|-------------|
| SITE : liver<br>TUMOR : hemangiosarcoma             |             |             |             |             |
| Tumor rate  |             |             |             |             |
| Overall rates(a)                                    | 2/50( 4.0)  | 3/50( 6.0)  | 4/50( 8.0)  | 2/50( 4.0)  |
| Adjusted rates(b)                                   | 0.0         | 9.09        | 9.09        | 2.44        |
| Terminal rates(c)                                   | 0/32( 0.0)  | 3/33( 9.1)  | 3/33( 9.1)  | 1/41( 2.4)  |
| Statistical analysis                                |             |             |             |             |
| Peto test   |             |             |             |             |
| Standard method(d)                                  | P = 0.6074  |             |             |             |
| Prevalence method(d)                                | P = 0.6056  |             |             |             |
| Combined analysis(d)                                | P = 0.6641  |             |             |             |
| Cochran-Armitage test(e)                            | P = 0.8639  |             |             |             |
| Fisher Exact test(e)                                |             | P = 0.5000  | P = 0.3389  | P = 0.6913  |
| SITE : liver<br>TUMOR : hepatocellular carcinoma    |             |             |             |             |
| Tumor rate  |             |             |             |             |
| Overall rates(a)                                    | 5/50( 10.0) | 5/50( 10.0) | 3/50( 6.0)  | 6/50( 12.0) |
| Adjusted rates(b)                                   | 6.25        | 5.71        | 6.06        | 12.20       |
| Terminal rates(c)                                   | 2/32( 6.3)  | 1/33( 3.0)  | 2/33( 6.1)  | 5/41( 12.2) |
| Statistical analysis                                |             |             |             |             |
| Peto test   |             |             |             |             |
| Standard method(d)                                  | P = 0.9047  |             |             |             |
| Prevalence method(d)                                | P = 0.1345  |             |             |             |
| Combined analysis(d)                                | P = 0.4926  |             |             |             |
| Cochran Armitage test(e)                            | P = 0.7080  |             |             |             |
| Fisher Exact test(e)                                |             | P = 0.6297  | P = 0.3575  | P = 0.5000  |
| SITE : liver<br>TUMOR : hemangioma, hemangiosarcoma |             |             |             |             |
| Tumor rate  |             |             |             |             |
| Overall rates(a)                                    | 3/50( 6.0)  | 5/50( 10.0) | 8/50( 16.0) | 7/50( 14.0) |
| Adjusted rates(b)                                   | 2.70        | 13.89       | 15.15       | 11.63       |
| Terminal rates(c)                                   | 0/32( 0.0)  | 4/33( 12.1) | 5/33( 15.2) | 4/41( 9.8)  |
| Statistical analysis                                |             |             |             |             |
| Peto test   |             |             |             |             |
| Standard method(d)                                  | P = 0.3793  |             |             |             |
| Prevalence method(d)                                | P = 0.2325  |             |             |             |
| Combined analysis(d)                                | P = 0.2234  |             |             |             |
| Cochran-Armitage test(e)                            | P = 0.2362  |             |             |             |
| Fisher Exact test(e)                                |             | P = 0.3575  | P = 0.0999  | P = 0.1589  |

STUDY No. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 5

| Group Name   | Control      | 32 ppm       | 80 ppm       | 200 ppm      |
|--|--------------|--------------|--------------|--------------|
| SITE : liver   |              |              |              |              |
| TUMOR : hepatocellular adenoma, hepatocellular carcinoma |              |              |              |              |
| Tumor rate   |              |              |              |              |
| Overall rates(a)   | 16/50( 32.0) | 14/50( 28.0) | 17/50( 34.0) | 18/50( 36.0) |
| Adjusted rates(b)  | 34.38        | 27.78        | 42.42        | 41.46        |
| Terminal rates(c)  | 11/32( 34.4) | 7/33( 21.2)  | 14/33( 42.4) | 17/41( 41.5) |
| Statistical analysis                                     |              |              |              |              |
| Peto test  |              |              |              |              |
| Standard method(d)                                       | P = 0.9380   |              |              |              |
| Prevalence method(d)                                     | P = 0.2425   |              |              |              |
| Combined analysis(d)                                     | P = 0.5282   |              |              |              |
| Cochran-Armitage test(e)                                 | P = 0.5018   |              |              |              |
| Fisher Exact test(e)                                     |              | P = 0.4138   | P = 0.5000   | P = 0.4165   |
| SITE : Harderian gland                                   |              |              |              |              |
| TUMOR : adenoma  |              |              |              |              |
| Tumor rate   |              |              |              |              |
| Overall rates(a)   | 1/50( 2.0)   | 2/50( 4.0)   | 3/49( 6.1)   | 6/50( 12.0)  |
| Adjusted rates(b)  | 3.13         | 6.06         | 7.32         | 14.63        |
| Terminal rates(c)  | 1/32( 3.1)   | 2/33( 6.1)   | 2/33( 6.1)   | 6/41( 14.6)  |
| Statistical analysis                                     |              |              |              |              |
| Peto test  |              |              |              |              |
| Standard method(d)                                       | P = -----    |              |              |              |
| Prevalence method(d)                                     | P = 0.0312*  |              |              |              |
| Combined analysis(d)                                     | P = -----    |              |              |              |
| Cochran-Armitage test(e)                                 | P = 0.0263*  |              |              |              |
| Fisher Exact test(e)                                     |              | P = 0.5000   | P = 0.3010   | P = 0.0559   |

(HPT360A)

BATS4

- (a): Number of tumor-bearing animals/number of animals examined at the site.  
 (b): Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.  
 (c): Observed tumor incidence at terminal kill.  
 (d): Beneath the control incidence are the P-values associated with the trend test.  
     Standard method : Death analysis  
     Prevalence method : Incidental tumor test  
     Combined analysis : Death analysis + Incidental tumor test  
 (e): The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.  
 ? : The conditional probabilities of the largest and smallest possible out comes can not estimated or this P-value is beyond the estimated P-value.  
 ----- : There is no data which should be statistical analysis.  
 Significant difference ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$   
 N.C. : Statistical value cannot be calculated and was not significant.

STUDY No. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 1

| Group Name                                     | Control     | 32 ppm      | 80 ppm      | 200 ppm      |
|--|-------------|-------------|-------------|--------------|
| SITE : ALL SITE<br>TUMOR : hemangioma          |             |             |             |              |
| Tumor rate                                     |             |             |             |              |
| Overall rates(a)                               | 2/50( 4.0)  | 4/50( 8.0)  | 5/50( 10.0) | 6/50( 12.0)  |
| Adjusted rates(b)                              | 5.41        | 11.11       | 9.09        | 11.63        |
| Terminal rates(c)                              | 1/32( 3.1)  | 3/33( 9.1)  | 3/33( 9.1)  | 4/41( 9.8)   |
| Statistical analysis                           |             |             |             |              |
| Peto test                                      |             |             |             |              |
| Standard method(d)                             | P = 0.2124  |             |             |              |
| Prevalence method(d)                           | P = 0.2439  |             |             |              |
| Combined analysis(d)                           | P = 0.1650  |             |             |              |
| Cochran-Armitage test(e)                       | P = 0.1797  |             |             |              |
| Fisher Exact test(e)                           |             | P = 0.3389  | P = 0.2180  | P = 0.1343   |
| SITE : ALL SITE<br>TUMOR : histiocytic sarcoma |             |             |             |              |
| Tumor rate                                     |             |             |             |              |
| Overall rates(a)                               | 5/50( 10.0) | 9/50( 18.0) | 8/50( 16.0) | 2/50( 4.0)   |
| Adjusted rates(b)                              | 6.25        | 15.15       | 9.09        | 2.44         |
| Terminal rates(c)                              | 2/32( 6.3)  | 5/33( 15.2) | 3/33( 9.1)  | 1/41( 2.4)   |
| Statistical analysis                           |             |             |             |              |
| Peto test                                      |             |             |             |              |
| Standard method(d)                             | P = 0.8789  |             |             |              |
| Prevalence method(d)                           | P = 0.9143  |             |             |              |
| Combined analysis(d)                           | P = 0.9657  |             |             |              |
| Cochran-Armitage test(e)                       | P = 0.1192  |             |             |              |
| Fisher Exact test(e)                           |             | P = 0.1940  | P = 0.2768  | P = 0.2180   |
| SITE : ALL SITE<br>TUMOR : malignant lymphoma  |             |             |             |              |
| Tumor rate                                     |             |             |             |              |
| Overall rates(a)                               | 9/50( 18.0) | 6/50( 12.0) | 5/50( 10.0) | 10/50( 20.0) |
| Adjusted rates(b)                              | 15.63       | 3.03        | 6.06        | 19.51        |
| Terminal rates(c)                              | 5/32( 15.6) | 1/33( 3.0)  | 2/33( 6.1)  | 8/41( 19.5)  |
| Statistical analysis                           |             |             |             |              |
| Peto test                                      |             |             |             |              |
| Standard method(d)                             | P = 0.8914  |             |             |              |
| Prevalence method(d)                           | P = 0.0818  |             |             |              |
| Combined analysis(d)                           | P = 0.4334  |             |             |              |
| Cochran-Armitage test(e)                       | P = 0.5113  |             |             |              |
| Fisher Exact test(e)                           |             | P = 0.2883  | P = 0.1940  | P = 0.5000   |

STUDY No. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 2

| Group Name               | Control    | 32 ppm      | 80 ppm      | 200 ppm     |
|--------------------------|------------|-------------|-------------|-------------|
| SITE : ALL SITE          |            |             |             |             |
| TUMOR : hemangiosarcoma  |            |             |             |             |
| Tumor rate               |            |             |             |             |
| Overall rates(a)         | 2/50( 4.0) | 7/50( 14.0) | 7/50( 14.0) | 7/50( 14.0) |
| Adjusted rates(b)        | 0.0        | 18.18       | 18.18       | 12.20       |
| Terminal rates(c)        | 0/32( 0.0) | 6/33( 18.2) | 6/33( 18.2) | 5/41( 12.2) |
| Statistical analysis     |            |             |             |             |
| Peto test                |            |             |             |             |
| Standard method(d)       | P = 0.4678 |             |             |             |
| Prevalence method(d)     | P = 0.2385 |             |             |             |
| Combined analysis(d)     | P = 0.2653 |             |             |             |
| Cochran-Armitage test(e) | P = 0.2552 |             |             |             |
| Fisher Exact test(e)     |            | P = 0.0798  | P = 0.0798  | P = 0.0798  |

(HPT360A)

BAIS4

- (a): Number of tumor-bearing animals/number of animals examined at the site.  
 (b): Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.  
 (c): Observed tumor incidence at terminal kill.  
 (d): Beneath the control incidence are the P-values associated with the trend test.  
     Standard method : Death analysis  
     Prevalence method : Incidental tumor test  
     Combined analysis : Death analysis + Incidental tumor test  
 (e): The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.  
 ? : The conditional probabilities of the largest and smallest possible outcomes can not be estimated or this P-value is beyond the estimated P-value.  
 — : There is no data which should be statistical analysis.  
 Significant difference ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$   
 N.C.: Statistical value cannot be calculated and was not significant.



## APPENDIX O 2

### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS : FEMALE

STUDY No. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 SEX : FEMALE

NEOPLASTIC LESIONS--INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 6

| Group Name   | Control     | 32 ppm      | 80 ppm     | 200 ppm     |
|--|-------------|-------------|------------|-------------|
| SITE : subcutis<br>TUMOR : hemangioma, hemangiosarcoma |             |             |            |             |
| Tumor rate   |             |             |            |             |
| Overall rates(a)                                       | 3/50( 6.0)  | 0/50( 0.0)  | 0/50( 0.0) | 0/50( 0.0)  |
| Adjusted rates(b)                                      | 9.09        | 0.0         | 0.0        | 0.0         |
| Terminal rates(c)                                      | 2/29( 6.9)  | 0/28( 0.0)  | 0/26( 0.0) | 0/30( 0.0)  |
| Statistical analysis                                   |             |             |            |             |
| Peto test  |             |             |            |             |
| Standard method(d)                                     | P = -----   |             |            |             |
| Prevalence method(d)                                   | P = 0.9846  |             |            |             |
| Combined analysis(d)                                   | P = -----   |             |            |             |
| Cochran-Armitage test(e)                               | P = 0.0732  |             |            |             |
| Fisher Exact test(e)                                   |             | P = 0.1212  | P = 0.1212 | P = 0.1212  |
| SITE : lung<br>TUMOR : bronchiolar-alveolar adenoma    |             |             |            |             |
| Tumor rate   |             |             |            |             |
| Overall rates(a)                                       | 1/50( 2.0)  | 4/50( 8.0)  | 4/50( 8.0) | 4/50( 8.0)  |
| Adjusted rates(b)                                      | 3.45        | 10.71       | 11.43      | 11.76       |
| Terminal rates(c)                                      | 1/29( 3.4)  | 3/28( 10.7) | 2/26( 7.7) | 3/30( 10.0) |
| Statistical analysis                                   |             |             |            |             |
| Peto test  |             |             |            |             |
| Standard method(d)                                     | P = -----   |             |            |             |
| Prevalence method(d)                                   | P = 0.1631  |             |            |             |
| Combined analysis(d)                                   | P = -----   |             |            |             |
| Cochran-Armitage test(e)                               | P = 0.3770  |             |            |             |
| Fisher Exact test(e)                                   |             | P = 0.1811  | P = 0.1811 | P = 0.1811  |
| SITE : lung<br>TUMOR : bronchiolar-alveolar carcinoma  |             |             |            |             |
| Tumor rate   |             |             |            |             |
| Overall rates(a)                                       | 1/50( 2.0)  | 1/50( 2.0)  | 1/50( 2.0) | 4/50( 8.0)  |
| Adjusted rates(b)                                      | 2.17        | 3.57        | 3.85       | 9.38        |
| Terminal rates(c)                                      | 0/29( 0.0)  | 1/28( 3.6)  | 1/26( 3.8) | 2/30( 6.7)  |
| Statistical analysis                                   |             |             |            |             |
| Peto test  |             |             |            |             |
| Standard method(d)                                     | P = 0.1183  |             |            |             |
| Prevalence method(d)                                   | P = 0.0887  |             |            |             |
| Combined analysis(d)                                   | P = 0.0345* |             |            |             |
| Cochran-Armitage test(e)                               | P = 0.0638  |             |            |             |
| Fisher Exact test(e)                                   |             | P = 0.7525  | P = 0.7525 | P = 0.1811  |

STUDY No. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name  | Control      | 32 ppm       | 80 ppm       | 200 ppm      |
|---|--------------|--------------|--------------|--------------|
| SITE : lung<br>TUMOR : bronchiolar-alveolar adenoma, bronchiolar-alveolar carcinoma |              |              |              |              |
| Tumor rate  |              |              |              |              |
| Overall rates(a)  | 2/50( 4.0)   | 4/50( 8.0)   | 5/50( 10.0)  | 8/50( 16.0)  |
| Adjusted rates(b)   | 4.35         | 10.71        | 14.81        | 20.59        |
| Terminal rates(c)   | 1/29( 3.4)   | 3/28( 10.7)  | 3/26( 11.5)  | 5/30( 16.7)  |
| Statistical analysis  |              |              |              |              |
| Peto test   |              |              |              |              |
| Standard method(d)  | P = 0.1183   |              |              |              |
| Prevalence method(d)  | P = 0.0365*  |              |              |              |
| Combined analysis(d)  | P = 0.0175*  |              |              |              |
| Cochran-Armitage test(e)  | P = 0.0403*  |              |              |              |
| Fisher Exact test(e)  |              | P = 0.3389   | P = 0.2180   | P = 0.0458*  |
| SITE : lymph node<br>TUMOR : malignant lymphoma                                     |              |              |              |              |
| Tumor rate  |              |              |              |              |
| Overall rates(a)  | 14/50( 28.0) | 21/50( 42.0) | 16/50( 32.0) | 11/50( 22.0) |
| Adjusted rates(b)   | 31.03        | 32.14        | 26.92        | 16.13        |
| Terminal rates(c)   | 9/29( 31.0)  | 9/28( 32.1)  | 7/26( 26.9)  | 4/30( 13.3)  |
| Statistical analysis  |              |              |              |              |
| Peto test   |              |              |              |              |
| Standard method(d)  | P = 0.5856   |              |              |              |
| Prevalence method(d)  | P = 0.9098   |              |              |              |
| Combined analysis(d)  | P = 0.8521   |              |              |              |
| Cochran-Armitage test(e)  | P = 0.1687   |              |              |              |
| Fisher Exact test(e)  |              | P = 0.1041   | P = 0.4138   | P = 0.3224   |
| SITE : stomach<br>TUMOR : squamous cell papilloma                                   |              |              |              |              |
| Tumor rate  |              |              |              |              |
| Overall rates(a)  | 3/50( 6.0)   | 0/50( 0.0)   | 1/50( 2.0)   | 3/50( 6.0)   |
| Adjusted rates(b)   | 6.90         | 0.0          | 3.70         | 6.67         |
| Terminal rates(c)   | 2/29( 6.9)   | 0/28( 0.0)   | 0/26( 0.0)   | 2/30( 6.7)   |
| Statistical analysis  |              |              |              |              |
| Peto test   |              |              |              |              |
| Standard method(d)  | P = -----    |              |              |              |
| Prevalence method(d)  | P = 0.2519   |              |              |              |
| Combined analysis(d)  | P = -----    |              |              |              |
| Cochran-Armitage test(e)  | P = 0.4974   |              |              |              |
| Fisher Exact test(e)  |              | P = 0.1212   | P = 0.3087   | P = 0.6611   |

STUDY No. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 8

| Group Name  | Control     | 32 ppm      | 80 ppm      | 200 ppm     |
|---|-------------|-------------|-------------|-------------|
| SITE : liver<br>TUMOR : hemangioma                  |             |             |             |             |
| Tumor rate  |             |             |             |             |
| Overall rates(a)                                    | 1/50( 2.0)  | 1/50( 2.0)  | 1/50( 2.0)  | 3/50( 6.0)  |
| Adjusted rates(b)                                   | 3.45        | 3.57        | 3.85        | 6.98        |
| Terminal rates(c)                                   | 1/29( 3.4)  | 1/28( 3.6)  | 1/26( 3.8)  | 2/30( 6.7)  |
| Statistical analysis                                |             |             |             |             |
| Peto test   |             |             |             |             |
| Standard method(d)                                  | P = -----   |             |             |             |
| Prevalence method(d)                                | P = 0.1050  |             |             |             |
| Combined analysis(d)                                | P = -----   |             |             |             |
| Cochran-Armitage test(e)                            | P = 0.1831  |             |             |             |
| Fisher Exact test(e)                                |             | P = 0.7525  | P = 0.7525  | P = 0.3087  |
| SITE : liver<br>TUMOR : hepatocellular adenoma      |             |             |             |             |
| Tumor rate  |             |             |             |             |
| Overall rates(a)                                    | 6/50( 12.0) | 7/50( 14.0) | 9/50( 18.0) | 8/50( 16.0) |
| Adjusted rates(b)                                   | 17.24       | 23.33       | 30.77       | 26.67       |
| Terminal rates(c)                                   | 5/29( 17.2) | 6/28( 21.4) | 8/26( 30.8) | 8/30( 26.7) |
| Statistical analysis                                |             |             |             |             |
| Peto test   |             |             |             |             |
| Standard method(d)                                  | P = -----   |             |             |             |
| Prevalence method(d)                                | P = 0.2368  |             |             |             |
| Combined analysis(d)                                | P = -----   |             |             |             |
| Cochran-Armitage test(e)                            | P = 0.5949  |             |             |             |
| Fisher Exact test(e)                                |             | P = 0.5000  | P = 0.2883  | P = 0.3871  |
| SITE : liver<br>TUMOR : hemangioma, hemangiosarcoma |             |             |             |             |
| Tumor rate  |             |             |             |             |
| Overall rates(a)                                    | 3/50( 6.0)  | 1/50( 2.0)  | 1/50( 2.0)  | 4/50( 8.0)  |
| Adjusted rates(b)                                   | 8.57        | 3.57        | 3.85        | 10.00       |
| Terminal rates(c)                                   | 2/29( 6.9)  | 1/28( 3.6)  | 1/26( 3.8)  | 3/30( 10.0) |
| Statistical analysis                                |             |             |             |             |
| Peto test   |             |             |             |             |
| Standard method(d)                                  | P = -----   |             |             |             |
| Prevalence method(d)                                | P = 0.1566  |             |             |             |
| Combined analysis(d)                                | P = -----   |             |             |             |
| Cochran-Armitage test(e)                            | P = 0.3458  |             |             |             |
| Fisher Exact test(e)                                |             | P = 0.3087  | P = 0.3087  | P = 0.5000  |

STUDY No. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name   | Control      | 32 ppm       | 80 ppm       | 200 ppm      |
|--|--------------|--------------|--------------|--------------|
| SITE : liver<br>TUMOR : hepatocellular adenoma, hepatocellular carcinoma |              |              |              |              |
| Tumor rate   |              |              |              |              |
| Overall rates(a)   | 7/50( 14.0)  | 8/50( 16.0)  | 9/50( 18.0)  | 8/50( 16.0)  |
| Adjusted rates(b)  | 20.69        | 23.33        | 30.77        | 26.67        |
| Terminal rates(c)  | 6/29( 20.7)  | 6/28( 21.4)  | 8/26( 30.8)  | 8/30( 26.7)  |
| Statistical analysis   |              |              |              |              |
| Peto test  |              |              |              |              |
| Standard method(d)   | P = -----    |              |              |              |
| Prevalence method(d)   | P = 0.3531   |              |              |              |
| Combined analysis(d)   | P = -----    |              |              |              |
| Cochran-Armitage test(e)   | P = 0.8391   |              |              |              |
| Fisher Exact test(e)   |              | P = 0.5000   | P = 0.3929   | P = 0.5000   |
| SITE : pituitary gland<br>TUMOR : adenoma                                |              |              |              |              |
| Tumor rate   |              |              |              |              |
| Overall rates(a)   | 16/49( 32.7) | 9/50( 18.0)  | 16/50( 32.0) | 14/50( 28.0) |
| Adjusted rates(b)  | 40.63        | 25.00        | 50.00        | 40.00        |
| Terminal rates(c)  | 11/29( 37.9) | 7/28( 25.0)  | 13/26( 50.0) | 12/30( 40.0) |
| Statistical analysis   |              |              |              |              |
| Peto test  |              |              |              |              |
| Standard method(d)   | P = 0.5075   |              |              |              |
| Prevalence method(d)   | P = 0.3019   |              |              |              |
| Combined analysis(d)   | P = 0.3233   |              |              |              |
| Cochran-Armitage test(e)   | P = 0.9062   |              |              |              |
| Fisher Exact test(e)   |              | P = 0.0737   | P = 0.6119   | P = 0.3879   |
| SITE : uterus<br>TUMOR : histiocytic sarcoma                             |              |              |              |              |
| Tumor rate   |              |              |              |              |
| Overall rates(a)   | 16/50( 32.0) | 15/50( 30.0) | 15/50( 30.0) | 11/50( 22.0) |
| Adjusted rates(b)  | 17.24        | 28.57        | 15.38        | 20.00        |
| Terminal rates(c)  | 5/29( 17.2)  | 8/28( 28.6)  | 4/26( 15.4)  | 6/30( 20.0)  |
| Statistical analysis   |              |              |              |              |
| Peto test  |              |              |              |              |
| Standard method(d)   | P = 0.7918   |              |              |              |
| Prevalence method(d)   | P = 0.6763   |              |              |              |
| Combined analysis(d)   | P = 0.8249   |              |              |              |
| Cochran-Armitage test(e)   | P = 0.2432   |              |              |              |
| Fisher Exact test(e)   |              | P = 0.5000   | P = 0.5000   | P = 0.1839   |

STUDY No. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 SEX : FEMALE

NEOPLASTIC LESIONS--INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 10

| Group Name                                     | Control    | 32 ppm     | 80 ppm     | 200 ppm    |
|--|------------|------------|------------|------------|
| SITE : mammary gland<br>TUMOR : adenocarcinoma |            |            |            |            |
| Tumor rate                                     |            |            |            |            |
| Overall rates(a)                               | 0/50( 0.0) | 0/50( 0.0) | 3/50( 6.0) | 1/50( 2.0) |
| Adjusted rates(b)                              | 0.0        | 0.0        | 3.85       | 3.33       |
| Terminal rates(c)                              | 0/29( 0.0) | 0/28( 0.0) | 1/26( 3.8) | 1/30( 3.3) |
| Statistical analysis                           |            |            |            |            |
| Peto test                                      |            |            |            |            |
| Standard method(d)                             | P = 0.4235 |            |            |            |
| Prevalence method(d)                           | P = 0.1596 |            |            |            |
| Combined analysis(d)                           | P = 0.2035 |            |            |            |
| Cochran-Armitage test(e)                       | P = 0.3948 |            |            |            |
| Fisher Exact test(e)                           |            | P = N.C.   | P = 0.1212 | P = 0.5000 |

(HPT360A)

BAIS4

- (a): Number of tumor-bearing animals/number of animals examined at the site.  
 (b): Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.  
 (c): Observed tumor incidence at terminal kill.  
 (d): Beneath the control incidence are the P-values associated with the trend test.  
     Standard method : Death analysis  
     Prevalence method : Incidental tumor test  
     Combined analysis : Death analysis + Incidental tumor test  
 (e): The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.  
 ? : The conditional probabilities of the largest and smallest possible outcomes can not be estimated or this P-value is beyond the estimated P-value.  
 — : There is no data which should be statistical analysis.  
 Significant difference ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$   
 N.C.: Statistical value cannot be calculated and was not significant.

STUDY No. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 3

| Group Name                                     | Control      | 32 ppm       | 80 ppm       | 200 ppm      |
|--|--------------|--------------|--------------|--------------|
| SITE : ALL SITE<br>TUMOR : hemangioma          |              |              |              |              |
| Tumor rate                                     |              |              |              |              |
| Overall rates(a)                               | 2/50( 4.0)   | 2/50( 4.0)   | 2/50( 4.0)   | 3/50( 6.0)   |
| Adjusted rates(b)                              | 6.06         | 7.14         | 7.69         | 6.98         |
| Terminal rates(c)                              | 1/29( 3.4)   | 2/28( 7.1)   | 2/26( 7.7)   | 2/30( 6.7)   |
| Statistical analysis                           |              |              |              |              |
| Peto test                                      |              |              |              |              |
| Standard method(d)                             | P = -----    |              |              |              |
| Prevalence method(d)                           | P = 0.2697   |              |              |              |
| Combined analysis(d)                           | P = -----    |              |              |              |
| Cochran-Armitage test(e)                       | P = 0.5839   |              |              |              |
| Fisher Exact test(e)                           |              | P = 0.6913   | P = 0.6913   | P = 0.5000   |
| SITE : ALL SITE<br>TUMOR : histiocytic sarcoma |              |              |              |              |
| Tumor rate                                     |              |              |              |              |
| Overall rates(a)                               | 16/50( 32.0) | 17/50( 34.0) | 17/50( 34.0) | 13/50( 26.0) |
| Adjusted rates(b)                              | 17.24        | 28.57        | 19.23        | 26.67        |
| Terminal rates(c)                              | 5/29( 17.2)  | 8/28( 28.6)  | 5/26( 19.2)  | 8/30( 26.7)  |
| Statistical analysis                           |              |              |              |              |
| Peto test                                      |              |              |              |              |
| Standard method(d)                             | P = 0.8396   |              |              |              |
| Prevalence method(d)                           | P = 0.4097   |              |              |              |
| Combined analysis(d)                           | P = 0.7311   |              |              |              |
| Cochran-Armitage test(e)                       | P = 0.4114   |              |              |              |
| Fisher Exact test(e)                           |              | P = 0.5000   | P = 0.5000   | P = 0.3299   |
| SITE : ALL SITE<br>TUMOR : malignant lymphoma  |              |              |              |              |
| Tumor rate                                     |              |              |              |              |
| Overall rates(a)                               | 15/50( 30.0) | 23/50( 46.0) | 16/50( 32.0) | 13/50( 26.0) |
| Adjusted rates(b)                              | 34.48        | 35.71        | 26.92        | 22.58        |
| Terminal rates(c)                              | 10/29( 34.5) | 10/28( 35.7) | 7/26( 26.9)  | 6/30( 20.0)  |
| Statistical analysis                           |              |              |              |              |
| Peto test                                      |              |              |              |              |
| Standard method(d)                             | P = 0.6213   |              |              |              |
| Prevalence method(d)                           | P = 0.8356   |              |              |              |
| Combined analysis(d)                           | P = 0.8132   |              |              |              |
| Cochran-Armitage test(e)                       | P = 0.2290   |              |              |              |
| Fisher Exact test(e)                           |              | P = 0.0744   | P = 0.5000   | P = 0.4120   |

STUDY No. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 4

| Group Name               | Control       | 32 ppm     | 80 ppm     | 200 ppm    |
|--------------------------|---------------|------------|------------|------------|
| SITE : ALL SITE          |               |            |            |            |
| TUMOR : hemangiosarcoma  |               |            |            |            |
| Tumor rate               |               |            |            |            |
| Overall rates(a)         | 4/50( 8.0)    | 0/50( 0.0) | 0/50( 0.0) | 3/50( 6.0) |
| Adjusted rates(b)        | 11.43         | 0.0        | 0.0        | 3.33       |
| Terminal rates(c)        | 3/29( 10.3)   | 0/28( 0.0) | 0/26( 0.0) | 1/30( 3.3) |
| Statistical analysis     |               |            |            |            |
| Peto test                |               |            |            |            |
| Standard method(d)       | P = 0.0169* ? |            |            |            |
| Prevalence method(d)     | P = 0.8476    |            |            |            |
| Combined analysis(d)     | P = 0.3468    |            |            |            |
| Cochran-Armitage test(e) | P = 0.7845    |            |            |            |
| Fisher Exact test(e)     |               | P = 0.0587 | P = 0.0587 | P = 0.5000 |

(HPT360A)

BAIS4

- (a): Number of tumor-bearing animals/number of animals examined at the site.  
 (b): Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.  
 (c): Observed tumor incidence at terminal kill.  
 (d): Beneath the control incidence are the P-values associated with the trend test.  
     Standard method : Death analysis  
     Prevalence method : Incidental tumor test  
     Combined analysis : Death analysis + Incidental tumor test  
 (e): The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.  
 ? : The conditional probabilities of the largest and smallest possible outcomes can not be estimated or this P-value is beyond the estimated P-value.  
 — : There is no data which should be statistical analysis.  
 Significant difference : \* :  $P \leq 0.05$     \*\* :  $P \leq 0.01$   
 N.C.:Statistical value cannot be calculated and was not significant.



## APPENDIX P 1

HISTOPATHOLOGICAL FINDINGS :

METASTASIS OF TUMOR :

MALE : ALL ANIMALS

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 1

|                                  |                                   | Group Name              | Control | 32 ppm | 80 ppm | 200 ppm |
|----------------------------------|-----------------------------------|-------------------------|---------|--------|--------|---------|
|                                  |                                   | No. of Animals on Study | 50      | 50     | 50     | 50      |
| Organ                            | Findings                          |                         |         |        |        |         |
| {Integumentary system/appandage} |                                   |                         |         |        |        |         |
| skin/app                         |                                   |                         | <50>    | <50>   | <50>   | <50>    |
|                                  | leukemic cell infiltration        |                         | 1       | 1      | 0      | 1       |
| subcutis                         |                                   |                         | <50>    | <50>   | <50>   | <50>    |
|                                  | leukemic cell infiltration        |                         | 1       | 0      | 0      | 0       |
| {Respiratory system}             |                                   |                         |         |        |        |         |
| nasal cavit                      |                                   |                         | <50>    | <50>   | <50>   | <50>    |
|                                  | leukemic cell infiltration        |                         | 2       | 1      | 0      | 1       |
|                                  | metastasis:subcutis tumor         |                         | 0       | 0      | 0      | 1       |
| lung                             | metastasis:peripheral nerve tumor |                         | 0       | 1      | 0      | 0       |
|                                  |                                   |                         | <50>    | <50>   | <50>   | <50>    |
|                                  | leukemic cell infiltration        |                         | 4       | 3      | 3      | 2       |
| lung                             | metastasis:liver tumor            |                         | 0       | 3      | 3      | 4       |
|                                  | metastasis:subcutis tumor         |                         | 0       | 0      | 2      | 0       |
|                                  | metastasis:peripheral nerve tumor |                         | 0       | 1      | 0      | 0       |
|                                  | metastasis:mammary gland tumor    |                         | 0       | 0      | 0      | 1       |
|                                  | metastasis:nasal tumor            |                         | 0       | 0      | 1      | 0       |
|                                  | metastasis:epididymis tumor       |                         | 1       | 0      | 0      | 0       |
|                                  |                                   |                         |         |        |        |         |
| {Hematopoietic system}           |                                   |                         |         |        |        |         |
| bone marrow                      |                                   |                         | <50>    | <50>   | <50>   | <50>    |
|                                  | leukemic cell infiltration        |                         | 4       | 4      | 1      | 0       |

< a > a : Number of animals examined at the site  
 b b : Number of animals with lesion

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 2

|                        |  | Group Name<br>No. of Animals on Study | Control<br>50 | 32 ppm<br>50 | 80 ppm<br>50 | 200 ppm<br>50 |
|------------------------|--|---------------------------------------|---------------|--------------|--------------|---------------|
| Organ                  | Findings                                   |                                       |               |              |              |               |
| {Hematopoietic system} |  |                                       |               |              |              |               |
| bone marrow            |  |                                       | <50>          | <50>         | <50>         | <50>          |
|                        | metastasis:liver tumor                     |                                       | 0             | 1            | 2            | 0             |
|                        | metastasis:nasal tumor                     |                                       | 0             | 0            | 1            | 0             |
| lymph node             |  |                                       | <50>          | <50>         | <50>         | <50>          |
|                        | metastasis:subcutis tumor                  |                                       | 0             | 0            | 1            | 0             |
| spleen                 |  |                                       | <50>          | <50>         | <50>         | <50>          |
|                        | leukemic cell infiltration                 |                                       | 7             | 5            | 4            | 8             |
|                        | metastasis:liver tumor                     |                                       | 0             | 1            | 1            | 0             |
| {Circulatory system}   |  |                                       |               |              |              |               |
| heart                  |  |                                       | <50>          | <50>         | <50>         | <50>          |
|                        | leukemic cell infiltration                 |                                       | 1             | 3            | 0            | 0             |
|                        | metastasis:liver tumor                     |                                       | 0             | 0            | 1            | 0             |
|                        | metastasis:mammary gland tumor             |                                       | 0             | 0            | 0            | 1             |
| {Digestive system}     |  |                                       |               |              |              |               |
| tooth                  |  |                                       | <50>          | <50>         | <50>         | <50>          |
|                        | leukemic cell infiltration                 |                                       | 1             | 0            | 0            | 0             |
| tongue                 |  |                                       | <50>          | <50>         | <50>         | <50>          |
|                        | leukemic cell infiltration                 |                                       | 0             | 1            | 0            | 1             |
| salivary gl            |  |                                       | <50>          | <50>         | <50>         | <50>          |
|                        | leukemic cell infiltration                 |                                       | 3             | 1            | 0            | 1             |
| stomach                |  |                                       | <50>          | <50>         | <50>         | <50>          |
|                        | leukemic cell infiltration                 |                                       | 2             | 1            | 0            | 0             |
| < a >                  | a : Number of animals examined at the site |                                       |               |              |              |               |
| b                      | b : Number of animals with lesion          |                                       |               |              |              |               |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 3

|                    |  | Group Name              | Control | 32 ppm | 80 ppm | 200 ppm |
|--------------------|--|-------------------------|---------|--------|--------|---------|
|                    |  | No. of Animals on Study | 50      | 50     | 50     | 50      |
| Organ              | Findings                                   |                         |         |        |        |         |
| {Digestive system} |  |                         |         |        |        |         |
| small intes        |  |                         | <50>    | <50>   | <50>   | <50>    |
|                    | leukemic cell infiltration                 |                         | 1       | 0      | 1      | 1       |
|                    | metastasis:epididymis tumor                |                         | 1       | 0      | 0      | 0       |
| liver              |  |                         | <50>    | <50>   | <50>   | <50>    |
|                    | leukemic cell infiltration                 |                         | 4       | 5      | 2      | 2       |
|                    | metastasis:subcutis tumor                  |                         | 1       | 0      | 1      | 0       |
|                    | metastasis:spleen tumor                    |                         | 0       | 0      | 1      | 0       |
|                    | metastasis:nasal tumor                     |                         | 1       | 0      | 0      | 0       |
|                    | metastasis:stomach tumor                   |                         | 0       | 1      | 0      | 0       |
|                    | metastasis:epididymis tumor                |                         | 1       | 0      | 0      | 1       |
| gall bladd         |  |                         | <50>    | <50>   | <50>   | <50>    |
|                    | leukemic cell infiltration                 |                         | 0       | 1      | 0      | 0       |
| pancreas           |  |                         | <50>    | <50>   | <50>   | <50>    |
|                    | leukemic cell infiltration                 |                         | 1       | 1      | 0      | 0       |
|                    | metastasis:liver tumor                     |                         | 0       | 1      | 0      | 0       |
|                    | metastasis:stomach tumor                   |                         | 0       | 1      | 0      | 0       |
| {Urinary system}   |  |                         |         |        |        |         |
| kidney             |  |                         | <50>    | <50>   | <50>   | <50>    |
|                    | leukemic cell infiltration                 |                         | 3       | 0      | 0      | 2       |
|                    | metastasis:liver tumor                     |                         | 0       | 1      | 0      | 0       |
| < a >              | a : Number of animals examined at the site |                         |         |        |        |         |
| b                  | b : Number of animals with lesion          |                         |         |        |        |         |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 4

|                       |                                | Group Name                                 | Control   | 32 ppm    | 80 ppm    | 200 ppm   |
|-----------------------|--------------------------------|--|-----------|-----------|-----------|-----------|
|                       |                                | No. of Animals on Study                    | 50        | 50        | 50        | 50        |
| Organ                 | Findings                       |  |           |           |           |           |
| {Urinary system}      |                                |  |           |           |           |           |
| kidney                | metastasis:subcutis tumor      |  | <50><br>0 | <50><br>0 | <50><br>1 | <50><br>0 |
|                       | metastasis:epididymis tumor    |  | 1         | 0         | 0         | 0         |
| urin bladd            | leukemic cell infiltration     |  | <50><br>3 | <50><br>2 | <50><br>0 | <50><br>1 |
| {Endocrine system}    |                                |  |           |           |           |           |
| thyroid               | leukemic cell infiltration     |  | <50><br>1 | <50><br>2 | <50><br>1 | <50><br>0 |
|                       | metastasis:subcutis tumor      |  | <50><br>0 | <50><br>0 | <50><br>1 | <50><br>0 |
| {Reproductive system} |                                |  |           |           |           |           |
| testis                | leukemic cell infiltration     |  | <50><br>0 | <50><br>1 | <50><br>0 | <50><br>0 |
|                       | metastasis:mammary gland tumor |  | 0         | 0         | 0         | 1         |
| epididymis            | leukemic cell infiltration     |  | <50><br>2 | <50><br>2 | <50><br>0 | <50><br>0 |
|                       | metastasis:subcutis tumor      |  | 1         | 0         | 0         | 0         |
| semin ves             | leukemic cell infiltration     |  | <50><br>0 | <50><br>3 | <50><br>0 | <50><br>0 |
|                       | leukemic cell infiltration     |  | <50><br>1 | <50><br>3 | <50><br>0 | <50><br>0 |
| < a >                 |                                | a : Number of animals examined at the site |           |           |           |           |
| b                     |                                | b : Number of animals with lesion          |           |           |           |           |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 5

| Group Name<br>No. of Animals on Study |                            | Control<br>50                              | 32 ppm<br>50 | 80 ppm<br>50 | 200 ppm<br>50 |
|---------------------------------------|----------------------------|--|--------------|--------------|---------------|
| Organ                                 | Findings                   |  |              |              |               |
| {Nervous system}                      |                            |  |              |              |               |
| brain                                 | leukemic cell infiltration | <50><br>0                                  | <50><br>1    | <50><br>0    | <50><br>0     |
|                                       | metastasis: nasal tumor    | 1  | 0            | 0            | 0             |
| {Special sense organs/appendage}      |                            |  |              |              |               |
| Harder gl                             | leukemic cell infiltration | <50><br>2                                  | <50><br>1    | <50><br>0    | <50><br>1     |
|                                       |                            |  |              |              |               |
| {Musculoskeletal system}              |                            |  |              |              |               |
| muscle                                | leukemic cell infiltration | <50><br>1                                  | <50><br>0    | <50><br>0    | <50><br>0     |
|                                       |                            |  |              |              |               |
| {Body cavities}                       |                            |  |              |              |               |
| mediastinum                           | metastasis: liver tumor    | <50><br>0                                  | <50><br>0    | <50><br>1    | <50><br>0     |
|                                       | metastasis: subcutis tumor | 0  | 0            | 1            | 0             |
| peritoneum                            | metastasis: stomach tumor  | <50><br>0                                  | <50><br>1    | <50><br>0    | <50><br>0     |
|                                       |                            |  |              |              |               |
| retroperit                            | leukemic cell infiltration | <50><br>0                                  | <50><br>0    | <50><br>0    | <50><br>1     |
|                                       |                            |  |              |              |               |
| < a >                                 |                            | a : Number of animals examined at the site |              |              |               |
| b                                     |                            | b : Number of animals with lesion          |              |              |               |

## APPENDIX P 2

HISTOPATHOLOGICAL FINDINGS :

METASTASIS OF TUMOR :

MALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 1

|                                  |                                   | Group Name<br>No. of Animals on Study | Control<br>18 | 32 ppm<br>17 | 80 ppm<br>17 | 200 ppm<br>9 |
|----------------------------------|-----------------------------------|---------------------------------------|---------------|--------------|--------------|--------------|
| Organ                            | Findings                          |                                       |               |              |              |              |
| {Integumentary system/appandage} |                                   |                                       |               |              |              |              |
| skin/app                         |                                   |                                       | <18>          | <17>         | <17>         | < 9>         |
|                                  | leukemic cell infiltration        |                                       | 1             | 1            | 0            | 1            |
| subcutis                         |                                   |                                       | <18>          | <17>         | <17>         | < 9>         |
|                                  | leukemic cell infiltration        |                                       | 1             | 0            | 0            | 0            |
| {Respiratory system}             |                                   |                                       |               |              |              |              |
| nasal cavit                      |                                   |                                       | <18>          | <17>         | <17>         | < 9>         |
|                                  | leukemic cell infiltration        |                                       | 2             | 1            | 0            | 1            |
|                                  | metastasis:peripheral nerve tumor |                                       | 0             | 1            | 0            | 0            |
| lung                             |                                   |                                       | <18>          | <17>         | <17>         | < 9>         |
|                                  | leukemic cell infiltration        |                                       | 3             | 3            | 3            | 2            |
|                                  | metastasis:liver tumor            |                                       | 0             | 3            | 3            | 1            |
|                                  | metastasis:subcutis tumor         |                                       | 0             | 0            | 1            | 0            |
|                                  | metastasis:peripheral nerve tumor |                                       | 0             | 1            | 0            | 0            |
|                                  | metastasis:mammary gland tumor    |                                       | 0             | 0            | 0            | 1            |
|                                  | metastasis:nasal tumor            |                                       | 0             | 0            | 1            | 0            |
|                                  | metastasis:epididymis tumor       |                                       | 1             | 0            | 0            | 0            |
| {Hematopoietic system}           |                                   |                                       |               |              |              |              |
| bone marrow                      |                                   |                                       | <18>          | <17>         | <17>         | < 9>         |
|                                  | leukemic cell infiltration        |                                       | 1             | 4            | 1            | 0            |
|                                  | metastasis:liver tumor            |                                       | 0             | 1            | 2            | 0            |

< a > a : Number of animals examined at the site  
 b b : Number of animals with lesion



STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 2

| Group Name<br>No. of Animals on Study |                                 | Control<br>18 | 32 ppm<br>17 | 80 ppm<br>17 | 200 ppm<br>9 |
|---------------------------------------|---------------------------------|---------------|--------------|--------------|--------------|
| Organ                                 | Findings                        |               |              |              |              |
| {Hematopoietic system}                |                                 |               |              |              |              |
| bone marrow                           | metastasis: nasal tumor         | <18><br>0     | <17><br>0    | <17><br>1    | < 9><br>0    |
| spleen                                | leukemic cell infiltration      | <18><br>4     | <17><br>4    | <17><br>3    | < 9><br>2    |
|                                       | metastasis: liver tumor         | 0             | 1            | 1            | 0            |
| {Circulatory system}                  |                                 |               |              |              |              |
| heart                                 | leukemic cell infiltration      | <18><br>1     | <17><br>3    | <17><br>0    | < 9><br>0    |
|                                       | metastasis: liver tumor         | 0             | 0            | 1            | 0            |
|                                       | metastasis: mammary gland tumor | 0             | 0            | 0            | 1            |
| {Digestive system}                    |                                 |               |              |              |              |
| tooth                                 | leukemic cell infiltration      | <18><br>1     | <17><br>0    | <17><br>0    | < 9><br>0    |
| tongue                                | leukemic cell infiltration      | <18><br>0     | <17><br>1    | <17><br>0    | < 9><br>1    |
| salivary gl                           | leukemic cell infiltration      | <18><br>2     | <17><br>1    | <17><br>0    | < 9><br>1    |
| stomach                               | leukemic cell infiltration      | <18><br>2     | <17><br>1    | <17><br>0    | < 9><br>0    |
| small intes                           | leukemic cell infiltration      | <18><br>1     | <17><br>0    | <17><br>1    | < 9><br>0    |

< a > a : Number of animals examined at the site  
 b b : Number of animals with lesion

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : MALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 3

|                    |                             | Group Name<br>No. of Animals on Study | Control<br>18 | 32 ppm<br>17 | 80 ppm<br>17 | 200 ppm<br>9 |
|--------------------|-----------------------------|---------------------------------------|---------------|--------------|--------------|--------------|
| Organ              | Findings                    |                                       |               |              |              |              |
| {Digestive system} |                             |                                       |               |              |              |              |
| small intes        |                             |                                       | <18>          | <17>         | <17>         | < 9>         |
|                    | metastasis:epididymis tumor |                                       | 1             | 0            | 0            | 0            |
| liver              |                             |                                       | <18>          | <17>         | <17>         | < 9>         |
|                    | leukemic cell infiltration  |                                       | 3             | 4            | 2            | 1            |
|                    | metastasis:subcutis tumor   |                                       | 1             | 0            | 0            | 0            |
|                    | metastasis:nasal tumor      |                                       | 1             | 0            | 0            | 0            |
|                    | metastasis:stomach tumor    |                                       | 0             | 1            | 0            | 0            |
|                    | metastasis:epididymis tumor |                                       | 1             | 0            | 0            | 1            |
| gall bladd         |                             |                                       | <18>          | <17>         | <17>         | < 9>         |
|                    | leukemic cell infiltration  |                                       | 0             | 1            | 0            | 0            |
| pancreas           |                             |                                       | <18>          | <17>         | <17>         | < 9>         |
|                    | leukemic cell infiltration  |                                       | 1             | 1            | 0            | 0            |
|                    | metastasis:liver tumor      |                                       | 0             | 1            | 0            | 0            |
|                    | metastasis:stomach tumor    |                                       | 0             | 1            | 0            | 0            |
| {Urinary system}   |                             |                                       |               |              |              |              |
| kidney             |                             |                                       | <18>          | <17>         | <17>         | < 9>         |
|                    | leukemic cell infiltration  |                                       | 2             | 0            | 0            | 0            |
|                    | metastasis:liver tumor      |                                       | 0             | 1            | 0            | 0            |
|                    | metastasis:epididymis tumor |                                       | 1             | 0            | 0            | 0            |
| urin bladd         |                             |                                       | <18>          | <17>         | <17>         | < 9>         |
|                    | leukemic cell infiltration  |                                       | 2             | 2            | 0            | 1            |

< a > a : Number of animals examined at the site  
b b : Number of animals with lesion

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 4

|                                  |                                | Group Name<br>No. of Animals on Study | Control<br>18 | 32 ppm<br>17 | 80 ppm<br>17 | 200 ppm<br>9 |
|----------------------------------|--------------------------------|---------------------------------------|---------------|--------------|--------------|--------------|
| Organ                            | Findings                       |                                       |               |              |              |              |
| {Endocrine system}               |                                |                                       |               |              |              |              |
| thyroid                          | leukemic cell infiltration     |                                       | <18><br>1     | <17><br>2    | <17><br>1    | < 9><br>0    |
| {Reproductive system}            |                                |                                       |               |              |              |              |
| testis                           | leukemic cell infiltration     |                                       | <18><br>0     | <17><br>1    | <17><br>0    | < 9><br>0    |
|                                  | metastasis:mammary gland tumor |                                       | 0             | 0            | 0            | 1            |
| epididymis                       | leukemic cell infiltration     |                                       | <18><br>2     | <17><br>2    | <17><br>0    | < 9><br>0    |
|                                  | metastasis:subcutis tumor      |                                       | 1             | 0            | 0            | 0            |
| semin ves                        | leukemic cell infiltration     |                                       | <18><br>0     | <17><br>3    | <17><br>0    | < 9><br>0    |
| prostate                         | leukemic cell infiltration     |                                       | <18><br>1     | <17><br>3    | <17><br>0    | < 9><br>0    |
| {Nervous system}                 |                                |                                       |               |              |              |              |
| brain                            | leukemic cell infiltration     |                                       | <18><br>0     | <17><br>1    | <17><br>0    | < 9><br>0    |
|                                  | metastasis:nasal tumor         |                                       | 1             | 0            | 0            | 0            |
| {Special sense organs/appendage} |                                |                                       |               |              |              |              |
| Harder gl                        | leukemic cell infiltration     |                                       | <18><br>2     | <17><br>1    | <17><br>0    | < 9><br>1    |

< a > a : Number of animals examined at the site  
 b b : Number of animals with lesion

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : MALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 5

| Group Name               |                            | Control | 32 ppm | 80 ppm | 200 ppm |
|--------------------------|----------------------------|---------|--------|--------|---------|
| No. of Animals on Study  |                            | 18      | 17     | 17     | 9       |
| Organ                    | Findings                   |         |        |        |         |
| {Musculoskeletal system} |                            |         |        |        |         |
| muscle                   |                            | <18>    | <17>   | <17>   | < 9>    |
|                          | leukemic cell infiltration | 1       | 0      | 0      | 0       |
| {Body cavities}          |                            |         |        |        |         |
| mediastinum              |                            | <18>    | <17>   | <17>   | < 9>    |
|                          | metastasis:liver tumor     | 0       | 0      | 1      | 0       |
|                          | metastasis:subcutis tumor  | 0       | 0      | 1      | 0       |
| peritoneum               |                            | <18>    | <17>   | <17>   | < 9>    |
|                          | metastasis:stomach tumor   | 0       | 1      | 0      | 0       |
| retroperit               |                            | <18>    | <17>   | <17>   | < 9>    |
|                          | leukemic cell infiltration | 0       | 0      | 0      | 1       |

< a > a : Number of animals examined at the site  
b b : Number of animals with lesion

(JPT150)

BAIS4

## APPENDIX P 3

HISTOPATHOLOGICAL FINDINGS :

METASTASIS OF TUMOR :

MALE : SACRIFICED ANIMALS

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Crlj[Crlj:BDF1]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 SACRIFICED ANIMALS (105W)

PAGE : 1

|                        |                            | Group Name              | Control | 32 ppm | 80 ppm | 200 ppm |
|------------------------|----------------------------|-------------------------|---------|--------|--------|---------|
|                        |                            | No. of Animals on Study | 32      | 33     | 33     | 41      |
| Organ                  | Findings                   |                         |         |        |        |         |
| {Respiratory system}   |                            |                         |         |        |        |         |
| nasal cavit            |                            |                         | <32>    | <33>   | <33>   | <41>    |
|                        | metastasis:subcutis tumor  |                         | 0       | 0      | 0      | 1       |
| lung                   |                            |                         | <32>    | <33>   | <33>   | <41>    |
|                        | leukemic cell infiltration |                         | 1       | 0      | 0      | 0       |
|                        | metastasis:liver tumor     |                         | 0       | 0      | 0      | 3       |
|                        | metastasis:subcutis tumor  |                         | 0       | 0      | 1      | 0       |
| {Hematopoietic system} |                            |                         |         |        |        |         |
| bone marrow            |                            |                         | <32>    | <33>   | <33>   | <41>    |
|                        | leukemic cell infiltration |                         | 3       | 0      | 0      | 0       |
| lymph node             |                            |                         | <32>    | <33>   | <33>   | <41>    |
|                        | metastasis:subcutis tumor  |                         | 0       | 0      | 1      | 0       |
| spleen                 |                            |                         | <32>    | <33>   | <33>   | <41>    |
|                        | leukemic cell infiltration |                         | 3       | 1      | 1      | 6       |
| {Digestive system}     |                            |                         |         |        |        |         |
| salivary gl            |                            |                         | <32>    | <33>   | <33>   | <41>    |
|                        | leukemic cell infiltration |                         | 1       | 0      | 0      | 0       |
| small intes            |                            |                         | <32>    | <33>   | <33>   | <41>    |
|                        | leukemic cell infiltration |                         | 0       | 0      | 0      | 1       |
| liver                  |                            |                         | <32>    | <33>   | <33>   | <41>    |
|                        | leukemic cell infiltration |                         | 1       | 1      | 0      | 1       |
|                        | metastasis:subcutis tumor  |                         | 0       | 0      | 1      | 0       |

< a > a : Number of animals examined at the site  
 b b : Number of animals with lesion

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Crlj[Crlj:BDF1]  
REPORT TYPE : A1  
SEX : MALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
SACRIFICED ANIMALS (105W)

PAGE : 2

|                    |  | Group Name              | Control | 32 ppm | 80 ppm | 200 ppm |
|--------------------|--|-------------------------|---------|--------|--------|---------|
|                    |  | No. of Animals on Study | 32      | 33     | 33     | 41      |
| Organ              | Findings                                   |                         |         |        |        |         |
| {Digestive system} |  |                         |         |        |        |         |
| liver              |  |                         | <32>    | <33>   | <33>   | <41>    |
|                    | metastasis:spleen tumor                    |                         | 0       | 0      | 1      | 0       |
| {Urinary system}   |  |                         |         |        |        |         |
| kidney             |  |                         | <32>    | <33>   | <33>   | <41>    |
|                    | leukemic cell infiltration                 |                         | 1       | 0      | 0      | 2       |
| urin bladd         |  |                         | <32>    | <33>   | <33>   | <41>    |
|                    | metastasis:subcutis tumor                  |                         | 0       | 0      | 1      | 0       |
| urin bladd         |  |                         | <32>    | <33>   | <33>   | <41>    |
|                    | leukemic cell infiltration                 |                         | 1       | 0      | 0      | 0       |
| {Endocrine system} |  |                         |         |        |        |         |
| adrenal            |  |                         | <32>    | <33>   | <33>   | <41>    |
|                    | metastasis:subcutis tumor                  |                         | 0       | 0      | 1      | 0       |
| < a >              | a : Number of animals examined at the site |                         |         |        |        |         |
| b                  | b : Number of animals with lesion          |                         |         |        |        |         |

## APPENDIX P 4

HISTOPATHOLOGICAL FINDINGS :

METASTASIS OF TUMOR :

FEMALE : ALL ANIMALS



STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 6

|                                  |                                | Group Name              | Control | 32 ppm | 80 ppm | 200 ppm |
|----------------------------------|--------------------------------|-------------------------|---------|--------|--------|---------|
|                                  |                                | No. of Animals on Study | 50      | 50     | 50     | 50      |
| Organ_____                       | Findings_____                  |                         |         |        |        |         |
|                                  |                                |                         |         |        |        |         |
| {Integumentary system/appandage} |                                |                         |         |        |        |         |
| skin/app                         |                                | <50>                    | <50>    | <50>   | <50>   |         |
|                                  | leukemic cell infiltration     | 2                       | 3       | 1      | 3      |         |
| subcutis                         |                                | <50>                    | <50>    | <50>   | <50>   |         |
|                                  | leukemic cell infiltration     | 0                       | 2       | 1      | 1      |         |
|                                  | metastasis:liver tumor         | 0                       | 0       | 0      | 1      |         |
|                                  | metastasis:uterus tumor        | 1                       | 0       | 0      | 0      |         |
|                                  | metastasis:mammary gland tumor | 0                       | 0       | 3      | 1      |         |
| {Respiratory system}             |                                |                         |         |        |        |         |
| nasal cavit                      |                                | <50>                    | <50>    | <50>   | <50>   |         |
|                                  | leukemic cell infiltration     | 1                       | 3       | 1      | 2      |         |
|                                  | metastasis:uterus tumor        | 0                       | 1       | 0      | 0      |         |
| larynx                           |                                | <50>                    | <50>    | <50>   | <50>   |         |
|                                  | leukemic cell infiltration     | 1                       | 0       | 0      | 0      |         |
| trachea                          |                                | <50>                    | <50>    | <50>   | <50>   |         |
|                                  | leukemic cell infiltration     | 1                       | 0       | 0      | 1      |         |
| lung                             |                                | <50>                    | <50>    | <50>   | <50>   |         |
|                                  | leukemic cell infiltration     | 5                       | 10      | 9      | 7      |         |
|                                  | metastasis:liver tumor         | 0                       | 1       | 0      | 0      |         |
|                                  | metastasis:uterus tumor        | 4                       | 3       | 5      | 1      |         |
|                                  | metastasis:mammary gland tumor | 0                       | 0       | 1      | 0      |         |
| {Hematopoietic system}           |                                |                         |         |        |        |         |
| bone marrow                      |                                | <50>                    | <50>    | <50>   | <50>   |         |
|                                  | leukemic cell infiltration     | 3                       | 6       | 3      | 5      |         |

< a > a : Number of animals examined at the site  
 b b : Number of animals with lesion

STUDY NO. : 0458  
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
REPORT TYPE : A1  
SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
ALL ANIMALS (0-105W)

PAGE : 7

|                        |  | Group Name<br>No. of Animals on Study | Control<br>50 | 32 ppm<br>50 | 80 ppm<br>50 | 200 ppm<br>50 |
|------------------------|--|---------------------------------------|---------------|--------------|--------------|---------------|
| Organ                  | Findings                                   |                                       |               |              |              |               |
| {Hematopoietic system} |  |                                       |               |              |              |               |
| bone marrow            |  |                                       | <50>          | <50>         | <50>         | <50>          |
|                        | metastasis:liver tumor                     |                                       | 0             | 1            | 0            | 0             |
|                        | metastasis:uterus tumor                    |                                       | 4             | 2            | 0            | 2             |
| lymph node             |  |                                       | <50>          | <50>         | <50>         | <50>          |
|                        | leukemic cell infiltration                 |                                       | 0             | 1            | 0            | 0             |
|                        | metastasis:uterus tumor                    |                                       | 3             | 0            | 1            | 0             |
| spleen                 |  |                                       | <50>          | <50>         | <50>         | <50>          |
|                        | leukemic cell infiltration                 |                                       | 3             | 13           | 12           | 8             |
|                        | metastasis:liver tumor                     |                                       | 0             | 1            | 0            | 0             |
|                        | metastasis:uterus tumor                    |                                       | 1             | 0            | 0            | 0             |
|                        | metastasis:lymph node tumor                |                                       | 0             | 0            | 1            | 0             |
| {Circulatory system}   |  |                                       |               |              |              |               |
| heart                  |  |                                       | <50>          | <50>         | <50>         | <50>          |
|                        | leukemic cell infiltration                 |                                       | 1             | 6            | 6            | 4             |
|                        | metastasis:uterus tumor                    |                                       | 0             | 1            | 0            | 0             |
| {Digestive system}     |  |                                       |               |              |              |               |
| tooth                  |  |                                       | <50>          | <50>         | <50>         | <50>          |
|                        | leukemic cell infiltration                 |                                       | 1             | 1            | 0            | 1             |
|                        | metastasis:uterus tumor                    |                                       | 1             | 0            | 2            | 0             |
| tongue                 |  |                                       | <50>          | <50>         | <50>         | <50>          |
|                        | leukemic cell infiltration                 |                                       | 1             | 3            | 1            | 3             |
|                        |  |                                       |               |              |              |               |
| < a >                  | a : Number of animals examined at the site |                                       |               |              |              |               |
| b                      | b : Number of animals with lesion          |                                       |               |              |              |               |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 8

|                    |                             | Group Name              | Control | 32 ppm | 80 ppm | 200 ppm |
|--------------------|-----------------------------|-------------------------|---------|--------|--------|---------|
|                    |                             | No. of Animals on Study | 50      | 50     | 50     | 50      |
| Organ              | Findings                    |                         |         |        |        |         |
| {Digestive system} |                             |                         |         |        |        |         |
| salivary gl        |                             |                         | <50>    | <50>   | <50>   | <50>    |
|                    | leukemic cell infiltration  |                         | 3       | 8      | 4      | 3       |
| stomach            |                             |                         | <50>    | <50>   | <50>   | <50>    |
|                    | leukemic cell infiltration  |                         | 2       | 3      | 1      | 1       |
|                    | metastasis:uterus tumor     |                         | 0       | 0      | 1      | 0       |
|                    | metastasis:lymph node tumor |                         | 0       | 0      | 1      | 0       |
| small intes        |                             |                         | <50>    | <50>   | <50>   | <50>    |
|                    | leukemic cell infiltration  |                         | 1       | 1      | 0      | 0       |
| liver              |                             |                         | <50>    | <50>   | <50>   | <50>    |
|                    | leukemic cell infiltration  |                         | 4       | 13     | 7      | 9       |
|                    | metastasis:uterus tumor     |                         | 10      | 6      | 12     | 6       |
|                    | metastasis:subcutis tumor   |                         | 1       | 0      | 0      | 0       |
|                    | metastasis:lymph node tumor |                         | 0       | 0      | 1      | 0       |
| gall bladd         |                             |                         | <50>    | <50>   | <50>   | <50>    |
|                    | leukemic cell infiltration  |                         | 1       | 1      | 1      | 0       |
| pancreas           |                             |                         | <50>    | <50>   | <50>   | <50>    |
|                    | leukemic cell infiltration  |                         | 2       | 5      | 2      | 3       |
|                    | metastasis:uterus tumor     |                         | 4       | 0      | 3      | 0       |
| {Urinary system}   |                             |                         |         |        |        |         |
| kidney             |                             |                         | <50>    | <50>   | <50>   | <50>    |
|                    | leukemic cell infiltration  |                         | 2       | 12     | 3      | 5       |

< a > a : Number of animals examined at the site  
 b b : Number of animals with lesion

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 9

|                       |  | Group Name              | Control | 32 ppm | 80 ppm | 200 ppm |
|-----------------------|--|-------------------------|---------|--------|--------|---------|
|                       |  | No. of Animals on Study | 50      | 50     | 50     | 50      |
| Organ                 | Findings                                   |                         |         |        |        |         |
| {Urinary system}      |  |                         |         |        |        |         |
| kidney                |  |                         | <50>    | <50>   | <50>   | <50>    |
|                       | metastasis:uterus tumor                    |                         | 4       | 0      | 2      | 0       |
| urin bladd            |  |                         | <50>    | <50>   | <50>   | <50>    |
|                       | leukemic cell infiltration                 |                         | 0       | 12     | 7      | 6       |
|                       | metastasis:uterus tumor                    |                         | 3       | 1      | 1      | 0       |
| {Endocrine system}    |  |                         |         |        |        |         |
| pituitary             |  |                         | <50>    | <50>   | <50>   | <50>    |
|                       | leukemic cell infiltration                 |                         | 0       | 1      | 0      | 1       |
|                       | metastasis:peripheral nerve tumor          |                         | 0       | 0      | 1      | 0       |
| thyroid               |  |                         | <50>    | <50>   | <50>   | <50>    |
|                       | leukemic cell infiltration                 |                         | 0       | 0      | 0      | 1       |
| adrenal               |  |                         | <50>    | <50>   | <50>   | <50>    |
|                       | leukemic cell infiltration                 |                         | 1       | 1      | 0      | 2       |
| {Reproductive system} |  |                         |         |        |        |         |
| ovary                 |  |                         | <50>    | <50>   | <50>   | <50>    |
|                       | leukemic cell infiltration                 |                         | 1       | 10     | 6      | 7       |
|                       | metastasis:uterus tumor                    |                         | 6       | 4      | 8      | 7       |
|                       | metastasis:retroperitoneum tumor           |                         | 0       | 1      | 0      | 0       |
| uterus                |  |                         | <50>    | <50>   | <50>   | <50>    |
|                       | leukemic cell infiltration                 |                         | 0       | 2      | 1      | 3       |
| vagina                |  |                         | <50>    | <50>   | <50>   | <50>    |
|                       | leukemic cell infiltration                 |                         | 1       | 4      | 0      | 3       |
|                       |  |                         |         |        |        |         |
| < a >                 | a : Number of animals examined at the site |                         |         |        |        |         |
| b                     | b : Number of animals with lesion          |                         |         |        |        |         |

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 10

| Group Name<br>No. of Animals on Study |  | Control<br>50 | 32 ppm<br>50 | 80 ppm<br>50 | 200 ppm<br>50 |
|---------------------------------------|--|---------------|--------------|--------------|---------------|
| Organ                                 | Findings                                   |               |              |              |               |
| {Reproductive system}                 |  |               |              |              |               |
| vagina                                | metastasis:uterus tumor                    | <50><br>4     | <50><br>0    | <50><br>0    | <50><br>0     |
| mammary gl                            | leukemic cell infiltration                 | <50><br>1     | <50><br>1    | <50><br>0    | <50><br>0     |
| {Nervous system}                      |  |               |              |              |               |
| brain                                 | leukemic cell infiltration                 | <50><br>0     | <50><br>1    | <50><br>0    | <50><br>2     |
| spinal cord                           | leukemic cell infiltration                 | <50><br>0     | <50><br>1    | <50><br>0    | <50><br>0     |
| {Special sense organs/appendage}      |  |               |              |              |               |
| Harder gl                             | leukemic cell infiltration                 | <50><br>1     | <50><br>6    | <50><br>2    | <50><br>2     |
| {Musculoskeletal system}              |  |               |              |              |               |
| muscle                                | leukemic cell infiltration                 | <50><br>2     | <50><br>3    | <50><br>1    | <50><br>3     |
| {Body cavities}                       |  |               |              |              |               |
| mediastinum                           | leukemic cell infiltration                 | <50><br>1     | <50><br>1    | <50><br>3    | <50><br>1     |
| peritoneum                            | leukemic cell infiltration                 | <50><br>0     | <50><br>2    | <50><br>0    | <50><br>1     |
| < a >                                 | a : Number of animals examined at the site |               |              |              |               |
| b                                     | b : Number of animals with lesion          |               |              |              |               |

## APPENDIX P 5

HISTOPATHOLOGICAL FINDINGS :

METASTASIS OF TUMOR :

FEMALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 6

|                                  |                                | Group Name<br>No. of Animals on Study | Control<br>21 | 32 ppm<br>22 | 80 ppm<br>24 | 200 ppm<br>20 |
|----------------------------------|--------------------------------|---------------------------------------|---------------|--------------|--------------|---------------|
| Organ                            | Findings                       |                                       |               |              |              |               |
| {Integumentary system/appandage} |                                |                                       |               |              |              |               |
| skin/app                         |                                |                                       | <21>          | <22>         | <24>         | <20>          |
|                                  | leukemic cell infiltration     |                                       | 1             | 2            | 1            | 2             |
| subcutis                         |                                |                                       | <21>          | <22>         | <24>         | <20>          |
|                                  | leukemic cell infiltration     |                                       | 0             | 1            | 0            | 1             |
|                                  | metastasis:uterus tumor        |                                       | 1             | 0            | 0            | 0             |
|                                  | metastasis:mammary gland tumor |                                       | 0             | 0            | 2            | 0             |
| {Respiratory system}             |                                |                                       |               |              |              |               |
| nasal cavit                      |                                |                                       | <21>          | <22>         | <24>         | <20>          |
|                                  | leukemic cell infiltration     |                                       | 1             | 2            | 1            | 2             |
| larynx                           |                                |                                       | <21>          | <22>         | <24>         | <20>          |
|                                  | leukemic cell infiltration     |                                       | 1             | 0            | 0            | 0             |
| trachea                          |                                |                                       | <21>          | <22>         | <24>         | <20>          |
|                                  | leukemic cell infiltration     |                                       | 1             | 0            | 0            | 1             |
| lung                             |                                |                                       | <21>          | <22>         | <24>         | <20>          |
|                                  | leukemic cell infiltration     |                                       | 3             | 8            | 7            | 4             |
|                                  | metastasis:liver tumor         |                                       | 0             | 1            | 0            | 0             |
|                                  | metastasis:uterus tumor        |                                       | 4             | 2            | 5            | 0             |
|                                  | metastasis:mammary gland tumor |                                       | 0             | 0            | 1            | 0             |
| {Hematopoietic system}           |                                |                                       |               |              |              |               |
| bone marrow                      |                                |                                       | <21>          | <22>         | <24>         | <20>          |
|                                  | leukemic cell infiltration     |                                       | 1             | 6            | 3            | 4             |

< a > a : Number of animals examined at the site  
 b b : Number of animals with lesion

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 7

|                        |                            | Group Name<br>No. of Animals on Study      | Control<br>21 | 32 ppm<br>22 | 80 ppm<br>24 | 200 ppm<br>20 |
|------------------------|----------------------------|--|---------------|--------------|--------------|---------------|
| Organ                  | Findings                   |  |               |              |              |               |
| {Hematopoietic system} |                            |  |               |              |              |               |
| bone marrow            | metastasis:liver tumor     |  | <21><br>0     | <22><br>1    | <24><br>0    | <20><br>0     |
|                        | metastasis:uterus tumor    |  | 4             | 2            | 0            | 1             |
| lymph node             | leukemic cell infiltration |  | <21><br>0     | <22><br>1    | <24><br>0    | <20><br>0     |
|                        | metastasis:uterus tumor    |  | 3             | 0            | 1            | 0             |
| spleen                 | leukemic cell infiltration |  | <21><br>0     | <22><br>8    | <24><br>6    | <20><br>4     |
|                        | metastasis:liver tumor     |  | 0             | 1            | 0            | 0             |
|                        | metastasis:uterus tumor    |  | 1             | 0            | 0            | 0             |
| {Circulatory system}   |                            |  |               |              |              |               |
| heart                  | leukemic cell infiltration |  | <21><br>1     | <22><br>4    | <24><br>5    | <20><br>2     |
|                        | metastasis:uterus tumor    |  | 0             | 1            | 0            | 0             |
| {Digestive system}     |                            |  |               |              |              |               |
| tooth                  | leukemic cell infiltration |  | <21><br>1     | <22><br>1    | <24><br>0    | <20><br>1     |
|                        | metastasis:uterus tumor    |  | 1             | 0            | 2            | 0             |
| tongue                 | leukemic cell infiltration |  | <21><br>1     | <22><br>2    | <24><br>1    | <20><br>2     |
| < a >                  |                            | a : Number of animals examined at the site |               |              |              |               |
| b                      |                            | b : Number of animals with lesion          |               |              |              |               |



STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 8

|                    |                            | Group Name<br>No. of Animals on Study | Control<br>21 | 32 ppm<br>22 | 80 ppm<br>24 | 200 ppm<br>20 |
|--------------------|----------------------------|---------------------------------------|---------------|--------------|--------------|---------------|
| Organ              | Findings                   |                                       |               |              |              |               |
| {Digestive system} |                            |                                       |               |              |              |               |
| salivary gl        |                            |                                       | <21>          | <22>         | <24>         | <20>          |
|                    | leukemic cell infiltration |                                       | 2             | 4            | 3            | 1             |
| stomach            |                            |                                       | <21>          | <22>         | <24>         | <20>          |
|                    | leukemic cell infiltration |                                       | 2             | 2            | 1            | 0             |
|                    | metastasis:uterus tumor    |                                       | 0             | 0            | 1            | 0             |
| liver              |                            |                                       | <21>          | <22>         | <24>         | <20>          |
|                    | leukemic cell infiltration |                                       | 1             | 10           | 6            | 5             |
|                    | metastasis:uterus tumor    |                                       | 10            | 5            | 11           | 4             |
| gall bladd         |                            |                                       | <21>          | <22>         | <24>         | <20>          |
|                    | leukemic cell infiltration |                                       | 1             | 1            | 1            | 0             |
| pancreas           |                            |                                       | <21>          | <22>         | <24>         | <20>          |
|                    | leukemic cell infiltration |                                       | 2             | 4            | 2            | 3             |
|                    | metastasis:uterus tumor    |                                       | 4             | 0            | 3            | 0             |
| {Urinary system}   |                            |                                       |               |              |              |               |
| kidney             |                            |                                       | <21>          | <22>         | <24>         | <20>          |
|                    | leukemic cell infiltration |                                       | 1             | 8            | 3            | 3             |
|                    | metastasis:uterus tumor    |                                       | 4             | 0            | 2            | 0             |
| urin bladd         |                            |                                       | <21>          | <22>         | <24>         | <20>          |
|                    | leukemic cell infiltration |                                       | 0             | 9            | 5            | 3             |
| {Endocrine system} |                            |                                       |               |              |              |               |
| pituitary          |                            |                                       | <21>          | <22>         | <24>         | <20>          |
|                    | leukemic cell infiltration |                                       | 0             | 1            | 0            | 0             |

< a > a : Number of animals examined at the site  
 b b : Number of animals with lesion

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 9

|                       |                                   | Group Name<br>No. of Animals on Study | Control<br>21 | 32 ppm<br>22 | 80 ppm<br>24 | 200 ppm<br>20 |
|-----------------------|-----------------------------------|---------------------------------------|---------------|--------------|--------------|---------------|
| Organ                 | Findings                          |                                       |               |              |              |               |
| {Endocrine system}    |                                   |                                       |               |              |              |               |
| pituitary             |                                   |                                       | <21>          | <22>         | <24>         | <20>          |
|                       | metastasis:peripheral nerve tumor |                                       | 0             | 0            | 1            | 0             |
| thyroid               |                                   |                                       | <21>          | <22>         | <24>         | <20>          |
|                       | leukemic cell infiltration        |                                       | 0             | 0            | 0            | 1             |
| adrenal               |                                   |                                       | <21>          | <22>         | <24>         | <20>          |
|                       | leukemic cell infiltration        |                                       | 1             | 1            | 0            | 2             |
| {Reproductive system} |                                   |                                       |               |              |              |               |
| ovary                 |                                   |                                       | <21>          | <22>         | <24>         | <20>          |
|                       | leukemic cell infiltration        |                                       | 1             | 8            | 4            | 5             |
|                       | metastasis:uterus tumor           |                                       | 6             | 3            | 8            | 4             |
| uterus                |                                   |                                       | <21>          | <22>         | <24>         | <20>          |
|                       | leukemic cell infiltration        |                                       | 0             | 2            | 1            | 2             |
|                       | metastasis:retroperitoneum tumor  |                                       | 0             | 1            | 0            | 0             |
| vagina                |                                   |                                       | <21>          | <22>         | <24>         | <20>          |
|                       | leukemic cell infiltration        |                                       | 1             | 4            | 0            | 2             |
| mammary gl            |                                   |                                       | <21>          | <22>         | <24>         | <20>          |
|                       | leukemic cell infiltration        |                                       | 1             | 1            | 0            | 0             |
| {Nervous system}      |                                   |                                       |               |              |              |               |
| brain                 |                                   |                                       | <21>          | <22>         | <24>         | <20>          |
|                       | leukemic cell infiltration        |                                       | 0             | 1            | 0            | 2             |

< a > a : Number of animals examined at the site  
 b b : Number of animals with lesion

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 10

|                                  |  | Group Name              | Control | 32 ppm | 80 ppm | 200 ppm |
|----------------------------------|--|-------------------------|---------|--------|--------|---------|
|                                  |  | No. of Animals on Study | 21      | 22     | 24     | 20      |
| Organ                            | Findings                                   |                         |         |        |        |         |
| {Nervous system}                 |  |                         |         |        |        |         |
| spinal cord                      |  |                         | <21>    | <22>   | <24>   | <20>    |
|                                  | leukemic cell infiltration                 |                         | 0       | 1      | 0      | 0       |
| {Special sense organs/appendage} |  |                         |         |        |        |         |
| Harder gl                        |  |                         | <21>    | <22>   | <24>   | <20>    |
|                                  | leukemic cell infiltration                 |                         | 1       | 3      | 2      | 2       |
| {Musculoskeletal system}         |  |                         |         |        |        |         |
| muscle                           |  |                         | <21>    | <22>   | <24>   | <20>    |
|                                  | leukemic cell infiltration                 |                         | 2       | 2      | 1      | 2       |
| {Body cavities}                  |  |                         |         |        |        |         |
| mediastinum                      |  |                         | <21>    | <22>   | <24>   | <20>    |
|                                  | leukemic cell infiltration                 |                         | 1       | 1      | 3      | 1       |
| peritoneum                       |  |                         | <21>    | <22>   | <24>   | <20>    |
|                                  | leukemic cell infiltration                 |                         | 0       | 2      | 0      | 1       |
|                                  |  |                         |         |        |        |         |
| < a >                            | a : Number of animals examined at the site |                         |         |        |        |         |
| b                                | b : Number of animals with lesion          |                         |         |        |        |         |

## APPENDIX P 6

HISTOPATHOLOGICAL FINDINGS :

METASTASIS OF TUMOR :

FEMALE : SACRIFICED ANIMALS

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 SACRIFICED ANIMALS (105W)

PAGE : 3

|                                  |                                | Group Name<br>No. of Animals on Study | Control<br>29 | 32 ppm<br>28 | 80 ppm<br>26 | 200 ppm<br>30 |
|----------------------------------|--------------------------------|---------------------------------------|---------------|--------------|--------------|---------------|
| Organ                            | Findings                       |                                       |               |              |              |               |
| {Integumentary system/appandage} |                                |                                       |               |              |              |               |
| skin/app                         |                                |                                       | <29>          | <28>         | <26>         | <30>          |
|                                  | leukemic cell infiltration     |                                       | 1             | 1            | 0            | 1             |
| subcutis                         |                                |                                       | <29>          | <28>         | <26>         | <30>          |
|                                  | leukemic cell infiltration     |                                       | 0             | 1            | 1            | 0             |
|                                  | metastasis:liver tumor         |                                       | 0             | 0            | 0            | 1             |
|                                  | metastasis:mammary gland tumor |                                       | 0             | 0            | 1            | 1             |
| {Respiratory system}             |                                |                                       |               |              |              |               |
| nasal cavit                      |                                |                                       | <29>          | <28>         | <26>         | <30>          |
|                                  | leukemic cell infiltration     |                                       | 0             | 1            | 0            | 0             |
|                                  | metastasis:uterus tumor        |                                       | 0             | 1            | 0            | 0             |
| lung                             |                                |                                       | <29>          | <28>         | <26>         | <30>          |
|                                  | leukemic cell infiltration     |                                       | 2             | 2            | 2            | 3             |
|                                  | metastasis:uterus tumor        |                                       | 0             | 1            | 0            | 1             |
| {Hematopoietic system}           |                                |                                       |               |              |              |               |
| bone marrow                      |                                |                                       | <29>          | <28>         | <26>         | <30>          |
|                                  | leukemic cell infiltration     |                                       | 2             | 0            | 0            | 1             |
|                                  | metastasis:uterus tumor        |                                       | 0             | 0            | 0            | 1             |
| spleen                           |                                |                                       | <29>          | <28>         | <26>         | <30>          |
|                                  | leukemic cell infiltration     |                                       | 3             | 5            | 6            | 4             |
|                                  | metastasis:lymph node tumor    |                                       | 0             | 0            | 1            | 0             |

< a > a : Number of animals examined at the site  
 b b : Number of animals with lesion

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 SACRIFICED ANIMALS (105W)

PAGE : 4

|                      |                             | Group Name<br>No. of Animals on Study | Control<br>29 | 32 ppm<br>28 | 80 ppm<br>26 | 200 ppm<br>30 |
|----------------------|-----------------------------|---------------------------------------|---------------|--------------|--------------|---------------|
| Organ                | Findings                    |                                       |               |              |              |               |
| {Circulatory system} |                             |                                       |               |              |              |               |
| heart                | leukemic cell infiltration  |                                       | <29><br>0     | <28><br>2    | <26><br>1    | <30><br>2     |
| {Digestive system}   |                             |                                       |               |              |              |               |
| tongue               | leukemic cell infiltration  |                                       | <29><br>0     | <28><br>1    | <26><br>0    | <30><br>1     |
| salivary gl          | leukemic cell infiltration  |                                       | <29><br>1     | <28><br>4    | <26><br>1    | <30><br>2     |
| stomach              | leukemic cell infiltration  |                                       | <29><br>0     | <28><br>1    | <26><br>0    | <30><br>1     |
|                      | metastasis:lymph node tumor |                                       | 0             | 0            | 1            | 0             |
| small intes          | leukemic cell infiltration  |                                       | <29><br>1     | <28><br>1    | <26><br>0    | <30><br>0     |
| liver                | leukemic cell infiltration  |                                       | <29><br>3     | <28><br>3    | <26><br>1    | <30><br>4     |
|                      | metastasis:uterus tumor     |                                       | 0             | 1            | 1            | 2             |
|                      | metastasis:subcutis tumor   |                                       | 1             | 0            | 0            | 0             |
|                      | metastasis:lymph node tumor |                                       | 0             | 0            | 1            | 0             |
| pancreas             | leukemic cell infiltration  |                                       | <29><br>0     | <28><br>1    | <26><br>0    | <30><br>0     |
| {Urinary system}     |                             |                                       |               |              |              |               |
| kidney               | leukemic cell infiltration  |                                       | <29><br>1     | <28><br>4    | <26><br>0    | <30><br>2     |

< a > a : Number of animals examined at the site  
 b b : Number of animals with lesion

STUDY NO. : 0458  
 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 SACRIFICED ANIMALS (105W)

PAGE : 5

|                                  |                            | Group Name<br>No. of Animals on Study | Control<br>29 | 32 ppm<br>28 | 80 ppm<br>26 | 200 ppm<br>30 |
|----------------------------------|----------------------------|---------------------------------------|---------------|--------------|--------------|---------------|
| Organ                            | Findings                   |                                       |               |              |              |               |
| {Urinary system}                 |                            |                                       |               |              |              |               |
| urin bladd                       | leukemic cell infiltration |                                       | <29><br>0     | <28><br>3    | <26><br>2    | <30><br>3     |
|                                  | metastasis:uterus tumor    |                                       | 3             | 1            | 1            | 0             |
| {Endocrine system}               |                            |                                       |               |              |              |               |
| pituitary                        | leukemic cell infiltration |                                       | <29><br>0     | <28><br>0    | <26><br>0    | <30><br>1     |
| {Reproductive system}            |                            |                                       |               |              |              |               |
| ovary                            | leukemic cell infiltration |                                       | <29><br>0     | <28><br>2    | <26><br>2    | <30><br>2     |
|                                  | metastasis:uterus tumor    |                                       | 0             | 1            | 0            | 3             |
| uterus                           | leukemic cell infiltration |                                       | <29><br>0     | <28><br>0    | <26><br>0    | <30><br>1     |
| vagina                           | leukemic cell infiltration |                                       | <29><br>0     | <28><br>0    | <26><br>0    | <30><br>1     |
|                                  | metastasis:uterus tumor    |                                       | 1             | 0            | 0            | 0             |
| {Special sense organs/appendage} |                            |                                       |               |              |              |               |
| Harder gl                        | leukemic cell infiltration |                                       | <29><br>0     | <28><br>3    | <26><br>0    | <30><br>0     |
| {Musculoskeletal system}         |                            |                                       |               |              |              |               |
| muscle                           | leukemic cell infiltration |                                       | <29><br>0     | <28><br>1    | <26><br>0    | <30><br>1     |

< a > a : Number of animals examined at the site  
 b b : Number of animals with lesion

## APPENDIX Q

METHODS, UNITS AND DECIMAL PLACE FOR  
HEMATOLOGY AND BIOCHEMISTRY IN THE 2-YEAR  
INHALATION STUDY OF 1,2-DICHLOROPROPANE



METHODS, UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY  
IN THE 2-YEAR INHALATION STUDY OF 1,2-DICHLOROPROPANE

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

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

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

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