

ブチル 2,3-エポキシプロピル エーテルのラット  
を用いた吸入によるがん原性試験報告書

試験番号 : 0437

## APPENDICES

## APPENDICES

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## APPENDIX A 1

### IDENTITY OF BUTYL 2,3-EPOXYPROPYL ETHER IN THE 2-YEAR INHALATION STUDY

## IDENTITY OF BUTYL 2,3-EPOXYPROPYL ETHER IN THE 2-YEAR INHALATION STUDY

Test Substance : Butyl 2,3-epoxypropyl ether (Wako Pure Chemical Industries, Ltd.)

A. Lot No. : LDJ4265

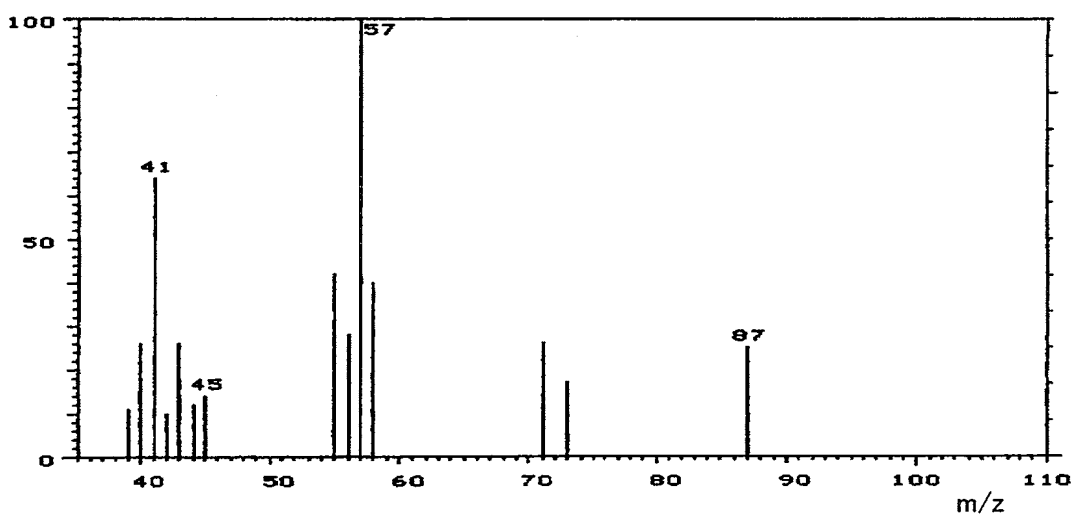
## 1. Spectral Data

Mass Spectrometry

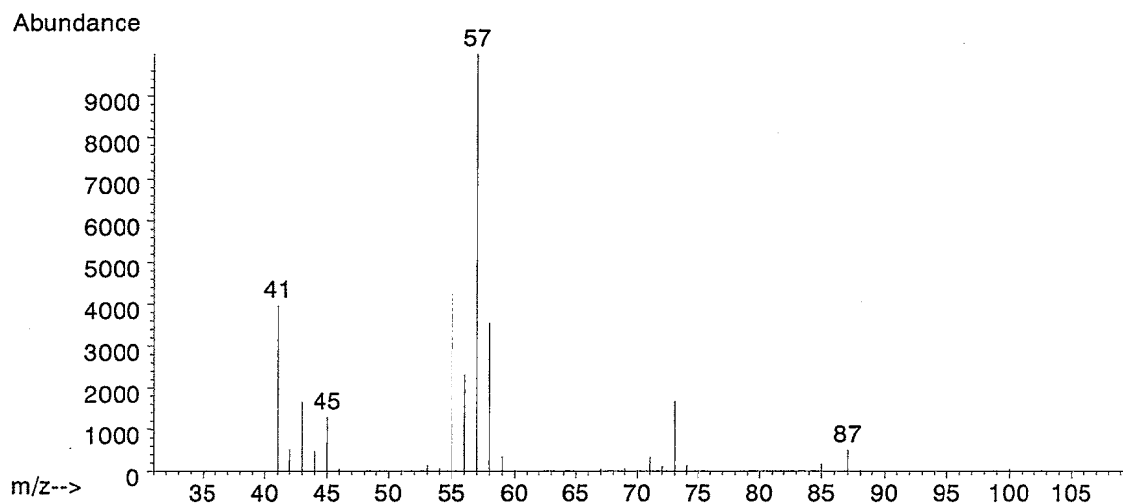
Instrument : Hitachi M-80B Mass Spectrometer

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.

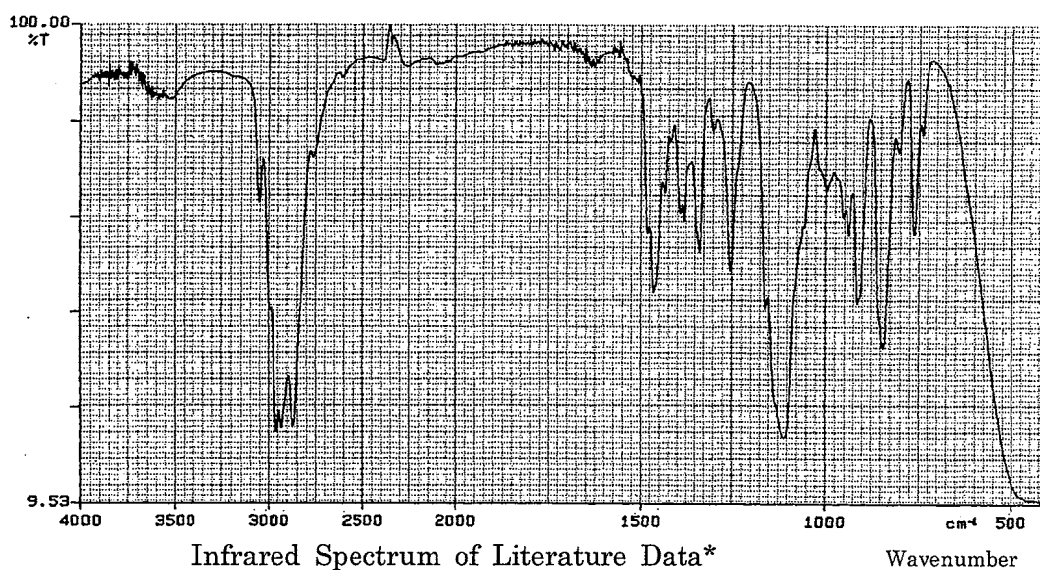
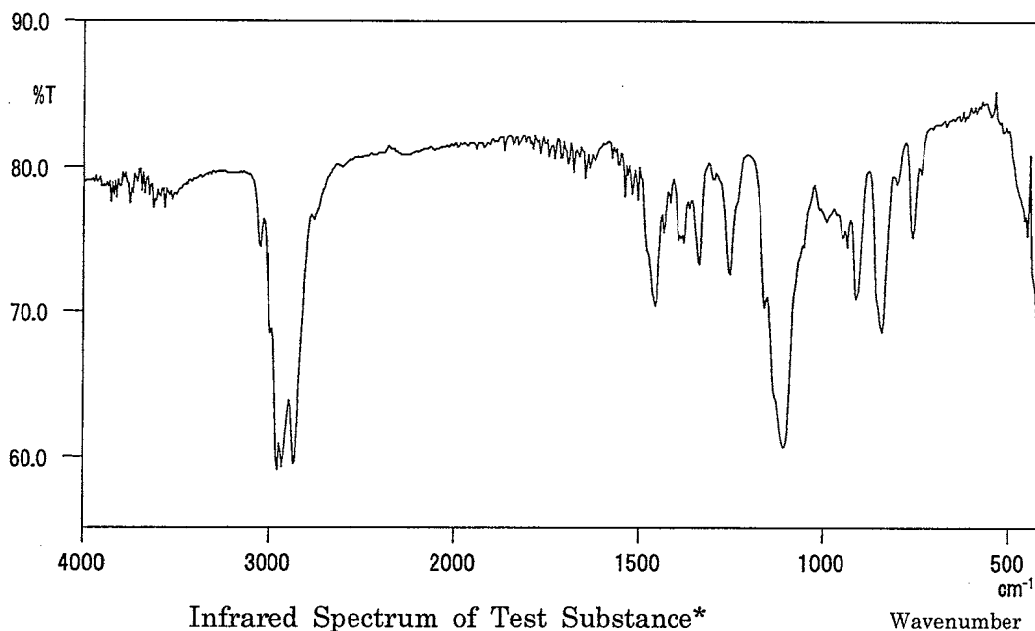
(\*McLafferty FW, ed. 1994. Wiley Registry of Mass Spectral Data. 6th ed. New York, NY:John Wiley and Sons.)

Infrared Spectrometry

Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

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



Result: The infrared spectrum was consistent with literature spectrum.

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

2. Conclusion: The test substance was identified as butyl 2,3-epoxypropyl ether by mass spectrum and infrared spectrum.

B. Lot No. : LDE4969

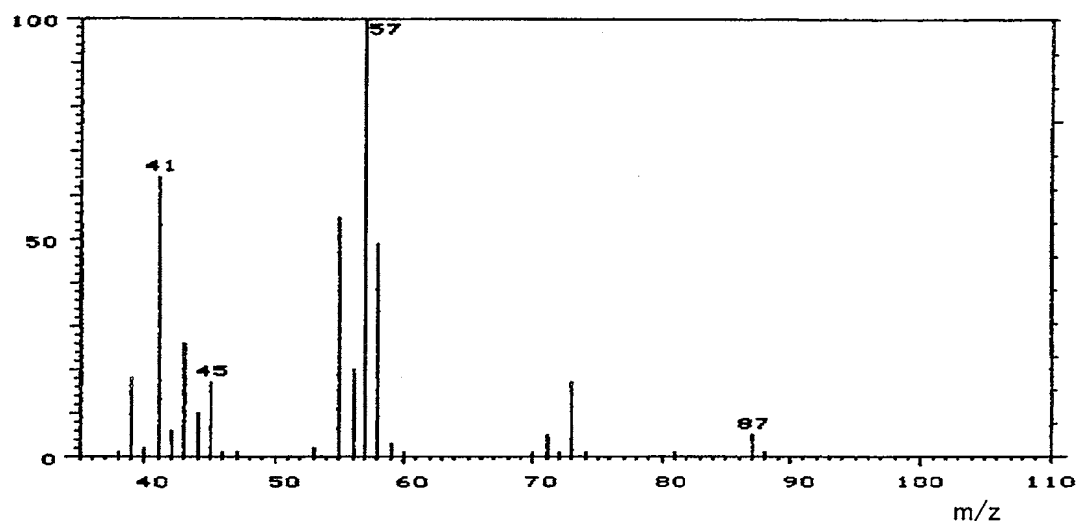
1. Spectral Data

Mass Spectrometry

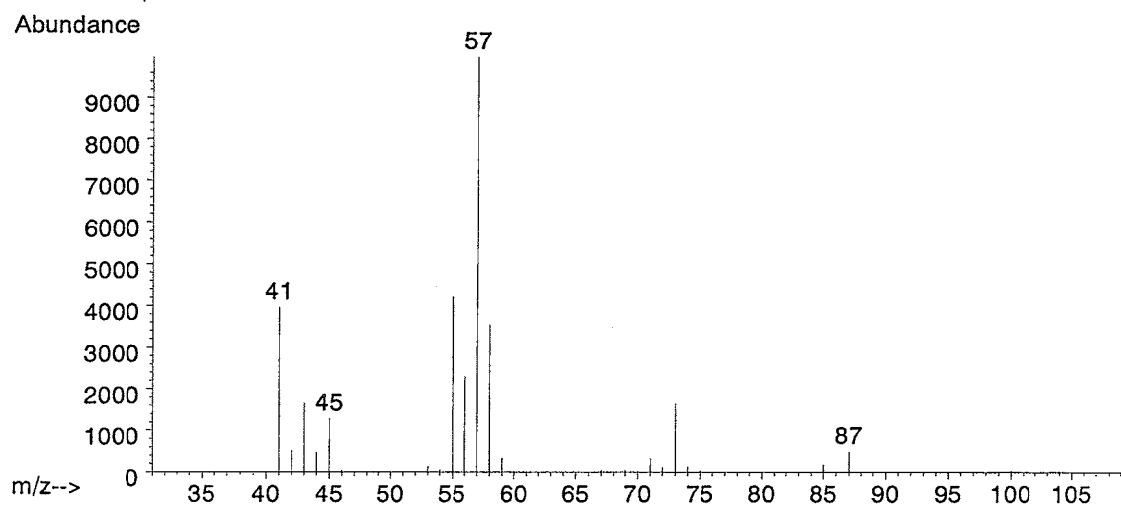
Instrument : Hitachi M-80B Mass Spectrometer

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.)

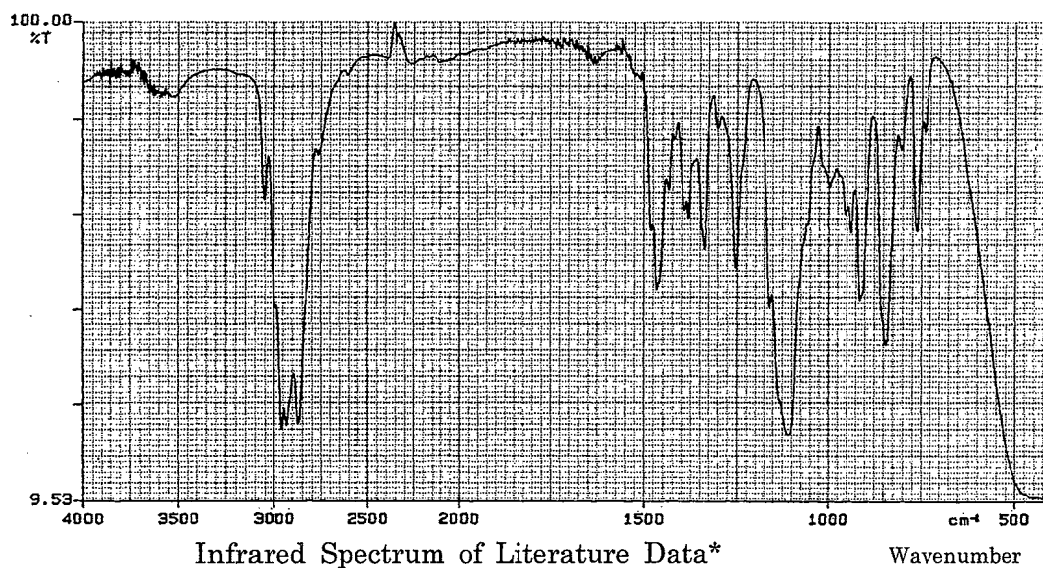
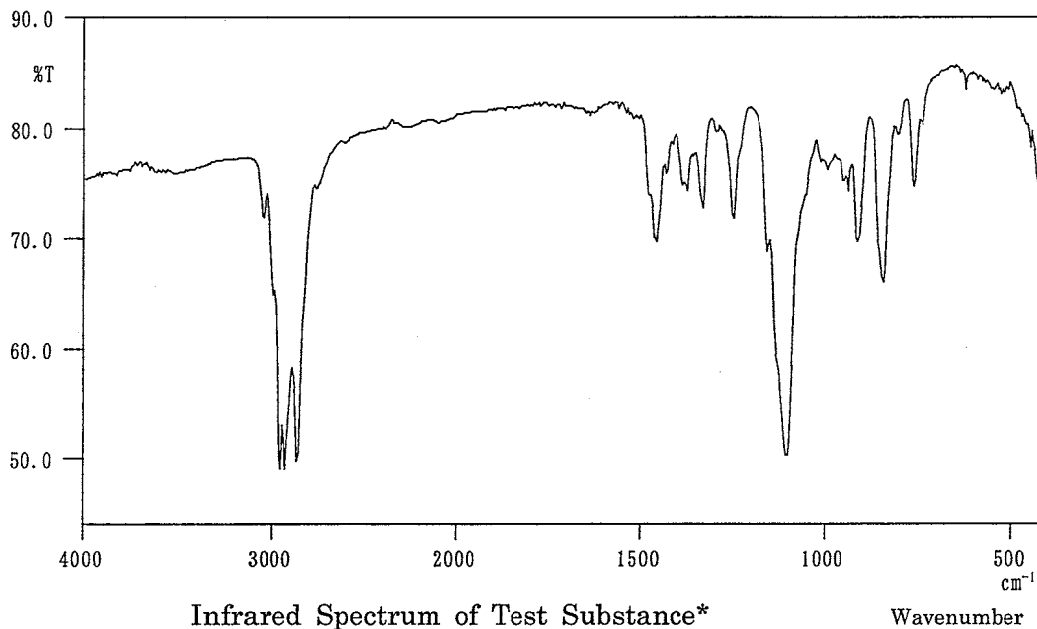


Infrared Spectrometry

Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

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



Result: The infrared spectrum was consistent with literature spectrum.

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

2. Conclusion: The test substance was identified as butyl 2,3-epoxypropyl ether by mass spectrum and infrared spectrum.

C. Lot No. : WAK4372

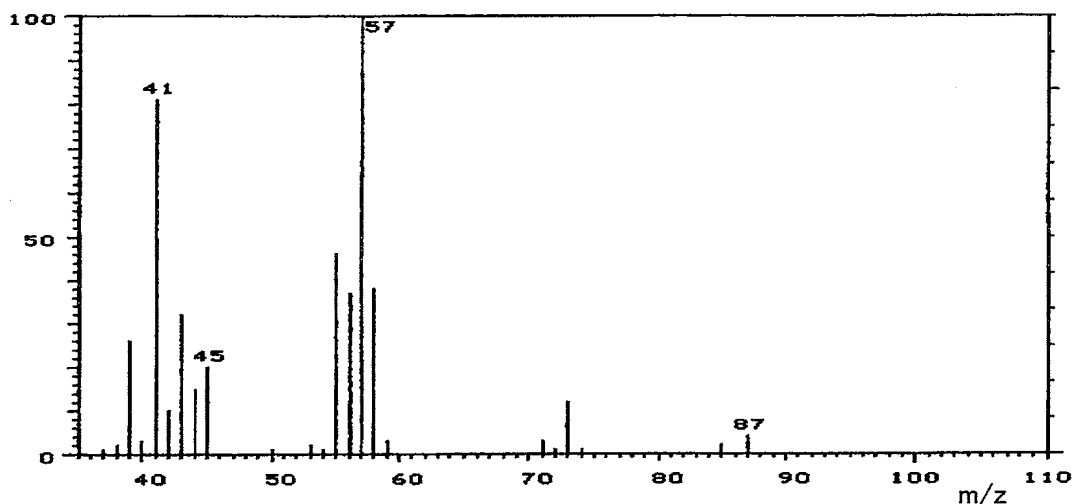
# 1. Spectral Data

## Mass Spectrometry

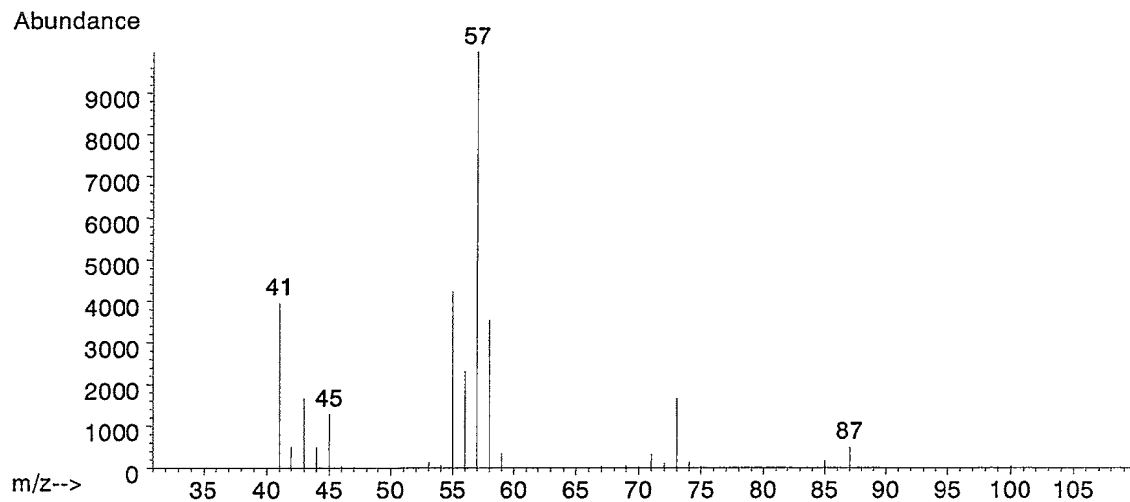
Instrument : Hitachi M-80B Mass Spectrometer

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.

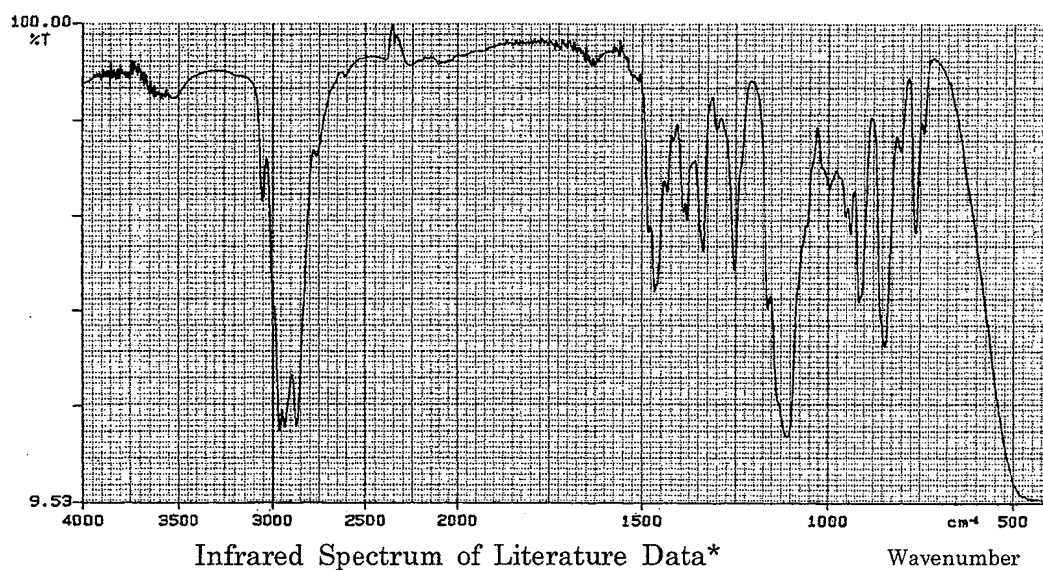
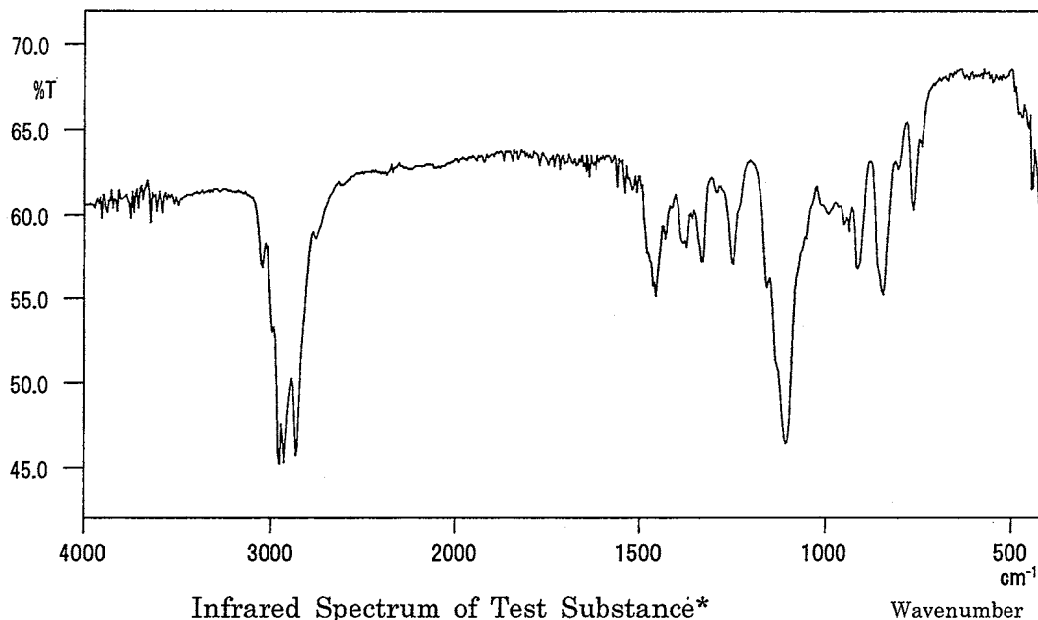
(\*McLafferty FW, ed. 1994. Wiley Registry of Mass Spectral Data. 6th ed. New York, NY:John Wiley and Sons.)

Infrared Spectrometry

Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

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



Result: The infrared spectrum was consistent with literature spectrum.

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

2. Conclusion: The test substance was identified as butyl 2,3-epoxypropyl ether by mass spectrum and infrared spectrum.

D. Lot No. : PKQ5714

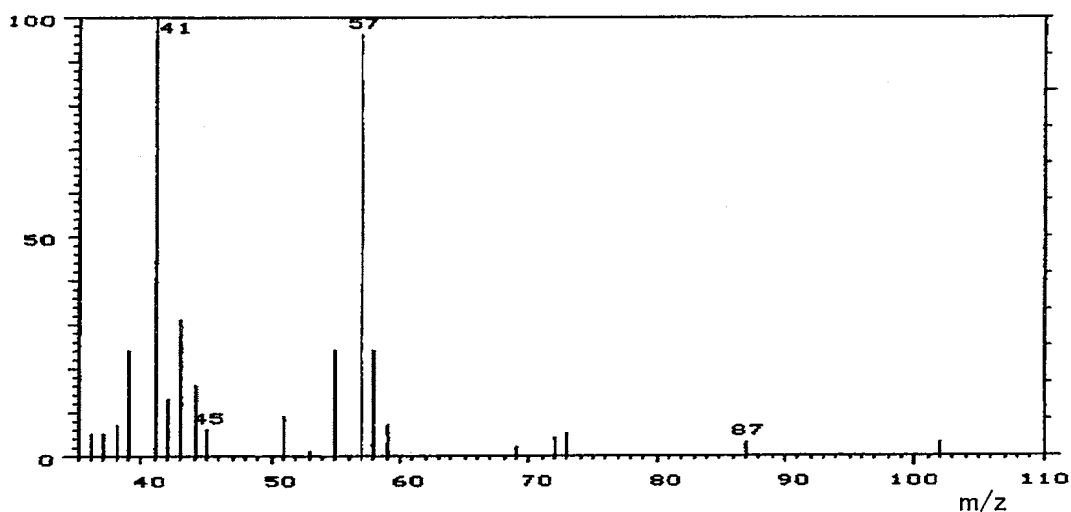
# 1. Spectral Data

## Mass Spectrometry

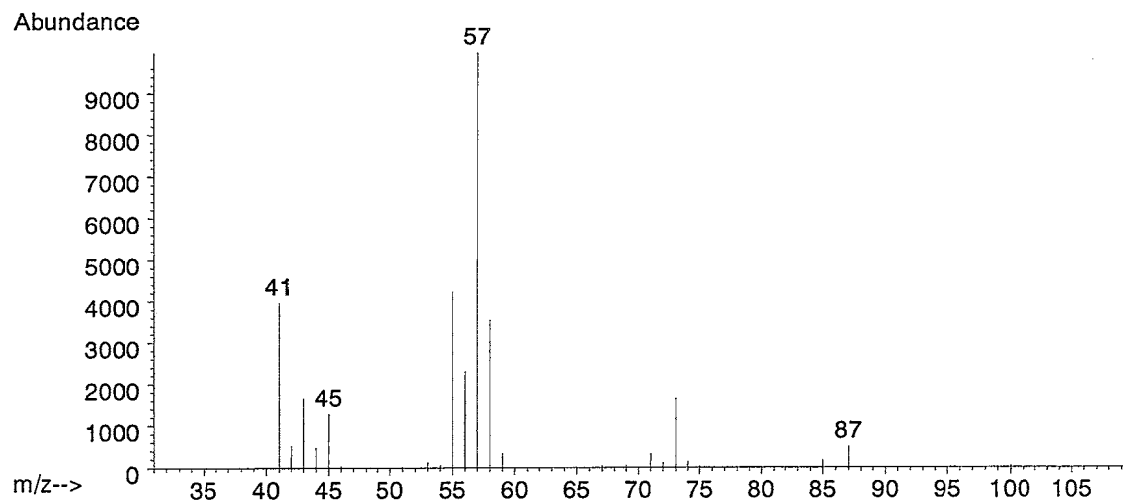
Instrument : Hitachi M-80B Mass Spectrometer

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.

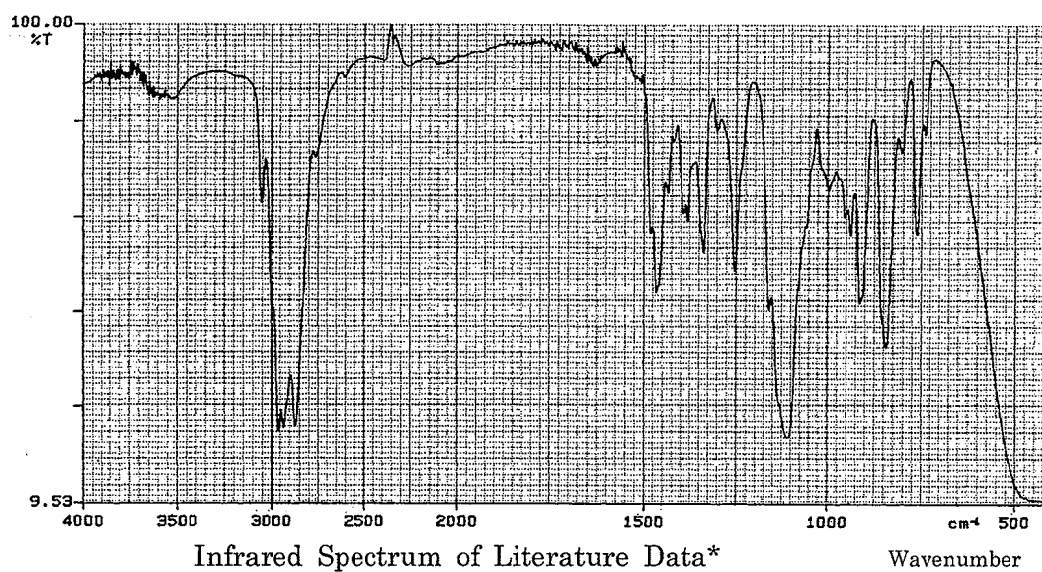
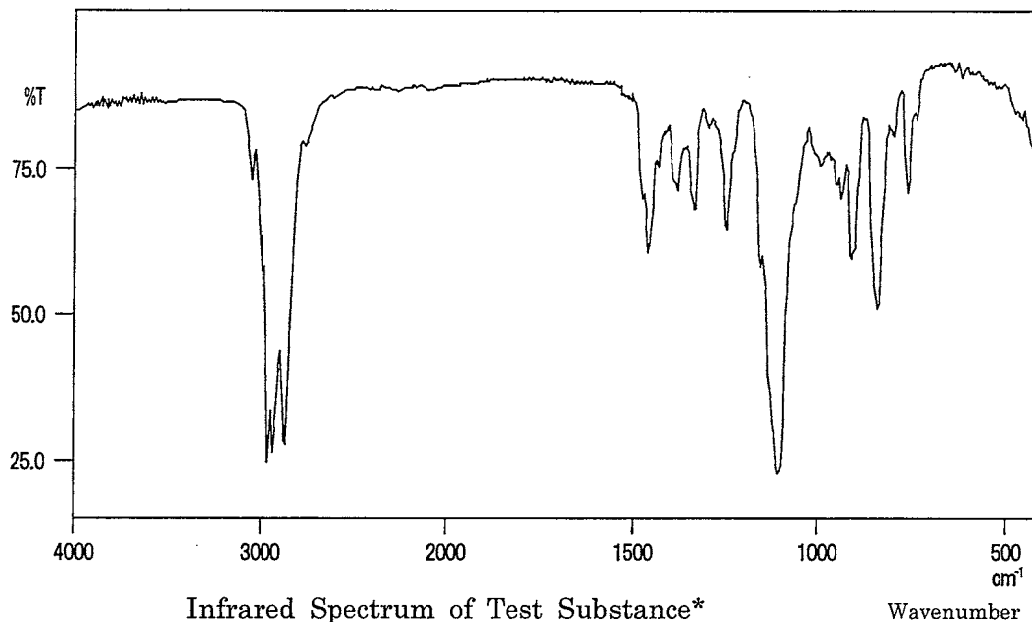
(\*McLafferty FW, ed. 1994. Wiley Registry of Mass Spectral Data. 6th ed. New York, NY:John Wiley and Sons.)

Infrared Spectrometry

Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

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



Result: The infrared spectrum was consistent with literature spectrum.

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

2. Conclusion: The test substance was identified as butyl 2,3-epoxypropyl ether by mass spectrum and infrared spectrum.

## APPENDIX A 2

### STABILITY OF BUTYL 2,3-EPOXYPROPYL ETHER IN THE 2-YEAR INHALATION STUDY

## STABILITY OF BUTYL 2,3-EPOXYPROPYL ETHER IN THE 2-YEAR INHALATION STUDY

Test Substance : Butyl 2,3-epoxypropyl ether (Wako Pure Chemical Industries, Ltd.)

A. Lot No. : LDJ4265

1. Sample : This lot was used from 2001.10.15 to 2002.2.18. The 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: 160° C

Flow Rate : 20 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1  $\mu$ L

| Date<br>(date analyzed) | Peak No. | Retention Time<br>(min) | Area<br>(%) |
|-------------------------|----------|-------------------------|-------------|
| 2001.10.10              | 1        | 2.893                   | 100         |
| 2002.02.19              | 1        | 2.899                   | 100         |

Result: Gas chromatography indicated one major peak (peak No.1) analyzed on 2001.10.10 and one major peak (peak No.1) analyzed on 2002.2.19. No new trace impurity peak in the test substance analyzed on 2002.2.19 was detected.

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

B. Lot No. : LDE4969

1. Sample : This lot was used from 2002.2.19 to 2002.10.7. The 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: 160° C

Flow Rate : 20 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1  $\mu$ L

| Date<br>(date analyzed) | Peak No. | Retention Time<br>(min) | Area<br>(%) |
|-------------------------|----------|-------------------------|-------------|
| 2002.02.18              | 1        | 2.901                   | 100         |
| 2002.10.09              | 1        | 3.135                   | 100         |

Result: Gas chromatography indicated one major peak (peak No.1) analyzed on 2001.2.18 and one major peak (peak No.1) analyzed on 2002.10.9. No new trace impurity peak in the test substance analyzed on 2002.10.9 was detected.

3. Conclusion: The test substance was stable for about 7 months in a dark place at room temperature.



C. Lot No. : WAK4372

1. Sample : This lot was used from 2002.10.8 to 2003.5.23. The 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: 160° C

Flow Rate : 20 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1  $\mu$ L

| Date<br>(date analyzed) | Peak No. | Retention Time<br>(min) | Area<br>(%) |
|-------------------------|----------|-------------------------|-------------|
| 2002.10.07              | 1        | 3.131                   | 100         |
| 2003.05.26              | 1        | 3.127                   | 100         |

Result: Gas chromatography indicated one major peak (peak No.1) analyzed on 2002.10.7 and one major peak (peak No.1) analyzed on 2003.5.26. No new trace impurity peak in the test substance analyzed on 2003.5.26 was detected.

3. Conclusion: The test substance was stable for about 7 months in a dark place at room temperature.

D. Lot No. : PKQ5714

1. Sample : This lot was used from 2003.5.26 to 2003.10.10. The 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: 160° C

Flow Rate : 20 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1  $\mu$ L

| Date<br>(date analyzed) | Peak No. | Retention Time<br>(min) | Area<br>(%) |
|-------------------------|----------|-------------------------|-------------|
| 2003.05.23              | 1        | 3.129                   | 100         |
| 2003.11.19              | 1        | 3.113                   | 100         |

Result: Gas chromatography indicated one major peak (peak No.1) analyzed on 2003.5.23 and one major peak (peak No.1) analyzed on 2003.11.19. No new trace impurity peak in the test substance analyzed on 2003.11.19 was detected.

3. Conclusion: The test substance was stable for about 5 months in a dark place at room temperature.

## APPENDIX B

### ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 2-YEAR INHALATION STUDY OF BUTYL 2,3-EPOXYPROPYL ETHER

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 2-YEAR  
INHALATION STUDY OF BUTYL 2,3-EPOXYPROPYL ETHER

| Group Name | Temperature<br>(°C) | Humidity<br>(%) | Ventilation Rate<br>(L/min) |                           | Air Change<br>(time/h) |                    |
|------------|---------------------|-----------------|-----------------------------|---------------------------|------------------------|--------------------|
|            | Mean ± S.D.         | Mean ± S.D.     | Mean ± S.D.* <sup>1</sup>   | Mean ± S.D.* <sup>2</sup> | Mean* <sup>1</sup>     | Mean* <sup>2</sup> |
| Control    | 23.1 ± 0.2          | 56.4 ± 1.7      | 856.8 ± 4.2                 | 1708.3 ± 11.6             | 6.0                    | 12.1               |
| 10 ppm     | 23.1 ± 0.2          | 55.1 ± 2.1      | 854.8 ± 2.8                 | 1704.0 ± 12.1             | 6.0                    | 12.0               |
| 30 ppm     | 23.0 ± 0.1          | 54.0 ± 2.3      | 854.8 ± 3.1                 | 1706.6 ± 11.7             | 6.0                    | 12.0               |
| 90 ppm     | 23.0 ± 0.1          | 53.7 ± 3.1      | 853.3 ± 3.5                 | 1707.1 ± 12.7             | 6.0                    | 12.1               |

\* 1: Exposure period      \* 2: After exposure period

## APPENDIX C 1

### CLINICAL OBSERVATION : MALE

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCrj  
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    |
|                         | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0   | 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    |
|                         | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 1   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| LATERAL                 | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 1   | 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    |
|                         | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| ABNORMAL GAIT           | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 1                       | 1   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCrj  
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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LATERAL                 | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ABNORMAL GAIT           | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LATERAL                 | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ABNORMAL GAIT           | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |



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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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LATERAL                 | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ABNORMAL GAIT           | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |

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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    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    |
|                         | 90 ppm     | 1                       | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
| MORIBUND SACRIFICE      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LATERAL                 | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ABNORMAL GAIT           | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 1                       | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |

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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    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                         | 30 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 2    | 3    | 3    | 3    | 3    | 3    |
|                         | 90 ppm     | 2                       | 2    | 2    | 2    | 2    | 3    | 5    | 5    | 6    | 7    | 9    | 9    | 9    | 10   |
| MORIBUND SACRIFICE      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 2    | 2    | 2    |
|                         | 30 ppm     | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                         | 90 ppm     | 1                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 3    | 4    | 4    | 5    | 5    | 6    |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LATERAL                 | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ABNORMAL GAIT           | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 3    | 3    | 2    | 1    | 1    | 3    | 2    |

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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 |      |      |      |      |      |      |      |      |      |      |      |
| DEATH                   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 2    | 2    | 2    | 5    | 6    | 6    | 6    | 7    |
|                         | 10 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 2    |
|                         | 30 ppm     | 3                       | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 4    | 4    | 4    | 5    |
|                         | 90 ppm     | 10                      | 11   | 13   | 15   | 16   | 16   | 16   | 16   | 16   | 16   | 19   | 20   | 21   | 23   |
| MORIBUND SACRIFICE      | Control    | 0                       | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 2    | 2    | 3    | 3    | 3    | 3    |
|                         | 10 ppm     | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 6    | 6    |
|                         | 30 ppm     | 2                       | 2    | 2    | 4    | 5    | 5    | 5    | 5    | 5    | 5    | 5    | 5    | 5    | 5    |
|                         | 90 ppm     | 6                       | 7    | 8    | 8    | 9    | 10   | 10   | 11   | 11   | 11   | 11   | 12   | 12   | 12   |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LATERAL                 | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    | 1    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ABNORMAL GAIT           | Control    | 0                       | 0    | 0    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    | 2    | 1    | 0    | 0    | 2    | 1    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 1    | 0    | 0    | 0    | 0    | 1    | 1    | 2    | 1    | 1    | 1    | 1    |
|                         | 90 ppm     | 2                       | 4    | 3    | 2    | 1    | 0    | 0    | 0    | 1    | 4    | 2    | 1    | 2    | 0    |

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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    | 7                       | 7     | 7     | 7     | 7     | 8     |
|                         | 10 ppm     | 3                       | 3     | 3     | 5     | 6     | 6     |
|                         | 30 ppm     | 5                       | 5     | 5     | 5     | 5     | 5     |
|                         | 90 ppm     | 23                      | 23    | 23    | 24    | 24    | 24    |
| MORIBUND SACRIFICE      | Control    | 4                       | 4     | 4     | 4     | 4     | 4     |
|                         | 10 ppm     | 6                       | 6     | 6     | 6     | 6     | 6     |
|                         | 30 ppm     | 6                       | 6     | 7     | 7     | 7     | 7     |
|                         | 90 ppm     | 12                      | 13    | 14    | 14    | 15    | 15    |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| LATERAL                 | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| HUNCHBACK POSITION      | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| PARALYTIC GAIT          | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 30 ppm     | 1                       | 1     | 0     | 0     | 0     | 0     |
|                         | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| ABNORMAL GAIT           | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| WASTING                 | Control    | 0                       | 1     | 1     | 1     | 2     | 1     |
|                         | 10 ppm     | 0                       | 0     | 1     | 0     | 0     | 0     |
|                         | 30 ppm     | 1                       | 1     | 0     | 0     | 0     | 0     |
|                         | 90 ppm     | 0                       | 0     | 1     | 0     | 0     | 2     |

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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 |
| SOILED                | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 90 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    |
|                       | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 90 ppm     | 0                       | 1   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| TRAUMA                | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 90 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    |
|                       | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 90 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    |
|                       | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 90 ppm     | 0                       | 1   | 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    |
|                       | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| EYE OPACITY           | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| CATARACT              | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                       | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |

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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 |
| SOILED                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PILOERRECTION         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| TRAUMA                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 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    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 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    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 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    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                       | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EYE OPACITY           | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CATARACT              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
|                       | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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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 |
|-----------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                       |            | 29-7                    | 30-7 | 31-7 |      |      |      |      |      |      |      |      |      |      |      |      |      |      |
| SOILED                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 ppm     | 0                       | 0    | 0    | 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    | 0    | 0    | 0    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| TRAUMA                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 ppm     | 0                       | 0    | 0    | 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    | 0    | 0    | 0    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 ppm     | 0                       | 0    | 0    | 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    | 0    | 0    | 0    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 ppm     | 0                       | 0    | 0    | 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    | 0    | 0    | 0    |
|                       | 10 ppm     | 0                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                       | 30 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                       | 90 ppm     | 0                       | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| EYE OPACITY           | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CATARACT              | Control    | 0                       | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 2    | 2    | 2    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
|                       | 30 ppm     | 1                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 3    | 3    | 3    |
|                       | 90 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 2    |



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 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 |
| SOILED                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 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    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| TRAUMA                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 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    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 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    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    |
| EXOPHTHALMOS          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 10 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                       | 30 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                       | 90 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| EYE OPACITY           | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CATARACT              | Control    | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 3    | 4    | 4    |
|                       | 10 ppm     | 1                       | 1    | 1    | 1    | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                       | 30 ppm     | 3                       | 3    | 3    | 3    | 4    | 4    | 4    | 5    | 5    | 5    | 5    | 5    | 5    | 5    |
|                       | 90 ppm     | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |

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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 |
| SOILED                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 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    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    |
| TRAUMA                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 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    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 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    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 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    |
|                       | 10 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                       | 90 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| EYE OPACITY           | Control    | 0                       | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CATARACT              | Control    | 4                       | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 5    | 5    | 5    | 5    | 5    |
|                       | 10 ppm     | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                       | 30 ppm     | 5                       | 5    | 5    | 5    | 5    | 5    | 5    | 5    | 5    | 5    | 5    | 5    | 5    | 5    |
|                       | 90 ppm     | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |

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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 |
| SOILED                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 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    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 ppm     | 0                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| TRAUMA                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 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    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 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    |
|                       | 10 ppm     | 0                       | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    |
| EXOPHTHALMOS          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    |
|                       | 90 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    |
| EYE OPACITY           | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CATARACT              | Control    | 5                       | 5    | 6    | 7    | 7    | 7    | 7    | 7    | 7    | 7    | 7    | 7    | 7    | 7    |
|                       | 10 ppm     | 2                       | 2    | 2    | 2    | 2    | 2    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    |
|                       | 30 ppm     | 5                       | 5    | 5    | 5    | 5    | 5    | 5    | 5    | 5    | 4    | 4    | 4    | 4    | 4    |
|                       | 90 ppm     | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 1    | 1    | 1    | 1    | 1    | 1    |

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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 |      |      |      |      |      |      |      |      |      |      |      |
| SOILED                | Control    | 1                       | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    |
|                       | 90 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    | 1    | 0    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 ppm     | 1                       | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| TRAUMA                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 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    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED PERI-GENITALIA | Control    | 0                       | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 1    | 1    | 0    | 0    | 0    | 0    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 ppm     | 1                       | 1    | 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    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EYE OPACITY           | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CATARACT              | Control    | 8                       | 8    | 8    | 8    | 8    | 8    | 8    | 8    | 8    | 8    | 8    | 8    | 8    | 8    |
|                       | 10 ppm     | 3                       | 3    | 3    | 3    | 4    | 4    | 4    | 4    | 4    | 5    | 5    | 5    | 3    | 3    |
|                       | 30 ppm     | 4                       | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    |
|                       | 90 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    |

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCrj  
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 |
| SOILED                | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 30 ppm     | 1                       | 1     | 0     | 0     | 0     | 0     |
|                       | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| PILOERECTOR           | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| TRAUMA                | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| FROG BELLY            | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 1     |
| SOILED PERI-GENITALIA | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| EXOPHTHALMOS          | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| EYE OPACITY           | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                       | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| CATARACT              | Control    | 8                       | 8     | 8     | 8     | 8     | 8     |
|                       | 10 ppm     | 3                       | 3     | 3     | 3     | 3     | 3     |
|                       | 30 ppm     | 4                       | 4     | 4     | 4     | 4     | 4     |
|                       | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |

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 ANIMAL : RAT F344/DuCrj  
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CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

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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 |
| CORNEAL OPACITY          | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| ANTERIOR CHAMBER OPACITY | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 90 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    |
|                          | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 90 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    |
|                          | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. NOSE                  | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. PERI-MOUTH            | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. PERI EAR              | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. NECK                  | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |

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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 |
| CORNEAL OPACITY          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 1    | 1    | 1    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ANTERIOR CHAMBER OPACITY | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 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    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 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    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NOSE                  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI-MOUTH            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI EAR              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NECK                  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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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 |
| CORNEAL OPACITY          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ANTERIOR CHAMBER OPACITY | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 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    |
|                          | 10 ppm     | 0                       | 0    | 1    | 1    | 1    | 0    | 0    | 1    | 1    | 1    | 1    | 2    | 1    | 1    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                          | 90 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    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NOSE                  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI-MOUTH            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI EAR              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NECK                  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |



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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 |
| CORNEAL OPACITY          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ANTERIOR CHAMBER OPACITY | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXTERNAL MASS            | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 2    | 2    | 2    | 2    | 2    |
|                          | 10 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 2    | 2    | 2    | 2    | 2    | 1    | 1    | 1    |
|                          | 30 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                          | 90 ppm     | 1                       | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 3    | 3    | 4    |
| INTERNAL MASS            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NOSE                  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    |
| M. PERI-MOUTH            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI EAR              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NECK                  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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 ANIMAL : RAT F344/DuCrj  
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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 |
| CORNEAL OPACITY          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ANTERIOR CHAMBER OPACITY | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXTERNAL MASS            | Control    | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 3    | 3    | 3    | 2    | 2    |
|                          | 10 ppm     | 1                       | 1    | 1    | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                          | 30 ppm     | 1                       | 2    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 3    | 3    |
|                          | 90 ppm     | 4                       | 4    | 3    | 3    | 3    | 3    | 3    | 4    | 3    | 4    | 4    | 4    | 4    | 5    |
| INTERNAL MASS            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NOSE                  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
|                          | 90 ppm     | 1                       | 1    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 1    |
| M. PERI-MOUTH            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI EAR              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NECK                  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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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 |
| CORNEAL OPACITY          | Control    | 0                       | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 1    | 1    | 2    | 3    | 2    | 1    | 1    | 2    | 1    |
| ANTERIOR CHAMBER OPACITY | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXTERNAL MASS            | Control    | 3                       | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 4    | 4    | 6    | 5    | 5    | 5    |
|                          | 10 ppm     | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 3    | 3    |
|                          | 30 ppm     | 3                       | 3    | 4    | 5    | 5    | 5    | 5    | 5    | 5    | 4    | 4    | 4    | 4    | 4    |
|                          | 90 ppm     | 5                       | 4    | 4    | 5    | 6    | 6    | 6    | 6    | 4    | 3    | 2    | 3    | 3    | 1    |
| INTERNAL MASS            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 1    |
| M. NOSE                  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 1                       | 0    | 0    | 1    | 1    | 1    | 2    | 2    | 1    | 0    | 0    | 1    | 1    | 0    |
| M. PERI-MOUTH            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI EAR              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NECK                  | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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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 |  |      |      |      |      |      |      |      |      |      |      |      |
| CORNEAL OPACITY          | Control    | 0                       | 0    | 0    |  | 0    | 1    | 1    | 1    | 0    | 0    | 0    | 1    | 1    | 1    | 1    |
|                          | 10 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 1                       | 1    | 0    |  | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    | 0    | 0    |
| ANTERIOR CHAMBER OPACITY | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXTERNAL MASS            | Control    | 5                       | 5    | 5    |  | 5    | 5    | 7    | 6    | 6    | 6    | 5    | 5    | 8    | 8    | 8    |
|                          | 10 ppm     | 3                       | 3    | 3    |  | 3    | 3    | 3    | 3    | 3    | 3    | 4    | 4    | 6    | 5    | 6    |
|                          | 30 ppm     | 4                       | 4    | 4    |  | 4    | 4    | 5    | 5    | 6    | 6    | 6    | 5    | 5    | 5    | 5    |
|                          | 90 ppm     | 2                       | 1    | 2    |  | 1    | 1    | 1    | 1    | 1    | 2    | 2    | 1    | 1    | 1    | 1    |
| INTERNAL MASS            | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    |
|                          | 30 ppm     | 0                       | 1    | 1    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 2                       | 2    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NOSE                  | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 1                       | 0    | 1    |  | 0    | 0    | 1    | 1    | 1    | 2    | 2    | 1    | 1    | 1    | 0    |
| M. PERI-MOUTH            | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI EAR              | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NECK                  | Control    | 1                       | 1    | 1    |  | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                          | 10 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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| Clinical sign            | Group Name | Administration Week-day |       |       |       |       |       |
|--------------------------|------------|-------------------------|-------|-------|-------|-------|-------|
|                          |            | 99-7                    | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| CORNEAL OPACITY          | Control    | 1                       | 1     | 1     | 1     | 1     | 1     |
|                          | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| ANTERIOR CHAMBER OPACITY | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 1     |
| EXTERNAL MASS            | Control    | 8                       | 9     | 9     | 9     | 10    | 10    |
|                          | 10 ppm     | 6                       | 6     | 6     | 7     | 9     | 10    |
|                          | 30 ppm     | 6                       | 6     | 6     | 8     | 8     | 8     |
|                          | 90 ppm     | 1                       | 2     | 1     | 2     | 1     | 1     |
| INTERNAL MASS            | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. NOSE                  | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 90 ppm     | 0                       | 1     | 0     | 1     | 1     | 1     |
| M. PERI-MOUTH            | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. PERI EAR              | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. NECK                  | Control    | 1                       | 1     | 1     | 1     | 1     | 0     |
|                          | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |

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ANIMAL : RAT F344/DuCrj  
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CLINICAL OBSERVATION (SUMMARY)  
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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. FORELIMB         | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. ANTERIOR. DORSUM | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. POSTERIOR DORSUM | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. SCROTUM          | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |

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CLINICAL OBSERVATION (SUMMARY)  
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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. FORELIMB         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ANTERIOR. DORSUM | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. POSTERIOR DORSUM | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. SCROTUM          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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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. FORELIMB         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 1    | 1    | 1    | 0    | 0    | 1    | 1    | 1    | 1    | 2    | 1    | 1    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ANTERIOR DORSUM  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. POSTERIOR DORSUM | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. SCROTUM          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |



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ANIMAL : RAT F344/DuCrj  
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. FORELIMB         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 2    | 2    | 2    | 2    | 2    | 1    | 1    | 1    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 2    |
| M. ANTERIOR DORSUM  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. POSTERIOR DORSUM | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. SCROTUM          | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1 104

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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. FORELIMB         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
|                     | 90 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    |
|                     | 10 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
| M. ANTERIOR. DORSUM | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    |
| M. POSTERIOR DORSUM | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. GENITALIA        | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. SCROTUM          | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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 |      |      |      |      |      |      |      |      |      |      |      |      |      |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                     |            | 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. FORELIMB         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 90 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    | 1    | 1    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
|                     | 30 ppm     | 1                       | 1    | 2    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    |
|                     | 90 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    |
|                     | 10 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 30 ppm     | 1                       | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 2                       | 2    | 2    | 2    | 3    | 3    | 3    | 3    | 2    | 1    | 0    | 0    | 0    | 0    |
| M. ANTERIOR. DORSUM | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| M. POSTERIOR DORSUM | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 2    | 2    | 2    | 2    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. GENITALIA        | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. SCROTUM          | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    |

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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. FORELIMB         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    | 1    | 1    | 1    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. BREAST           | Control    | 0                       | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 10 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    |
|                     | 30 ppm     | 3                       | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    |
|                     | 90 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    | 1    | 2    | 2    | 2    |
|                     | 10 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 2    | 1    | 1    | 2    | 2    | 3    | 3    | 3    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ANTERIOR. DORSUM | Control    | 0                       | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 2    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 1    | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                     | 90 ppm     | 1                       | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
| M. POSTERIOR DORSUM | Control    | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 3    | 2    | 2    | 2    | 2    |
|                     | 10 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    | 1    | 1    | 1    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. GENITALIA        | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. SCROTUM          | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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| Clinical sign       | Group Name | Administration Week-day |       |       |       |       |       |
|---------------------|------------|-------------------------|-------|-------|-------|-------|-------|
|                     |            | 99-7                    | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| M. FORELIMB         | Control    | 1                       | 1     | 1     | 1     | 1     | 2     |
|                     | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 1     |
|                     | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. BREAST           | Control    | 1                       | 1     | 1     | 2     | 2     | 2     |
|                     | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 30 ppm     | 4                       | 4     | 4     | 4     | 4     | 4     |
|                     | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. ABDOMEN          | Control    | 2                       | 3     | 3     | 3     | 3     | 3     |
|                     | 10 ppm     | 3                       | 3     | 3     | 3     | 4     | 4     |
|                     | 30 ppm     | 0                       | 0     | 0     | 1     | 1     | 1     |
|                     | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. ANTERIOR. DORSUM | Control    | 1                       | 1     | 1     | 0     | 1     | 1     |
|                     | 10 ppm     | 2                       | 2     | 2     | 2     | 3     | 3     |
|                     | 30 ppm     | 2                       | 2     | 2     | 3     | 3     | 3     |
|                     | 90 ppm     | 1                       | 1     | 1     | 1     | 0     | 0     |
| M. POSTERIOR DORSUM | Control    | 2                       | 2     | 2     | 2     | 2     | 2     |
|                     | 10 ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
|                     | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. HINDLIMB         | Control    | 1                       | 1     | 1     | 1     | 1     | 1     |
|                     | 10 ppm     | 0                       | 1     | 1     | 2     | 2     | 2     |
|                     | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. GENITALIA        | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 1     |
|                     | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. SCROTUM          | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |

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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 |
| ANEMIA              | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| JAUNDICE            | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| HEMORRHAGE          | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |

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ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1 104

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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 |
| ANEMIA              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| JAUNDICE            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HEMORRHAGE          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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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 |
| ANEMIA              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| JAUNDICE            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HEMORRHAGE          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |



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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 |
| ANEMIA              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| JAUNDICE            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HEMORRHAGE          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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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 |
| ANEMIA              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| JAUNDICE            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 1                       | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HEMORRHAGE          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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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 |
| ANEMIA              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                     | 10 ppm     | 0                       | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| JAUNDICE            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    |
| ULCER               | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HEMORRHAGE          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    | 1    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 1    | 2    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 1    | 1    | 1    | 1    | 2    | 1    | 3    | 3    | 1    | 1    | 2    | 2    | 2    |

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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 |
| ANEMIA              | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 2    | 1    | 0    | 0    | 0    | 1    | 1    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 1                       | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| JAUNDICE            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 2    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 1                       | 1    | 1    | 1    | 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    | 1    | 1    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CRUSTA              | Control    | 1                       | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HEMORRHAGE          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    | 1    | 1    | 0    | 0    | 1    | 1    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    | 1    | 0    | 1    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                     | 90 ppm     | 4                       | 3    | 1    | 3    | 1    | 0    | 1    | 0    | 0    | 2    | 2    | 2    | 2    | 0    |

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CLINICAL OBSERVATION (SUMMARY)  
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| Clinical sign       | Group Name | Administration Week-day |       |       |       |       |       |
|---------------------|------------|-------------------------|-------|-------|-------|-------|-------|
|                     |            | 99-7                    | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| ANEMIA              | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 10 ppm     | 0                       | 0     | 0     | 1     | 1     | 1     |
|                     | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| JAUNDICE            | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 10 ppm     | 0                       | 0     | 1     | 0     | 0     | 0     |
|                     | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| ULCER               | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 10 ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
|                     | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| EROSION             | Control    | 1                       | 1     | 1     | 1     | 1     | 1     |
|                     | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| CRUSTA              | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 10 ppm     | 0                       | 0     | 0     | 2     | 2     | 2     |
|                     | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| HEMORRHAGE          | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| PROLAPSE OF PENIS   | Control    | 1                       | 1     | 1     | 1     | 1     | 0     |
|                     | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| IRREGULAR BREATHING | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 30 ppm     | 1                       | 1     | 0     | 0     | 0     | 0     |
|                     | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |

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 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
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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 |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| NOISY                   | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| DEEP BREATHING          | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| ABNORMAL RESPIRA. SOUND | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |

(HAN190)

BAIS 4

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1 104

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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 |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| NOISY                   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| DEEP BREATHING          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ABNORMAL RESPIRA. SOUND | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
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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 |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| NOISY                   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| DEEP BREATHING          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ABNORMAL RESPIRA. SOUND | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

(HAN190)

BAIS 4



STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
 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 |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| NOISY                   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    |
| DEEP BREATHING          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ABNORMAL RESPIRA. SOUND | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
 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 |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    |
| NOISY                   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 1                       | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| DEEP BREATHING          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    |
| ABNORMAL RESPIRA. SOUND | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
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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 |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 1    | 2    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    |
| NOISY                   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 1    | 2    | 1    | 1    | 2    | 2    | 1    | 2    | 2    | 2    |
| DEEP BREATHING          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 1    | 0    | 2    | 1    | 1    | 0    | 0    | 1    | 0    |
| ABNORMAL RESPIRA. SOUND | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 1                       | 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
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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 |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 3                       | 5    | 4    | 2    | 1    | 1    | 0    | 2    | 3    | 6    | 7    | 5    | 4    | 4    |
| NOISY                   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 2                       | 1    | 1    | 1    | 1    | 1    | 3    | 1    | 2    | 2    | 0    | 0    | 1    | 0    |
| DEEP BREATHING          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 2    | 1    | 0    | 0    | 0    | 0    | 0    | 3    | 1    | 0    | 0    | 2    |
| ABNORMAL RESPIRA. SOUND | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    | 1    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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STUDY NO. : 0437  
ANIMAL : RAT F344/DuCrj  
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 |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 90 ppm     | 4                       | 3     | 3     | 2     | 2     | 3     |
| NOISY                   | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 90 ppm     | 0                       | 1     | 0     | 0     | 0     | 0     |
| DEEP BREATHING          | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 90 ppm     | 2                       | 2     | 1     | 0     | 0     | 0     |
| ABNORMAL RESPIRA. SOUND | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| SUBNORMAL TEMP          | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |

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BAIS 4

## APPENDIX C 2

### CLINICAL OBSERVATION : FEMALE

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
 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    |
|                         | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCrj  
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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |



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REPORT TYPE : A1 104

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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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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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    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
|                         | 90 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    | 1    | 1    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    | 1    | 1    | 1    | 1    | 1    | 1    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 1    | 1    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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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    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                         | 90 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 2    | 3    | 3    | 4    | 4    | 4    | 4    | 5    |
| MORIBUND SACRIFICE      | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 2    | 3    | 3    | 3    | 3    | 3    | 3    | 3    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 2    | 2    | 2    |
|                         | 90 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 4    | 4    | 4    | 4    | 4    | 4    |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| WASTING                 | Control    | 0                       | 0    | 0    | 1    | 1    | 2    | 2    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 2    | 1    | 0    | 0    | 1    | 1    | 1    |
| SOILED                  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PILOERECTION            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED PERI-GENITALIA   | Control    | 1                       | 1    | 0    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 1    | 0    |

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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    | 0                       | 0    | 0    | 1    | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 3    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                         | 30 ppm     | 2                       | 3    | 3    | 4    | 4    | 4    | 5    | 5    | 5    | 5    | 6    | 6    | 6    | 6    |
|                         | 90 ppm     | 6                       | 8    | 8    | 8    | 8    | 9    | 11   | 13   | 13   | 13   | 14   | 14   | 15   | 15   |
| MORIBUND SACRIFICE      | Control    | 3                       | 3    | 3    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 5    | 5    | 5    | 5    |
|                         | 10 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                         | 30 ppm     | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                         | 90 ppm     | 5                       | 5    | 5    | 5    | 5    | 5    | 6    | 7    | 7    | 7    | 8    | 8    | 8    | 10   |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| WASTING                 | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 1    | 1    | 1    | 2    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 1    | 1    | 1    | 3    | 0    | 0    | 2    | 1    | 1    | 2    | 3    |
| SOILED                  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PILOERECTION            | Control    | 0                       | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 2    |
| FROG BELLY              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 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    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 1    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |

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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    | 3                       | 3     | 4     | 4     | 4     | 4     |
|                         | 10 ppm     | 1                       | 1     | 2     | 2     | 2     | 2     |
|                         | 30 ppm     | 6                       | 6     | 6     | 6     | 6     | 6     |
|                         | 90 ppm     | 15                      | 16    | 18    | 19    | 20    | 21    |
| MORIBUND SACRIFICE      | Control    | 5                       | 5     | 6     | 6     | 6     | 6     |
|                         | 10 ppm     | 1                       | 1     | 2     | 2     | 2     | 3     |
|                         | 30 ppm     | 2                       | 2     | 2     | 2     | 2     | 3     |
|                         | 90 ppm     | 12                      | 12    | 12    | 13    | 13    | 14    |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 10 ppm     | 0                       | 1     | 0     | 0     | 0     | 0     |
|                         | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| WASTING                 | Control    | 2                       | 3     | 2     | 2     | 2     | 2     |
|                         | 10 ppm     | 0                       | 1     | 0     | 1     | 1     | 0     |
|                         | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 1     |
|                         | 90 ppm     | 2                       | 3     | 1     | 1     | 1     | 1     |
| SOILED                  | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| PILOERECTION            | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 1     |
| FROG BELLY              | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| SOILED PERI-GENITALIA   | Control    | 0                       | 1     | 0     | 0     | 0     | 0     |
|                         | 10 ppm     | 0                       | 0     | 1     | 1     | 1     | 0     |
|                         | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 1     |
|                         | 90 ppm     | 0                       | 0     | 0     | 1     | 0     | 1     |

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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 |
| EXOPHTHALMOS             | Control    | 0                       | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 1    | 1    | 1    | 1    | 1    |
|                          | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0   | 0   | 0   | 1   | 1   | 1   | 1   | 1   | 1    | 1    | 1    | 1    | 1    |
|                          | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| EYE OPACITY              | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| CATARACT                 | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 90 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    |
|                          | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| ANTERIOR CHAMBER OPACITY | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 1    | 1    |
|                          | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 90 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    |
|                          | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 90 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    |
|                          | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. NOSE                  | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |

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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 |
| EXOPHTHALMOS             | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EYE OPACITY              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CATARACT                 | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                          | 30 ppm     | 0                       | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    |
| CORNEAL OPACITY          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ANTERIOR CHAMBER OPACITY | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 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    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 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    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NOSE                  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |



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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 |
| EXOPHTHALMOS             | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 1                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EYE OPACITY              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CATARACT                 | Control    | 1                       | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                          | 10 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 2    |
|                          | 30 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 2    | 2    |
|                          | 90 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
| CORNEAL OPACITY          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ANTERIOR CHAMBER OPACITY | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 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    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 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    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NOSE                  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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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 |
| EXOPHTHALMOS             | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EYE OPACITY              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CATARACT                 | Control    | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                          | 10 ppm     | 2                       | 2    | 2    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    |
|                          | 30 ppm     | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 3    | 3    |
|                          | 90 ppm     | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
| CORNEAL OPACITY          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ANTERIOR CHAMBER OPACITY | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXTERNAL MASS            | Control    | 0                       | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| INTERNAL MASS            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NOSE                  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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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 |
| EXOPHTHALMOS             | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 1    | 1    | 1    | 1    | 1    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EYE OPACITY              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 1                       | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CATARACT                 | Control    | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                          | 10 ppm     | 3                       | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    |
|                          | 30 ppm     | 3                       | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    |
|                          | 90 ppm     | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
| CORNEAL OPACITY          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ANTERIOR CHAMBER OPACITY | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXTERNAL MASS            | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 2    | 2    | 2    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    |
| INTERNAL MASS            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NOSE                  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    |

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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 |
| EXOPHTHALMOS             | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 1                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EYE OPACITY              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 1                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CATARACT                 | Control    | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 3    |
|                          | 10 ppm     | 3                       | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    |
|                          | 30 ppm     | 3                       | 3    | 3    | 3    | 3    | 3    | 3    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                          | 90 ppm     | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 1    | 2    | 2    | 2    | 2    | 2    |
| CORNEAL OPACITY          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 2    | 3    | 2    | 1    | 0    | 0    | 1    | 1    | 0    |
| ANTERIOR CHAMBER OPACITY | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXTERNAL MASS            | Control    | 2                       | 3    | 3    | 3    | 4    | 4    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 1                       | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 2    | 1    | 1    | 1    | 1    | 1    | 3    | 2    |
| INTERNAL MASS            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 1    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NOSE                  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 1    |

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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 |
| EXOPHTHALMOS             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
| EYE OPACITY              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CATARACT                 | Control    | 3                       | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    |
|                          | 10 ppm     | 3                       | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    |
|                          | 30 ppm     | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                          | 90 ppm     | 2                       | 2    | 2    | 2    | 2    | 2    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| CORNEAL OPACITY          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 1    | 0    | 0    | 0    | 1    |
| ANTERIOR CHAMBER OPACITY | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    | 0    | 0    |
| EXTERNAL MASS            | Control    | 3                       | 3    | 4    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 4    | 5    | 5    | 6    |
|                          | 10 ppm     | 0                       | 0    | 0    | 1    | 1    | 1    | 1    | 2    | 2    | 2    | 2    | 3    | 3    | 4    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                          | 90 ppm     | 1                       | 1    | 1    | 1    | 1    | 4    | 4    | 2    | 2    | 2    | 1    | 1    | 3    | 2    |
| INTERNAL MASS            | Control    | 0                       | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 1                       | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 1                       | 0    | 1    | 1    | 1    | 2    | 0    | 0    | 1    | 1    | 0    | 0    | 1    | 1    |
| M. NOSE                  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                          | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 3    | 3    | 1    | 1    | 1    | 0    | 0    | 1    | 0    |

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| Clinical sign            | Group Name | Administration Week-day |       |       |       |       |       |
|--------------------------|------------|-------------------------|-------|-------|-------|-------|-------|
|                          |            | 99-7                    | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| EXOPHTHALMOS             | Control    | 1                       | 1     | 0     | 0     | 0     | 1     |
|                          | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| EYE OPACITY              | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| CATARACT                 | Control    | 3                       | 3     | 3     | 3     | 3     | 3     |
|                          | 10 ppm     | 3                       | 3     | 3     | 3     | 3     | 3     |
|                          | 30 ppm     | 2                       | 2     | 2     | 2     | 2     | 2     |
|                          | 90 ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
| CORNEAL OPACITY          | Control    | 1                       | 1     | 0     | 0     | 0     | 1     |
|                          | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| ANTERIOR CHAMBER OPACITY | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 1     |
| EXTERNAL MASS            | Control    | 6                       | 6     | 5     | 5     | 5     | 5     |
|                          | 10 ppm     | 4                       | 7     | 5     | 5     | 5     | 4     |
|                          | 30 ppm     | 2                       | 2     | 3     | 3     | 3     | 3     |
|                          | 90 ppm     | 2                       | 2     | 2     | 2     | 2     | 3     |
| INTERNAL MASS            | Control    | 1                       | 1     | 1     | 1     | 2     | 2     |
|                          | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 30 ppm     | 0                       | 0     | 1     | 1     | 1     | 1     |
|                          | 90 ppm     | 0                       | 0     | 1     | 2     | 2     | 0     |
| M. NOSE                  | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                          | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |

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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. EYE              | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. PERI-MOUTH       | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. PERI EAR         | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. HEAD             | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. NECK             | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. ANTERIOR. DORSUM | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |

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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. EYE              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI-MOUTH       | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI EAR         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. HEAD             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NECK             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ANTERIOR. DORSUM | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |



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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. EYE              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI-MOUTH       | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI EAR         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. HEAD             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NECK             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ANTERIOR. DORSUM | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                     |            | 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. EYE              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI-MOUTH       | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI EAR         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. HEAD             | Control    | 0                       | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NECK             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ANTERIOR. DORSUM | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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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. EYE              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI-MOUTH       | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI EAR         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. HEAD             | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NECK             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    | 1    | 1    | 1    | 1    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ANTERIOR. DORSUM | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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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. EYE              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI-MOUTH       | Control    | 0                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI EAR         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 1                       | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. HEAD             | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NECK             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. BREAST           | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 1                       | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ABDOMEN          | Control    | 0                       | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ANTERIOR. DORSUM | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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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. EYE              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
| M. PERI-MOUTH       | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 2    | 2    | 2    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI EAR         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. HEAD             | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NECK             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 2    | 2    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ABDOMEN          | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 2    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ANTERIOR. DORSUM | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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| Clinical sign       | Group Name | Administration Week-day |       |       |       |       |       |
|---------------------|------------|-------------------------|-------|-------|-------|-------|-------|
|                     |            | 99-7                    | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| M. EYE              | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 90 ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
| M. PERI-MOUTH       | Control    | 2                       | 2     | 1     | 1     | 1     | 1     |
|                     | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. PERI EAR         | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. HEAD             | Control    | 1                       | 1     | 1     | 1     | 1     | 1     |
|                     | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. NECK             | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 10 ppm     | 1                       | 1     | 1     | 1     | 1     | 0     |
|                     | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. BREAST           | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 10 ppm     | 2                       | 5     | 4     | 4     | 4     | 4     |
|                     | 30 ppm     | 1                       | 1     | 2     | 2     | 2     | 2     |
|                     | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. ABDOMEN          | Control    | 2                       | 2     | 2     | 2     | 2     | 2     |
|                     | 10 ppm     | 0                       | 0     | 0     | 0     | 1     | 1     |
|                     | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 1     |
| M. ANTERIOR. DORSUM | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |

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ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1 104

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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 |
| M. HINDLIMB         | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| JAUNDICE            | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| HEMORRHAGE          | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |

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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. HINDLIMB         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| JAUNDICE            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HEMORRHAGE          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |



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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. HINDLIMB         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| JAUNDICE            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HEMORRHAGE          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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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. HINDLIMB         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| JAUNDICE            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HEMORRHAGE          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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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. HINDLIMB         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
| JAUNDICE            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HEMORRHAGE          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    |
|                     | 30 ppm     | 1                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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 ANIMAL : RAT F344/DuCrj  
 REPORT TYPE : A1 104

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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. HINDLIMB         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
| ANEMIA              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 1                       | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| JAUNDICE            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HEMORRHAGE          | Control    | 0                       | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 2    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    |
| IRREGULAR BREATHING | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    | 0    | 0    | 1    | 1    | 2    |

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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. HINDLIMB         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. GENITALIA        | Control    | 0                       | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| ANEMIA              | Control    | 0                       | 0    | 1    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 2    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 1                       | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
| JAUNDICE            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 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    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HEMORRHAGE          | Control    | 0                       | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 1    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 1                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| IRREGULAR BREATHING | Control    | 0                       | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 3    | 1    | 0    | 1    | 1    | 0    | 0    | 0    | 0    |

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| Clinical sign       | Group Name | Administration Week-day |       |       |       |       |       |
|---------------------|------------|-------------------------|-------|-------|-------|-------|-------|
|                     |            | 99-7                    | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| M. HINDLIMB         | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 30 ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
|                     | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. GENITALIA        | Control    | 1                       | 1     | 1     | 1     | 1     | 1     |
|                     | 10 ppm     | 1                       | 1     | 0     | 0     | 0     | 0     |
|                     | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 1     |
|                     | 90 ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
| ANEMIA              | Control    | 2                       | 3     | 1     | 1     | 1     | 1     |
|                     | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 90 ppm     | 0                       | 1     | 1     | 1     | 1     | 0     |
| JAUNDICE            | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 90 ppm     | 0                       | 0     | 0     | 1     | 1     | 0     |
| EROSION             | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 30 ppm     | 0                       | 0     | 1     | 0     | 0     | 0     |
|                     | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| CRUSTA              | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 30 ppm     | 0                       | 0     | 0     | 1     | 1     | 1     |
|                     | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| HEMORRHAGE          | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| IRREGULAR BREATHING | Control    | 1                       | 1     | 0     | 0     | 0     | 0     |
|                     | 10 ppm     | 0                       | 1     | 0     | 0     | 0     | 0     |
|                     | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 90 ppm     | 0                       | 0     | 1     | 1     | 0     | 0     |

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ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1 104

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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 |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| NOISY                   | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| TACHYPNEA               | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| DEEP BREATHING          | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |

(HAN190)

BAIS 4

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
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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 |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| NOISY                   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| TACHYPNEA               | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| DEEP BREATHING          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

(HAN190)

BAIS 4



STUDY NO. : 0437  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : FEMALE

PAGE : 83

| 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 |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| NOISY                   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| TACHYPNEA               | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| DEEP BREATHING          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

(HAN190)

BAIS 4

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : FEMALE

PAGE : 84

| 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 |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| NOISY                   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| TACHYPNEA               | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| DEEP BREATHING          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

(HAN190)

BAIS 4

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : FEMALE

PAGE : 85

| 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 |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| NOISY                   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    |
| TACHYPNEA               | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 1                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| DEEP BREATHING          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : FEMALE

PAGE : 86

| 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 |  |      |      |      |      |      |      |      |      |      |      |      |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
| NOISY                   | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 1    | 0    |
| TACHYPNEA               | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| DEEP BREATHING          | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    |  | 0    | 0    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : FEMALE

PAGE : 87

| 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 |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 2    | 3    | 2    | 5    | 6    | 4    |
| NOISY                   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    |
| TACHYPNEA               | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| DEEP BREATHING          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 30 ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 90 ppm     | 1                       | 0    | 0    | 0    | 0    | 2    | 3    | 0    | 0    | 2    | 1    | 2    | 1    | 4    |

(HAN190)

BAIS 4

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCrj  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : FEMALE

PAGE : 88

| Clinical sign           | Group Name | Administration Week-day |       |       |       |       |       |
|-------------------------|------------|-------------------------|-------|-------|-------|-------|-------|
|                         |            | 99-7                    | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 10 ppm     | 0                       | 1     | 0     | 0     | 0     | 0     |
|                         | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 90 ppm     | 4                       | 5     | 4     | 2     | 1     | 1     |
| NOISY                   | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| TACHYPNEA               | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 90 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
| DEEP BREATHING          | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 10 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 30 ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 90 ppm     | 4                       | 3     | 1     | 0     | 0     | 1     |

(HAN190)

BAIS 4

## APPENDIX D 1

### BODY WEIGHT CHANGES : MALE

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
 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  |      |
| Control    | 127±           | 5 | 159±     | 8    | 189± | 10   | 215± | 10   | 235± | 11   | 251± | 11   |
| 10 ppm     | 127±           | 5 | 156±     | 8    | 187± | 10   | 211± | 11   | 231± | 12   | 248± | 12   |
| 30 ppm     | 127±           | 5 | 155±     | 7    | 183± | 9*   | 208± | 9**  | 227± | 10** | 243± | 11** |
| 90 ppm     | 127±           | 5 | 145±     | 11** | 168± | 17** | 191± | 10** | 207± | 10** | 220± | 11** |

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

Test of Dunnett

(HAN260)

BAIS 4



STUDY NO. : 0437  
ANIMAL : RAT F344/DuCrj  
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    | 280±           | 13   | 293±     | 13   | 304± | 14   | 313± | 14   | 321± | 14   | 328± | 15   | 334± | 14   |  |  |
| 10 ppm     | 275±           | 12   | 288±     | 12   | 297± | 12** | 305± | 12*  | 314± | 12*  | 319± | 14** | 327± | 13*  |  |  |
| 30 ppm     | 270±           | 12** | 282±     | 13** | 292± | 12** | 300± | 12** | 308± | 12** | 317± | 13** | 323± | 13** |  |  |
| 90 ppm     | 240±           | 12** | 247±     | 12** | 254± | 12** | 259± | 12** | 266± | 12** | 283± | 13** | 280± | 14** |  |  |

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

Test of Dunnett

(HAN260)

BAIS 4

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
 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 |      |
| Control    | 339±           | 15   | 357±     | 18   | 372± | 19   | 384± | 21   | 393± | 22   | 404± | 23   |
| 10 ppm     | 332±           | 13*  | 351±     | 14   | 367± | 16   | 379± | 17   | 388± | 18   | 399± | 20   |
| 30 ppm     | 330±           | 14** | 348±     | 16*  | 363± | 17*  | 375± | 19*  | 385± | 19   | 394± | 21   |
| 90 ppm     | 280±           | 14** | 294±     | 15** | 304± | 17** | 314± | 16** | 320± | 17** | 326± | 18** |

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

Test of Dunnett

(HAN260)

BAIS 4

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
 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 |      |
| Control    | 422±           | 25   | 429±     | 26   | 435± | 26   | 439± | 27   | 442± | 27   | 444± | 27   |
| 10 ppm     | 418±           | 22   | 424±     | 22   | 431± | 23   | 433± | 23   | 436± | 23   | 437± | 22   |
| 30 ppm     | 413±           | 22   | 419±     | 24   | 424± | 25   | 424± | 26   | 431± | 26   | 429± | 28*  |
| 90 ppm     | 343±           | 19** | 342±     | 19** | 348± | 18** | 351± | 18** | 349± | 27** | 348± | 26** |

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

Test of Dunnett

(HAN260)

BAIS 4

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
 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 |      |
| Control    | 451±           | 27   | 454±     | 27   | 454± | 28   | 452± | 29   | 447± | 31   | 441± | 29   |
| 10 ppm     | 443±           | 23   | 447±     | 22   | 449± | 23   | 451± | 23   | 449± | 21   | 447± | 25   |
| 30 ppm     | 436±           | 28*  | 437±     | 28** | 438± | 28*  | 439± | 30   | 435± | 38   | 436± | 39   |
| 90 ppm     | 352±           | 26** | 347±     | 31** | 338± | 38** | 337± | 35** | 322± | 44** | 334± | 26** |

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

Test of Dunnett

(HAN260)

BAIS 4

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCrj  
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    | 432±                    | 34   | 431±  | 30   | 422±  | 34   |
| 10 ppm     | 434±                    | 27   | 428±  | 26   | 423±  | 26   |
| 30 ppm     | 423±                    | 38   | 421±  | 30   | 418±  | 31   |
| 90 ppm     | 319±                    | 27** | 310±  | 37** | 294±  | 32** |

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

Test of Dunnett

(HAN260)

BAIS 4

## APPENDIX D 2

### BODY WEIGHT CHANGES : FEMALE

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
 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  |     |
| Control    | 95±            | 3 | 110±     | 5   | 123± | 5   | 133± | 6   | 141± | 6   | 149± | 7   |
| 10 ppm     | 95±            | 3 | 108±     | 5   | 121± | 6   | 131± | 7   | 139± | 7   | 147± | 8   |
| 30 ppm     | 95±            | 3 | 108±     | 4   | 119± | 5*  | 130± | 6   | 136± | 6** | 145± | 7*  |
| 90 ppm     | 95±            | 3 | 102±     | 5** | 113± | 6** | 124± | 7** | 131± | 7** | 140± | 8** |

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

Test of Dunnett

(HAN260)

BAIS 4

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
 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 |     |
| Control    | 159±           | 9   | 162±     | 8   | 168± | 9   | 171± | 9   | 176± | 10  | 178± | 10  |
| 10 ppm     | 158±           | 10  | 160±     | 9   | 165± | 10  | 168± | 10  | 172± | 11  | 176± | 11  |
| 30 ppm     | 153±           | 8** | 156±     | 7** | 161± | 7** | 165± | 8** | 169± | 8** | 173± | 9*  |
| 90 ppm     | 148±           | 8** | 151±     | 8** | 155± | 8** | 157± | 9** | 162± | 9** | 168± | 9** |

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

Test of Dunnett

(HAN260)

BAIS 4



STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
 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 |     |
| Control    | 181±           | 11  | 188±     | 12  | 195± | 13  | 199± | 14  | 203± | 14  | 207± | 15  |
| 10 ppm     | 180±           | 11  | 187±     | 11  | 194± | 12  | 197± | 13  | 202± | 14  | 207± | 13  |
| 30 ppm     | 175±           | 9*  | 183±     | 10  | 189± | 11* | 194± | 10  | 200± | 12  | 205± | 12  |
| 90 ppm     | 165±           | 9** | 170±     | 9** | 175± | 9** | 179± | 9** | 182± | 9** | 185± | 9** |

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

Test of Dunnett

(HAN260)

BAIS 4

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
 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 |      |
| Control    | 217±           | 16   | 222±     | 17   | 226± | 18   | 229± | 18   | 233± | 20   | 234± | 21   |
| 10 ppm     | 216±           | 13   | 220±     | 14   | 228± | 16   | 229± | 16   | 232± | 16   | 236± | 18   |
| 30 ppm     | 216±           | 14   | 218±     | 14   | 227± | 15   | 229± | 16   | 233± | 17   | 235± | 17   |
| 90 ppm     | 195±           | 11** | 195±     | 11** | 201± | 13** | 201± | 11** | 201± | 12** | 203± | 12** |

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

Test of Dunnett

(HAN260)

BAIS 4

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
 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 |      |
| Control    | 242±           | 24   | 249±     | 27   | 255± | 29   | 258± | 30   | 261± | 31   | 267± | 28   |
| 10 ppm     | 248±           | 21   | 255±     | 21   | 260± | 22   | 262± | 21   | 267± | 20   | 271± | 22   |
| 30 ppm     | 245±           | 19   | 251±     | 21   | 256± | 24   | 260± | 22   | 263± | 21   | 266± | 22   |
| 90 ppm     | 212±           | 12** | 212±     | 13** | 211± | 19** | 213± | 14** | 214± | 11** | 210± | 17** |

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

Test of Dunnett

(HAN260)

BAIS 4

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCrj  
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   | 271±           | 33   | 271±     | 30   | 269±  | 35   |
| 10 ppm  | 274±           | 21   | 274±     | 23   | 272±  | 24   |
| 30 ppm  | 274±           | 21   | 274±     | 25   | 270±  | 28   |
| 90 ppm  | 206±           | 21** | 207±     | 24** | 206±  | 24** |
| Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett |                |      |          |      |       |      |

(HAN260)

BAIS 4

## APPENDIX E 1

### FOOD CONSUMPTION CHANGES : MALE

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
 UNIT : g  
 REPORT TYPE : A1 104  
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 1

| Group Name | Administration week-day(effective) |             |             |             |             |             |             |
|------------|------------------------------------|-------------|-------------|-------------|-------------|-------------|-------------|
|            | 1-7(4)                             | 2-7(7)      | 3-7(7)      | 4-7(7)      | 5-7(7)      | 6-7(7)      | 7-7(7)      |
| Control    | 15.6± 1.1                          | 16.4± 1.0   | 17.4± 1.3   | 17.4± 1.1   | 17.3± 1.2   | 17.1± 1.0   | 17.0± 1.0   |
| 10 ppm     | 15.4± 1.2                          | 16.1± 1.1   | 16.8± 1.3*  | 17.2± 1.1   | 16.6± 0.9** | 16.6± 0.9** | 16.6± 1.0   |
| 30 ppm     | 14.9± 1.2*                         | 15.7± 1.0*  | 16.5± 1.2** | 16.6± 1.1** | 16.4± 1.1** | 16.4± 0.9** | 16.4± 1.0** |
| 90 ppm     | 12.3± 1.5**                        | 13.7± 1.6** | 14.6± 1.0** | 14.9± 1.0** | 14.7± 1.0** | 14.6± 0.9** | 14.9± 1.0** |

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

Test of Dunnett

(HAN260)

BAIS 4

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
 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    | 16.9± 0.9                | 17.1± 1.0                     | 16.7± 0.9   | 16.2± 0.9   | 16.7± 1.0   | 16.3± 1.0   | 16.5± 1.0   |
| 10 ppm     | 16.4± 1.0*               | 16.4± 0.8**                   | 16.4± 0.8   | 15.8± 1.0   | 16.2± 0.9*  | 15.6± 1.0** | 16.0± 0.9*  |
| 30 ppm     | 16.0± 0.9**              | 16.3± 0.9**                   | 16.1± 0.9** | 16.0± 1.0   | 16.5± 1.0   | 16.0± 0.9   | 15.8± 0.8** |
| 90 ppm     | 14.0± 0.7**              | 14.0± 0.9**                   | 14.1± 0.7** | 14.5± 0.9** | 16.1± 1.1** | 14.3± 0.9** | 13.7± 0.7** |

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

Test of Dunnett

(HAN260)

BATS 4

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCrj  
UNIT : g  
REPORT TYPE : A1 104  
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
ALL ANIMALS

PAGE : 3

| 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    | 16.4± 1.0                          | 16.6± 1.1   | 16.8± 1.1   | 16.5± 0.9   | 16.9± 1.2   | 17.0± 1.0   | 17.2± 1.0   |
| 10 ppm     | 16.1± 1.0                          | 16.2± 1.5   | 16.3± 1.1   | 16.5± 1.0   | 16.7± 1.1   | 16.9± 1.1   | 17.0± 1.1   |
| 30 ppm     | 15.9± 1.0*                         | 16.1± 1.0   | 15.9± 1.1** | 16.2± 1.0   | 16.5± 1.1   | 16.6± 1.3   | 16.8± 1.1   |
| 90 ppm     | 14.5± 0.9**                        | 14.4± 0.9** | 14.7± 1.0** | 15.3± 1.0** | 15.2± 1.0** | 15.5± 1.1** | 15.9± 1.0** |

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

Test of Dunnett

(HAN260)

BAIS 4



STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
 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    | 16.9± 1.1                          | 17.0± 1.1   | 16.7± 0.9   | 16.9± 0.9   | 17.0± 1.1   | 17.2± 0.9   | 17.5± 1.1   |
| 10 ppm     | 16.8± 0.9                          | 16.9± 0.9   | 16.7± 1.0   | 16.9± 0.9   | 16.9± 1.0   | 17.3± 1.1   | 17.5± 1.0   |
| 30 ppm     | 16.6± 1.2                          | 16.7± 1.0   | 16.4± 1.1   | 16.7± 1.0   | 16.5± 1.4   | 16.8± 1.3   | 17.2± 1.2   |
| 90 ppm     | 15.3± 1.0**                        | 15.9± 1.0** | 15.4± 0.8** | 15.5± 1.4** | 15.4± 1.8** | 15.4± 1.0** | 16.0± 1.2** |

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

Test of Dunnett

(HAN260)

BAIS 4

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCrj  
UNIT : g  
REPORT TYPE : A1 104  
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
ALL ANIMALS

PAGE : 5

| Group Name  | Administration week-day(effective) |             |             |             |             |             |             |
|---|------------------------------------|-------------|-------------|-------------|-------------|-------------|-------------|
|   | 74-7(7)                            | 78-7(7)     | 82-7(7)     | 86-7(7)     | 90-7(7)     | 94-7(7)     | 98-7(7)     |
| Control   | 17.2± 1.1                          | 16.8± 1.0   | 17.0± 1.1   | 16.6± 1.1   | 16.0± 1.7   | 15.6± 3.0   | 16.6± 1.3   |
| 10 ppm  | 17.4± 1.2                          | 17.6± 1.5   | 17.6± 1.4   | 16.9± 1.1   | 16.6± 1.2   | 16.7± 2.5*  | 16.5± 1.8   |
| 30 ppm  | 16.6± 1.2*                         | 16.7± 1.9   | 16.9± 1.5   | 15.9± 2.8   | 16.6± 1.9   | 16.4± 1.9   | 16.4± 1.6   |
| 90 ppm  | 14.8± 1.2**                        | 14.7± 2.7** | 14.8± 1.8** | 13.9± 2.9** | 14.9± 1.2** | 13.9± 2.9** | 15.0± 1.3** |
| Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett |                                    |             |             |             |             |             |             |

(HAN260)

BAIS 4

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCrj  
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    | 17.1± 1.8                          | 16.3± 1.9   |
| 10 ppm     | 16.8± 2.0                          | 16.6± 1.8   |
| 30 ppm     | 16.6± 1.7                          | 16.7± 1.4   |
| 90 ppm     | 15.0± 2.6**                        | 13.6± 2.1** |

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

Test of Dunnett

## APPENDIX E 2

### FOOD CONSUMPTION CHANGES : FEMALE

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
 UNIT : g  
 REPORT TYPE : A1 104  
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 7

| Group Name  | Administration week-day(effective) |             |             |             |            |             |           |
|---|------------------------------------|-------------|-------------|-------------|------------|-------------|-----------|
|   | 1-7(4)                             | 2-7(7)      | 3-7(7)      | 4-7(7)      | 5-7(7)     | 6-7(7)      | 7-7(7)    |
| Control   | 10.9± 0.7                          | 11.0± 0.8   | 11.2± 0.8   | 11.1± 0.7   | 11.6± 1.2  | 10.9± 0.9   | 11.0± 0.9 |
| 10 ppm  | 10.8± 0.8                          | 10.9± 0.8   | 11.3± 0.9   | 11.2± 1.0   | 11.6± 1.5  | 10.9± 0.9   | 11.1± 1.3 |
| 30 ppm  | 10.7± 0.7                          | 10.5± 0.6** | 10.8± 0.6   | 10.8± 0.5   | 11.2± 0.8  | 10.5± 0.7*  | 10.7± 0.9 |
| 90 ppm  | 9.2± 0.6**                         | 9.9± 0.7**  | 10.6± 1.0** | 10.4± 0.7** | 11.0± 0.8* | 10.4± 0.7** | 10.9± 1.0 |
| Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett |                                    |             |             |             |            |             |           |

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
 UNIT : g  
 REPORT TYPE : A1 104  
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 8

| Group Name | Administration week-day(effective) |             |           |           |           |           |            |
|------------|------------------------------------|-------------|-----------|-----------|-----------|-----------|------------|
|            | 8-7(7)                             | 9-7(7)      | 10-7(7)   | 11-7(7)   | 12-7(7)   | 13-7(7)   | 14-7(7)    |
| Control    | 10.2± 0.8                          | 10.9± 0.9   | 10.1± 1.1 | 10.7± 1.1 | 10.4± 1.1 | 10.5± 0.9 | 10.2± 0.9  |
| 10 ppm     | 10.2± 0.7                          | 10.4± 0.8** | 10.1± 0.8 | 10.4± 0.9 | 10.2± 1.0 | 10.4± 1.2 | 10.1± 1.1  |
| 30 ppm     | 10.0± 0.7                          | 10.6± 1.0   | 10.1± 0.9 | 10.7± 1.2 | 10.4± 1.0 | 10.2± 0.8 | 10.1± 0.9  |
| 90 ppm     | 9.6± 0.7**                         | 10.0± 0.8** | 9.8± 0.9  | 10.7± 1.0 | 10.6± 1.0 | 10.0± 0.9 | 9.3± 0.9** |

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

Test of Dunnett

(HAN260)

BAIS 4

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
 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    | 9.9± 0.8                           | 10.2± 1.2 | 10.2± 1.1 | 10.4± 1.0 | 10.2± 0.8 | 10.4± 1.1 | 10.8± 0.9 |
| 10 ppm     | 10.0± 1.1                          | 10.3± 1.1 | 10.1± 0.9 | 10.3± 0.9 | 10.5± 0.8 | 10.5± 0.8 | 10.7± 0.7 |
| 30 ppm     | 10.0± 0.7                          | 10.1± 1.0 | 10.1± 0.7 | 10.6± 1.1 | 10.6± 0.8 | 10.7± 1.1 | 10.8± 1.0 |
| 90 ppm     | 9.9± 1.0                           | 10.0± 1.0 | 10.2± 1.0 | 10.4± 0.7 | 10.5± 0.9 | 10.5± 0.8 | 11.0± 1.3 |

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

Test of Dunnett

(HAN260)

BAIS 4

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
 UNIT : g  
 REPORT TYPE : A1 104  
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 10

| 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    | 10.7± 0.9                          | 10.9± 1.0 | 10.7± 0.8   | 10.8± 1.1 | 10.7± 1.3 | 11.5± 1.2 | 11.3± 1.1   |
| 10 ppm     | 10.6± 0.9                          | 11.1± 1.0 | 11.0± 0.8   | 10.9± 0.8 | 11.1± 1.0 | 12.0± 1.1 | 12.0± 1.2** |
| 30 ppm     | 10.4± 0.8                          | 11.3± 1.2 | 10.9± 1.1   | 10.8± 1.4 | 10.9± 1.0 | 11.6± 1.0 | 11.8± 1.1*  |
| 90 ppm     | 10.5± 0.7                          | 11.3± 1.2 | 10.2± 0.6** | 10.4± 0.8 | 10.7± 0.8 | 11.1± 1.0 | 11.7± 0.9   |

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

Test of Dunnett

(HAN260)

BAIS 4



STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
 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    | 11.5± 1.5                 | 11.5± 1.3                      | 11.6± 1.3   | 11.5± 1.2   | 11.4± 1.4   | 12.3± 1.8   | 12.2± 2.2  |
| 10 ppm     | 12.2± 1.1*                | 12.1± 1.4                      | 11.8± 1.0   | 12.1± 1.0*  | 12.1± 1.0*  | 12.0± 1.1   | 12.2± 1.1  |
| 30 ppm     | 11.8± 1.2                 | 11.8± 1.4                      | 11.9± 1.3   | 11.5± 1.0   | 11.7± 1.2   | 12.3± 2.1   | 12.2± 1.1  |
| 90 ppm     | 10.7± 0.9**               | 10.5± 1.9**                    | 10.8± 0.9** | 10.8± 0.7** | 10.1± 2.0** | 10.7± 1.2** | 9.9± 2.0** |

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

Test of Dunnett

(HAN260)

BAIS 4

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCrj  
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   | 11.7± 1.3                          | 11.5± 2.7 |
| 10 ppm  | 12.3± 1.3                          | 11.9± 1.2 |
| 30 ppm  | 12.4± 1.8                          | 11.7± 2.0 |
| 90 ppm  | 10.5± 3.3                          | 10.3± 2.8 |
| Significant difference : * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett |                                    |           |

(HAN260)

BAIS 4

## APPENDIX F 1

### HEMATOLOGY : MALE

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
 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>3</sup> /μl |     |
|------------|-------------------|---------------------------------------|------|--------------------|-------|-----------------|-------|-----------|------|-----------|-------|--------------|-------|---------------------------------|-----|
| Control    | 38                | 8.49±                                 | 1.44 | 14.5±              | 2.3   | 41.7±           | 5.6   | 49.9±     | 6.6  | 17.3±     | 1.5   | 34.7±        | 1.8   | 828±                            | 218 |
| 10 ppm     | 37                | 8.21±                                 | 1.53 | 14.0±              | 2.7   | 40.2±           | 6.6   | 49.3±     | 3.3  | 17.0±     | 1.2   | 34.6±        | 2.0   | 876±                            | 248 |
| 30 ppm     | 38                | 8.08±                                 | 1.69 | 13.7±              | 2.8   | 39.8±           | 6.5   | 50.4±     | 7.7  | 17.1±     | 1.9   | 34.1±        | 2.2   | 882±                            | 319 |
| 90 ppm     | 8                 | 6.93±                                 | 2.27 | 10.6±              | 3.0** | 33.2±           | 7.0** | 50.5±     | 11.4 | 15.8±     | 3.2** | 31.4±        | 2.7** | 997±                            | 399 |

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

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 4

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
 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>3</sup> /μl |      | Differential<br>N-BAND |   | WBC (%)<br>N-SEG |     | EOSINO |   | BASO |   | MONO |   | LYMPHO |    | OTHER |    |
|------------|-------------------|----------------------------|------|------------------------|---|------------------|-----|--------|---|------|---|------|---|--------|----|-------|----|
| Control    | 38                | 5.94±                      | 1.99 | 0±                     | 1 | 48±              | 8   | 2±     | 1 | 0±   | 0 | 5±   | 2 | 44±    | 9  | 2±    | 4  |
| 10 ppm     | 37                | 7.71±                      | 6.45 | 0±                     | 1 | 45±              | 11  | 2±     | 1 | 0±   | 0 | 5±   | 2 | 44±    | 10 | 4±    | 13 |
| 30 ppm     | 38                | 7.26±                      | 6.05 | 0±                     | 1 | 45±              | 9   | 2±     | 1 | 0±   | 0 | 4±   | 2 | 45±    | 9  | 4±    | 13 |
| 90 ppm     | 8                 | 9.74±                      | 5.56 | 1±                     | 1 | 37±              | 13* | 2±     | 2 | 0±   | 0 | 3±   | 2 | 45±    | 14 | 13±   | 19 |

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

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 4

## APPENDIX F 2

### HEMATOLOGY : FEMALE

STUDY NO. : 0437

ANIMAL : RAT F344/DuCrj

MEASURE. TIME : 1

SEX : FEMALE

REPORT TYPE : A1

## HEMATOLOGY (SUMMARY)

ALL ANIMALS (105W)

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>3</sup> /μl |     |
|------------|-------------------|---------------------------------------|------|--------------------|-----|-----------------|-----|-----------|-----|-----------|-----|--------------|-----|---------------------------------|-----|
| Control    | 38                | 7.86±                                 | 1.39 | 14.5±              | 2.6 | 40.4±           | 5.8 | 52.0±     | 4.3 | 18.4±     | 1.2 | 35.5±        | 2.6 | 621±                            | 153 |
| 10 ppm     | 45                | 8.16±                                 | 0.75 | 14.9±              | 1.3 | 41.2±           | 3.1 | 50.7±     | 2.5 | 18.3±     | 0.8 | 36.0±        | 0.8 | 622±                            | 82  |
| 30 ppm     | 41                | 7.94±                                 | 1.20 | 14.7±              | 1.9 | 40.9±           | 4.5 | 52.5±     | 8.3 | 18.8±     | 1.8 | 35.9±        | 1.5 | 636±                            | 155 |
| 90 ppm     | 15                | 8.00±                                 | 1.46 | 14.5±              | 2.8 | 41.1±           | 6.6 | 51.9±     | 3.6 | 18.1±     | 1.3 | 35.0±        | 2.5 | 624±                            | 161 |

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

Test of Dunnett

(HCL070)

BAIS 4

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
 MEASURE. TIME : 1  
 SEX : FEMALE

HEMATOLOGY (SUMMARY)  
 ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 4

| Group Name | NO. of<br>Animals | WBC<br>10 <sup>3</sup> /μl |       | Differential<br>N-BAND |   | WBC (%)<br>N-SEG |    | EOSINO |   | BASO |   | MONO |   | LYMPHO |    | OTHER |    |
|------------|-------------------|----------------------------|-------|------------------------|---|------------------|----|--------|---|------|---|------|---|--------|----|-------|----|
| Control    | 38                | 3.51±                      | 2.10  | 1±                     | 2 | 42±              | 10 | 2±     | 1 | 0±   | 0 | 4±   | 2 | 49±    | 9  | 2±    | 6  |
| 10 ppm     | 45                | 7.04±                      | 20.51 | 0±                     | 1 | 38±              | 11 | 2±     | 1 | 0±   | 0 | 4±   | 2 | 51±    | 12 | 4±    | 15 |
| 30 ppm     | 41                | 5.91±                      | 9.57  | 0±                     | 1 | 38±              | 12 | 2±     | 1 | 0±   | 0 | 4±   | 2 | 49±    | 15 | 8±    | 23 |
| 90 ppm     | 15                | 5.17±                      | 4.98  | 0±                     | 1 | 40±              | 8  | 1±     | 1 | 0±   | 0 | 3±   | 2 | 52±    | 4  | 3±    | 6  |

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

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 4



## APPENDIX G 1

BIOCHEMISTRY : MALE

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCrj  
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    | 38                | 6.7±                  | 0.4 | 2.9±            | 0.2   | 0.8±      | 0.1 | 0.23±                | 0.41 | 150±             | 27 | 190±                   | 84   | 154±                  | 173  |
| 10 ppm     | 37                | 6.6±                  | 0.4 | 2.8±            | 0.2   | 0.8±      | 0.1 | 0.16±                | 0.04 | 147±             | 22 | 194±                   | 76   | 146±                  | 107  |
| 30 ppm     | 38                | 6.5±                  | 0.4 | 2.8±            | 0.3   | 0.8±      | 0.1 | 0.21±                | 0.19 | 152±             | 23 | 172±                   | 54   | 112±                  | 62   |
| 90 ppm     | 8                 | 6.3±                  | 0.2 | 2.5±            | 0.3** | 0.7±      | 0.1 | 0.39±                | 0.74 | 129±             | 33 | 94±                    | 22** | 44±                   | 41** |

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

Test of Dunnett

(HCL074)

BAIS 4

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCrj  
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/l |    | LDH<br>IU/l |     | ALP<br>IU/l |       | G-GTP<br>IU/l |   | CK<br>IU/l |       |
|------------|-------------------|-----------------------|------|-------------|-------|-------------|----|-------------|-----|-------------|-------|---------------|---|------------|-------|
| Control    | 38                | 275±                  | 130  | 103±        | 121   | 42±         | 19 | 194±        | 88  | 205±        | 57    | 6±            | 3 | 119±       | 146   |
| 10 ppm     | 37                | 280±                  | 110  | 91±         | 55    | 42±         | 24 | 186±        | 49  | 351±        | 849   | 7±            | 4 | 109±       | 48    |
| 30 ppm     | 38                | 250±                  | 63   | 87±         | 67    | 38±         | 17 | 198±        | 112 | 237±        | 94    | 8±            | 5 | 111±       | 73    |
| 90 ppm     | 8                 | 164±                  | 34** | 156±        | 111** | 62±         | 32 | 202±        | 93  | 370±        | 144** | 6±            | 4 | 169±       | 105** |

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

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 4

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
 MEASURE. TIME : 1  
 SEX : MALE

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 3

| Group Name | NO. of Animals | UREA NITROGEN<br>mg/dl |     | CREATININE<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    | 38             | 20.7±                  | 8.6 | 0.6±                | 0.1 | 142±            | 2 | 3.8±               | 0.3  | 104±              | 2 | 10.4±            | 0.4  | 4.0±                          | 0.8   |
| 10 ppm     | 37             | 19.3±                  | 2.4 | 0.6±                | 0.1 | 142±            | 2 | 3.8±               | 0.3  | 104±              | 2 | 10.3±            | 0.4  | 4.2±                          | 0.5   |
| 30 ppm     | 38             | 19.7±                  | 3.1 | 0.6±                | 0.1 | 142±            | 1 | 3.9±               | 0.3  | 105±              | 1 | 10.2±            | 0.3  | 4.2±                          | 0.7   |
| 90 ppm     | 8              | 18.9±                  | 2.1 | 0.5±                | 0.0 | 143±            | 1 | 4.2±               | 0.4* | 104±              | 2 | 10.0±            | 0.2* | 4.9±                          | 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. : 0437  
 ANIMAL : RAT F344/DuCrj  
 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    | 38                | 6.7±                  | 0.6   | 3.4±            | 0.4  | 1.1±      | 0.1 | 0.16±                | 0.18 | 140±             | 14 | 126±                   | 23   | 62±                   | 62  |
| 10 ppm     | 45                | 7.0±                  | 0.4** | 3.5±            | 0.3  | 1.0±      | 0.2 | 0.14±                | 0.06 | 135±             | 20 | 138±                   | 28*  | 62±                   | 30  |
| 30 ppm     | 41                | 7.0±                  | 0.4   | 3.5±            | 0.4  | 1.0±      | 0.1 | 0.22±                | 0.47 | 140±             | 19 | 150±                   | 53** | 81±                   | 65* |
| 90 ppm     | 15                | 6.4±                  | 0.7   | 3.1±            | 0.5* | 0.9±      | 0.2 | 0.15±                | 0.09 | 126±             | 32 | 104±                   | 38   | 35±                   | 20  |

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

Test of Dunnett

(HCL074)

BAIS 4

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCrj  
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    | 38                | 226±                  | 38   | 115±        | 40  | 54±         | 19 | 214±        | 64  | 142±        | 59    | 2±            | 1  | 95±        | 18    |
| 10 ppm     | 45                | 245±                  | 43   | 150±        | 107 | 66±         | 34 | 242±        | 97  | 140±        | 62    | 3±            | 2  | 108±       | 62    |
| 30 ppm     | 41                | 267±                  | 81** | 192±        | 210 | 70±         | 49 | 436±        | 871 | 170±        | 150   | 4±            | 4  | 117±       | 82    |
| 90 ppm     | 15                | 192±                  | 62   | 135±        | 73  | 71±         | 47 | 233±        | 94  | 236±        | 150** | 4±            | 4* | 181±       | 188** |

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

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 4

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
 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 |      | CREATININE<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    | 38                | 17.7±                  | 3.5  | 0.5±                | 0.1 | 141±            | 2  | 3.8±               | 0.4 | 102±              | 2 | 10.1±            | 0.3   | 3.9±                          | 0.8 |
| 10 ppm     | 45                | 17.2±                  | 2.3  | 0.5±                | 0.1 | 140±            | 2  | 3.7±               | 0.4 | 101±              | 2 | 10.3±            | 0.3** | 3.8±                          | 0.8 |
| 30 ppm     | 41                | 17.2±                  | 2.8  | 0.5±                | 0.1 | 141±            | 1  | 3.7±               | 0.4 | 102±              | 2 | 10.4±            | 0.4** | 4.1±                          | 0.9 |
| 90 ppm     | 15                | 22.4±                  | 15.8 | 0.5±                | 0.1 | 140±            | 2* | 4.0±               | 0.5 | 102±              | 2 | 10.0±            | 0.3   | 4.5±                          | 1.0 |

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

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 4



## APPENDIX H 1

### URINALYSIS : MALE

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
 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 | Bilirubin |   |    |    | 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    | 38                | 0   | 0   | 2   | 7   | 15  | 14  | 0   |     | 0       | 0 | 1 | 3  | 17 | 17 |     | 38      | 0 | 0 | 0  | 0  | 0  |     | 38          | 0 | 0 | 0  | 0  | 0  |     | 38        | 0 | 0  | 0  |     |
| 10 ppm     | 38                | 0   | 2   | 4   | 7   | 15  | 10  | 0   |     | 0       | 0 | 0 | 2  | 12 | 24 |     | 38      | 0 | 0 | 0  | 0  | 0  |     | 38          | 0 | 0 | 0  | 0  | 0  |     | 37        | 0 | 0  | 1  |     |
| 30 ppm     | 38                | 0   | 0   | 2   | 1   | 27  | 8   | 0   | *   | 0       | 0 | 0 | 0  | 16 | 22 |     | 38      | 0 | 0 | 0  | 0  | 0  |     | 35          | 3 | 0 | 0  | 0  | 0  |     | 35        | 2 | 1  | 0  |     |
| 90 ppm     | 11                | 0   | 0   | 3   | 1   | 5   | 2   | 0   |     | 0       | 0 | 1 | 4  | 3  | 3  |     | 11      | 0 | 0 | 0  | 0  | 0  |     | 9           | 2 | 0 | 0  | 0  | 0  | **  | 10        | 0 | 1  | 0  |     |

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

Test of CHI SQUARE

(HCL101)

BAIS 4

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCrj  
MEASURE. TIME : 1  
SEX : MALE

URINALYSIS

REPORT TYPE : A1

PAGE : 2

| Group Name | NO. of<br>Animals | Occult blood |   |   |    |    | CHI | Urobilinogen |   |    |    |    | CHI |
|------------|-------------------|--------------|---|---|----|----|-----|--------------|---|----|----|----|-----|
|            |                   | -            | ± | + | 2+ | 3+ |     | ±            | + | 2+ | 3+ | 4+ |     |
| Control    | 38                | 37           | 1 | 0 | 0  | 0  |     | 38           | 0 | 0  | 0  | 0  |     |
| 10 ppm     | 38                | 38           | 0 | 0 | 0  | 0  |     | 38           | 0 | 0  | 0  | 0  |     |
| 30 ppm     | 38                | 38           | 0 | 0 | 0  | 0  |     | 38           | 0 | 0  | 0  | 0  |     |
| 90 ppm     | 11                | 7            | 4 | 0 | 0  | 0  | **  | 11           | 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. : 0437  
 ANIMAL : RAT F344/DuCrj  
 MEASURE. TIME : 1  
 SEX : FEMALE

URINALYSIS

REPORT TYPE : A1

PAGE : 3

| Group Name | NO. of<br>Animals | pH  |     |     |     |     |     |     | CHI | Protein |   |   |    |    |    | CHI | Glucose |   |   |    |    |    | CHI | Ketone body |    |   |    |    |    | CHI | Bilirubin |   |    |    | 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    | 39                | 0   | 1   | 2   | 3   | 6   | 21  | 6   |     | 1       | 5 | 7 | 10 | 11 | 5  |     | 39      | 0 | 0 | 0  | 0  | 0  |     | 27          | 10 | 2 | 0  | 0  | 0  |     | 39        | 0 | 0  | 0  |     |
| 10 ppm     | 46                | 1   | 1   | 2   | 5   | 7   | 27  | 3   |     | 0       | 4 | 8 | 13 | 14 | 7  |     | 46      | 0 | 0 | 0  | 0  | 0  |     | 39          | 7  | 0 | 0  | 0  | 0  |     | 46        | 0 | 0  | 0  |     |
| 30 ppm     | 42                | 0   | 3   | 2   | 5   | 6   | 21  | 5   |     | 0       | 4 | 3 | 9  | 21 | 5  |     | 42      | 0 | 0 | 0  | 0  | 0  |     | 30          | 11 | 1 | 0  | 0  | 0  |     | 42        | 0 | 0  | 0  |     |
| 90 ppm     | 15                | 0   | 1   | 3   | 1   | 5   | 3   | 2   |     | 1       | 5 | 7 | 2  | 0  | 0  | *   | 15      | 0 | 0 | 0  | 0  | 0  |     | 12          | 2  | 0 | 1  | 0  | 0  |     | 15        | 0 | 0  | 0  |     |

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

Test of CHI SQUARE

(HCL101)

BAIS 4

STUDY NO. : 0437

URINALYSIS

ANIMAL : RAT F344/DuCrj

MEASURE. TIME : 1

SEX : FEMALE

REPORT TYPE : A1

PAGE : 4

| Group Name | NO. of<br>Animals | Occult blood |   |   |    |    | Urobilinogen |   |    |    |    |
|------------|-------------------|--------------|---|---|----|----|--------------|---|----|----|----|
|            |                   | -            | ± | + | 2+ | 3+ | ±            | + | 2+ | 3+ | 4+ |
| Control    | 39                | 36           | 0 | 1 | 0  | 2  | 39           | 0 | 0  | 0  | 0  |
| 10 ppm     | 46                | 40           | 0 | 2 | 1  | 3  | 46           | 0 | 0  | 0  | 0  |
| 30 ppm     | 42                | 39           | 0 | 0 | 0  | 3  | 42           | 0 | 0  | 0  | 0  |
| 90 ppm     | 15                | 15           | 0 | 0 | 0  | 0  | 15           | 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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 1

| Organ       | Findings    | Group Name<br>NO. of Animals | Control |       | 10 ppm |       | 30 ppm |       | 90 ppm |       |
|-------------|-------------|------------------------------|---------|-------|--------|-------|--------|-------|--------|-------|
|             |             |                              | 50      | (%)   | 50     | (%)   | 50     | (%)   | 50     | (%)   |
| skin/app    | nodule      |                              | 3       | ( 6)  | 6      | ( 12) | 2      | ( 4)  | 1      | ( 2)  |
|             | scab        |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0      | ( 0)  |
| subcutis    | jaundice    |                              | 2       | ( 4)  | 1      | ( 2)  | 1      | ( 2)  | 2      | ( 4)  |
|             | dry         |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 2)  |
|             | mass        |                              | 11      | ( 22) | 9      | ( 18) | 8      | ( 16) | 4      | ( 8)  |
| trachea     | nodule      |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0      | ( 0)  |
| lung        | red         |                              | 1       | ( 2)  | 1      | ( 2)  | 0      | ( 0)  | 0      | ( 0)  |
|             | white zone  |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 2)  |
|             | red zone    |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 4      | ( 8)  |
|             | yellow zone |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 2)  |
|             | brown zone  |                              | 2       | ( 4)  | 0      | ( 0)  | 0      | ( 0)  | 2      | ( 4)  |
|             | edema       |                              | 0       | ( 0)  | 2      | ( 4)  | 0      | ( 0)  | 0      | ( 0)  |
|             | nodule      |                              | 2       | ( 4)  | 3      | ( 6)  | 1      | ( 2)  | 2      | ( 4)  |
| lymph node  | enlarged    |                              | 2       | ( 4)  | 1      | ( 2)  | 1      | ( 2)  | 1      | ( 2)  |
| spleen      | enlarged    |                              | 6       | ( 12) | 6      | ( 12) | 8      | ( 16) | 7      | ( 14) |
|             | pale        |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 2)  |
|             | nodule      |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0      | ( 0)  |
| heart       | white zone  |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 1      | ( 2)  |
| oral cavity | nodule      |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0      | ( 0)  |
| tongue      | nodule      |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
| salivary gl | nodule      |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 2)  |
| forestomach | ulcer       |                              | 1       | ( 2)  | 1      | ( 2)  | 0      | ( 0)  | 0      | ( 0)  |



STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 2

| Organ       | Findings               | Group Name<br>NO. of Animals | Control | 10 ppm  |         | 30 ppm  |          | 90 ppm |        |
|-------------|------------------------|------------------------------|---------|---------|---------|---------|----------|--------|--------|
|             |                        |                              | 50 (%)  | 50 (%)  | 50 (%)  | 50 (%)  | 50 (%)   | 50 (%) | 50 (%) |
| stomach     | gas                    |                              | 0 ( 0)  | 0 ( 0)  | 0 ( 0)  | 0 ( 0)  | 10 ( 20) |        |        |
| small intes | nodule                 |                              | 1 ( 2)  | 0 ( 0)  | 0 ( 0)  | 0 ( 0)  | 0 ( 0)   |        |        |
|             | gas                    |                              | 0 ( 0)  | 0 ( 0)  | 0 ( 0)  | 0 ( 0)  | 14 ( 28) |        |        |
| cecum       | gas                    |                              | 0 ( 0)  | 0 ( 0)  | 0 ( 0)  | 0 ( 0)  | 2 ( 4)   |        |        |
| large intes | gas                    |                              | 0 ( 0)  | 0 ( 0)  | 0 ( 0)  | 0 ( 0)  | 9 ( 18)  |        |        |
| liver       | enlarged               |                              | 1 ( 2)  | 0 ( 0)  | 0 ( 0)  | 0 ( 0)  | 0 ( 0)   |        |        |
|             | pale                   |                              | 0 ( 0)  | 0 ( 0)  | 0 ( 0)  | 0 ( 0)  | 1 ( 2)   |        |        |
|             | yellow                 |                              | 1 ( 2)  | 0 ( 0)  | 0 ( 0)  | 0 ( 0)  | 0 ( 0)   |        |        |
|             | white zone             |                              | 0 ( 0)  | 1 ( 2)  | 0 ( 0)  | 0 ( 0)  | 0 ( 0)   |        |        |
|             | red zone               |                              | 0 ( 0)  | 0 ( 0)  | 1 ( 2)  | 0 ( 0)  | 0 ( 0)   |        |        |
|             | nodule                 |                              | 0 ( 0)  | 2 ( 4)  | 5 ( 10) | 1 ( 2)  |          |        |        |
|             | cyst                   |                              | 0 ( 0)  | 0 ( 0)  | 0 ( 0)  | 1 ( 2)  | 0 ( 0)   |        |        |
|             | deformed               |                              | 0 ( 0)  | 0 ( 0)  | 1 ( 2)  | 0 ( 0)  |          |        |        |
|             | rough                  |                              | 0 ( 0)  | 2 ( 4)  | 2 ( 4)  | 1 ( 2)  |          |        |        |
|             | nodular                |                              | 1 ( 2)  | 0 ( 0)  | 0 ( 0)  | 0 ( 0)  | 0 ( 0)   |        |        |
|             | herniation             |                              | 3 ( 6)  | 5 ( 10) | 4 ( 8)  | 9 ( 18) |          |        |        |
| pancreas    | nodule                 |                              | 0 ( 0)  | 1 ( 2)  | 0 ( 0)  | 0 ( 0)  |          |        |        |
| kidney      | white zone             |                              | 1 ( 2)  | 0 ( 0)  | 1 ( 2)  | 0 ( 0)  | 0 ( 0)   |        |        |
|             | yellow zone            |                              | 0 ( 0)  | 1 ( 2)  | 0 ( 0)  | 0 ( 0)  |          |        |        |
|             | granular               |                              | 4 ( 8)  | 5 ( 10) | 5 ( 10) | 0 ( 0)  |          |        |        |
| urin bladd  | urine:marked retention |                              | 0 ( 0)  | 1 ( 2)  | 2 ( 4)  | 0 ( 0)  |          |        |        |
|             | urine:red              |                              | 0 ( 0)  | 0 ( 0)  | 1 ( 2)  | 1 ( 2)  |          |        |        |

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 3

| Organ       | Findings | Group Name<br>NO. of Animals | Control |       | 10 ppm |       | 30 ppm |       | 90 ppm |       |
|-------------|----------|------------------------------|---------|-------|--------|-------|--------|-------|--------|-------|
|             |          |                              | 50      | (%)   | 50     | (%)   | 50     | (%)   | 50     | (%)   |
| pituitary   | enlarged |                              | 5       | ( 10) | 9      | ( 18) | 3      | ( 6)  | 0      | ( 0)  |
|             | red zone |                              | 1       | ( 2)  | 0      | ( 0)  | 1      | ( 2)  | 0      | ( 0)  |
|             | nodule   |                              | 1       | ( 2)  | 7      | ( 14) | 5      | ( 10) | 2      | ( 4)  |
|             | cyst     |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0      | ( 0)  |
| thyroid     | enlarged |                              | 1       | ( 2)  | 2      | ( 4)  | 4      | ( 8)  | 2      | ( 4)  |
|             | nodule   |                              | 1       | ( 2)  | 1      | ( 2)  | 0      | ( 0)  | 0      | ( 0)  |
| adrenal     | enlarged |                              | 3       | ( 6)  | 3      | ( 6)  | 3      | ( 6)  | 1      | ( 2)  |
| testis      | enlarged |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0      | ( 0)  |
|             | atrophic |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 4      | ( 8)  |
|             | nodule   |                              | 44      | ( 88) | 39     | ( 78) | 38     | ( 76) | 23     | ( 46) |
| prostate    | nodule   |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0      | ( 0)  |
| brain       | red zone |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
|             | nodule   |                              | 0       | ( 0)  | 1      | ( 2)  | 1      | ( 2)  | 0      | ( 0)  |
| spinal cord | red zone |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
| eye         | turbid   |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 5      | ( 10) |
|             | white    |                              | 8       | ( 16) | 5      | ( 10) | 4      | ( 8)  | 1      | ( 2)  |
|             | red      |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 2)  |
| mediastinum | mass     |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 2)  |
| peritoneum  | nodule   |                              | 0       | ( 0)  | 1      | ( 2)  | 3      | ( 6)  | 1      | ( 2)  |
|             | mass     |                              | 1       | ( 2)  | 1      | ( 2)  | 0      | ( 0)  | 0      | ( 0)  |
| retroperit  | mass     |                              | 0       | ( 0)  | 1      | ( 2)  | 3      | ( 6)  | 0      | ( 0)  |
| abdominal c | ascites  |                              | 1       | ( 2)  | 0      | ( 0)  | 2      | ( 4)  | 4      | ( 8)  |

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 4

| Organ       | Findings         | Group Name<br>NO. of Animals | Control |      | 10 ppm |      | 30 ppm |      | 90 ppm |       |
|-------------|------------------|------------------------------|---------|------|--------|------|--------|------|--------|-------|
|             |                  |                              | 50      | (%)  | 50     | (%)  | 50     | (%)  | 50     | (%)   |
| thoracic ca | hemorrhage       |                              | 0       | ( 0) | 0      | ( 0) | 0      | ( 0) | 1      | ( 2)  |
|             | pleural fluid    |                              | 1       | ( 2) | 3      | ( 6) | 0      | ( 0) | 2      | ( 4)  |
| other       | hindlimb:nodule  |                              | 0       | ( 0) | 2      | ( 4) | 0      | ( 0) | 0      | ( 0)  |
|             | forelimb:swollen |                              | 0       | ( 0) | 1      | ( 2) | 0      | ( 0) | 0      | ( 0)  |
|             | lower jaw:nodule |                              | 0       | ( 0) | 0      | ( 0) | 0      | ( 0) | 1      | ( 2)  |
|             | nose:elevated    |                              | 0       | ( 0) | 0      | ( 0) | 0      | ( 0) | 6      | ( 12) |
|             | nose:nodule      |                              | 0       | ( 0) | 0      | ( 0) | 0      | ( 0) | 15     | ( 30) |
| whole body  | anemic           |                              | 0       | ( 0) | 1      | ( 2) | 0      | ( 0) | 0      | ( 0)  |

(HPT080)

BAIS 4

## APPENDIX I 2

### GROSS FINDINGS : MALE DEAD AND MORIBUND ANIMALS

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 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 |       | 10 ppm |       | 30 ppm |       | 90 ppm |       |
|-------------|-------------|------------------------------|---------|-------|--------|-------|--------|-------|--------|-------|
|             |             |                              | 12      | (%)   | 12     | (%)   | 12     | (%)   | 39     | (%)   |
| skin/app    | nodule      |                              | 0       | ( 0)  | 1      | ( 8)  | 0      | ( 0)  | 1      | ( 3)  |
| subcutis    | jaundice    |                              | 1       | ( 8)  | 1      | ( 8)  | 1      | ( 8)  | 2      | ( 5)  |
|             | dry         |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 3)  |
|             | mass        |                              | 3       | ( 25) | 1      | ( 8)  | 2      | ( 17) | 4      | ( 10) |
| lung        | red         |                              | 1       | ( 8)  | 1      | ( 8)  | 0      | ( 0)  | 0      | ( 0)  |
|             | white zone  |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 3)  |
|             | red zone    |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 8)  | 4      | ( 10) |
|             | yellow zone |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 3)  |
|             | brown zone  |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 3)  |
|             | edema       |                              | 0       | ( 0)  | 2      | ( 17) | 0      | ( 0)  | 0      | ( 0)  |
|             | nodule      |                              | 2       | ( 17) | 0      | ( 0)  | 0      | ( 0)  | 2      | ( 5)  |
| lymph node  | enlarged    |                              | 1       | ( 8)  | 1      | ( 8)  | 0      | ( 0)  | 1      | ( 3)  |
| spleen      | enlarged    |                              | 4       | ( 33) | 3      | ( 25) | 3      | ( 25) | 4      | ( 10) |
|             | pale        |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 3)  |
|             | nodule      |                              | 0       | ( 0)  | 1      | ( 8)  | 0      | ( 0)  | 0      | ( 0)  |
| heart       | white zone  |                              | 0       | ( 0)  | 1      | ( 8)  | 0      | ( 0)  | 1      | ( 3)  |
| tongue      | nodule      |                              | 1       | ( 8)  | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
| salivary gl | nodule      |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 3)  |
| forestomach | ulcer       |                              | 1       | ( 8)  | 1      | ( 8)  | 0      | ( 0)  | 0      | ( 0)  |
| stomach     | gas         |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 7      | ( 18) |
| small intes | gas         |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 11     | ( 28) |
| cecum       | gas         |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 2      | ( 5)  |

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 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 |       | 10 ppm |       | 30 ppm |       | 90 ppm |       |
|-------------|------------------------|------------------------------|---------|-------|--------|-------|--------|-------|--------|-------|
|             |                        |                              | 12      | (%)   | 12     | (%)   | 12     | (%)   | 39     | (%)   |
| large intes | gas                    |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 6      | ( 15) |
| liver       | enlarged               |                              | 1       | ( 8)  | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
|             | pale                   |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 3)  |
|             | yellow                 |                              | 1       | ( 8)  | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
|             | nodule                 |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 8)  | 0      | ( 0)  |
|             | cyst                   |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 3)  |
|             | rough                  |                              | 0       | ( 0)  | 1      | ( 8)  | 0      | ( 0)  | 0      | ( 0)  |
|             | herniation             |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 7      | ( 18) |
| pancreas    | nodule                 |                              | 0       | ( 0)  | 1      | ( 8)  | 0      | ( 0)  | 0      | ( 0)  |
| kidney      | white zone             |                              | 1       | ( 8)  | 0      | ( 0)  | 1      | ( 8)  | 0      | ( 0)  |
|             | yellow zone            |                              | 0       | ( 0)  | 1      | ( 8)  | 0      | ( 0)  | 0      | ( 0)  |
| urin bladd  | urine:marked retention |                              | 0       | ( 0)  | 1      | ( 8)  | 2      | ( 17) | 0      | ( 0)  |
|             | urine:red              |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 8)  | 1      | ( 3)  |
| pituitary   | enlarged               |                              | 1       | ( 8)  | 3      | ( 25) | 1      | ( 8)  | 0      | ( 0)  |
|             | nodule                 |                              | 0       | ( 0)  | 1      | ( 8)  | 0      | ( 0)  | 1      | ( 3)  |
|             | cyst                   |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 8)  | 0      | ( 0)  |
| thyroid     | enlarged               |                              | 0       | ( 0)  | 1      | ( 8)  | 0      | ( 0)  | 2      | ( 5)  |
|             | nodule                 |                              | 1       | ( 8)  | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
| adrenal     | enlarged               |                              | 1       | ( 8)  | 1      | ( 8)  | 1      | ( 8)  | 1      | ( 3)  |
| testis      | atrophic               |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 4      | ( 10) |
|             | nodule                 |                              | 8       | ( 67) | 7      | ( 58) | 3      | ( 25) | 12     | ( 31) |
| brain       | red zone               |                              | 1       | ( 8)  | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 3

| Organ       | Findings         | Group Name<br>NO. of Animals | Control |      | 10 ppm |       | 30 ppm |       | 90 ppm |       |
|-------------|------------------|------------------------------|---------|------|--------|-------|--------|-------|--------|-------|
|             |                  |                              | 12      | (%)  | 12     | (%)   | 12     | (%)   | 39     | (%)   |
| brain       | nodule           |                              | 0       | ( 0) | 1      | ( 8)  | 1      | ( 8)  | 0      | ( 0)  |
| spinal cord | red zone         |                              | 1       | ( 8) | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
| eye         | turbid           |                              | 0       | ( 0) | 0      | ( 0)  | 1      | ( 8)  | 4      | ( 10) |
|             | white            |                              | 0       | ( 0) | 2      | ( 17) | 0      | ( 0)  | 1      | ( 3)  |
|             | red              |                              | 0       | ( 0) | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 3)  |
| mediastinum | mass             |                              | 0       | ( 0) | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 3)  |
| peritoneum  | nodule           |                              | 0       | ( 0) | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 3)  |
|             | mass             |                              | 1       | ( 8) | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
| retroperit  | mass             |                              | 0       | ( 0) | 0      | ( 0)  | 3      | ( 25) | 0      | ( 0)  |
| abdominal c | ascites          |                              | 0       | ( 0) | 0      | ( 0)  | 0      | ( 0)  | 4      | ( 10) |
| thoracic ca | hemorrhage       |                              | 0       | ( 0) | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 3)  |
|             | pleural fluid    |                              | 1       | ( 8) | 3      | ( 25) | 0      | ( 0)  | 2      | ( 5)  |
| other       | lower jaw:nodule |                              | 0       | ( 0) | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 3)  |
|             | nose:elevated    |                              | 0       | ( 0) | 0      | ( 0)  | 0      | ( 0)  | 6      | ( 15) |
|             | nose:nodule      |                              | 0       | ( 0) | 0      | ( 0)  | 0      | ( 0)  | 13     | ( 33) |
| whole body  | anemic           |                              | 0       | ( 0) | 1      | ( 8)  | 0      | ( 0)  | 0      | ( 0)  |

## APPENDIX I 3

### GROSS FINDINGS : MALE SACRIFICED ANIMALS



STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

GROSS FINDINGS (SUMMARY)  
 SACRIFICED ANIMALS (105W)

PAGE : 1

| Organ       | Findings   | Group Name<br>NO. of Animals | Control |       | 10 ppm |       | 30 ppm |       | 90 ppm |       |
|-------------|------------|------------------------------|---------|-------|--------|-------|--------|-------|--------|-------|
|             |            |                              | 38      | (%)   | 38     | (%)   | 38     | (%)   | 11     | (%)   |
| skin/app    | nodule     |                              | 3       | ( 8)  | 5      | ( 13) | 2      | ( 5)  | 0      | ( 0)  |
|             | scab       |                              | 0       | ( 0)  | 1      | ( 3)  | 0      | ( 0)  | 0      | ( 0)  |
| subcutis    | jaundice   |                              | 1       | ( 3)  | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
|             | mass       |                              | 8       | ( 21) | 8      | ( 21) | 6      | ( 16) | 0      | ( 0)  |
| trachea     | nodule     |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 3)  | 0      | ( 0)  |
| lung        | white zone |                              | 1       | ( 3)  | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
|             | brown zone |                              | 2       | ( 5)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 9)  |
|             | nodule     |                              | 0       | ( 0)  | 3      | ( 8)  | 1      | ( 3)  | 0      | ( 0)  |
| lymph node  | enlarged   |                              | 1       | ( 3)  | 0      | ( 0)  | 1      | ( 3)  | 0      | ( 0)  |
| spleen      | enlarged   |                              | 2       | ( 5)  | 3      | ( 8)  | 5      | ( 13) | 3      | ( 27) |
| oral cavity | nodule     |                              | 0       | ( 0)  | 1      | ( 3)  | 0      | ( 0)  | 0      | ( 0)  |
| stomach     | gas        |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 3      | ( 27) |
| small intes | nodule     |                              | 1       | ( 3)  | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
|             | gas        |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 3      | ( 27) |
| large intes | gas        |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 3      | ( 27) |
| liver       | white zone |                              | 0       | ( 0)  | 1      | ( 3)  | 0      | ( 0)  | 0      | ( 0)  |
|             | red zone   |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 3)  | 0      | ( 0)  |
|             | nodule     |                              | 0       | ( 0)  | 2      | ( 5)  | 4      | ( 11) | 1      | ( 9)  |
|             | deformed   |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 3)  | 0      | ( 0)  |
|             | rough      |                              | 0       | ( 0)  | 1      | ( 3)  | 2      | ( 5)  | 1      | ( 9)  |
|             | nodular    |                              | 1       | ( 3)  | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
|             | herniation |                              | 3       | ( 8)  | 5      | ( 13) | 4      | ( 11) | 2      | ( 18) |

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

GROSS FINDINGS (SUMMARY)  
 SACRIFICED ANIMALS (105W)

PAGE : 2

| Organ       | Findings         | Group Name<br>NO. of Animals | Control |       | 10 ppm |       | 30 ppm |       | 90 ppm |       |
|-------------|------------------|------------------------------|---------|-------|--------|-------|--------|-------|--------|-------|
|             |                  |                              | 38      | (%)   | 38     | (%)   | 38     | (%)   | 11     | (%)   |
| kidney      | granular         |                              | 4       | ( 11) | 5      | ( 13) | 5      | ( 13) | 0      | ( 0)  |
| pituitary   | enlarged         |                              | 4       | ( 11) | 6      | ( 16) | 2      | ( 5)  | 0      | ( 0)  |
|             | red zone         |                              | 1       | ( 3)  | 0      | ( 0)  | 1      | ( 3)  | 0      | ( 0)  |
|             | nodule           |                              | 1       | ( 3)  | 6      | ( 16) | 5      | ( 13) | 1      | ( 9)  |
| thyroid     | enlarged         |                              | 1       | ( 3)  | 1      | ( 3)  | 4      | ( 11) | 0      | ( 0)  |
|             | nodule           |                              | 0       | ( 0)  | 1      | ( 3)  | 0      | ( 0)  | 0      | ( 0)  |
| adrenal     | enlarged         |                              | 2       | ( 5)  | 2      | ( 5)  | 2      | ( 5)  | 0      | ( 0)  |
| testis      | enlarged         |                              | 0       | ( 0)  | 1      | ( 3)  | 0      | ( 0)  | 0      | ( 0)  |
|             | atrophic         |                              | 1       | ( 3)  | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
|             | nodule           |                              | 36      | ( 95) | 32     | ( 84) | 35     | ( 92) | 11     | (100) |
| prostate    | nodule           |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 3)  | 0      | ( 0)  |
| eye         | turbid           |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 9)  |
|             | white            |                              | 8       | ( 21) | 3      | ( 8)  | 4      | ( 11) | 0      | ( 0)  |
| peritoneum  | nodule           |                              | 0       | ( 0)  | 1      | ( 3)  | 3      | ( 8)  | 0      | ( 0)  |
|             | mass             |                              | 0       | ( 0)  | 1      | ( 3)  | 0      | ( 0)  | 0      | ( 0)  |
| retroperit  | mass             |                              | 0       | ( 0)  | 1      | ( 3)  | 0      | ( 0)  | 0      | ( 0)  |
| abdominal c | ascites          |                              | 1       | ( 3)  | 0      | ( 0)  | 2      | ( 5)  | 0      | ( 0)  |
| other       | hindlimb:nodule  |                              | 0       | ( 0)  | 2      | ( 5)  | 0      | ( 0)  | 0      | ( 0)  |
|             | forelimb:swollen |                              | 0       | ( 0)  | 1      | ( 3)  | 0      | ( 0)  | 0      | ( 0)  |
|             | nose:nodule      |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 2      | ( 18) |

## APPENDIX I 4

GROSS FINDINGS : FEMALE

ALL ANIMALS

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 5

| Organ       | Findings   | Group Name<br>NO. of Animals | Control |       | 10 ppm |       | 30 ppm |       | 90 ppm |       |
|-------------|------------|------------------------------|---------|-------|--------|-------|--------|-------|--------|-------|
|             |            |                              | 50      | (%)   | 50     | (%)   | 50     | (%)   | 50     | (%)   |
| skin/app    | nodule     |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 2      | ( 4)  |
|             | scab       |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0      | ( 0)  |
| subcutis    | jaundice   |                              | 2       | ( 4)  | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
|             | mass       |                              | 6       | ( 12) | 10     | ( 20) | 6      | ( 12) | 2      | ( 4)  |
| nasal cavit | nodule     |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 2)  |
| lung        | red        |                              | 1       | ( 2)  | 0      | ( 0)  | 1      | ( 2)  | 1      | ( 2)  |
|             | white zone |                              | 2       | ( 4)  | 0      | ( 0)  | 1      | ( 2)  | 1      | ( 2)  |
|             | red zone   |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 3      | ( 6)  |
|             | brown zone |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0      | ( 0)  |
|             | edema      |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 2)  |
|             | nodule     |                              | 1       | ( 2)  | 1      | ( 2)  | 1      | ( 2)  | 0      | ( 0)  |
| lymph node  | enlarged   |                              | 0       | ( 0)  | 1      | ( 2)  | 1      | ( 2)  | 3      | ( 6)  |
| spleen      | enlarged   |                              | 4       | ( 8)  | 6      | ( 12) | 5      | ( 10) | 7      | ( 14) |
|             | white zone |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 2)  |
|             | nodule     |                              | 2       | ( 4)  | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
| heart       | nodule     |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
| forestomach | nodule     |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0      | ( 0)  |
|             | ulcer      |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 2)  |
| stomach     | gas        |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 5      | ( 10) |
| small intes | nodule     |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0      | ( 0)  |
|             | gas        |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 4      | ( 8)  |
| large intes | gas        |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 3      | ( 6)  |

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 6

| Organ      | Findings               | Group Name<br>NO. of Animals | Control |       | 10 ppm |       | 30 ppm |       | 90 ppm |       |
|------------|------------------------|------------------------------|---------|-------|--------|-------|--------|-------|--------|-------|
|            |                        |                              | 50      | (%)   | 50     | (%)   | 50     | (%)   | 50     | (%)   |
| liver      | white zone             |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0      | ( 0)  |
|            | yellow zone            |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
|            | nodule                 |                              | 1       | ( 2)  | 1      | ( 2)  | 1      | ( 2)  | 0      | ( 0)  |
|            | deformed               |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0      | ( 0)  |
|            | rough                  |                              | 2       | ( 4)  | 2      | ( 4)  | 2      | ( 4)  | 0      | ( 0)  |
|            | nodular                |                              | 0       | ( 0)  | 2      | ( 4)  | 0      | ( 0)  | 0      | ( 0)  |
|            | herniation             |                              | 9       | ( 18) | 10     | ( 20) | 6      | ( 12) | 12     | ( 24) |
| pancreas   | nodule                 |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0      | ( 0)  |
| kidney     | nodule                 |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0      | ( 0)  |
|            | granular               |                              | 0       | ( 0)  | 1      | ( 2)  | 2      | ( 4)  | 0      | ( 0)  |
|            | hydronephrosis         |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
| urin bladd | urine:marked retention |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0      | ( 0)  |
| pituitary  | enlarged               |                              | 7       | ( 14) | 15     | ( 30) | 11     | ( 22) | 2      | ( 4)  |
|            | red zone               |                              | 5       | ( 10) | 4      | ( 8)  | 0      | ( 0)  | 3      | ( 6)  |
|            | nodule                 |                              | 10      | ( 20) | 10     | ( 20) | 9      | ( 18) | 6      | ( 12) |
|            | cyst                   |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 2)  |
| thyroid    | enlarged               |                              | 1       | ( 2)  | 0      | ( 0)  | 5      | ( 10) | 1      | ( 2)  |
|            | nodule                 |                              | 0       | ( 0)  | 1      | ( 2)  | 1      | ( 2)  | 0      | ( 0)  |
| adrenal    | enlarged               |                              | 2       | ( 4)  | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
| ovary      | enlarged               |                              | 0       | ( 0)  | 0      | ( 0)  | 2      | ( 4)  | 1      | ( 2)  |
|            | nodule                 |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0      | ( 0)  |
| uterus     | nodule                 |                              | 6       | ( 12) | 5      | ( 10) | 6      | ( 12) | 8      | ( 16) |

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 7

| Organ       | Findings      | Group Name<br>NO. of Animals | Control |      | 10 ppm |      | 30 ppm |      | 90 ppm |       |
|-------------|---------------|------------------------------|---------|------|--------|------|--------|------|--------|-------|
|             |               |                              | 50      | (%)  | 50     | (%)  | 50     | (%)  | 50     | (%)   |
| uterus      | cyst          |                              | 0       | ( 0) | 1      | ( 2) | 0      | ( 0) | 1      | ( 2)  |
|             | dilated lumen |                              | 0       | ( 0) | 0      | ( 0) | 1      | ( 2) | 0      | ( 0)  |
|             | fluid:black   |                              | 0       | ( 0) | 0      | ( 0) | 1      | ( 2) | 0      | ( 0)  |
| vagina      | nodule        |                              | 1       | ( 2) | 0      | ( 0) | 0      | ( 0) | 0      | ( 0)  |
| spinal cord | brown zone    |                              | 1       | ( 2) | 0      | ( 0) | 0      | ( 0) | 0      | ( 0)  |
| eye         | turbid        |                              | 1       | ( 2) | 0      | ( 0) | 0      | ( 0) | 8      | ( 16) |
|             | white         |                              | 3       | ( 6) | 4      | ( 8) | 2      | ( 4) | 2      | ( 4)  |
|             | nodule        |                              | 0       | ( 0) | 0      | ( 0) | 0      | ( 0) | 2      | ( 4)  |
| Zymbal gl   | nodule        |                              | 0       | ( 0) | 0      | ( 0) | 1      | ( 2) | 0      | ( 0)  |
| bone        | nodule        |                              | 0       | ( 0) | 0      | ( 0) | 0      | ( 0) | 1      | ( 2)  |
| peritoneum  | nodule        |                              | 2       | ( 4) | 0      | ( 0) | 0      | ( 0) | 0      | ( 0)  |
| retroperit  | mass          |                              | 0       | ( 0) | 1      | ( 2) | 1      | ( 2) | 0      | ( 0)  |
| abdominal c | hemorrhage    |                              | 0       | ( 0) | 1      | ( 2) | 2      | ( 4) | 0      | ( 0)  |
|             | ascites       |                              | 2       | ( 4) | 0      | ( 0) | 0      | ( 0) | 0      | ( 0)  |
| thoracic ca | pleural fluid |                              | 1       | ( 2) | 0      | ( 0) | 0      | ( 0) | 0      | ( 0)  |
| other       | lip:nodule    |                              | 1       | ( 2) | 0      | ( 0) | 0      | ( 0) | 0      | ( 0)  |
|             | nose:elevated |                              | 0       | ( 0) | 0      | ( 0) | 0      | ( 0) | 4      | ( 8)  |
|             | nose:nodule   |                              | 0       | ( 0) | 0      | ( 0) | 0      | ( 0) | 11     | ( 22) |

## APPENDIX I 5

### GROSS FINDINGS : FEMALE DEAD AND MORIBUND ANIMALS

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1j[F344/DuCrj]  
 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 |       | 10 ppm |       | 30 ppm |       | 90 ppm |       |
|-------------|------------------------|------------------------------|---------|-------|--------|-------|--------|-------|--------|-------|
|             |                        |                              | 10      | (%)   | 5      | (%)   | 9      | (%)   | 35     | (%)   |
| subcutis    | jaundice               |                              | 1       | ( 10) | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
|             | mass                   |                              | 2       | ( 20) | 3      | ( 60) | 2      | ( 22) | 2      | ( 6)  |
| lung        | red                    |                              | 1       | ( 10) | 0      | ( 0)  | 1      | ( 11) | 1      | ( 3)  |
|             | white zone             |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 3)  |
|             | red zone               |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 3      | ( 9)  |
|             | edema                  |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 3)  |
|             | nodule                 |                              | 1       | ( 10) | 1      | ( 20) | 0      | ( 0)  | 0      | ( 0)  |
| lymph node  | enlarged               |                              | 0       | ( 0)  | 1      | ( 20) | 1      | ( 11) | 2      | ( 6)  |
| spleen      | enlarged               |                              | 0       | ( 0)  | 2      | ( 40) | 2      | ( 22) | 5      | ( 14) |
|             | nodule                 |                              | 1       | ( 10) | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
| forestomach | nodule                 |                              | 0       | ( 0)  | 1      | ( 20) | 0      | ( 0)  | 0      | ( 0)  |
|             | ulcer                  |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 3)  |
| stomach     | gas                    |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 5      | ( 14) |
| small intes | gas                    |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 4      | ( 11) |
| large intes | gas                    |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 3      | ( 9)  |
| liver       | white zone             |                              | 0       | ( 0)  | 1      | ( 20) | 0      | ( 0)  | 0      | ( 0)  |
|             | yellow zone            |                              | 1       | ( 10) | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
|             | nodule                 |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 11) | 0      | ( 0)  |
|             | herniation             |                              | 0       | ( 0)  | 1      | ( 20) | 0      | ( 0)  | 10     | ( 29) |
| pancreas    | nodule                 |                              | 0       | ( 0)  | 1      | ( 20) | 0      | ( 0)  | 0      | ( 0)  |
| urin bladd  | urine:marked retention |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 11) | 0      | ( 0)  |
| pituitary   | enlarged               |                              | 3       | ( 30) | 3      | ( 60) | 3      | ( 33) | 2      | ( 6)  |



STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 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 |       | 10 ppm |       | 30 ppm |       | 90 ppm |       |
|-------------|---------------|------------------------------|---------|-------|--------|-------|--------|-------|--------|-------|
|             |               |                              | 10      | (%)   | 5      | (%)   | 9      | (%)   | 35     | (%)   |
| pituitary   | red zone      |                              | 1       | ( 10) | 1      | ( 20) | 0      | ( 0)  | 3      | ( 9)  |
|             | nodule        |                              | 2       | ( 20) | 0      | ( 0)  | 2      | ( 22) | 2      | ( 6)  |
|             | cyst          |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 3)  |
| thyroid     | enlarged      |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 11) | 0      | ( 0)  |
| adrenal     | enlarged      |                              | 1       | ( 10) | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
| ovary       | enlarged      |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 11) | 1      | ( 3)  |
|             | nodule        |                              | 0       | ( 0)  | 1      | ( 20) | 0      | ( 0)  | 0      | ( 0)  |
| uterus      | nodule        |                              | 1       | ( 10) | 1      | ( 20) | 2      | ( 22) | 4      | ( 11) |
| vagina      | nodule        |                              | 1       | ( 10) | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
| spinal cord | brown zone    |                              | 1       | ( 10) | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
| eye         | turbid        |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 7      | ( 20) |
|             | white         |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 3)  |
|             | nodule        |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 2      | ( 6)  |
| Zymbal gl   | nodule        |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 11) | 0      | ( 0)  |
| bone        | nodule        |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 3)  |
| retroperit  | mass          |                              | 0       | ( 0)  | 1      | ( 20) | 1      | ( 11) | 0      | ( 0)  |
| abdominal c | hemorrhage    |                              | 0       | ( 0)  | 1      | ( 20) | 2      | ( 22) | 0      | ( 0)  |
| thoracic ca | pleural fluid |                              | 1       | ( 10) | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
| other       | nose:elevated |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 4      | ( 11) |
|             | nose:nodule   |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 10     | ( 29) |

## APPENDIX I 6

### GROSS FINDINGS : FEMALE SACRIFICED ANIMALS

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : FEMALE

GROSS FINDINGS (SUMMARY)  
SACRIFICED ANIMALS (105W)

PAGE : 3

| Organ       | Findings   | Group Name<br>NO. of Animals | Control |       | 10 ppm |       | 30 ppm |       | 90 ppm |       |
|-------------|------------|------------------------------|---------|-------|--------|-------|--------|-------|--------|-------|
|             |            |                              | 40      | (%)   | 45     | (%)   | 41     | (%)   | 15     | (%)   |
| skin/app    | nodule     |                              | 1       | ( 3)  | 0      | ( 0)  | 0      | ( 0)  | 2      | ( 13) |
|             | scab       |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0      | ( 0)  |
| subcutis    | jaundice   |                              | 1       | ( 3)  | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
|             | mass       |                              | 4       | ( 10) | 7      | ( 16) | 4      | ( 10) | 0      | ( 0)  |
| nasal cavit | nodule     |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 7)  |
| lung        | white zone |                              | 2       | ( 5)  | 0      | ( 0)  | 1      | ( 2)  | 0      | ( 0)  |
|             | red zone   |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0      | ( 0)  |
|             | brown zone |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0      | ( 0)  |
|             | nodule     |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0      | ( 0)  |
| lymph node  | enlarged   |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 7)  |
| spleen      | enlarged   |                              | 4       | ( 10) | 4      | ( 9)  | 3      | ( 7)  | 2      | ( 13) |
|             | white zone |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 7)  |
|             | nodule     |                              | 1       | ( 3)  | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
| heart       | nodule     |                              | 1       | ( 3)  | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
| small intes | nodule     |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0      | ( 0)  |
| liver       | nodule     |                              | 1       | ( 3)  | 1      | ( 2)  | 0      | ( 0)  | 0      | ( 0)  |
|             | deformed   |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0      | ( 0)  |
|             | rough      |                              | 2       | ( 5)  | 2      | ( 4)  | 2      | ( 5)  | 0      | ( 0)  |
|             | nodular    |                              | 0       | ( 0)  | 2      | ( 4)  | 0      | ( 0)  | 0      | ( 0)  |
|             | herniation |                              | 9       | ( 23) | 9      | ( 20) | 6      | ( 15) | 2      | ( 13) |
| kidney      | nodule     |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0      | ( 0)  |
|             | granular   |                              | 0       | ( 0)  | 1      | ( 2)  | 2      | ( 5)  | 0      | ( 0)  |

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

GROSS FINDINGS (SUMMARY)  
 SACRIFICED ANIMALS (105W)

PAGE : 4

| Organ       | Findings       | Group Name<br>NO. of Animals | Control |       | 10 ppm |       | 30 ppm |       | 90 ppm |       |
|-------------|----------------|------------------------------|---------|-------|--------|-------|--------|-------|--------|-------|
|             |                |                              | 40      | (%)   | 45     | (%)   | 41     | (%)   | 15     | (%)   |
| kidney      | hydronephrosis |                              | 1       | ( 3)  | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
| pituitary   | enlarged       |                              | 4       | ( 10) | 12     | ( 27) | 8      | ( 20) | 0      | ( 0)  |
|             | red zone       |                              | 4       | ( 10) | 3      | ( 7)  | 0      | ( 0)  | 0      | ( 0)  |
|             | nodule         |                              | 8       | ( 20) | 10     | ( 22) | 7      | ( 17) | 4      | ( 27) |
| thyroid     | enlarged       |                              | 1       | ( 3)  | 0      | ( 0)  | 4      | ( 10) | 1      | ( 7)  |
|             | nodule         |                              | 0       | ( 0)  | 1      | ( 2)  | 1      | ( 2)  | 0      | ( 0)  |
| adrenal     | enlarged       |                              | 1       | ( 3)  | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
| ovary       | enlarged       |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0      | ( 0)  |
| uterus      | nodule         |                              | 5       | ( 13) | 4      | ( 9)  | 4      | ( 10) | 4      | ( 27) |
|             | cyst           |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 1      | ( 7)  |
|             | dilated lumen  |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0      | ( 0)  |
|             | fluid:black    |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0      | ( 0)  |
| eye         | turbid         |                              | 1       | ( 3)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 7)  |
|             | white          |                              | 3       | ( 8)  | 4      | ( 9)  | 2      | ( 5)  | 1      | ( 7)  |
| peritoneum  | nodule         |                              | 2       | ( 5)  | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
| abdominal c | ascites        |                              | 2       | ( 5)  | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
| other       | lip:nodule     |                              | 1       | ( 3)  | 0      | ( 0)  | 0      | ( 0)  | 0      | ( 0)  |
|             | nose:nodule    |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1      | ( 7)  |

## APPENDIX J 1

ORGAN WEIGHT, ABSOLUTE : MALE

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
 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    | 38                | 396± 33     | 0.155± 0.519 | 3.435± 1.140 | 1.176± 0.094 | 1.476± 0.343   | 2.771± 0.217   |
| 10 ppm     | 38                | 395± 27     | 0.104± 0.141 | 3.371± 2.326 | 1.249± 0.116 | 1.620± 0.470*  | 2.819± 0.228   |
| 30 ppm     | 38                | 390± 32     | 0.103± 0.164 | 3.765± 1.384 | 1.214± 0.091 | 1.498± 0.252   | 2.844± 0.278   |
| 90 ppm     | 11                | 275± 35**   | 0.068± 0.016 | 2.702± 1.063 | 1.204± 0.162 | 1.810± 0.498** | 2.470± 0.209** |

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

Test of Dunnett

(HCL040)

BAIS 4

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCrj  
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    | 38                | 1.276± | 1.895 | 11.561± | 2.041 | 2.068± | 0.051 |
| 10 ppm     | 38                | 1.192± | 0.633 | 11.752± | 1.680 | 2.083± | 0.052 |
| 30 ppm     | 38                | 1.445± | 1.634 | 11.790± | 2.997 | 2.097± | 0.063 |
| 90 ppm     | 11                | 1.512± | 1.972 | 9.581±  | 3.890 | 2.036± | 0.067 |

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. : 0437  
 ANIMAL : RAT F344/DuCrj  
 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    | 40                | 251± 35     | 0.082± 0.097 | 0.164± 0.332 | 0.858± 0.106  | 1.017± 0.123 | 1.710± 0.136 |
| 10 ppm     | 45                | 254± 24     | 0.068± 0.010 | 0.116± 0.023 | 0.837± 0.052  | 1.039± 0.218 | 1.754± 0.134 |
| 30 ppm     | 41                | 252± 27     | 0.065± 0.013 | 0.192± 0.490 | 0.862± 0.087  | 1.050± 0.234 | 1.816± 0.309 |
| 90 ppm     | 15                | 195± 24**   | 0.065± 0.009 | 0.106± 0.015 | 0.796± 0.048* | 1.043± 0.179 | 1.610± 0.140 |

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

Test of Dunnett

(HCL040)

BAIS 4

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCrj  
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   | 40                | 0.877± | 1.416 | 6.474± | 1.279 | 1.864± | 0.046 |
| 10 ppm  | 45                | 0.779± | 1.076 | 6.831± | 1.292 | 1.866± | 0.046 |
| 30 ppm  | 41                | 0.928± | 1.854 | 6.814± | 1.601 | 1.872± | 0.042 |
| 90 ppm  | 15                | 0.745± | 0.796 | 5.695± | 0.989 | 1.864± | 0.033 |
| Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett |                   |        |       |        |       |        |       |

(HCL040)

BAIS 4

## APPENDIX K 1

ORGAN WEIGHT, RELATIVE : MALE

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

| Group | Name    | NO. of<br>Animals | Body Weight<br>(g) | ADRENALS     | TESTES       | HEART          | LUNGS          | KIDNEYS        |
|-------|---------|-------------------|--------------------|--------------|--------------|----------------|----------------|----------------|
|       | Control | 38                | 396± 33            | 0.047± 0.182 | 0.868± 0.293 | 0.298± 0.023   | 0.376± 0.101   | 0.705± 0.072   |
|       | 10 ppm  | 38                | 395± 27            | 0.026± 0.035 | 0.853± 0.595 | 0.317± 0.038*  | 0.413± 0.134   | 0.715± 0.071   |
|       | 30 ppm  | 38                | 390± 32            | 0.026± 0.038 | 0.965± 0.350 | 0.312± 0.023*  | 0.384± 0.046   | 0.732± 0.078   |
|       | 90 ppm  | 11                | 275± 35**          | 0.025± 0.007 | 0.979± 0.394 | 0.446± 0.097** | 0.682± 0.270** | 0.909± 0.129** |

Test of Dunnett

BAIS 4

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCrj  
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    | 38                | 0.328± 0.521 | 2.921± 0.481 | 0.526± 0.045   |
| 10 ppm     | 38                | 0.304± 0.181 | 2.977± 0.421 | 0.529± 0.039   |
| 30 ppm     | 38                | 0.357± 0.324 | 3.016± 0.685 | 0.540± 0.042   |
| 90 ppm     | 11                | 0.498± 0.576 | 3.460± 1.297 | 0.752± 0.113** |

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

Test of Dunnett

(HCL042)

BAIS 4

## APPENDIX K 2

ORGAN WEIGHT, RELATIVE : FEMALE

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCrj  
 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    | 40                | 251± 35            | 0.034± 0.044   | 0.070± 0.159   | 0.347± 0.056   | 0.413± 0.076   | 0.691± 0.088   |
| 10 ppm     | 45                | 254± 24            | 0.027± 0.006   | 0.046± 0.009   | 0.332± 0.025   | 0.413± 0.096   | 0.697± 0.085   |
| 30 ppm     | 41                | 252± 27            | 0.026± 0.005   | 0.071± 0.159   | 0.345± 0.050   | 0.425± 0.146   | 0.726± 0.120   |
| 90 ppm     | 15                | 195± 24**          | 0.034± 0.007** | 0.055± 0.010** | 0.415± 0.055** | 0.544± 0.115** | 0.836± 0.096** |

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

Test of Dunnett

(HCL042)

BAIS 4

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCrj  
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    | 40                | 0.356± 0.560 | 2.590± 0.418 | 0.757± 0.107   |
| 10 ppm     | 45                | 0.310± 0.440 | 2.703± 0.487 | 0.742± 0.072   |
| 30 ppm     | 41                | 0.413± 1.043 | 2.710± 0.545 | 0.751± 0.083   |
| 90 ppm     | 15                | 0.378± 0.394 | 2.936± 0.414 | 0.976± 0.163** |

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

Test of Dunnett

(HCL042)

BAIS 4



## APPENDIX L 1

HISTOPATHOLOGICAL FINDINGS :  
NON-NEOPLASTIC LESIONS : MALE  
ALL ANIMALS

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 1

| Organ                            | Findings                              | Group Name<br>No. of Animals on Study |       |       |       | Control |       |       |       | 10 ppm |       |       |       | 30 ppm |       |       |       | 90 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     |
|                                  |                                       | (%)                                   | (%)   | (%)   | (%)   | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   |
| {Integumentary system/appandage} |                                       |                                       |       |       |       |         |       |       |       |        |       |       |       |        |       |       |       |        |        |       |       |
| skin/app                         |                                       | <50>                                  |       |       |       | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |        |       |       |
|                                  | mineralization                        | 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 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                                  | scab                                  | 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 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                                  | epidermal cyst                        | 0                                     | 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 ) |
| subcutis                         |                                       | <50>                                  |       |       |       | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |        |       |       |
|                                  | abscess                               | 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 )  | ( 0 )  | ( 0 ) | ( 0 ) |
| {Respiratory system}             |                                       |                                       |       |       |       |         |       |       |       |        |       |       |       |        |       |       |       |        |        |       |       |
| nasal cavit                      |                                       | <50>                                  |       |       |       | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |        |       |       |
|                                  | exudate                               | 0                                     | 0     | 0     | 0     | 0       | 1     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 3      | 0     | 0     |
|                                  |                                       | ( 0 )                                 | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 6 )  | ( 0 ) | ( 0 ) |
|                                  | squamous cell hyperplasia with atypia | 0                                     | 0     | 0     | 0     | 0       | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 1      | 30     | 1     | 0 **  |
|                                  |                                       | ( 0 )                                 | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 60 ) | ( 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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 2

| Organ                | Findings  | Group Name              | Control     |             |           |           | 10 ppm      |             |           |           | 30 ppm      |             |           |              | 90 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            |
|                      |   |                         | (%)         | (%)         | (%)       | (%)       | (%)         | (%)         | (%)       | (%)       | (%)         | (%)         | (%)       | (%)          | (%)        | (%)         | (%)       | (%)          |
| {Respiratory system} |   |                         |             |             |           |           |             |             |           |           |             |             |           |              |            |             |           |              |
| nasal cavit          |   |                         |             |             |           |           |             |             |           |           |             |             |           |              |            |             |           |              |
|                      | eosinophilic change:olfactory epithelium        |                         | 18<br>( 36) | 23<br>( 46) | 1<br>( 2) | 0<br>( 0) | 20<br>( 40) | 20<br>( 40) | 1<br>( 2) | 0<br>( 0) | 11<br>( 22) | 22<br>( 44) | 1<br>( 2) | 0<br>( 0)    | 9<br>( 18) | 6<br>( 12)  | 0<br>( 0) | 0 **<br>( 0) |
|                      | eosinophilic change:respiratory epithelium      |                         | 2<br>( 4)   | 3<br>( 6)   | 0<br>( 0) | 0<br>( 0) | 4<br>( 8)   | 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)    |
|                      | inflammation:foreign body                       |                         | 7<br>( 14)  | 17<br>( 34) | 0<br>( 0) | 0<br>( 0) | 8<br>( 16)  | 15<br>( 30) | 0<br>( 0) | 0<br>( 0) | 6<br>( 12)  | 23<br>( 46) | 0<br>( 0) | 0<br>( 0)    | 2<br>( 4)  | 7<br>( 14)  | 0<br>( 0) | 0 **<br>( 0) |
|                      | inflammation:respiratory epithelium             |                         | 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)   | 2<br>( 4)   | 0<br>( 0) | 0<br>( 0)    | 4<br>( 8)  | 17<br>( 34) | 1<br>( 2) | 0 **<br>( 0) |
|                      | respiratory metaplasia:olfactory epithelium     |                         | 3<br>( 6)   | 0<br>( 0)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)   | 1<br>( 2)   | 0<br>( 0) | 0<br>( 0) | 4<br>( 8)   | 1<br>( 2)   | 0<br>( 0) | 0<br>( 0)    | 2<br>( 4)  | 6<br>( 12)  | 0<br>( 0) | 0 *<br>( 0)  |
|                      | respiratory metaplasia:gland                    |                         | 5<br>( 10)  | 14<br>( 28) | 0<br>( 0) | 0<br>( 0) | 9<br>( 18)  | 10<br>( 20) | 0<br>( 0) | 0<br>( 0) | 5<br>( 10)  | 12<br>( 24) | 0<br>( 0) | 0<br>( 0)    | 3<br>( 6)  | 17<br>( 34) | 1<br>( 2) | 0<br>( 0)    |
|                      | squamous cell metaplasia:respiratory epithelium |                         | 0<br>( 0)   | 0<br>( 0)   | 0<br>( 0) | 0<br>( 0) | 1<br>( 2)   | 1<br>( 2)   | 0<br>( 0) | 0<br>( 0) | 4<br>( 8)   | 6<br>( 12)  | 0<br>( 0) | 0 **<br>( 0) | 4<br>( 8)  | 38<br>( 76) | 0<br>( 0) | 0 **<br>( 0) |
|                      | squamous cell metaplasia: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) | 0<br>( 0)   | 0<br>( 0)   | 0<br>( 0) | 0<br>( 0)    | 5<br>( 10) | 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. : 0437  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 3

| Organ | Findings | Group Name              | Control |     |     |     | 10 ppm |     |     |     | 30 ppm |     |     |     | 90 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   |
|       |          |                         | (%)     | (%) | (%) | (%) | (%)    | (%) | (%) | (%) | (%)    | (%) | (%) | (%) | (%)    | (%) | (%) | (%) |

---

|                      |  |       |       |       |       |       |       |       |       |        |       |       |       |        |        |       |       |       |
|----------------------|--|-------|-------|-------|-------|-------|-------|-------|-------|--------|-------|-------|-------|--------|--------|-------|-------|-------|
| {Respiratory system} |  |       |       |       |       |       |       |       |       |        |       |       |       |        |        |       |       |       |
| nasal cavit          |  | <50>  |       |       |       |       |       |       |       |        |       |       |       |        |        |       |       |       |
|                      | hyperplasia with atypia:respiratory epithelium | 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 )  | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                      | hyperplasia:submucosal gland                   | 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 )  | ( 6 ) | ( 0 ) | ( 0 ) |
|                      | hyperplasia:transitional epithelium            | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 5      | 3     | 0     | 0 *   | 0      | 0      | 0     | 0     | 0     |
|                      |  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 10 ) | ( 6 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                      | atrophy:olfactory epithelium                   | 0     | 0     | 0     | 0     | 0     | 1     | 0     | 0     | 7      | 2     | 0     | 0 **  | 10     | 14     | 0     | 0 **  | 0     |
|                      |  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 ) | ( 0 ) | ( 0 ) | ( 14 ) | ( 4 ) | ( 0 ) | ( 0 ) | ( 20 ) | ( 28 ) | ( 0 ) | ( 0 ) | ( 0 ) |
| lung                 |  | <50>  |       |       |       |       |       |       |       |        |       |       |       |        |        |       |       |       |
|                      | congestion                                     | 0     | 1     | 0     | 0     | 0     | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 1      | 0     | 0     | 0     |
|                      |  | ( 0 ) | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                      | hemorrhage                                     | 0     | 0     | 0     | 0     | 0     | 1     | 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 ) |
|                      | inflammatory infiltration                      | 0     | 0     | 0     | 0     | 1     | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 0      | 0     | 0     | 0     |
|                      |  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                      | accumulation of foamy cells                    | 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 ) | ( 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. : 0437  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : MALE

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

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|                        |                                       | Group Name              | Control |       |       |       | 10 ppm |       |       |       | 30 ppm |       |       |       | 90 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                              |                         | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   |
|                        |                                       |                         |         |       |       |       |        |       |       |       |        |       |       |       |        |        |       |       |
| {Respiratory system}   |                                       |                         |         |       |       |       |        |       |       |       |        |       |       |       |        |        |       |       |
|                        |                                       |                         |         |       |       |       |        |       |       |       |        |       |       |       |        |        |       |       |
| lung                   |                                       |                         | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |        |       |       |
|                        | bronchiolar-alveolar cell hyperplasia |                         | 0       | 3     | 0     | 0     | 0      | 1     | 0     | 0     | 0      | 2     | 0     | 0     | 0      | 1      | 0     | 0     |
|                        |                                       |                         | ( 0 )   | ( 6 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 4 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 )  | ( 0 ) | ( 0 ) |
|                        | inflammation:foreign body             |                         | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 8      | 0     | 0 **  |
|                        |                                       |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 16 ) | ( 0 ) | ( 0 ) |
|                        |                                       |                         |         |       |       |       |        |       |       |       |        |       |       |       |        |        |       |       |
| {Hematopoietic system} |                                       |                         |         |       |       |       |        |       |       |       |        |       |       |       |        |        |       |       |
|                        |                                       |                         |         |       |       |       |        |       |       |       |        |       |       |       |        |        |       |       |
| bone marrow            |                                       |                         | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |        |       |       |
|                        | thrombus                              |                         | 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 ) |
|                        | granulation                           |                         | 1       | 0     | 0     | 0     | 3      | 1     | 0     | 0     | 0      | 1     | 0     | 0     | 0      | 0      | 0     | 0     |
|                        |                                       |                         | ( 2 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 6 )  | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                        | increased hematopoiesis               |                         | 4       | 0     | 0     | 0     | 5      | 0     | 0     | 0     | 5      | 0     | 0     | 0     | 14     | 0      | 0     | 0 *   |
|                        |                                       |                         | ( 8 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 10 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 10 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 28 ) | ( 0 )  | ( 0 ) | ( 0 ) |
|                        | decreased hematopoiesis               |                         | 0       | 1     | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 1      | 0     | 0     |
|                        |                                       |                         | ( 0 )   | ( 2 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 )  | ( 0 ) | ( 0 ) |
|                        |                                       |                         |         |       |       |       |        |       |       |       |        |       |       |       |        |        |       |       |
| lymph node             |                                       |                         | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |        |       |       |
|                        | lymphadenitis                         |                         | 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 ) |

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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 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 |       |       |       | 10 ppm |       |       |       | 30 ppm |       |       |       | 90 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     |
|                        |  | (%)                                   | (%)    | (%)   | (%)   | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   |
| {Hematopoietic system} |  |                                       |        |       |       |         |       |       |       |        |       |       |       |        |       |       |       |        |       |       |       |
| spleen                 |  | <50>                                  |        |       |       | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |       |       |       |
|                        | congestion                             | 0                                     | 6      | 0     | 0     | 1       | 3     | 0     | 0     | 1      | 3     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0 *   |
|                        |  | ( 0 )                                 | ( 12 ) | ( 0 ) | ( 0 ) | ( 2 )   | ( 6 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 6 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                        | deposit of hemosiderin                 | 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 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                        | inflammatory cell nest                 | 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 ) | ( 0 ) |
|                        | fibrosis                               | 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 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                        | increased extramedullary hematopoiesis | 1                                     | 3      | 0     | 0     | 0       | 4     | 0     | 0     | 2      | 1     | 1     | 0     | 0      | 2     | 0     | 0     | 0      | 0     | 0     | 0     |
|                        |  | ( 2 )                                 | ( 6 )  | ( 0 ) | ( 0 ) | ( 0 )   | ( 8 ) | ( 0 ) | ( 0 ) | ( 4 )  | ( 2 ) | ( 2 ) | ( 0 ) | ( 0 )  | ( 4 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
| {Circulatory system}   |  |                                       |        |       |       |         |       |       |       |        |       |       |       |        |       |       |       |        |       |       |       |
| heart                  |  | <50>                                  |        |       |       | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |       |       |       |
|                        | thrombus                               | 0                                     | 1      | 0     | 0     | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 2      | 0     | 0     | 0     |
|                        |  | ( 0 )                                 | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                        | necrosis:focal                         | 0                                     | 1      | 0     | 0     | 0       | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 1      | 1     | 0     | 0     | 1      | 1     | 0     | 0     |
|                        |  | ( 0 )                                 | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 2 ) | ( 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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 6

|                      |                           | Group Name              | Control |        |       |       | 10 ppm |        |       |       | 30 ppm |        |       |       | 90 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                  |                         | (%)     | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   |
| {Circulatory system} |                           |                         |         |        |       |       |        |        |       |       |        |        |       |       |        |        |       |       |
| heart                |                           |                         | <50>    |        |       |       | <50>   |        |       |       | <50>   |        |       |       | <50>   |        |       |       |
|                      | mineralization            |                         | 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 ) |
|                      | inflammatory cell nest    |                         | 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 )  | ( 0 ) | ( 0 ) |
|                      | myocardial fibrosis       |                         | 14      | 36     | 0     | 0     | 15     | 31     | 0     | 0     | 22     | 27     | 0     | 0     | 24     | 21     | 0     | 0 **  |
|                      |                           |                         | ( 28 )  | ( 72 ) | ( 0 ) | ( 0 ) | ( 30 ) | ( 62 ) | ( 0 ) | ( 0 ) | ( 44 ) | ( 54 ) | ( 0 ) | ( 0 ) | ( 48 ) | ( 42 ) | ( 0 ) | ( 0 ) |
|                      | subendocardial fibrosis   |                         | 1       | 0      | 0     | 0     | 0      | 1      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0     | 0     |
|                      |                           |                         | ( 2 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                      | arteritis                 |                         | 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 ) |
| {Digestive system}   |                           |                         |         |        |       |       |        |        |       |       |        |        |       |       |        |        |       |       |
| oral cavity          |                           |                         | <50>    |        |       |       | <50>   |        |       |       | <50>   |        |       |       | <50>   |        |       |       |
|                      | squamous cell hyperplasia |                         | 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 ) |
| tooth                |                           |                         | <50>    |        |       |       | <50>   |        |       |       | <50>   |        |       |       | <50>   |        |       |       |
|                      | inflammation              |                         | 0       | 1      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 1      | 0     | 0     | 1      | 2      | 0     | 0     |
|                      |                           |                         | ( 0 )   | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 )  | ( 0 ) | ( 0 ) | ( 2 )  | ( 4 )  | ( 0 ) | ( 0 ) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 7

| Organ              | Findings                  | Group Name<br>No. of Animals on Study |       |       |       | Control |       |       |       | 10 ppm |       |       |       | 30 ppm |       |       |       | 90 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             | inflammatory infiltration | <50>                                  |       |       |       | <49>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |       |       |       |
|                    |                           | 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 ) |
| stomach            | mineralization            | <50>                                  |       |       |       | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |       |       |       |
|                    |                           | 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 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                    | epidermal 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 ) |
|                    | atrophy:glandular mucosa  | 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 ) |
|                    | erosion:forestomach       | 2                                     | 0     | 0     | 0     | 1       | 0     | 0     | 0     | 1      | 1     | 0     | 0     | 4      | 0     | 0     | 0     | 4      | 0     | 0     | 0     |
|                    |                           | ( 4 )                                 | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 2 ) | ( 0 ) | ( 0 ) | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                    | ulcer:forestomach         | 0                                     | 2     | 0     | 0     | 1       | 3     | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 1      | 0     | 0     | 0     |
|                    |                           | ( 0 )                                 | ( 4 ) | ( 0 ) | ( 0 ) | ( 2 )   | ( 6 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                    | hyperplasia:forestomach   | 0                                     | 4     | 0     | 0     | 2       | 3     | 0     | 0     | 1      | 2     | 0     | 0     | 3      | 0     | 0     | 0 *   | 3      | 0     | 0     | 0 *   |
|                    |                           | ( 0 )                                 | ( 8 ) | ( 0 ) | ( 0 ) | ( 4 )   | ( 6 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 4 ) | ( 0 ) | ( 0 ) | ( 6 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 6 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                    | erosion:glandular stomach | 7                                     | 1     | 0     | 0     | 1       | 0     | 0     | 0 *   | 3      | 0     | 0     | 0     | 8      | 1     | 0     | 0     | 8      | 1     | 0     | 0     |
|                    |                           | ( 14 )                                | ( 2 ) | ( 0 ) | ( 0 ) | ( 2 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 6 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 16 ) | ( 2 ) | ( 0 ) | ( 0 ) | ( 16 ) | ( 2 ) | ( 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  
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STUDY NO. : 0437  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 8

| Organ              | Findings                | Group Name              |       |       |       | Control |       |       |       | 10 ppm |       |       |       | 30 ppm |       |       |       | 90 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     |
|                    |                         | (%)                     | (%)   | (%)   | (%)   | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   |
| {Digestive system} |                         |                         |       |       |       |         |       |       |       |        |       |       |       |        |       |       |       |        |       |       |       |
| stomach            | ulcer:glandular stomach | <50>                    |       |       |       | 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 ) |
| small intes        | inflammation            | <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 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
| liver              | herniation              | <50>                    |       |       |       | 3       | 0     | 0     | 0     | 5      | 0     | 0     | 0     | 4      | 0     | 0     | 0     | 9      | 0     | 0     | 0     |
|                    |                         | ( 6 )                   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 10 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 18 ) | ( 0 ) | ( 0 ) | ( 0 ) |
|                    | hemorrhage              | 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 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                    | necrosis:central        | 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 )  | ( 4 ) | ( 0 ) | ( 0 ) |
|                    | necrosis:focal          | 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 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                    | fatty change            | 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 )  | ( 0 ) | ( 0 ) | ( 0 ) |

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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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 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 9

| Organ              | Findings               | Group Name              | Control |       |      |      | 10 ppm |       |      |      | 30 ppm |       |      |      | 90 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    |
|                    |                        |                         | (%)     | (%)   | (%)  | (%)  | (%)    | (%)   | (%)  | (%)  | (%)    | (%)   | (%)  | (%)  | (%)    | (%)   | (%)  | (%)  |
| {Digestive system} |                        |                         |         |       |      |      |        |       |      |      |        |       |      |      |        |       |      |      |
| liver              |                        |                         |         |       |      |      |        |       |      |      |        |       |      |      |        |       |      |      |
|                    | fatty change:central   |                         | <50>    |       |      |      | <50>   |       |      |      | <50>   |       |      |      | <50>   |       |      |      |
|                    |                        |                         | 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) |
|                    | granulation            |                         | 3       | 1     | 0    | 0    | 2      | 0     | 0    | 0    | 2      | 1     | 0    | 0    | 0      | 0     | 0    | 0    |
|                    |                        |                         | ( 6)    | ( 2)  | ( 0) | ( 0) | ( 4)   | ( 0)  | ( 0) | ( 0) | ( 4)   | ( 2)  | ( 0) | ( 0) | ( 0)   | ( 0)  | ( 0) | ( 0) |
|                    | inflammatory cell nest |                         | 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) |
|                    | clear cell focus       |                         | 7       | 4     | 0    | 0    | 5      | 8     | 0    | 0    | 3      | 5     | 0    | 0    | 1      | 1     | 0    | 0 *  |
|                    |                        |                         | ( 14)   | ( 8)  | ( 0) | ( 0) | ( 10)  | ( 16) | ( 0) | ( 0) | ( 6)   | ( 10) | ( 0) | ( 0) | ( 2)   | ( 2)  | ( 0) | ( 0) |
|                    | acidophilic cell focus |                         | 0       | 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) | ( 0)   | ( 0)  | ( 0) | ( 0) |
|                    | basophilic cell focus  |                         | 3       | 1     | 0    | 0    | 0      | 1     | 0    | 0    | 1      | 1     | 0    | 0    | 1      | 0     | 0    | 0    |
|                    |                        |                         | ( 6)    | ( 2)  | ( 0) | ( 0) | ( 0)   | ( 2)  | ( 0) | ( 0) | ( 2)   | ( 2)  | ( 0) | ( 0) | ( 2)   | ( 0)  | ( 0) | ( 0) |
|                    | spongiosis hepatitis   |                         | 3       | 0     | 0    | 0    | 1      | 1     | 0    | 0    | 7      | 0     | 0    | 0    | 2      | 0     | 0    | 0    |
|                    |                        |                         | ( 6)    | ( 0)  | ( 0) | ( 0) | ( 2)   | ( 2)  | ( 0) | ( 0) | ( 14)  | ( 0)  | ( 0) | ( 0) | ( 4)   | ( 0)  | ( 0) | ( 0) |
|                    | bile duct hyperplasia  |                         | 0       | 48    | 0    | 0    | 1      | 47    | 1    | 0    | 5      | 44    | 0    | 0    | 5      | 43    | 0    | 0    |
|                    |                        |                         | ( 0)    | ( 96) | ( 0) | ( 0) | ( 2)   | ( 94) | ( 2) | ( 0) | ( 10)  | ( 88) | ( 0) | ( 0) | ( 10)  | ( 86) | ( 0) | ( 0) |

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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
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PAGE : 10

| Organ              | Findings               | Group Name              | Control |       |       |       | 10 ppm |       |       |        | 30 ppm |       |       |       | 90 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   |
|                    |                        |                         | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%) |
| {Digestive system} |                        |                         |         |       |       |       |        |       |       |        |        |       |       |       |        |       |       |     |
| liver              | biliary cyst           |                         | <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 ) |     |
| pancreas           | atrophy                |                         | <50>    |       |       |       | <50>   |       |       |        | <50>   |       |       |       | <50>   |       |       |     |
|                    |                        | 1                       | 7       | 1     | 0     | 4     | 11     | 1     | 0     | 5      | 8      | 0     | 0     | 1     | 2      | 0     | 0     |     |
|                    |                        | ( 2 )                   | ( 14 )  | ( 2 ) | ( 0 ) | ( 8 ) | ( 22 ) | ( 2 ) | ( 0 ) | ( 10 ) | ( 16 ) | ( 0 ) | ( 0 ) | ( 2 ) | ( 4 )  | ( 0 ) | ( 0 ) |     |
|                    | islet cell hyperplasia |                         | 0       | 2     | 0     | 0     | 0      | 4     | 0     | 0      | 1      | 0     | 0     | 0     | 0      | 0     | 0     |     |
|                    |                        | ( 0 )                   | ( 4 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) |     |
| {Urinary system}   |                        |                         |         |       |       |       |        |       |       |        |        |       |       |       |        |       |       |     |
| kidney             | necrosis:focal         |                         | <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 ) |     |
|                    | deposit of hemosiderin |                         | 0       | 0     | 0     | 0     | 0      | 1     | 0     | 0      | 0      | 0     | 0     | 0     | 1      | 0     | 0     |     |
|                    |                        | ( 0 )                   | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) |     |
|                    | inflammatory cell nest |                         | 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 ) |     |

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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 |        |       |       | 10 ppm |        |       |       | 30 ppm |       |       |       | 90 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>   |       |       |       |
|                  | mineralization:central                    | 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 ) |
|                  | chronic nephropathy                       | 16                                    | 26     | 2     | 0     | 12      | 31     | 2     | 0     | 14     | 25     | 2     | 0     | 18     | 1     | 0     | 0     | 18     | 1     | 0     | 0 **  |
|                  |   | ( 32 )                                | ( 52 ) | ( 4 ) | ( 0 ) | ( 24 )  | ( 62 ) | ( 4 ) | ( 0 ) | ( 28 ) | ( 50 ) | ( 4 ) | ( 0 ) | ( 36 ) | ( 2 ) | ( 0 ) | ( 0 ) | ( 36 ) | ( 2 ) | ( 0 ) | ( 0 ) |
|                  | hydronephrosis                            | 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 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                  | tubular necrosis                          | 0                                     | 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 ) |
|                  | mineralization:cortico-medullary junction | 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 ) |
|                  | mineralization:papilla                    | 4                                     | 0      | 0     | 0     | 5       | 0      | 0     | 0     | 3      | 0      | 0     | 0     | 4      | 2     | 0     | 0     | 4      | 2     | 0     | 0     |
|                  |   | ( 8 )                                 | ( 0 )  | ( 0 ) | ( 0 ) | ( 10 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 6 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 8 )  | ( 4 ) | ( 0 ) | ( 0 ) | ( 8 )  | ( 4 ) | ( 0 ) | ( 0 ) |
|                  | mineralization:pelvis                     | 4                                     | 0      | 0     | 0     | 2       | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     |
|                  |   | ( 8 )                                 | ( 0 )  | ( 0 ) | ( 0 ) | ( 4 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                  | mineralization:cortex                     | 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 )  | ( 0 ) | ( 0 ) | ( 0 ) |

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ALL ANIMALS (0-105W)

PAGE : 12

| Organ              | Findings                                   | Group Name              | Control |        |       |       | 10 ppm |        |       |       | 30 ppm |       |       |       | 90 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     |
|                    |  |                         | (%)     | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   |
| {Urinary system}   |  |                         |         |        |       |       |        |        |       |       |        |       |       |       |        |       |       |       |
| urin bladd         |  |                         | <50>    |        |       |       | <50>   |        |       |       | <50>   |       |       |       | <50>   |       |       |       |
|                    | hemorrhage                                 |                         | 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 ) |
|                    | simple hyperplasia:transitional epithelium |                         | 1       | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 0     | 0     | 0     |
|                    |  |                         | ( 2 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
| {Endocrine system} |  |                         |         |        |       |       |        |        |       |       |        |       |       |       |        |       |       |       |
| pituitary          |  |                         | <50>    |        |       |       | <50>   |        |       |       | <50>   |       |       |       | <50>   |       |       |       |
|                    | cyst                                       |                         | 0       | 0      | 0     | 0     | 1      | 0      | 0     | 0     | 0      | 1     | 0     | 0     | 0      | 2     | 0     | 0     |
|                    |  |                         | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 4 ) | ( 0 ) | ( 0 ) |
|                    | hyperplasia                                |                         | 2       | 6      | 0     | 0     | 0      | 8      | 0     | 0     | 1      | 4     | 0     | 0     | 0      | 2     | 0     | 0     |
|                    |  |                         | ( 4 )   | ( 12 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 16 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 8 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 4 ) | ( 0 ) | ( 0 ) |
|                    | Rathke pouch                               |                         | 1       | 2      | 0     | 0     | 0      | 0      | 0     | 0     | 2      | 1     | 0     | 0     | 0      | 3     | 0     | 0     |
|                    |  |                         | ( 2 )   | ( 4 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 4 )  | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 6 ) | ( 0 ) | ( 0 ) |
| thyroid            |  |                         | <50>    |        |       |       | <49>   |        |       |       | <50>   |       |       |       | <50>   |       |       |       |
|                    | cyst                                       |                         | 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 ) |

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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

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

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|                       |                                   | Group Name              | Control |      |       |      | 10 ppm |       |       |      | 30 ppm |       |       |      | 90 ppm |       |       |      |
|-----------------------|-----------------------------------|-------------------------|---------|------|-------|------|--------|-------|-------|------|--------|-------|-------|------|--------|-------|-------|------|
|                       |                                   | No. of Animals on Study | 50      |      |       |      | 50     |       |       |      | 50     |       |       |      | 50     |       |       |      |
| Organ                 | Findings                          | Grade                   | 1       | 2    | 3     | 4    | 1      | 2     | 3     | 4    | 1      | 2     | 3     | 4    | 1      | 2     | 3     | 4    |
|                       |                                   |                         | (%)     | (%)  | (%)   | (%)  | (%)    | (%)   | (%)   | (%)  | (%)    | (%)   | (%)   | (%)  | (%)    | (%)   | (%)   | (%)  |
| {Endocrine system}    |                                   |                         |         |      |       |      |        |       |       |      |        |       |       |      |        |       |       |      |
| thyroid               |                                   |                         | <50>    |      |       |      | <49>   |       |       |      | <50>   |       |       |      | <50>   |       |       |      |
|                       | C-cell hyperplasia                |                         | 6       | 1    | 0     | 0    | 7      | 5     | 0     | 0    | 3      | 5     | 0     | 0    | 2      | 2     | 0     | 0    |
|                       |                                   |                         | ( 12)   | ( 2) | ( 0)  | ( 0) | ( 14)  | ( 10) | ( 0)  | ( 0) | ( 6)   | ( 10) | ( 0)  | ( 0) | ( 4)   | ( 4)  | ( 0)  | ( 0) |
|                       | focal follicular cell hyperplasia |                         | 0       | 0    | 0     | 0    | 0      | 0     | 0     | 0    | 1      | 1     | 0     | 0    | 0      | 0     | 0     | 0    |
|                       |                                   |                         | ( 0)    | ( 0) | ( 0)  | ( 0) | ( 0)   | ( 0)  | ( 0)  | ( 0) | ( 2)   | ( 2)  | ( 0)  | ( 0) | ( 0)   | ( 0)  | ( 0)  | ( 0) |
| parathyroid           |                                   |                         | <50>    |      |       |      | <49>   |       |       |      | <50>   |       |       |      | <50>   |       |       |      |
|                       | hyperplasia                       |                         | 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) |
| adrenal               |                                   |                         | <50>    |      |       |      | <50>   |       |       |      | <50>   |       |       |      | <50>   |       |       |      |
|                       | hyperplasia:cortical cell         |                         | 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) |
|                       | hyperplasia:medulla               |                         | 2       | 4    | 0     | 0    | 1      | 4     | 0     | 0    | 0      | 4     | 0     | 0    | 0      | 1     | 0     | 0    |
|                       |                                   |                         | ( 4)    | ( 8) | ( 0)  | ( 0) | ( 2)   | ( 8)  | ( 0)  | ( 0) | ( 0)   | ( 8)  | ( 0)  | ( 0) | ( 0)   | ( 2)  | ( 0)  | ( 0) |
|                       | focal fatty change:cortex         |                         | 0       | 2    | 0     | 0    | 0      | 3     | 0     | 0    | 1      | 1     | 0     | 0    | 3      | 1     | 0     | 0    |
|                       |                                   |                         | ( 0)    | ( 4) | ( 0)  | ( 0) | ( 0)   | ( 6)  | ( 0)  | ( 0) | ( 2)   | ( 2)  | ( 0)  | ( 0) | ( 6)   | ( 2)  | ( 0)  | ( 0) |
| {Reproductive system} |                                   |                         |         |      |       |      |        |       |       |      |        |       |       |      |        |       |       |      |
| testis                |                                   |                         | <50>    |      |       |      | <50>   |       |       |      | <50>   |       |       |      | <50>   |       |       |      |
|                       | atrophy                           |                         | 0       | 3    | 44    | 0    | 0      | 1     | 47    | 0    | 2      | 2     | 43    | 0    | 10     | 6     | 24    | 0 ** |
|                       |                                   |                         | ( 0)    | ( 6) | ( 88) | ( 0) | ( 0)   | ( 2)  | ( 94) | ( 0) | ( 4)   | ( 4)  | ( 86) | ( 0) | ( 20)  | ( 12) | ( 48) | ( 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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

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|                       |                               | Group Name              | Control |       |       |       | 10 ppm |        |       |       | 30 ppm |        |       |       | 90 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} |                               |                         |         |       |       |       |        |        |       |       |        |        |       |       |        |       |       |       |
| testis                |                               |                         | <50>    |       |       |       | <50>   |        |       |       | <50>   |        |       |       | <50>   |       |       |       |
|                       | mineralization                |                         | 10      | 1     | 0     | 0     | 8      | 0      | 0     | 0     | 8      | 0      | 0     | 0     | 11     | 0     | 0     | 0     |
|                       |                               |                         | ( 20 )  | ( 2 ) | ( 0 ) | ( 0 ) | ( 16 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 16 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 22 ) | ( 0 ) | ( 0 ) | ( 0 ) |
|                       |                               |                         |         |       |       |       |        |        |       |       |        |        |       |       |        |       |       |       |
|                       | arteritis                     |                         | 1       | 1     | 0     | 0     | 2      | 1      | 0     | 0     | 0      | 0      | 1     | 0     | 0      | 0     | 0     | 0     |
|                       |                               |                         | ( 2 )   | ( 2 ) | ( 0 ) | ( 0 ) | ( 4 )  | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 2 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                       | interstitial cell hyperplasia |                         | 0       | 1     | 0     | 0     | 6      | 0      | 0     | 0 *   | 4      | 0      | 0     | 0     | 10     | 0     | 0     | 0 **  |
|                       |                               |                         | ( 0 )   | ( 2 ) | ( 0 ) | ( 0 ) | ( 12 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 8 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 20 ) | ( 0 ) | ( 0 ) | ( 0 ) |
| prostate              |                               |                         | <50>    |       |       |       | <50>   |        |       |       | <50>   |        |       |       | <50>   |       |       |       |
|                       | inflammation                  |                         | 9       | 3     | 1     | 0     | 6      | 7      | 0     | 0     | 5      | 6      | 2     | 0     | 4      | 1     | 0     | 0     |
|                       |                               |                         | ( 18 )  | ( 6 ) | ( 2 ) | ( 0 ) | ( 12 ) | ( 14 ) | ( 0 ) | ( 0 ) | ( 10 ) | ( 12 ) | ( 4 ) | ( 0 ) | ( 8 )  | ( 2 ) | ( 0 ) | ( 0 ) |
|                       | hyperplasia                   |                         | 7       | 1     | 0     | 0     | 9      | 0      | 0     | 0     | 8      | 0      | 0     | 0     | 1      | 0     | 0     | 0 *   |
|                       |                               |                         | ( 14 )  | ( 2 ) | ( 0 ) | ( 0 ) | ( 18 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 16 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) |
| mammary gl            |                               |                         | <50>    |       |       |       | <50>   |        |       |       | <50>   |        |       |       | <50>   |       |       |       |
|                       | galactoceles                  |                         | 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 )  | ( 0 ) | ( 0 ) | ( 0 ) |
| {Nervous system}      |                               |                         |         |       |       |       |        |        |       |       |        |        |       |       |        |       |       |       |
| brain                 |                               |                         | <50>    |       |       |       | <50>   |        |       |       | <50>   |        |       |       | <50>   |       |       |       |
|                       | hemorrhage                    |                         | 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 ) |       |

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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

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|                                  |                               | Group Name              | Control |       |       |       | 10 ppm |       |       |       | 30 ppm |       |       |       | 90 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                      |                         | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   |
| {Nervous system}                 |                               |                         |         |       |       |       |        |       |       |       |        |       |       |       |        |       |       |       |
| brain                            |                               |                         | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |       |       |       |
|                                  | necrosis:focal                |                         | 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 ) |
|                                  | vacuolic change               |                         | 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 ) |
|                                  | mineralization                |                         | 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 ) | ( 0 ) |       |
|                                  | gliosis                       |                         | 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 ) | ( 0 ) |
|                                  | dilatation:cerebral ventricle |                         | 0       | 1     | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 1     | 0     | 0     |
|                                  |                               |                         | ( 0 )   | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 ) | ( 0 ) | ( 0 ) |
| spinal cord                      |                               |                         | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |       |       |       |
|                                  | hemorrhage                    |                         | 0       | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 0     | 0     | 0     |
|                                  |                               |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                                  | gliosis                       |                         | 0       | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 1     | 0     | 0     | 0      | 0     | 0     | 0     |
|                                  |                               |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
| {Special sense organs/appendage} |                               |                         |         |       |       |       |        |       |       |       |        |       |       |       |        |       |       |       |
| eye                              |                               |                         | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |       |       |       |
|                                  | hemorrhage                    |                         | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 1     | 0     | 0     | 0      | 0     | 1     | 0     |
|                                  |                               | ( 0 )                   | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 ) | ( 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 ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$  Test of Chi Square



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ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
ALL ANIMALS (0-105W)

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| Organ                            | Findings                  | Group Name<br>No. of Animals on Study |             |             |            | Control      |            |             |            | 10 ppm       |             |             |            | 30 ppm       |              |            |            | 90 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          |
|                                  |                           | (%)                                   | (%)         | (%)         | (%)        | (%)          | (%)        | (%)         | (%)        | (%)          | (%)         | (%)         | (%)        | (%)          | (%)          | (%)        | (%)        | (%)        | (%)        | (%)        | (%)        |
| (Special sense organs/appendage) |                           |                                       |             |             |            |              |            |             |            |              |             |             |            |              |              |            |            |            |            |            |            |
| eye                              |                           | <50>                                  |             |             |            | <50>         |            |             |            | <50>         |             |             |            | <50>         |              |            |            | <50>       |            |            |            |
|                                  | cataract                  | 3<br>( 6 )                            | 5<br>( 10 ) | 0<br>( 0 )  | 0<br>( 0 ) | 3<br>( 6 )   | 3<br>( 6 ) | 0<br>( 0 )  | 0<br>( 0 ) | 0<br>( 0 )   | 5<br>( 10 ) | 0<br>( 0 )  | 0<br>( 0 ) | 0<br>( 0 )   | 5<br>( 10 )  | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 2<br>( 4 ) | 0<br>( 0 ) | 0<br>( 0 ) |
|                                  | retinal atrophy           | 32<br>( 64 )                          | 0<br>( 0 )  | 8<br>( 16 ) | 0<br>( 0 ) | 36<br>( 72 ) | 0<br>( 0 ) | 5<br>( 10 ) | 0<br>( 0 ) | 40<br>( 80 ) | 0<br>( 0 )  | 5<br>( 10 ) | 0<br>( 0 ) | 18<br>( 36 ) | 0<br>( 0 )   | 2<br>( 4 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |
|                                  | keratitis                 | 3<br>( 6 )                            | 0<br>( 0 )  | 0<br>( 0 )  | 0<br>( 0 ) | 3<br>( 6 )   | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 ) | 0<br>( 0 )   | 0<br>( 0 )  | 0<br>( 0 )  | 0<br>( 0 ) | 10<br>( 20 ) | 13<br>( 26 ) | 3<br>( 6 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |
| Harder gl                        |                           | <50>                                  |             |             |            | <50>         |            |             |            | <50>         |             |             |            | <50>         |              |            |            | <50>       |            |            |            |
|                                  | degeneration              | 0<br>( 0 )                            | 0<br>( 0 )  | 0<br>( 0 )  | 0<br>( 0 ) | 0<br>( 0 )   | 1<br>( 2 ) | 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 ) |
|                                  | 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 ) | 1<br>( 2 )   | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |
|                                  | lymphocytic infiltration  | 3<br>( 6 )                            | 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 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |
| (Musculoskeletal system)         |                           |                                       |             |             |            |              |            |             |            |              |             |             |            |              |              |            |            |            |            |            |            |
| muscle                           |                           | <50>                                  |             |             |            | <50>         |            |             |            | <50>         |             |             |            | <50>         |              |            |            | <50>       |            |            |            |
|                                  | mineralization            | 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 ) |

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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 17

| Organ | Findings | Group Name              |  |  |  | Control         |  |  |  | 10 ppm          |  |  |  | 30 ppm          |  |  |  | 90 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         |  |  |  |
|       |          | (%) (%) (%) (%)         |  |  |  | (%) (%) (%) (%) |  |  |  | (%) (%) (%) (%) |  |  |  | (%) (%) (%) (%) |  |  |  | (%) (%) (%) (%) |  |  |  |

{Body cavities}

|            |              |                         |                         |                         |                         |                         |                         |                         |                         |                         |                         |                         |                         |                         |                         |                         |                         |
|------------|--------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| peritoneum | inflammation | <50>                    |                         |                         |                         | <50>                    |                         |                         |                         | <50>                    |                         |                         |                         | <50>                    |                         |                         |                         |
|            |              | 0 1 0 0                 | 0 0 0 0                 | 0 0 0 0                 | 0 0 0 0                 | 0 0 0 0                 | 0 0 0 0                 | 0 0 0 0                 | 0 0 0 0                 | 0 0 0 0                 | 0 0 0 0                 | 0 0 0 0                 | 0 0 0 0                 | 0 0 0 0                 | 0 0 0 0                 | 0 0 0 0                 | 0 0 0 0                 |
|            |              | ( 0 ) ( 2 ) ( 0 ) ( 0 ) | ( 0 ) ( 0 ) ( 0 ) ( 0 ) | ( 0 ) ( 0 ) ( 0 ) ( 0 ) | ( 0 ) ( 0 ) ( 0 ) ( 0 ) | ( 0 ) ( 0 ) ( 0 ) ( 0 ) | ( 0 ) ( 0 ) ( 0 ) ( 0 ) | ( 0 ) ( 0 ) ( 0 ) ( 0 ) | ( 0 ) ( 0 ) ( 0 ) ( 0 ) | ( 0 ) ( 0 ) ( 0 ) ( 0 ) | ( 0 ) ( 0 ) ( 0 ) ( 0 ) | ( 0 ) ( 0 ) ( 0 ) ( 0 ) | ( 0 ) ( 0 ) ( 0 ) ( 0 ) | ( 0 ) ( 0 ) ( 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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 1

|                                  |  | Group Name              | Control |        |       |       | 10 ppm |        |       |       | 30 ppm |        |       |       | 90 ppm |        |       |       |
|----------------------------------|--|-------------------------|---------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|
|                                  |  | No. of Animals on Study | 12      |        |       |       | 12     |        |       |       | 12     |        |       |       | 39     |        |       |       |
| Organ                            | Findings                                   | Grade                   | 1       | 2      | 3     | 4     | 1      | 2      | 3     | 4     | 1      | 2      | 3     | 4     | 1      | 2      | 3     | 4     |
|                                  |  |                         | (%)     | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   |
| {Integumentary system/appandage} |  |                         |         |        |       |       |        |        |       |       |        |        |       |       |        |        |       |       |
| skin/app                         |  |                         | <12>    |        |       |       | <12>   |        |       |       | <12>   |        |       |       | <39>   |        |       |       |
|                                  | epidermal cyst                             |                         | 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 )  | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |
| {Respiratory system}             |  |                         |         |        |       |       |        |        |       |       |        |        |       |       |        |        |       |       |
| nasal cavit                      |  |                         | <12>    |        |       |       | <12>   |        |       |       | <12>   |        |       |       | <39>   |        |       |       |
|                                  | exudate                                    |                         | 0       | 0      | 0     | 0     | 0      | 1      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 3      | 0     | 0     |
|                                  |  |                         | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 8 )  | ( 0 ) | ( 0 ) |
|                                  | squamous cell hyperplasia with atypia      |                         | 0       | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 1      | 0      | 0     | 0     | 0      | 23     | 0     | 0 **  |
|                                  |  |                         | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 8 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 59 ) | ( 0 ) | ( 0 ) |
|                                  | eosinophilic change:olfactory epithelium   |                         | 3       | 3      | 0     | 0     | 4      | 2      | 0     | 0     | 0      | 1      | 0     | 0     | 3      | 4      | 0     | 0     |
|                                  |  |                         | ( 25 )  | ( 25 ) | ( 0 ) | ( 0 ) | ( 33 ) | ( 17 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 8 )  | ( 0 ) | ( 0 ) | ( 8 )  | ( 10 ) | ( 0 ) | ( 0 ) |
|                                  | eosinophilic change:respiratory epithelium |                         | 0       | 1      | 0     | 0     | 1      | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0     | 0     |
|                                  |  |                         | ( 0 )   | ( 8 )  | ( 0 ) | ( 0 ) | ( 8 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                                  | inflammation:foreign body                  |                         | 0       | 4      | 0     | 0     | 2      | 3      | 0     | 0     | 0      | 4      | 0     | 0     | 2      | 2      | 0     | 0 *   |
|                                  |  |                         | ( 0 )   | ( 33 ) | ( 0 ) | ( 0 ) | ( 17 ) | ( 25 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 33 ) | ( 0 ) | ( 0 ) | ( 5 )  | ( 5 )  | ( 0 ) | ( 0 ) |
|                                  | inflammation:respiratory epithelium        |                         | 0       | 0      | 0     | 0     | 0      | 1      | 0     | 0     | 0      | 2      | 0     | 0     | 4      | 9      | 0     | 0     |
|                                  |  |                         | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 17 ) | ( 0 ) | ( 0 ) | ( 10 ) | ( 23 ) | ( 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. : 0437  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 2

|                      |   | Group Name              | Control |        |       |       | 10 ppm |        |       |       | 30 ppm |        |       |       | 90 ppm |        |       |       |
|----------------------|---|-------------------------|---------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|
|                      |   | No. of Animals on Study | 12      |        |       |       | 12     |        |       |       | 12     |        |       |       | 39     |        |       |       |
|                      |   | Grade                   | 1       | 2      | 3     | 4     | 1      | 2      | 3     | 4     | 1      | 2      | 3     | 4     | 1      | 2      | 3     | 4     |
| Organ                | Findings  |                         | (%)     | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   |
| {Respiratory system} |   |                         |         |        |       |       |        |        |       |       |        |        |       |       |        |        |       |       |
| nasal cavit          |   |                         | <12>    |        |       |       | <12>   |        |       |       | <12>   |        |       |       | <39>   |        |       |       |
|                      | respiratory metaplasia:olfactory epithelium     |                         | 0       | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 1      | 0      | 0     | 0     | 1      | 5      | 0     | 0     |
|                      |   |                         | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 8 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 3 )  | ( 13 ) | ( 0 ) | ( 0 ) |
|                      | respiratory metaplasia:gland                    |                         | 0       | 5      | 0     | 0     | 1      | 2      | 0     | 0     | 0      | 5      | 0     | 0     | 1      | 12     | 1     | 0     |
|                      |   |                         | ( 0 )   | ( 42 ) | ( 0 ) | ( 0 ) | ( 8 )  | ( 17 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 42 ) | ( 0 ) | ( 0 ) | ( 3 )  | ( 31 ) | ( 3 ) | ( 0 ) |
|                      | squamous cell metaplasia:respiratory epithelium |                         | 0       | 0      | 0     | 0     | 0      | 1      | 0     | 0     | 1      | 4      | 0     | 0 *   | 3      | 29     | 0     | 0 **  |
|                      |   |                         | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 8 )  | ( 0 ) | ( 0 ) | ( 8 )  | ( 33 ) | ( 0 ) | ( 0 ) | ( 8 )  | ( 74 ) | ( 0 ) | ( 0 ) |
|                      | squamous cell metaplasia:olfactory epithelium   |                         | 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 ) | ( 10 ) | ( 0 )  | ( 0 ) | ( 0 ) |
|                      | hyperplasia:submucosal gland                    |                         | 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 )  | ( 8 )  | ( 0 ) | ( 0 ) |
|                      | atrophy:olfactory epithelium                    |                         | 0       | 0      | 0     | 0     | 0      | 1      | 0     | 0     | 5      | 2      | 0     | 0 **  | 9      | 10     | 0     | 0 **  |
|                      |   |                         | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 8 )  | ( 0 ) | ( 0 ) | ( 42 ) | ( 17 ) | ( 0 ) | ( 0 ) | ( 23 ) | ( 26 ) | ( 0 ) | ( 0 ) |
| lung                 |   |                         | <12>    |        |       |       | <12>   |        |       |       | <12>   |        |       |       | <39>   |        |       |       |
|                      | congestion                                      |                         | 0       | 1      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 1      | 0     | 0     |
|                      |   |                         | ( 0 )   | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 3 )  | ( 0 ) | ( 0 ) |
|                      | hemorrhage                                      |                         | 0       | 0      | 0     | 0     | 0      | 1      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0     | 0     |
|                      |   |                         | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 8 )  | ( 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. : 0437  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 3

|                        |                                       | Group Name              | Control |       |       |       | 10 ppm |       |       |       | 30 ppm |       |       |       | 90 ppm |        |       |       |
|------------------------|---------------------------------------|-------------------------|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|--------|-------|-------|
|                        |                                       | No. of Animals on Study | 12      |       |       |       | 12     |       |       |       | 12     |       |       |       | 39     |        |       |       |
| Organ                  | Findings                              | Grade                   | 1       | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2      | 3     | 4     |
|                        |                                       |                         | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   |
| {Respiratory system}   |                                       |                         |         |       |       |       |        |       |       |       |        |       |       |       |        |        |       |       |
| lung                   |                                       |                         | <12>    |       |       |       | <12>   |       |       |       | <12>   |       |       |       | <39>   |        |       |       |
|                        | inflammatory infiltration             |                         | 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 ) |
|                        | bronchiolar-alveolar cell hyperplasia |                         | 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 )  | ( 8 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 3 )  | ( 0 ) | ( 0 ) |
|                        | inflammation:foreign body             |                         | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 7      | 0     | 0     |
|                        |                                       |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 3 )  | ( 18 ) | ( 0 ) | ( 0 ) |
| {Hematopoietic system} |                                       |                         |         |       |       |       |        |       |       |       |        |       |       |       |        |        |       |       |
| bone marrow            |                                       |                         | <12>    |       |       |       | <12>   |       |       |       | <12>   |       |       |       | <39>   |        |       |       |
|                        | granulation                           |                         | 0       | 0     | 0     | 0     | 0      | 1     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0      | 0     | 0     |
|                        |                                       |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 8 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                        | increased hematopoiesis               |                         | 3       | 0     | 0     | 0     | 2      | 0     | 0     | 0     | 3      | 0     | 0     | 0     | 9      | 0      | 0     | 0     |
|                        |                                       |                         | ( 25 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 17 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 25 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 23 ) | ( 0 )  | ( 0 ) | ( 0 ) |
|                        | decreased hematopoiesis               |                         | 0       | 1     | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 1      | 0     | 0     |
|                        |                                       |                         | ( 0 )   | ( 8 ) | ( 0 ) | ( 0 ) | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 3 )  | ( 0 ) | ( 0 ) |
| lymph node             |                                       |                         | <12>    |       |       |       | <12>   |       |       |       | <12>   |       |       |       | <39>   |        |       |       |
|                        | lymphadenitis                         |                         | 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 ) |

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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 4

|                        |  | Group Name              | Control |        |       |       | 10 ppm |        |       |       | 30 ppm |        |       |       | 90 ppm |        |       |       |
|------------------------|--|-------------------------|---------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|
|                        |  | No. of Animals on Study | 12      |        |       |       | 12     |        |       |       | 12     |        |       |       | 39     |        |       |       |
| Organ                  | Findings                               | Grade                   | 1       | 2      | 3     | 4     | 1      | 2      | 3     | 4     | 1      | 2      | 3     | 4     | 1      | 2      | 3     | 4     |
|                        |  |                         | (%)     | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   |
| {Hematopoietic system} |  |                         |         |        |       |       |        |        |       |       |        |        |       |       |        |        |       |       |
| spleen                 |  |                         | <12>    |        |       |       | <12>   |        |       |       | <12>   |        |       |       | <39>   |        |       |       |
|                        | deposit of hemosiderin                 |                         | 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 )  | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                        | increased extramedullary hematopoiesis |                         | 0       | 2      | 0     | 0     | 0      | 1      | 0     | 0     | 0      | 1      | 0     | 0     | 0      | 2      | 0     | 0     |
|                        |  |                         | ( 0 )   | ( 17 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 5 )  | ( 0 ) | ( 0 ) |
| {Circulatory system}   |  |                         |         |        |       |       |        |        |       |       |        |        |       |       |        |        |       |       |
| heart                  |  |                         | <12>    |        |       |       | <12>   |        |       |       | <12>   |        |       |       | <39>   |        |       |       |
|                        | thrombus                               |                         | 0       | 1      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 2     | 0     |
|                        |  |                         | ( 0 )   | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 5 ) | ( 0 ) |
|                        | necrosis:focal                         |                         | 0       | 1      | 0     | 0     | 0      | 0      | 0     | 0     | 1      | 0      | 0     | 0     | 1      | 1      | 0     | 0     |
|                        |  |                         | ( 0 )   | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 8 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 3 )  | ( 3 )  | ( 0 ) | ( 0 ) |
|                        | mineralization                         |                         | 0       | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 2      | 0      | 0     | 0     | 0      | 0      | 0     | 0     |
|                        |  |                         | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 17 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                        | inflammatory cell nest                 |                         | 0       | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 1      | 0      | 0     | 0     | 0      | 0      | 0     | 0     |
|                        |  |                         | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 8 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                        | myocardial fibrosis                    |                         | 3       | 9      | 0     | 0     | 5      | 5      | 0     | 0     | 5      | 6      | 0     | 0     | 19     | 15     | 0     | 0     |
|                        |  |                         | ( 25 )  | ( 75 ) | ( 0 ) | ( 0 ) | ( 42 ) | ( 42 ) | ( 0 ) | ( 0 ) | ( 42 ) | ( 50 ) | ( 0 ) | ( 0 ) | ( 49 ) | ( 38 ) | ( 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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 5

| Organ                | Findings                  | Group Name              | Control |       |       |       | 10 ppm |       |       |       | 30 ppm |       |       |       | 90 ppm |       |       |       |
|----------------------|---------------------------|-------------------------|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
|                      |                           | No. of Animals on Study | 12      |       |       |       | 12     |       |       |       | 12     |       |       |       | 39     |       |       |       |
|                      |                           | Grade                   | 1       | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     |
|                      |                           |                         | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   |
| {Circulatory system} |                           |                         |         |       |       |       |        |       |       |       |        |       |       |       |        |       |       |       |
| heart                |                           |                         | <12>    |       |       |       | <12>   |       |       |       | <12>   |       |       |       | <39>   |       |       |       |
|                      | subendocardial fibrosis   |                         | 0       | 0     | 0     | 0     | 0      | 1     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     |
|                      |                           |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 8 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
| {Digestive system}   |                           |                         |         |       |       |       |        |       |       |       |        |       |       |       |        |       |       |       |
| oral cavity          |                           |                         | <12>    |       |       |       | <12>   |       |       |       | <12>   |       |       |       | <39>   |       |       |       |
|                      | squamous cell hyperplasia |                         | 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 ) |
| tooth                |                           |                         | <12>    |       |       |       | <12>   |       |       |       | <12>   |       |       |       | <39>   |       |       |       |
|                      | inflammation              |                         | 0       | 1     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 2     | 0     | 0     |
|                      |                           |                         | ( 0 )   | ( 8 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 3 ) | ( 5 )  | ( 0 ) | ( 0 ) |       |
| tongue               |                           |                         | <12>    |       |       |       | <12>   |       |       |       | <12>   |       |       |       | <39>   |       |       |       |
|                      | inflammatory infiltration |                         | 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 ) | ( 3 ) | ( 0 ) | ( 0 )  | ( 0 ) |       |       |
| stomach              |                           |                         | <12>    |       |       |       | <12>   |       |       |       | <12>   |       |       |       | <39>   |       |       |       |
|                      | mineralization            |                         | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 1     | 0     | 0     | 0      | 0     | 0     | 0     |
|                      |                           |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 8 )  | ( 8 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                      | epidermal 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 ) | ( 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 ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square



STUDY NO. : 0437  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
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 |       |      |      | Control |       |      |      | 10 ppm |       |      |      | 30 ppm |      |      |      | 90 ppm |      |      |      |
|--------------------|---------------------------|---------------------------------------|-------|------|------|---------|-------|------|------|--------|-------|------|------|--------|------|------|------|--------|------|------|------|
|                    |                           | Grade                                 |       |      |      | 12      |       |      |      | 12     |       |      |      | 12     |      |      |      | 39     |      |      |      |
|                    |                           | 1                                     | 2     | 3    | 4    | 1       | 2     | 3    | 4    | 1      | 2     | 3    | 4    | 1      | 2    | 3    | 4    | 1      | 2    | 3    | 4    |
|                    |                           | (%)                                   | (%)   | (%)  | (%)  | (%)     | (%)   | (%)  | (%)  | (%)    | (%)   | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  |
| {Digestive system} |                           |                                       |       |      |      |         |       |      |      |        |       |      |      |        |      |      |      |        |      |      |      |
| stomach            |                           | <12>                                  |       |      |      | <12>    |       |      |      | <12>   |       |      |      | <39>   |      |      |      |        |      |      |      |
|                    | atrophy:glandular mucosa  | 1                                     | 0     | 0    | 0    | 0       | 0     | 0    | 0    | 0      | 0     | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0    | 0    | 0    |
|                    |                           | ( 8)                                  | ( 0)  | ( 0) | ( 0) | ( 0)    | ( 0)  | ( 0) | ( 0) | ( 0)   | ( 0)  | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) |
|                    | erosion:forestomach       | 2                                     | 0     | 0    | 0    | 0       | 0     | 0    | 0    | 1      | 1     | 0    | 0    | 4      | 0    | 0    | 0    | 4      | 0    | 0    | 0    |
|                    |                           | ( 17)                                 | ( 0)  | ( 0) | ( 0) | ( 0)    | ( 0)  | ( 0) | ( 0) | ( 8)   | ( 8)  | ( 0) | ( 0) | ( 10)  | ( 0) | ( 0) | ( 0) | ( 10)  | ( 0) | ( 0) | ( 0) |
|                    | ulcer:forestomach         | 0                                     | 2     | 0    | 0    | 1       | 3     | 0    | 0    | 0      | 0     | 0    | 0    | 1      | 0    | 0    | 0    | 1      | 0    | 0    | 0 *  |
|                    |                           | ( 0)                                  | ( 17) | ( 0) | ( 0) | ( 8)    | ( 25) | ( 0) | ( 0) | ( 0)   | ( 0)  | ( 0) | ( 0) | ( 3)   | ( 0) | ( 0) | ( 0) | ( 3)   | ( 0) | ( 0) | ( 0) |
|                    | hyperplasia:forestomach   | 0                                     | 4     | 0    | 0    | 1       | 3     | 0    | 0    | 1      | 2     | 0    | 0    | 3      | 0    | 0    | 0    | 3      | 0    | 0    | 0 ** |
|                    |                           | ( 0)                                  | ( 33) | ( 0) | ( 0) | ( 8)    | ( 25) | ( 0) | ( 0) | ( 8)   | ( 17) | ( 0) | ( 0) | ( 8)   | ( 0) | ( 0) | ( 0) | ( 8)   | ( 0) | ( 0) | ( 0) |
|                    | erosion:glandular stomach | 2                                     | 1     | 0    | 0    | 1       | 0     | 0    | 0    | 2      | 0     | 0    | 0    | 5      | 1    | 0    | 0    | 5      | 1    | 0    | 0    |
|                    |                           | ( 17)                                 | ( 8)  | ( 0) | ( 0) | ( 8)    | ( 0)  | ( 0) | ( 0) | ( 17)  | ( 0)  | ( 0) | ( 0) | ( 13)  | ( 3) | ( 0) | ( 0) | ( 13)  | ( 3) | ( 0) | ( 0) |
|                    | ulcer:glandular stomach   | 0                                     | 0     | 0    | 0    | 1       | 0     | 0    | 0    | 0      | 0     | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0    | 0    | 0    |
|                    |                           | ( 0)                                  | ( 0)  | ( 0) | ( 0) | ( 8)    | ( 0)  | ( 0) | ( 0) | ( 0)   | ( 0)  | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) |
| liver              |                           | <12>                                  |       |      |      | <12>    |       |      |      | <12>   |       |      |      | <39>   |      |      |      |        |      |      |      |
|                    | herniation                | 0                                     | 0     | 0    | 0    | 0       | 0     | 0    | 0    | 0      | 0     | 0    | 0    | 7      | 0    | 0    | 0    | 7      | 0    | 0    | 0    |
|                    |                           | ( 0)                                  | ( 0)  | ( 0) | ( 0) | ( 0)    | ( 0)  | ( 0) | ( 0) | ( 0)   | ( 0)  | ( 0) | ( 0) | ( 18)  | ( 0) | ( 0) | ( 0) | ( 18)  | ( 0) | ( 0) | ( 0) |
|                    | hemorrhage                | 0                                     | 1     | 0    | 0    | 0       | 0     | 0    | 0    | 0      | 0     | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0    | 0    | 0    |
|                    |                           | ( 0)                                  | ( 8)  | ( 0) | ( 0) | ( 0)    | ( 0)  | ( 0) | ( 0) | ( 0)   | ( 0)  | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) |

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

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 7

| Organ                 | Findings             | Group Name              | Control |       |       |       | 10 ppm |       |       |        | 30 ppm |       |       |        | 90 ppm |       |       |       |
|-----------------------|----------------------|-------------------------|---------|-------|-------|-------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|-------|
|                       |                      | No. of Animals on Study | 12      |       |       |       | 12     |       |       |        | 12     |       |       |        | 39     |       |       |       |
|                       |                      | Grade                   | 1       | 2     | 3     | 4     | 1      | 2     | 3     | 4      | 1      | 2     | 3     | 4      | 1      | 2     | 3     | 4     |
|                       |                      |                         | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)   |
| {Digestive system}    |                      |                         |         |       |       |       |        |       |       |        |        |       |       |        |        |       |       |       |
| liver                 |                      |                         | <12>    |       |       |       | <12>   |       |       |        | <12>   |       |       |        | <39>   |       |       |       |
|                       | necrosis:central     |                         | 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 )  | ( 5 ) | ( 0 ) | ( 0 ) |
|                       | necrosis:focal       |                         | 0       | 0     | 0     | 0     | 0      | 1     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 0     |
|                       |                      |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 8 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                       | fatty change         |                         | 0       | 1     | 0     | 0     | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 0     |
|                       |                      |                         | ( 0 )   | ( 8 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                       | fatty change:central |                         | 0       | 0     | 1     | 0     | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 0     |
|                       |                      | ( 0 )                   | ( 0 )   | ( 8 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |       |
| granulation           |                      | 0                       | 0       | 0     | 0     | 1     | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0     | 0     |       |
|                       |                      | ( 0 )                   | ( 0 )   | ( 0 ) | ( 0 ) | ( 8 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |       |
| spongiosis hepatis    |                      | 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 ) |       |
| bile duct hyperplasia |                      | 0                       | 10      | 0     | 0     | 1     | 9      | 1     | 0     | 4      | 7      | 0     | 0     | 5      | 32     | 0     | 0     |       |
|                       |                      | ( 0 )                   | ( 83 )  | ( 0 ) | ( 0 ) | ( 8 ) | ( 75 ) | ( 8 ) | ( 0 ) | ( 33 ) | ( 58 ) | ( 0 ) | ( 0 ) | ( 13 ) | ( 82 ) | ( 0 ) | ( 0 ) |       |
| biliary 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 ) |       |

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

PAGE : 8

|                    |                        | Group Name              | Control |       |       |       | 10 ppm |        |       |       | 30 ppm |        |       |       | 90 ppm |       |       |       |       |
|--------------------|------------------------|-------------------------|---------|-------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|--------|-------|-------|-------|-------|
|                    |                        | No. of Animals on Study | 12      |       |       |       | 12     |        |       |       | 12     |        |       |       | 39     |       |       |       |       |
| Organ              | Findings               | Grade                   | 1       | 2     | 3     | 4     | 1      | 2      | 3     | 4     | 1      | 2      | 3     | 4     | 1      | 2     | 3     | 4     |       |
|                    |                        |                         | (%)     | (%)   | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   |       |
| {Digestive system} |                        |                         |         |       |       |       |        |        |       |       |        |        |       |       |        |       |       |       |       |
| pancreas           |                        |                         | <12>    |       |       |       | <12>   |        |       |       | <12>   |        |       |       | <39>   |       |       |       |       |
|                    | atrophy                |                         | 1       | 0     | 1     | 0     | 2      | 0      | 1     | 0     | 0      | 2      | 0     | 0     | 0      | 1     | 0     | 0     |       |
|                    |                        |                         | ( 8 )   | ( 0 ) | ( 8 ) | ( 0 ) | ( 17 ) | ( 0 )  | ( 8 ) | ( 0 ) | ( 0 )  | ( 17 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 3 ) | ( 0 ) | ( 0 ) |
|                    | islet cell hyperplasia |                         | 0       | 0     | 0     | 0     | 0      | 2      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0     | 0     | 0     | 0     |
|                    |                        |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 17 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) |
| {Urinary system}   |                        |                         |         |       |       |       |        |        |       |       |        |        |       |       |        |       |       |       |       |
| kidney             |                        |                         | <12>    |       |       |       | <12>   |        |       |       | <12>   |        |       |       | <39>   |       |       |       |       |
|                    | necrosis:focal         |                         | 0       | 0     | 0     | 0     | 0      | 1      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0     | 0     | 0     | 0     |
|                    |                        |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) |
|                    | deposit of hemosiderin |                         | 0       | 0     | 0     | 0     | 0      | 1      | 0     | 0     | 1      | 0      | 0     | 0     | 0      | 1     | 0     | 0     | 0     |
|                    |                        |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 8 )  | ( 0 ) | ( 0 ) | ( 8 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 3 ) | ( 0 ) | ( 0 ) |
|                    | inflammatory cell nest |                         | 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 )  | ( 3 ) | ( 0 ) | ( 0 ) |       |
|                    | mineralization:central |                         | 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 ) |       |
|                    | chronic nephropathy    |                         | 8       | 1     | 0     | 0     | 7      | 1      | 0     | 0     | 1      | 3      | 0     | 0 *   | 11     | 0     | 0     | 0 **  |       |
|                    |                        |                         | ( 67 )  | ( 8 ) | ( 0 ) | ( 0 ) | ( 58 ) | ( 8 )  | ( 0 ) | ( 0 ) | ( 8 )  | ( 25 ) | ( 0 ) | ( 0 ) | ( 28 ) | ( 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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 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 9

|                    |  | Group Name              | Control |       |       |       | 10 ppm |       |       |       | 30 ppm |       |       |       | 90 ppm |       |       |       |
|--------------------|--|-------------------------|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
|                    |  | No. of Animals on Study | 12      |       |       |       | 12     |       |       |       | 12     |       |       |       | 39     |       |       |       |
|                    |  | Grade                   | 1       | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     |
| Organ              | Findings                                   |                         | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   |
| {Urinary system}   |  |                         |         |       |       |       |        |       |       |       |        |       |       |       |        |       |       |       |
| kidney             |  |                         | <12>    |       |       |       | <12>   |       |       |       | <12>   |       |       |       | <39>   |       |       |       |
|                    | hydronephrosis                             |                         | 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 )  | ( 8 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                    | mineralization:cortico-medullary junction  |                         | 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 ) |
|                    | mineralization:papilla                     |                         | 1       | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 3      | 2     | 0     | 0     |
|                    |  |                         | ( 8 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 8 )  | ( 5 ) | ( 0 ) | ( 0 ) |
|                    | mineralization:pelvis                      |                         | 2       | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     |
|                    |  |                         | ( 17 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                    | mineralization:cortex                      |                         | 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 )  | ( 8 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
| urin bladd         |  |                         | <12>    |       |       |       | <12>   |       |       |       | <12>   |       |       |       | <39>   |       |       |       |
|                    | hemorrhage                                 |                         | 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 ) |
|                    | simple hyperplasia:transitional epithelium |                         | 1       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 1     | 0     | 0     | 0      | 0     | 0     | 0     |
|                    |  |                         | ( 8 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 8 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
| {Endocrine system} |  |                         |         |       |       |       |        |       |       |       |        |       |       |       |        |       |       |       |
| pituitary          |  |                         | <12>    |       |       |       | <12>   |       |       |       | <12>   |       |       |       | <39>   |       |       |       |
|                    | cyst                                       |                         | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 1     | 0     | 0     | 0      | 2     | 0     | 0     |
|                    |  |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 8 )  | ( 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. : 0437  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 10

|                       |                           | Group Name              | Control |        |        |       | 10 ppm |        |        |       | 30 ppm |        |        |       | 90 ppm |        |        |       |
|-----------------------|---------------------------|-------------------------|---------|--------|--------|-------|--------|--------|--------|-------|--------|--------|--------|-------|--------|--------|--------|-------|
|                       |                           | No. of Animals on Study | 12      |        |        |       | 12     |        |        |       | 12     |        |        |       | 39     |        |        |       |
| Organ                 | Findings                  | Grade                   | 1       | 2      | 3      | 4     | 1      | 2      | 3      | 4     | 1      | 2      | 3      | 4     | 1      | 2      | 3      | 4     |
|                       |                           |                         |         |        |        |       |        |        |        |       |        |        |        |       |        |        |        |       |
| {Endocrine system}    |                           |                         |         |        |        |       |        |        |        |       |        |        |        |       |        |        |        |       |
| pituitary             |                           |                         | <12>    |        |        |       | <12>   |        |        |       | <12>   |        |        |       | <39>   |        |        |       |
|                       | hyperplasia               |                         | 0       | 0      | 0      | 0     | 0      | 2      | 0      | 0     | 0      | 1      | 0      | 0     | 0      | 1      | 0      | 0     |
|                       |                           |                         | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 17 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 8 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 3 )  | ( 0 )  | ( 0 ) |
|                       | Rathke pouch              |                         | 1       | 0      | 0      | 0     | 0      | 0      | 0      | 0     | 0      | 0      | 0      | 0     | 0      | 3      | 0      | 0     |
|                       |                           |                         | ( 8 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 8 )  | ( 0 )  | ( 0 ) |
| thyroid               |                           |                         | <12>    |        |        |       | <12>   |        |        |       | <12>   |        |        |       | <39>   |        |        |       |
|                       | C-cell hyperplasia        |                         | 1       | 0      | 0      | 0     | 3      | 1      | 0      | 0     | 0      | 1      | 0      | 0     | 0      | 2      | 0      | 0     |
|                       |                           |                         | ( 8 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 25 ) | ( 8 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 8 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 5 )  | ( 0 )  | ( 0 ) |
| parathyroid           |                           |                         | <12>    |        |        |       | <12>   |        |        |       | <12>   |        |        |       | <39>   |        |        |       |
|                       | hyperplasia               |                         | 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 ) |
| adrenal               |                           |                         | <12>    |        |        |       | <12>   |        |        |       | <12>   |        |        |       | <39>   |        |        |       |
|                       | hyperplasia:medulla       |                         | 0       | 0      | 0      | 0     | 0      | 2      | 0      | 0     | 0      | 0      | 0      | 0     | 0      | 0      | 0      | 0     |
|                       |                           |                         | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 17 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) |
|                       | focal fatty change:cortex |                         | 0       | 0      | 0      | 0     | 0      | 1      | 0      | 0     | 1      | 0      | 0      | 0     | 3      | 1      | 0      | 0     |
|                       |                           |                         | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 8 )  | ( 0 )  | ( 0 ) | ( 8 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 8 )  | ( 3 )  | ( 0 )  | ( 0 ) |
| {Reproductive system} |                           |                         |         |        |        |       |        |        |        |       |        |        |        |       |        |        |        |       |
| testis                |                           |                         | <12>    |        |        |       | <12>   |        |        |       | <12>   |        |        |       | <39>   |        |        |       |
|                       | atrophy                   |                         | 0       | 2      | 8      | 0     | 0      | 1      | 9      | 0     | 2      | 2      | 5      | 0     | 10     | 6      | 13     | 0     |
|                       |                           |                         | ( 0 )   | ( 17 ) | ( 67 ) | ( 0 ) | ( 0 )  | ( 8 )  | ( 75 ) | ( 0 ) | ( 17 ) | ( 17 ) | ( 42 ) | ( 0 ) | ( 26 ) | ( 15 ) | ( 33 ) | ( 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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 11

| Organ                         | Findings         | Group Name              | Control |      |       |       | 10 ppm |      |      |       | 30 ppm |       |      |       | 90 ppm |      |      |     |
|-------------------------------|------------------|-------------------------|---------|------|-------|-------|--------|------|------|-------|--------|-------|------|-------|--------|------|------|-----|
|                               |                  | No. of Animals on Study | 12      |      |       |       | 12     |      |      |       | 12     |       |      |       | 39     |      |      |     |
|                               |                  | Grade                   | 1       | 2    | 3     | 4     | 1      | 2    | 3    | 4     | 1      | 2     | 3    | 4     | 1      | 2    | 3    | 4   |
|                               |                  |                         | (%)     | (%)  | (%)   | (%)   | (%)    | (%)  | (%)  | (%)   | (%)    | (%)   | (%)  | (%)   | (%)    | (%)  | (%)  | (%) |
| {Reproductive system}         |                  |                         |         |      |       |       |        |      |      |       |        |       |      |       |        |      |      |     |
| testis                        | mineralization   |                         | <12>    |      |       |       | <12>   |      |      |       | <12>   |       |      |       | <39>   |      |      |     |
|                               |                  | 2                       | 0       | 0    | 0     | 2     | 0      | 0    | 0    | 0     | 0      | 0     | 0    | 7     | 0      | 0    | 0    |     |
|                               |                  | ( 17)                   | ( 0)    | ( 0) | ( 0)  | ( 17) | ( 0)   | ( 0) | ( 0) | ( 0)  | ( 0)   | ( 0)  | ( 0) | ( 18) | ( 0)   | ( 0) | ( 0) |     |
| interstitial cell hyperplasia |                  | 0                       | 0       | 0    | 0     | 3     | 0      | 0    | 0    | 3     | 0      | 0     | 0    | 10    | 0      | 0    | 0    |     |
|                               | ( 0)             | ( 0)                    | ( 0)    | ( 0) | ( 25) | ( 0)  | ( 0)   | ( 0) | ( 0) | ( 25) | ( 0)   | ( 0)  | ( 0) | ( 26) | ( 0)   | ( 0) | ( 0) |     |
|                               | prostate         | inflammation            |         | <12> |       |       |        | <12> |      |       |        | <12>  |      |       |        | <39> |      |     |
| 0                             |                  |                         | 1       | 1    | 0     | 1     | 2      | 0    | 0    | 1     | 2      | 2     | 0    | 3     | 1      | 0    | 0    |     |
| ( 0)                          |                  |                         | ( 8)    | ( 8) | ( 0)  | ( 8)  | ( 17)  | ( 0) | ( 0) | ( 8)  | ( 17)  | ( 17) | ( 0) | ( 8)  | ( 3)   | ( 0) | ( 0) |     |
| hyperplasia                   |                  | 1                       | 0       | 0    | 0     | 1     | 0      | 0    | 0    | 0     | 0      | 0     | 0    | 0     | 0      | 0    | 0    |     |
|                               | ( 8)             | ( 0)                    | ( 0)    | ( 0) | ( 8)  | ( 0)  | ( 0)   | ( 0) | ( 0) | ( 0)  | ( 0)   | ( 0)  | ( 0) | ( 0)  | ( 0)   | ( 0) | ( 0) |     |
|                               | {Nervous system} |                         |         |      |       |       |        |      |      |       |        |       |      |       |        |      |      |     |
| brain                         | hemorrhage       |                         | <12>    |      |       |       | <12>   |      |      |       | <12>   |       |      |       | <39>   |      |      |     |
|                               |                  | 1                       | 0       | 0    | 0     | 0     | 0      | 0    | 0    | 1     | 0      | 0     | 0    | 1     | 0      | 0    | 0    |     |
|                               |                  | ( 8)                    | ( 0)    | ( 0) | ( 0)  | ( 0)  | ( 0)   | ( 0) | ( 0) | ( 8)  | ( 0)   | ( 0)  | ( 0) | ( 3)  | ( 0)   | ( 0) | ( 0) |     |
| vacuolic change               |                  | 1                       | 0       | 0    | 0     | 0     | 0      | 0    | 0    | 0     | 0      | 0     | 0    | 0     | 0      | 0    | 0    |     |
|                               | ( 8)             | ( 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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 12

|                                  |                               | Group Name              | Control |       |       |       | 10 ppm |       |       |       | 30 ppm |       |       |       | 90 ppm |       |       |       |
|----------------------------------|-------------------------------|-------------------------|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
|                                  |                               | No. of Animals on Study | 12      |       |       |       | 12     |       |       |       | 12     |       |       |       | 39     |       |       |       |
| Organ                            | Findings                      | Grade                   | 1       | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     |
|                                  |                               |                         | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   |
| {Nervous system}                 |                               |                         |         |       |       |       |        |       |       |       |        |       |       |       |        |       |       |       |
| brain                            |                               |                         | <12>    |       |       |       | <12>   |       |       |       | <12>   |       |       |       | <39>   |       |       |       |
|                                  | mineralization                |                         | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 0     | 0     | 0     |
|                                  |                               |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                                  | gliosis                       |                         | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 0     | 0     | 0     |
|                                  |                               |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                                  | dilatation:cerebral ventricle |                         | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 1     | 0     | 0     |
|                                  |                               |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 3 ) | ( 0 ) | ( 0 ) |
| spinal cord                      |                               |                         | <12>    |       |       |       | <12>   |       |       |       | <12>   |       |       |       | <39>   |       |       |       |
|                                  | hemorrhage                    |                         | 0       | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 0     | 0     | 0     |
|                                  |                               |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 3 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                                  | gliosis                       |                         | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 0     | 0     | 0     |
|                                  |                               |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
| {Special sense organs/appendage} |                               |                         |         |       |       |       |        |       |       |       |        |       |       |       |        |       |       |       |
| eye                              |                               |                         | <12>    |       |       |       | <12>   |       |       |       | <12>   |       |       |       | <39>   |       |       |       |
|                                  | hemorrhage                    |                         | 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 )  | ( 8 ) | ( 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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 13

|                                  |                           | Group Name              | Control |       |       |       | 10 ppm |       |       |       | 30 ppm |       |       |       | 90 ppm |        |       |       |       |
|----------------------------------|---------------------------|-------------------------|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|--------|-------|-------|-------|
|                                  |                           | No. of Animals on Study | 12      |       |       |       | 12     |       |       |       | 12     |       |       |       | 39     |        |       |       |       |
| Organ                            | Findings                  | Grade                   | 1       | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2      | 3     | 4     |       |
|                                  |                           |                         | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   |       |
| {Special sense organs/appendage} |                           |                         |         |       |       |       |        |       |       |       |        |       |       |       |        |        |       |       |       |
| eye                              |                           |                         | <12>    |       |       |       | <12>   |       |       |       | <12>   |       |       |       | <39>   |        |       |       |       |
|                                  | cataract                  |                         | 0       | 0     | 0     | 0     | 1      | 1     | 0     | 0     | 0      | 1     | 0     | 0     | 0      | 2      | 0     | 0     |       |
|                                  |                           |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 8 )  | ( 8 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 8 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 5 ) | ( 0 ) | ( 0 ) |
|                                  | retinal atrophy           |                         | 4       | 0     | 0     | 0     | 4      | 0     | 1     | 0     | 6      | 0     | 1     | 0     | 9      | 0      | 2     | 0     |       |
|                                  |                           |                         | ( 33 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 33 ) | ( 0 ) | ( 8 ) | ( 0 ) | ( 50 ) | ( 0 ) | ( 8 ) | ( 0 ) | ( 23 ) | ( 0 )  | ( 5 ) | ( 0 ) |       |
|                                  | keratitis                 |                         | 1       | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 9      | 13     | 2     | 0 *   |       |
|                                  |                           |                         | ( 8 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 23 ) | ( 33 ) | ( 5 ) | ( 0 ) |       |
| Harder gl                        |                           |                         | <12>    |       |       |       | <12>   |       |       |       | <12>   |       |       |       | <39>   |        |       |       |       |
|                                  | degeneration              |                         | 0       | 0     | 0     | 0     | 0      | 1     | 0     | 0     | 0      | 1     | 0     | 0     | 0      | 0      | 0     | 0     |       |
|                                  |                           |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 8 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 8 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |       |
|                                  | inflammatory infiltration |                         | 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 ) |       |
|                                  | lymphocytic infiltration  |                         | 0       | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 0      | 0     | 0     |       |
|                                  |                           |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |       |
| {Musculoskeletal system}         |                           |                         |         |       |       |       |        |       |       |       |        |       |       |       |        |        |       |       |       |
| muscle                           |                           |                         | <12>    |       |       |       | <12>   |       |       |       | <12>   |       |       |       | <39>   |        |       |       |       |
|                                  | mineralization            |                         | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 0      | 0     | 0     |       |
|                                  |                           | ( 0 )                   | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 8 ) | ( 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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 14

| Organ_____      | Findings_____ | Group Name              | Control |       |       |       | 10 ppm |       |       |       | 30 ppm |       |       |       | 90 ppm |       |       |       |
|-----------------|---------------|-------------------------|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
|                 |               | No. of Animals on Study | 12      |       |       |       | 12     |       |       |       | 12     |       |       |       | 39     |       |       |       |
|                 |               | Grade                   | 1       | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     |
|                 |               |                         | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   |
| <hr/>           |               |                         |         |       |       |       |        |       |       |       |        |       |       |       |        |       |       |       |
| {Body cavities} |               |                         |         |       |       |       |        |       |       |       |        |       |       |       |        |       |       |       |
| peritoneum      | inflammation  |                         | <12>    |       |       |       | <12>   |       |       |       | <12>   |       |       |       | <39>   |       |       |       |
|                 |               |                         | 0       | 1     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     |
|                 |               |                         | ( 0 )   | ( 8 ) | ( 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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

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

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|                                  |  | Group Name              | Control |        |       |       | 10 ppm |        |       |       | 30 ppm |        |       |       | 90 ppm |        |       |       |
|----------------------------------|--|-------------------------|---------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|
|                                  |  | No. of Animals on Study | 38      |        |       |       | 38     |        |       |       | 38     |        |       |       | 11     |        |       |       |
| Organ                            | Findings                                 | Grade                   | 1       | 2      | 3     | 4     | 1      | 2      | 3     | 4     | 1      | 2      | 3     | 4     | 1      | 2      | 3     | 4     |
|                                  |  |                         | (%)     | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   |
| {Integumentary system/appandage} |  |                         |         |        |       |       |        |        |       |       |        |        |       |       |        |        |       |       |
| skin/app                         |  |                         | <38>    |        |       |       | <38>   |        |       |       | <38>   |        |       |       | <11>   |        |       |       |
|                                  | mineralization                           |                         | 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 ) |
|                                  | scab                                     |                         | 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 ) |
|                                  | epidermal cyst                           |                         | 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 ) |
| subcutis                         |  |                         | <38>    |        |       |       | <38>   |        |       |       | <38>   |        |       |       | <11>   |        |       |       |
|                                  | abscess                                  |                         | 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 ) |
| {Respiratory system}             |  |                         |         |        |       |       |        |        |       |       |        |        |       |       |        |        |       |       |
| nasal cavit                      |  |                         | <38>    |        |       |       | <38>   |        |       |       | <38>   |        |       |       | <11>   |        |       |       |
|                                  | squamous cell hyperplasia with atypia    |                         | 0       | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 1      | 7      | 1     | 0 **  |
|                                  |  |                         | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 9 )  | ( 64 ) | ( 9 ) | ( 0 ) |
|                                  | eosinophilic change:olfactory epithelium |                         | 15      | 20     | 1     | 0     | 16     | 18     | 1     | 0     | 11     | 21     | 1     | 0     | 6      | 2      | 0     | 0     |
|                                  |  |                         | ( 39 )  | ( 53 ) | ( 3 ) | ( 0 ) | ( 42 ) | ( 47 ) | ( 3 ) | ( 0 ) | ( 29 ) | ( 55 ) | ( 3 ) | ( 0 ) | ( 55 ) | ( 18 ) | ( 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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

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

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| Organ | Findings | Group Name              | Control |     |     |     | 10 ppm |     |     |     | 30 ppm |     |     |     | 90 ppm |     |     |     |
|-------|----------|-------------------------|---------|-----|-----|-----|--------|-----|-----|-----|--------|-----|-----|-----|--------|-----|-----|-----|
|       |          | No. of Animals on Study | 38      |     |     |     | 38     |     |     |     | 38     |     |     |     | 11     |     |     |     |
|       |          | Grade                   | 1       | 2   | 3   | 4   | 1      | 2   | 3   | 4   | 1      | 2   | 3   | 4   | 1      | 2   | 3   | 4   |
|       |          |                         | (%)     | (%) | (%) | (%) | (%)    | (%) | (%) | (%) | (%)    | (%) | (%) | (%) | (%)    | (%) | (%) | (%) |

---

|                      |   |  |       |       |      |      |       |       |      |      |       |       |      |      |       |       |      |      |
|----------------------|---|--|-------|-------|------|------|-------|-------|------|------|-------|-------|------|------|-------|-------|------|------|
| {Respiratory system} |   |  |       |       |      |      |       |       |      |      |       |       |      |      |       |       |      |      |
| nasal cavit          |   |  | <38>  |       |      |      | <38>  |       |      |      | <38>  |       |      |      | <11>  |       |      |      |
|                      | eosinophilic change:respiratory epithelium      |  | 2     | 2     | 0    | 0    | 3     | 0     | 0    | 0    | 2     | 0     | 0    | 0    | 0     | 0     | 0    | 0    |
|                      |   |  | ( 5)  | ( 5)  | ( 0) | ( 0) | ( 8)  | ( 0)  | ( 0) | ( 0) | ( 5)  | ( 0)  | ( 0) | ( 0) | ( 0)  | ( 0)  | ( 0) | ( 0) |
|                      | inflammation:foreign body                       |  | 7     | 13    | 0    | 0    | 6     | 12    | 0    | 0    | 6     | 19    | 0    | 0    | 0     | 5     | 0    | 0    |
|                      |   |  | ( 18) | ( 34) | ( 0) | ( 0) | ( 16) | ( 32) | ( 0) | ( 0) | ( 16) | ( 50) | ( 0) | ( 0) | ( 0)  | ( 45) | ( 0) | ( 0) |
|                      | inflammation:respiratory epithelium             |  | 0     | 0     | 0    | 0    | 1     | 0     | 0    | 0    | 0     | 0     | 0    | 0    | 0     | 8     | 1    | 0 ** |
|                      |   |  | ( 0)  | ( 0)  | ( 0) | ( 0) | ( 3)  | ( 0)  | ( 0) | ( 0) | ( 0)  | ( 0)  | ( 0) | ( 0) | ( 0)  | ( 73) | ( 9) | ( 0) |
|                      | respiratory metaplasia:olfactory epithelium     |  | 3     | 0     | 0    | 0    | 0     | 1     | 0    | 0    | 3     | 1     | 0    | 0    | 1     | 1     | 0    | 0    |
|                      |   |  | ( 8)  | ( 0)  | ( 0) | ( 0) | ( 0)  | ( 3)  | ( 0) | ( 0) | ( 8)  | ( 3)  | ( 0) | ( 0) | ( 9)  | ( 9)  | ( 0) | ( 0) |
|                      | respiratory metaplasia:gland                    |  | 5     | 9     | 0    | 0    | 8     | 8     | 0    | 0    | 5     | 7     | 0    | 0    | 2     | 5     | 0    | 0    |
|                      |   |  | ( 13) | ( 24) | ( 0) | ( 0) | ( 21) | ( 21) | ( 0) | ( 0) | ( 13) | ( 18) | ( 0) | ( 0) | ( 18) | ( 45) | ( 0) | ( 0) |
|                      | squamous cell metaplasia:respiratory epithelium |  | 0     | 0     | 0    | 0    | 1     | 0     | 0    | 0    | 3     | 2     | 0    | 0    | 1     | 9     | 0    | 0 ** |
|                      |   |  | ( 0)  | ( 0)  | ( 0) | ( 0) | ( 3)  | ( 0)  | ( 0) | ( 0) | ( 8)  | ( 5)  | ( 0) | ( 0) | ( 9)  | ( 82) | ( 0) | ( 0) |
|                      | squamous cell metaplasia:olfactory epithelium   |  | 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) | ( 9)  | ( 0)  | ( 0) | ( 0) |
|                      | hyperplasia with atypia:respiratory epithelium  |  | 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) |

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

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

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|                        |                                       | Group Name              | Control |       |       |       | 10 ppm |       |       |       | 30 ppm |       |       |       | 90 ppm |        |       |       |
|------------------------|---------------------------------------|-------------------------|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|--------|-------|-------|
|                        |                                       | No. of Animals on Study | 38      |       |       |       | 38     |       |       |       | 38     |       |       |       | 11     |        |       |       |
| Organ                  | Findings                              | Grade                   | 1       | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2      | 3     | 4     |
|                        |                                       |                         |         |       |       |       |        |       |       |       |        |       |       |       |        |        |       |       |
| {Respiratory system}   |                                       |                         |         |       |       |       |        |       |       |       |        |       |       |       |        |        |       |       |
| nasal cavit            |                                       |                         | <38>    |       |       |       | <38>   |       |       |       | <38>   |       |       |       | <11>   |        |       |       |
|                        | hyperplasia:transitional epithelium   |                         | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 5      | 3     | 0     | 0 *   | 0      | 0      | 0     | 0     |
|                        |                                       |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 13 ) | ( 8 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                        |                                       |                         | <38>    |       |       |       | <38>   |       |       |       | <38>   |       |       |       | <11>   |        |       |       |
|                        | atrophy:olfactory epithelium          |                         | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 2      | 0     | 0     | 0     | 1      | 4      | 0     | 0 **  |
|                        |                                       |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 5 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 9 )  | ( 36 ) | ( 0 ) | ( 0 ) |
| lung                   |                                       |                         | <38>    |       |       |       | <38>   |       |       |       | <38>   |       |       |       | <11>   |        |       |       |
|                        | inflammatory infiltration             |                         | 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 ) |
|                        |                                       |                         | <38>    |       |       |       | <38>   |       |       |       | <38>   |       |       |       | <11>   |        |       |       |
|                        | accumulation of foamy cells           |                         | 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 ) |
|                        |                                       |                         | <38>    |       |       |       | <38>   |       |       |       | <38>   |       |       |       | <11>   |        |       |       |
|                        | bronchiolar-alveolar cell hyperplasia |                         | 0       | 3     | 0     | 0     | 0      | 1     | 0     | 0     | 0      | 1     | 0     | 0     | 0      | 0      | 0     | 0     |
|                        |                                       |                         | ( 0 )   | ( 8 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 3 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 3 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                        |                                       |                         | <38>    |       |       |       | <38>   |       |       |       | <38>   |       |       |       | <11>   |        |       |       |
|                        | inflammation:foreign body             |                         | 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 )  | ( 9 )  | ( 0 ) | ( 0 ) |
| {Hematopoietic system} |                                       |                         |         |       |       |       |        |       |       |       |        |       |       |       |        |        |       |       |
| bone marrow            |                                       |                         | <38>    |       |       |       | <38>   |       |       |       | <38>   |       |       |       | <11>   |        |       |       |
|                        | thrombus                              |                         | 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 ) |

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 < a > a : Number of animals examined at the site  
 b b : Number of animals with lesion  
 ( c ) c : b / a \* 100  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS (105W)

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|                        |  | Group Name              | Control   |            |           |           | 10 ppm    |           |           |           | 30 ppm    |           |           |           | 90 ppm     |           |           |              |           |
|------------------------|--|-------------------------|-----------|------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|------------|-----------|-----------|--------------|-----------|
|                        |  | No. of Animals on Study | 38        |            |           |           | 38        |           |           |           | 38        |           |           |           | 11         |           |           |              |           |
| Organ                  | Findings                               | Grade                   | 1         | 2          | 3         | 4         | 1         | 2         | 3         | 4         | 1         | 2         | 3         | 4         | 1          | 2         | 3         | 4            |           |
|                        |  |                         |           |            |           |           |           |           |           |           |           |           |           |           |            |           |           |              |           |
| {Hematopoietic system} |  |                         |           |            |           |           |           |           |           |           |           |           |           |           |            |           |           |              |           |
| bone marrow            |  |                         | <38>      |            |           |           | <38>      |           |           |           | <38>      |           |           |           | <11>       |           |           |              |           |
|                        | granulation                            |                         | 1<br>( 3) | 0<br>( 0)  | 0<br>( 0) | 0<br>( 0) | 3<br>( 8) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 3) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)  | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)    | 0<br>( 0) |
|                        | increased hematopoiesis                |                         | 1<br>( 3) | 0<br>( 0)  | 0<br>( 0) | 0<br>( 0) | 3<br>( 8) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 2<br>( 5) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 5<br>( 45) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) ** |           |
| spleen                 |  |                         | <38>      |            |           |           | <38>      |           |           |           | <38>      |           |           |           | <11>       |           |           |              |           |
|                        | congestion                             |                         | 0<br>( 0) | 6<br>( 16) | 0<br>( 0) | 0<br>( 0) | 1<br>( 3) | 3<br>( 8) | 0<br>( 0) | 0<br>( 0) | 1<br>( 3) | 3<br>( 8) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)  | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)    | 0<br>( 0) |
|                        | inflammatory cell nest                 |                         | 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>( 9) | 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) | 1<br>( 3) | 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 extramedullary hematopoiesis |                         | 1<br>( 3) | 1<br>( 3)  | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 3<br>( 8) | 0<br>( 0) | 0<br>( 0) | 2<br>( 5) | 0<br>( 0) | 1<br>( 3) | 0<br>( 0) | 0<br>( 0)  | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)    | 0<br>( 0) |
| {Circulatory system}   |  |                         |           |            |           |           |           |           |           |           |           |           |           |           |            |           |           |              |           |
| heart                  |  |                         | <38>      |            |           |           | <38>      |           |           |           | <38>      |           |           |           | <11>       |           |           |              |           |
|                        | inflammatory cell nest                 |                         | 3<br>( 8) | 0<br>( 0)  | 0<br>( 0) | 0<br>( 0) | 1<br>( 3) | 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) |

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PAGE : 5

| Organ_____           | Findings_____           | Group Name              | Control |       |      |      | 10 ppm |       |      |      | 30 ppm |       |      |      | 90 ppm |       |      |      |
|----------------------|-------------------------|-------------------------|---------|-------|------|------|--------|-------|------|------|--------|-------|------|------|--------|-------|------|------|
|                      |                         | No. of Animals on Study | 38      |       |      |      | 38     |       |      |      | 38     |       |      |      | 11     |       |      |      |
|                      |                         | Grade                   | 1       | 2     | 3    | 4    | 1      | 2     | 3    | 4    | 1      | 2     | 3    | 4    | 1      | 2     | 3    | 4    |
|                      |                         |                         | (%)     | (%)   | (%)  | (%)  | (%)    | (%)   | (%)  | (%)  | (%)    | (%)   | (%)  | (%)  | (%)    | (%)   | (%)  | (%)  |
| {Circulatory system} |                         |                         |         |       |      |      |        |       |      |      |        |       |      |      |        |       |      |      |
| heart                |                         |                         | <38>    |       |      |      | <38>   |       |      |      | <38>   |       |      |      | <11>   |       |      |      |
|                      | myocardial fibrosis     |                         | 11      | 27    | 0    | 0    | 10     | 26    | 0    | 0    | 17     | 21    | 0    | 0    | 5      | 6     | 0    | 0    |
|                      |                         |                         | ( 29)   | ( 71) | ( 0) | ( 0) | ( 26)  | ( 68) | ( 0) | ( 0) | ( 45)  | ( 55) | ( 0) | ( 0) | ( 45)  | ( 55) | ( 0) | ( 0) |
|                      | subendocardial fibrosis |                         | 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) |
|                      | arteritis               |                         | 2       | 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) |
| {Digestive system}   |                         |                         |         |       |      |      |        |       |      |      |        |       |      |      |        |       |      |      |
| tooth                |                         |                         | <38>    |       |      |      | <38>   |       |      |      | <38>   |       |      |      | <11>   |       |      |      |
|                      | 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)   | ( 3)  | ( 0) | ( 0) | ( 0)   | ( 0)  | ( 0) | ( 0) |
| stomach              |                         |                         | <38>    |       |      |      | <38>   |       |      |      | <38>   |       |      |      | <11>   |       |      |      |
|                      | erosion:forestomach     |                         | 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) |
|                      | hyperplasia:forestomach |                         | 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) |

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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCr1j]  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 6

| Organ              | Findings                  | Control |       |      |      | 10 ppm |       |      |      | 30 ppm |       |      |      | 90 ppm |      |      |      |
|--------------------|---------------------------|---------|-------|------|------|--------|-------|------|------|--------|-------|------|------|--------|------|------|------|
|                    |                           | 38      |       |      |      | 38     |       |      |      | 38     |       |      |      | 11     |      |      |      |
|                    |                           | 1       | 2     | 3    | 4    | 1      | 2     | 3    | 4    | 1      | 2     | 3    | 4    | 1      | 2    | 3    | 4    |
|                    |                           | (%)     | (%)   | (%)  | (%)  | (%)    | (%)   | (%)  | (%)  | (%)    | (%)   | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  |
| (Digestive system) |                           |         |       |      |      |        |       |      |      |        |       |      |      |        |      |      |      |
| stomach            |                           | <38>    |       |      |      | <38>   |       |      |      | <38>   |       |      |      | <11>   |      |      |      |
|                    | erosion:glandular stomach | 5       | 0     | 0    | 0    | 0      | 0     | 0    | 0    | 1      | 0     | 0    | 0    | 3      | 0    | 0    | 0    |
|                    |                           | ( 13)   | ( 0)  | ( 0) | ( 0) | ( 0)   | ( 0)  | ( 0) | ( 0) | ( 3)   | ( 0)  | ( 0) | ( 0) | ( 27)  | ( 0) | ( 0) | ( 0) |
| small intes        |                           | <38>    |       |      |      | <38>   |       |      |      | <38>   |       |      |      | <11>   |      |      |      |
|                    | 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) |
| liver              |                           | <38>    |       |      |      | <38>   |       |      |      | <38>   |       |      |      | <11>   |      |      |      |
|                    | herniation                | 3       | 0     | 0    | 0    | 5      | 0     | 0    | 0    | 4      | 0     | 0    | 0    | 2      | 0    | 0    | 0    |
|                    |                           | ( 8)    | ( 0)  | ( 0) | ( 0) | ( 13)  | ( 0)  | ( 0) | ( 0) | ( 11)  | ( 0)  | ( 0) | ( 0) | ( 18)  | ( 0) | ( 0) | ( 0) |
|                    | granulation               | 3       | 1     | 0    | 0    | 1      | 0     | 0    | 0    | 2      | 1     | 0    | 0    | 0      | 0    | 0    | 0    |
|                    |                           | ( 8)    | ( 3)  | ( 0) | ( 0) | ( 3)   | ( 0)  | ( 0) | ( 0) | ( 5)   | ( 3)  | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) |
|                    | inflammatory cell nest    | 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          | 7       | 4     | 0    | 0    | 5      | 8     | 0    | 0    | 3      | 5     | 0    | 0    | 1      | 1    | 0    | 0    |
|                    |                           | ( 18)   | ( 11) | ( 0) | ( 0) | ( 13)  | ( 21) | ( 0) | ( 0) | ( 8)   | ( 13) | ( 0) | ( 0) | ( 9)   | ( 9) | ( 0) | ( 0) |
|                    | acidophilic cell focus    | 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) |

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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 7

|                    |                        | Group Name              | Control |         |       |       | 10 ppm |         |       |       | 30 ppm |        |       |       | 90 ppm |         |       |       |
|--------------------|------------------------|-------------------------|---------|---------|-------|-------|--------|---------|-------|-------|--------|--------|-------|-------|--------|---------|-------|-------|
|                    |                        | No. of Animals on Study | 38      |         |       |       | 38     |         |       |       | 38     |        |       |       | 11     |         |       |       |
| Organ              | Findings               | Grade                   | 1       | 2       | 3     | 4     | 1      | 2       | 3     | 4     | 1      | 2      | 3     | 4     | 1      | 2       | 3     | 4     |
|                    |                        |                         | (%)     | (%)     | (%)   | (%)   | (%)    | (%)     | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)     | (%)   | (%)   |
| {Digestive system} |                        |                         |         |         |       |       |        |         |       |       |        |        |       |       |        |         |       |       |
| liver              |                        |                         | <38>    |         |       |       | <38>   |         |       |       | <38>   |        |       |       | <11>   |         |       |       |
|                    | basophilic cell focus  |                         | 3       | 1       | 0     | 0     | 0      | 1       | 0     | 0     | 1      | 1      | 0     | 0     | 1      | 0       | 0     | 0     |
|                    |                        |                         | ( 8 )   | ( 3 )   | ( 0 ) | ( 0 ) | ( 0 )  | ( 3 )   | ( 0 ) | ( 0 ) | ( 3 )  | ( 3 )  | ( 0 ) | ( 0 ) | ( 9 )  | ( 0 )   | ( 0 ) | ( 0 ) |
|                    |                        |                         |         |         |       |       |        |         |       |       |        |        |       |       |        |         |       |       |
|                    | spongiosis hepatitis   |                         | 3       | 0       | 0     | 0     | 1      | 1       | 0     | 0     | 7      | 0      | 0     | 0     | 1      | 0       | 0     | 0     |
|                    |                        |                         | ( 8 )   | ( 0 )   | ( 0 ) | ( 0 ) | ( 3 )  | ( 3 )   | ( 0 ) | ( 0 ) | ( 18 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 9 )  | ( 0 )   | ( 0 ) | ( 0 ) |
|                    | bile duct hyperplasia  |                         | 0       | 38      | 0     | 0     | 0      | 38      | 0     | 0     | 1      | 37     | 0     | 0     | 0      | 11      | 0     | 0     |
|                    |                        |                         | ( 0 )   | ( 100 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 100 ) | ( 0 ) | ( 0 ) | ( 3 )  | ( 97 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 100 ) | ( 0 ) | ( 0 ) |
| pancreas           |                        |                         | <38>    |         |       |       | <38>   |         |       |       | <38>   |        |       |       | <11>   |         |       |       |
|                    | atrophy                |                         | 0       | 7       | 0     | 0     | 2      | 11      | 0     | 0     | 5      | 6      | 0     | 0     | 1      | 1       | 0     | 0     |
|                    |                        |                         | ( 0 )   | ( 18 )  | ( 0 ) | ( 0 ) | ( 5 )  | ( 29 )  | ( 0 ) | ( 0 ) | ( 13 ) | ( 16 ) | ( 0 ) | ( 0 ) | ( 9 )  | ( 9 )   | ( 0 ) | ( 0 ) |
|                    |                        |                         |         |         |       |       |        |         |       |       |        |        |       |       |        |         |       |       |
|                    | islet cell hyperplasia |                         | 0       | 2       | 0     | 0     | 0      | 2       | 0     | 0     | 0      | 1      | 0     | 0     | 0      | 0       | 0     | 0     |
|                    |                        |                         | ( 0 )   | ( 5 )   | ( 0 ) | ( 0 ) | ( 0 )  | ( 5 )   | ( 0 ) | ( 0 ) | ( 0 )  | ( 3 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )   | ( 0 ) | ( 0 ) |
| {Urinary system}   |                        |                         |         |         |       |       |        |         |       |       |        |        |       |       |        |         |       |       |
| kidney             |                        |                         | <38>    |         |       |       | <38>   |         |       |       | <38>   |        |       |       | <11>   |         |       |       |
|                    | chronic nephropathy    |                         | 8       | 25      | 2     | 0     | 5      | 30      | 2     | 0     | 13     | 22     | 2     | 0     | 7      | 1       | 0     | 0 **  |
|                    |                        |                         | ( 21 )  | ( 66 )  | ( 5 ) | ( 0 ) | ( 13 ) | ( 79 )  | ( 5 ) | ( 0 ) | ( 34 ) | ( 58 ) | ( 5 ) | ( 0 ) | ( 64 ) | ( 9 )   | ( 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  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS (105W)

PAGE : 8

|                    |                        | Group Name              | Control |        |       |       | 10 ppm |        |       |       | 30 ppm |       |       |       | 90 ppm |       |       |       |
|--------------------|------------------------|-------------------------|---------|--------|-------|-------|--------|--------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
|                    |                        | No. of Animals on Study | 38      |        |       |       | 38     |        |       |       | 38     |       |       |       | 11     |       |       |       |
|                    |                        | Grade                   | 1       | 2      | 3     | 4     | 1      | 2      | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     |
| Organ              | Findings               |                         | (%)     | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   |
| {Urinary system}   |                        |                         |         |        |       |       |        |        |       |       |        |       |       |       |        |       |       |       |
| kidney             |                        |                         | <38>    |        |       |       | <38>   |        |       |       | <38>   |       |       |       | <11>   |       |       |       |
|                    | tubular necrosis       |                         | 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 )  | ( 9 ) | ( 0 ) | ( 0 ) |
|                    | mineralization:papilla |                         | 3       | 0      | 0     | 0     | 4      | 0      | 0     | 0     | 2      | 0     | 0     | 0     | 1      | 0     | 0     | 0     |
|                    |                        |                         | ( 8 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 11 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 5 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 9 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                    | mineralization:pelvis  |                         | 2       | 0      | 0     | 0     | 1      | 0      | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     |
|                    |                        |                         | ( 5 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 3 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
| {Endocrine system} |                        |                         |         |        |       |       |        |        |       |       |        |       |       |       |        |       |       |       |
| pituitary          |                        |                         | <38>    |        |       |       | <38>   |        |       |       | <38>   |       |       |       | <11>   |       |       |       |
|                    | cyst                   |                         | 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 ) |
|                    | hyperplasia            |                         | 2       | 6      | 0     | 0     | 0      | 6      | 0     | 0     | 1      | 3     | 0     | 0     | 0      | 1     | 0     | 0     |
|                    |                        |                         | ( 5 )   | ( 16 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 16 ) | ( 0 ) | ( 0 ) | ( 3 )  | ( 8 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 9 ) | ( 0 ) | ( 0 ) |
|                    | Rathke pouch           |                         | 0       | 2      | 0     | 0     | 0      | 0      | 0     | 0     | 2      | 1     | 0     | 0     | 0      | 0     | 0     | 0     |
|                    |                        |                         | ( 0 )   | ( 5 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 5 )  | ( 3 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
| thyroid            |                        |                         | <38>    |        |       |       | <37>   |        |       |       | <38>   |       |       |       | <11>   |       |       |       |
|                    | cyst                   |                         | 0       | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 1     | 0     | 0     | 0      | 0     | 0     | 0     |
|                    |                        |                         | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 3 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |

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 < a > a : Number of animals examined at the site  
 b b : Number of animals with lesion  
 ( c ) c : b / a \* 100  
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ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 9

|                       |                                   | Group Name              | Control |       |       |      | 10 ppm |       |        |      | 30 ppm |       |        |      | 90 ppm |      |        |      |
|-----------------------|-----------------------------------|-------------------------|---------|-------|-------|------|--------|-------|--------|------|--------|-------|--------|------|--------|------|--------|------|
|                       |                                   | No. of Animals on Study | 38      |       |       |      | 38     |       |        |      | 38     |       |        |      | 11     |      |        |      |
| Organ                 | Findings                          | Grade                   | 1       | 2     | 3     | 4    | 1      | 2     | 3      | 4    | 1      | 2     | 3      | 4    | 1      | 2    | 3      | 4    |
|                       |                                   |                         |         |       |       |      |        |       |        |      |        |       |        |      |        |      |        |      |
| {Endocrine system}    |                                   |                         |         |       |       |      |        |       |        |      |        |       |        |      |        |      |        |      |
| thyroid               |                                   |                         | <38>    |       |       |      | <37>   |       |        |      | <38>   |       |        |      | <11>   |      |        |      |
|                       | C-cell hyperplasia                |                         | 5       | 1     | 0     | 0    | 4      | 4     | 0      | 0    | 3      | 4     | 0      | 0    | 2      | 0    | 0      | 0    |
|                       |                                   |                         | ( 13)   | ( 3)  | ( 0)  | ( 0) | ( 11)  | ( 11) | ( 0)   | ( 0) | ( 8)   | ( 11) | ( 0)   | ( 0) | ( 18)  | ( 0) | ( 0)   | ( 0) |
|                       | focal follicular cell hyperplasia |                         | 0       | 0     | 0     | 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) |
| adrenal               |                                   |                         | <38>    |       |       |      | <38>   |       |        |      | <38>   |       |        |      | <11>   |      |        |      |
|                       | hyperplasia:cortical cell         |                         | 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) |
|                       | hyperplasia:medulla               |                         | 2       | 4     | 0     | 0    | 1      | 2     | 0      | 0    | 0      | 4     | 0      | 0    | 0      | 1    | 0      | 0    |
|                       |                                   |                         | ( 5)    | ( 11) | ( 0)  | ( 0) | ( 3)   | ( 5)  | ( 0)   | ( 0) | ( 0)   | ( 11) | ( 0)   | ( 0) | ( 0)   | ( 9) | ( 0)   | ( 0) |
|                       | focal fatty change:cortex         |                         | 0       | 2     | 0     | 0    | 0      | 2     | 0      | 0    | 0      | 1     | 0      | 0    | 0      | 0    | 0      | 0    |
|                       |                                   |                         | ( 0)    | ( 5)  | ( 0)  | ( 0) | ( 0)   | ( 5)  | ( 0)   | ( 0) | ( 0)   | ( 3)  | ( 0)   | ( 0) | ( 0)   | ( 0) | ( 0)   | ( 0) |
| {Reproductive system} |                                   |                         |         |       |       |      |        |       |        |      |        |       |        |      |        |      |        |      |
| testis                |                                   |                         | <38>    |       |       |      | <38>   |       |        |      | <38>   |       |        |      | <11>   |      |        |      |
|                       | atrophy                           |                         | 0       | 1     | 36    | 0    | 0      | 0     | 38     | 0    | 0      | 0     | 38     | 0    | 0      | 0    | 11     | 0    |
|                       |                                   |                         | ( 0)    | ( 3)  | ( 95) | ( 0) | ( 0)   | ( 0)  | ( 100) | ( 0) | ( 0)   | ( 0)  | ( 100) | ( 0) | ( 0)   | ( 0) | ( 100) | ( 0) |

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 SACRIFICED ANIMALS (105W)

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|                       |                               | Group Name              | Control |      |      |      | 10 ppm |       |      |      | 30 ppm |       |      |      | 90 ppm |      |      |      |
|-----------------------|-------------------------------|-------------------------|---------|------|------|------|--------|-------|------|------|--------|-------|------|------|--------|------|------|------|
|                       |                               | No. of Animals on Study | 38      |      |      |      | 38     |       |      |      | 38     |       |      |      | 11     |      |      |      |
| Organ                 | Findings                      | Grade                   | 1       | 2    | 3    | 4    | 1      | 2     | 3    | 4    | 1      | 2     | 3    | 4    | 1      | 2    | 3    | 4    |
|                       |                               |                         |         |      |      |      |        |       |      |      |        |       |      |      |        |      |      |      |
| {Reproductive system} |                               |                         |         |      |      |      |        |       |      |      |        |       |      |      |        |      |      |      |
| testis                | mineralization                |                         | <38>    |      |      |      | <38>   |       |      |      | <38>   |       |      |      | <11>   |      |      |      |
|                       |                               |                         | 8       | 1    | 0    | 0    | 6      | 0     | 0    | 0    | 8      | 0     | 0    | 0    | 4      | 0    | 0    | 0    |
|                       |                               |                         | ( 21)   | ( 3) | ( 0) | ( 0) | ( 16)  | ( 0)  | ( 0) | ( 0) | ( 21)  | ( 0)  | ( 0) | ( 0) | ( 36)  | ( 0) | ( 0) | ( 0) |
|                       |                               |                         |         |      |      |      |        |       |      |      |        |       |      |      |        |      |      |      |
|                       | arteritis                     |                         | 1       | 1    | 0    | 0    | 2      | 1     | 0    | 0    | 0      | 0     | 1    | 0    | 0      | 0    | 0    | 0    |
|                       |                               |                         | ( 3)    | ( 3) | ( 0) | ( 0) | ( 5)   | ( 3)  | ( 0) | ( 0) | ( 0)   | ( 0)  | ( 3) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) |
|                       |                               |                         |         |      |      |      |        |       |      |      |        |       |      |      |        |      |      |      |
|                       |                               |                         |         |      |      |      |        |       |      |      |        |       |      |      |        |      |      |      |
|                       | interstitial cell hyperplasia |                         | 0       | 1    | 0    | 0    | 3      | 0     | 0    | 0    | 1      | 0     | 0    | 0    | 0      | 0    | 0    | 0    |
|                       |                               |                         | ( 0)    | ( 3) | ( 0) | ( 0) | ( 8)   | ( 0)  | ( 0) | ( 0) | ( 3)   | ( 0)  | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) |
|                       |                               |                         |         |      |      |      |        |       |      |      |        |       |      |      |        |      |      |      |
|                       |                               |                         |         |      |      |      |        |       |      |      |        |       |      |      |        |      |      |      |
| prostate              | inflammation                  |                         | <38>    |      |      |      | <38>   |       |      |      | <38>   |       |      |      | <11>   |      |      |      |
|                       |                               |                         | 9       | 2    | 0    | 0    | 5      | 5     | 0    | 0    | 4      | 4     | 0    | 0    | 1      | 0    | 0    | 0    |
|                       |                               |                         | ( 24)   | ( 5) | ( 0) | ( 0) | ( 13)  | ( 13) | ( 0) | ( 0) | ( 11)  | ( 11) | ( 0) | ( 0) | ( 9)   | ( 0) | ( 0) | ( 0) |
|                       |                               |                         |         |      |      |      |        |       |      |      |        |       |      |      |        |      |      |      |
|                       | hyperplasia                   |                         | 6       | 1    | 0    | 0    | 8      | 0     | 0    | 0    | 8      | 0     | 0    | 0    | 1      | 0    | 0    | 0    |
|                       |                               |                         | ( 16)   | ( 3) | ( 0) | ( 0) | ( 21)  | ( 0)  | ( 0) | ( 0) | ( 21)  | ( 0)  | ( 0) | ( 0) | ( 9)   | ( 0) | ( 0) | ( 0) |
|                       |                               |                         |         |      |      |      |        |       |      |      |        |       |      |      |        |      |      |      |
|                       |                               |                         |         |      |      |      |        |       |      |      |        |       |      |      |        |      |      |      |
| mammary gl            | galactocoele                  |                         | <38>    |      |      |      | <38>   |       |      |      | <38>   |       |      |      | <11>   |      |      |      |
|                       |                               |                         | 0       | 0    | 0    | 0    | 0      | 2     | 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) |
|                       |                               |                         |         |      |      |      |        |       |      |      |        |       |      |      |        |      |      |      |
| {Nervous system}      |                               |                         |         |      |      |      |        |       |      |      |        |       |      |      |        |      |      |      |
| brain                 | necrosis:focal                |                         | <38>    |      |      |      | <38>   |       |      |      | <38>   |       |      |      | <11>   |      |      |      |
|                       |                               |                         | 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) |
|                       |                               |                         |         |      |      |      |        |       |      |      |        |       |      |      |        |      |      |      |

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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 11

|                                  |                               | Group Name              | Control |        |        |       | 10 ppm |       |        |       | 30 ppm |        |        |       | 90 ppm |       |       |       |
|----------------------------------|-------------------------------|-------------------------|---------|--------|--------|-------|--------|-------|--------|-------|--------|--------|--------|-------|--------|-------|-------|-------|
|                                  |                               | No. of Animals on Study | 38      |        |        |       | 38     |       |        |       | 38     |        |        |       | 11     |       |       |       |
| Organ                            | Findings                      | Grade                   | 1       | 2      | 3      | 4     | 1      | 2     | 3      | 4     | 1      | 2      | 3      | 4     | 1      | 2     | 3     | 4     |
|                                  |                               |                         | (%)     | (%)    | (%)    | (%)   | (%)    | (%)   | (%)    | (%)   | (%)    | (%)    | (%)    | (%)   | (%)    | (%)   | (%)   | (%)   |
| {Nervous system}                 |                               |                         |         |        |        |       |        |       |        |       |        |        |        |       |        |       |       |       |
| brain                            |                               |                         | <38>    |        |        |       | <38>   |       |        |       | <38>   |        |        |       | <11>   |       |       |       |
|                                  | dilatation:cerebral ventricle |                         | 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 ) |
| spinal cord                      |                               |                         | <38>    |        |        |       | <38>   |       |        |       | <38>   |        |        |       | <11>   |       |       |       |
|                                  | gliosis                       |                         | 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 ) |
| {Special sense organs/appendage} |                               |                         |         |        |        |       |        |       |        |       |        |        |        |       |        |       |       |       |
| eye                              |                               |                         | <38>    |        |        |       | <38>   |       |        |       | <38>   |        |        |       | <11>   |       |       |       |
|                                  | cataract                      |                         | 3       | 5      | 0      | 0     | 2      | 2     | 0      | 0     | 0      | 4      | 0      | 0     | 0      | 0     | 0     | 0     |
|                                  |                               |                         | ( 8 )   | ( 13 ) | ( 0 )  | ( 0 ) | ( 5 )  | ( 5 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 11 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                                  | retinal atrophy               |                         | 28      | 0      | 8      | 0     | 32     | 0     | 4      | 0     | 34     | 0      | 4      | 0     | 9      | 0     | 0     | 0     |
|                                  |                               |                         | ( 74 )  | ( 0 )  | ( 21 ) | ( 0 ) | ( 84 ) | ( 0 ) | ( 11 ) | ( 0 ) | ( 89 ) | ( 0 )  | ( 11 ) | ( 0 ) | ( 82 ) | ( 0 ) | ( 0 ) | ( 0 ) |
|                                  | keratitis                     |                         | 2       | 0      | 0      | 0     | 2      | 0     | 0      | 0     | 0      | 0      | 0      | 0     | 1      | 0     | 1     | 0     |
|                                  |                               |                         | ( 5 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 5 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 9 )  | ( 0 ) | ( 9 ) | ( 0 ) |
| Harder gl                        |                               |                         | <38>    |        |        |       | <38>   |       |        |       | <38>   |        |        |       | <11>   |       |       |       |
|                                  | degeneration                  |                         | 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 ) |

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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 12

| Organ | Findings | Control                 |     |     |     | 10 ppm |     |     |     | 30 ppm |     |     |     | 90 ppm |     |     |     |
|-------|----------|-------------------------|-----|-----|-----|--------|-----|-----|-----|--------|-----|-----|-----|--------|-----|-----|-----|
|       |          | No. of Animals on Study |     |     |     | 38     |     |     |     | 38     |     |     |     | 11     |     |     |     |
|       |          | Grade                   |     |     |     | 1      |     |     |     | 1      |     |     |     | 1      |     |     |     |
|       |          | 1                       | 2   | 3   | 4   | 1      | 2   | 3   | 4   | 1      | 2   | 3   | 4   | 1      | 2   | 3   | 4   |
|       |          | (%)                     | (%) | (%) | (%) | (%)    | (%) | (%) | (%) | (%)    | (%) | (%) | (%) | (%)    | (%) | (%) | (%) |

{Special sense organs/appendage}

|           |                          |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
|-----------|--------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Harder gl | Lymphocytic infiltration | <38>  |       |       |       | <38>  |       |       |       | <38>  |       |       |       | <11>  |       |       |       |
|           |                          | 3     | 0     | 0     | 0     | 2     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 1     | 0     | 0     | 0     |
|           |                          | ( 8 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 5 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 9 ) | ( 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 4

HISTOPATHOLOGICAL FINDINGS :  
NON-NEOPLASTIC LESIONS : FEMALE  
ALL ANIMALS

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 18

| Organ                            | Findings                                   | Group Name<br>No. of Animals on Study |        |        |       | Control |        |       |       | 10 ppm |        |       |       | 30 ppm |        |       |       | 90 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     |
|                                  |  | (%)                                   | (%)    | (%)    | (%)   | (%)     | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   |
| {Integumentary system/appandage} |  |                                       |        |        |       |         |        |       |       |        |        |       |       |        |        |       |       |        |        |       |       |
| skin/app                         |  | <50>                                  |        |        |       | <50>    |        |       |       | <50>   |        |       |       | <50>   |        |       |       | <50>   |        |       |       |
|                                  | angiectasis                                | 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 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                                  | inflammation                               | 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 ) |
| {Respiratory system}             |  |                                       |        |        |       |         |        |       |       |        |        |       |       |        |        |       |       |        |        |       |       |
| nasal cavit                      |  | <50>                                  |        |        |       | <50>    |        |       |       | <50>   |        |       |       | <50>   |        |       |       | <50>   |        |       |       |
|                                  | squamous cell hyperplasia with atypia      | 0                                     | 0      | 0      | 0     | 0       | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 9      | 30     | 0     | 0 **  |
|                                  |  | ( 0 )                                 | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 18 ) | ( 60 ) | ( 0 ) | ( 0 ) |
|                                  | eosinophilic change:olfactory epithelium   | 1                                     | 35     | 13     | 0     | 2       | 46     | 2     | 0 *   | 3      | 46     | 1     | 0 **  | 10     | 25     | 0     | 0 **  | 10     | 25     | 0     | 0 **  |
|                                  |  | ( 2 )                                 | ( 70 ) | ( 26 ) | ( 0 ) | ( 4 )   | ( 92 ) | ( 4 ) | ( 0 ) | ( 6 )  | ( 92 ) | ( 2 ) | ( 0 ) | ( 20 ) | ( 50 ) | ( 0 ) | ( 0 ) | ( 20 ) | ( 50 ) | ( 0 ) | ( 0 ) |
|                                  | eosinophilic change:respiratory epithelium | 22                                    | 5      | 0      | 0     | 20      | 6      | 0     | 0     | 11     | 2      | 0     | 0 *   | 1      | 0      | 0     | 0 **  | 1      | 0      | 0     | 0 **  |
|                                  |  | ( 44 )                                | ( 10 ) | ( 0 )  | ( 0 ) | ( 40 )  | ( 12 ) | ( 0 ) | ( 0 ) | ( 22 ) | ( 4 )  | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                                  | inflammation:foreign body                  | 3                                     | 1      | 0      | 0     | 3       | 1      | 0     | 0     | 1      | 1      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0     | 0     |
|                                  |  | ( 6 )                                 | ( 2 )  | ( 0 )  | ( 0 ) | ( 6 )   | ( 2 )  | ( 0 ) | ( 0 ) | ( 2 )  | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                                  | inflammation:respiratory epithelium        | 0                                     | 0      | 0      | 0     | 0       | 0      | 0     | 0     | 2      | 0      | 0     | 0     | 8      | 23     | 1     | 0 **  | 8      | 23     | 1     | 0 **  |
|                                  |  | ( 0 )                                 | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 4 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 16 ) | ( 46 ) | ( 2 ) | ( 0 ) | ( 16 ) | ( 46 ) | ( 2 ) | ( 0 ) |

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( c ) c : b / a \* 100  
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 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 19

|                      |   | Group Name              | Control |       |       |       | 10 ppm |       |       |       | 30 ppm |       |       |       | 90 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  |                         | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   |
| {Respiratory system} |   |                         |         |       |       |       |        |       |       |       |        |       |       |       |        |        |       |       |
| nasal cavit          |   |                         | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |        |       |       |
|                      | inflammation:olfactory epithelium               |                         | 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 ) |
|                      | respiratory metaplasia:olfactory epithelium     |                         | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 5      | 0      | 0     | 0     |
|                      |   |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 10 ) | ( 0 )  | ( 0 ) | ( 0 ) |
|                      | respiratory metaplasia:gland                    |                         | 16      | 3     | 0     | 0     | 24     | 1     | 0     | 0     | 21     | 1     | 0     | 0     | 14     | 5      | 0     | 0     |
|                      |   |                         | ( 32 )  | ( 6 ) | ( 0 ) | ( 0 ) | ( 48 ) | ( 2 ) | ( 0 ) | ( 0 ) | ( 42 ) | ( 2 ) | ( 0 ) | ( 0 ) | ( 28 ) | ( 10 ) | ( 0 ) | ( 0 ) |
|                      | squamous cell metaplasia:respiratory epithelium |                         | 0       | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 6      | 0     | 0     | 0 *   | 2      | 41     | 0     | 0 **  |
|                      |   |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 12 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )  | ( 82 ) | ( 0 ) | ( 0 ) |
|                      | squamous cell metaplasia:olfactory epithelium   |                         | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 8      | 0      | 0     | 0 **  |
|                      |   |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 16 ) | ( 0 )  | ( 0 ) | ( 0 ) |
|                      | hyperplasia:transitional epithelium             |                         | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 6      | 0     | 0     | 0 *   | 0      | 0      | 0     | 0     |
|                      |   |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 12 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                      | atrophy:olfactory epithelium                    |                         | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 21     | 8      | 0     | 0 **  |
|                      |   |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 42 ) | ( 16 ) | ( 0 ) | ( 0 ) |
| lung                 |   |                         | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |        |       |       |
|                      | congestion                                      |                         | 0       | 1     | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 2      | 0     | 0     |
|                      |   |                         | ( 0 )   | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 4 )  | ( 0 ) | ( 0 ) |

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

PAGE : 20

|                        |                                       | Group Name              | Control |      |      |      | 10 ppm |      |      |      | 30 ppm |      |      |      | 90 ppm |      |      |      |
|------------------------|---------------------------------------|-------------------------|---------|------|------|------|--------|------|------|------|--------|------|------|------|--------|------|------|------|
|                        |                                       | No. of Animals on Study | 50      |      |      |      | 50     |      |      |      | 50     |      |      |      | 50     |      |      |      |
| Organ                  | Findings                              | Grade                   | 1       | 2    | 3    | 4    | 1      | 2    | 3    | 4    | 1      | 2    | 3    | 4    | 1      | 2    | 3    | 4    |
|                        |                                       |                         | (%)     | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  |
| {Respiratory system}   |                                       |                         |         |      |      |      |        |      |      |      |        |      |      |      |        |      |      |      |
| lung                   |                                       |                         | <50>    |      |      |      | <50>   |      |      |      | <50>   |      |      |      | <50>   |      |      |      |
|                        | hemorrhage                            |                         | 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) | ( 4)   | ( 0) | ( 0) | ( 0) |
|                        | inflammation                          |                         | 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 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) |
|                        | bronchiolar-alveolar cell hyperplasia |                         | 0       | 1    | 0    | 0    | 1      | 1    | 0    | 0    | 1      | 2    | 0    | 0    | 1      | 0    | 0    | 0    |
|                        |                                       |                         | ( 0)    | ( 2) | ( 0) | ( 0) | ( 2)   | ( 2) | ( 0) | ( 0) | ( 2)   | ( 4) | ( 0) | ( 0) | ( 2)   | ( 0) | ( 0) | ( 0) |
|                        | inflammation:foreign body             |                         | 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)   | ( 8) | ( 0) | ( 0) |
| {Hematopoietic system} |                                       |                         |         |      |      |      |        |      |      |      |        |      |      |      |        |      |      |      |
| bone marrow            |                                       |                         | <50>    |      |      |      | <50>   |      |      |      | <50>   |      |      |      | <50>   |      |      |      |
|                        | granulation                           |                         | 14      | 1    | 0    | 0    | 15     | 4    | 0    | 0    | 15     | 3    | 0    | 0    | 10     | 0    | 0    | 0    |
|                        |                                       |                         | ( 28)   | ( 2) | ( 0) | ( 0) | ( 30)  | ( 8) | ( 0) | ( 0) | ( 30)  | ( 6) | ( 0) | ( 0) | ( 20)  | ( 0) | ( 0) | ( 0) |
|                        | increased hematopoiesis               |                         | 6       | 0    | 0    | 0    | 3      | 0    | 0    | 0    | 4      | 0    | 0    | 0    | 5      | 0    | 0    | 0    |
|                        |                                       |                         | ( 12)   | ( 0) | ( 0) | ( 0) | ( 6)   | ( 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. : 0437  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
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 |       |       |       | 10 ppm |       |       |       | 30 ppm |        |       |       | 90 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     |
|                        |  | (%)                                   | (%)   | (%)   | (%)   | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   |
| {Hematopoietic system} |  |                                       |       |       |       |         |       |       |       |        |       |       |       |        |        |       |       |        |        |       |       |
| bone marrow            |  | <50>                                  |       |       |       | <50>    |       |       |       | <50>   |       |       |       | <50>   |        |       |       | <50>   |        |       |       |
|                        | decreased hematopoiesis                | 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 ) |
| spleen                 |  | <50>                                  |       |       |       | <50>    |       |       |       | <49>   |       |       |       | <50>   |        |       |       | <50>   |        |       |       |
|                        | congestion                             | 0                                     | 2     | 0     | 0     | 0       | 1     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 1      | 0     | 0     |
|                        |  | ( 0 )                                 | ( 4 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 )  | ( 0 ) | ( 0 ) |
|                        | deposit of hemosiderin                 | 0                                     | 2     | 0     | 0     | 0       | 1     | 0     | 0     | 0      | 3     | 0     | 0     | 0      | 5      | 0     | 0     | 0      | 10     | 0     | 0     |
|                        |  | ( 0 )                                 | ( 4 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 6 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 10 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 10 ) | ( 0 ) | ( 0 ) |
|                        | granulation                            | 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 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                        | fibrosis                               | 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 )  | ( 2 )  | ( 0 ) | ( 0 ) |
|                        | increased extramedullary hematopoiesis | 0                                     | 2     | 1     | 0     | 0       | 2     | 1     | 0     | 0      | 2     | 3     | 0     | 0      | 5      | 0     | 0     | 0      | 10     | 0     | 0     |
|                        |  | ( 0 )                                 | ( 4 ) | ( 2 ) | ( 0 ) | ( 0 )   | ( 4 ) | ( 2 ) | ( 0 ) | ( 0 )  | ( 4 ) | ( 6 ) | ( 0 ) | ( 0 )  | ( 10 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 10 ) | ( 0 ) | ( 0 ) |
| {Circulatory system}   |  |                                       |       |       |       |         |       |       |       |        |       |       |       |        |        |       |       |        |        |       |       |
| heart                  |  | <50>                                  |       |       |       | <50>    |       |       |       | <50>   |       |       |       | <50>   |        |       |       | <50>   |        |       |       |
|                        | thrombus                               | 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 )  | ( 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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 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 |        |       |       | Control |       |       |       | 10 ppm |        |       |       | 30 ppm |       |       |       | 90 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     |
|                      |                           | (%)                                   | (%)    | (%)   | (%)   | (%)     | (%)   | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   |
| {Circulatory system} |                           |                                       |        |       |       |         |       |       |       |        |        |       |       |        |       |       |       |        |       |       |       |
| heart                |                           | <50>                                  |        |       |       | <50>    |       |       |       | <50>   |        |       |       | <50>   |       |       |       | <50>   |       |       |       |
|                      | necrosis:focal            | 0                                     | 1      | 0     | 0     | 0       | 0     | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 0     | 0     | 0     |
|                      |                           | ( 0 )                                 | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                      | mineralization            | 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 ) |
|                      | 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 ) |
|                      | inflammatory cell nest    | 1                                     | 0      | 0     | 0     | 3       | 0     | 0     | 0     | 1      | 0      | 0     | 0     | 1      | 0     | 0     | 0     | 1      | 0     | 0     | 0     |
|                      |                           | ( 2 )                                 | ( 0 )  | ( 0 ) | ( 0 ) | ( 6 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                      | myocardial fibrosis       | 30                                    | 5      | 0     | 0     | 31      | 3     | 0     | 0     | 34     | 5      | 0     | 0     | 25     | 2     | 0     | 0     | 25     | 2     | 0     | 0     |
|                      |                           | ( 60 )                                | ( 10 ) | ( 0 ) | ( 0 ) | ( 62 )  | ( 6 ) | ( 0 ) | ( 0 ) | ( 68 ) | ( 10 ) | ( 0 ) | ( 0 ) | ( 50 ) | ( 4 ) | ( 0 ) | ( 0 ) | ( 50 ) | ( 4 ) | ( 0 ) | ( 0 ) |
|                      | subendocardial fibrosis   | 1                                     | 0      | 0     | 0     | 3       | 0     | 0     | 0     | 2      | 0      | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     |
|                      |                           | ( 2 )                                 | ( 0 )  | ( 0 ) | ( 0 ) | ( 6 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
| {Digestive system}   |                           |                                       |        |       |       |         |       |       |       |        |        |       |       |        |       |       |       |        |       |       |       |
| tongue               |                           | <50>                                  |        |       |       | <50>    |       |       |       | <50>   |        |       |       | <50>   |       |       |       | <50>   |       |       |       |
|                      | inflammatory infiltration | 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 ) | ( 4 )  | ( 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

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 23

|                    |                           | Group Name              | Control |       |       |       | 10 ppm |       |       |       | 30 ppm |       |       |       | 90 ppm |       |       |       |
|--------------------|---------------------------|-------------------------|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
|                    |                           | No. of Animals on Study | 50      |       |       |       | 50     |       |       |       | 50     |       |       |       | 50     |       |       |       |
| Organ              | Findings                  | Grade                   | 1       | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     |
|                    |                           |                         | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   |
| {Digestive system} |                           |                         |         |       |       |       |        |       |       |       |        |       |       |       |        |       |       |       |
| tongue             | arteritis                 |                         | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |       |       |       |
|                    |                           | 1                       | 0       | 0     | 0     | 2     | 0      | 0     | 0     | 1     | 0      | 0     | 0     | 2     | 0      | 0     | 0     |       |
|                    |                           | ( 2 )                   | ( 0 )   | ( 0 ) | ( 0 ) | ( 4 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 2 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 4 ) | ( 0 )  | ( 0 ) | ( 0 ) |       |
| stomach            | basal cell hyperplasia    |                         | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |       |       |       |
|                    |                           | 1                       | 0       | 0     | 0     | 3     | 0      | 0     | 0     | 1     | 0      | 0     | 0     | 4     | 0      | 0     | 0     |       |
|                    |                           | ( 2 )                   | ( 0 )   | ( 0 ) | ( 0 ) | ( 6 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 2 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 8 ) | ( 0 )  | ( 0 ) | ( 0 ) |       |
|                    | erosion:forestomach       |                         | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 1     | 0     | 0     | 4      | 0     | 0     | 0     |
|                    |                           |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 ) | ( 0 ) | ( 0 ) | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                    | ulcer:forestomach         |                         | 0       | 2     | 0     | 0     | 0      | 1     | 1     | 0     | 0      | 2     | 0     | 0     | 2      | 3     | 0     | 0     |
|                    |                           |                         | ( 0 )   | ( 4 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 ) | ( 2 ) | ( 0 ) | ( 0 )  | ( 4 ) | ( 0 ) | ( 0 ) | ( 4 )  | ( 6 ) | ( 0 ) | ( 0 ) |
|                    | hyperplasia:forestomach   |                         | 4       | 2     | 0     | 0     | 0      | 2     | 0     | 0     | 0      | 2     | 0     | 0     | 6      | 2     | 0     | 0     |
|                    |                           |                         | ( 8 )   | ( 4 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 4 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 4 ) | ( 0 ) | ( 0 ) | ( 12 ) | ( 4 ) | ( 0 ) | ( 0 ) |
|                    | erosion:glandular stomach |                         | 3       | 0     | 0     | 0     | 2      | 1     | 0     | 0     | 0      | 0     | 0     | 0     | 2      | 0     | 0     | 0     |
|                    |                           |                         | ( 6 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )  | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                    | ulcer:glandular stomach   |                         | 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 ) | ( 2 )  | ( 2 ) | ( 0 ) | ( 0 ) |
| small intes        | erosion                   |                         | <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 ) |       |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe  
 < a > a : Number of animals examined at the site  
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STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 24

|                    |                          | Group Name              | Control     |            |           |           | 10 ppm      |            |            |           | 30 ppm      |            |           |             | 90 ppm      |           |           |              |
|--------------------|--------------------------|-------------------------|-------------|------------|-----------|-----------|-------------|------------|------------|-----------|-------------|------------|-----------|-------------|-------------|-----------|-----------|--------------|
|                    |                          | No. of Animals on Study | 50          |            |           |           | 50          |            |            |           | 50          |            |           |             | 50          |           |           |              |
| Organ              | Findings                 | Grade                   | 1           | 2          | 3         | 4         | 1           | 2          | 3          | 4         | 1           | 2          | 3         | 4           | 1           | 2         | 3         | 4            |
|                    |                          |                         | (%)         | (%)        | (%)       | (%)       | (%)         | (%)        | (%)        | (%)       | (%)         | (%)        | (%)       | (%)         | (%)         | (%)       | (%)       | (%)          |
| {Digestive system} |                          |                         |             |            |           |           |             |            |            |           |             |            |           |             |             |           |           |              |
| liver              |                          |                         | <50>        |            |           |           | <50>        |            |            |           | <50>        |            |           |             | <50>        |           |           |              |
|                    | herniation               |                         | 9<br>( 18)  | 0<br>( 0)  | 0<br>( 0) | 0<br>( 0) | 10<br>( 20) | 0<br>( 0)  | 0<br>( 0)  | 0<br>( 0) | 6<br>( 12)  | 0<br>( 0)  | 0<br>( 0) | 0<br>( 0)   | 12<br>( 24) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)    |
|                    | necrosis:central         |                         | 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)    |
|                    | fatty change:central     |                         | 0<br>( 0)   | 3<br>( 6)  | 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)    |
|                    | lymphocytic infiltration |                         | 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)   | 1<br>( 2) | 0<br>( 0) | 0<br>( 0)    |
|                    | granulation              |                         | 12<br>( 24) | 7<br>( 14) | 2<br>( 4) | 0<br>( 0) | 14<br>( 28) | 8<br>( 16) | 6<br>( 12) | 0<br>( 0) | 13<br>( 26) | 8<br>( 16) | 3<br>( 6) | 0<br>( 0)   | 4<br>( 8)   | 1<br>( 2) | 1<br>( 2) | 0<br>( 0) ** |
|                    | inflammatory cell nest   |                         | 1<br>( 2)   | 3<br>( 6)  | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)   | 1<br>( 2)  | 0<br>( 0)  | 0<br>( 0) | 3<br>( 6)   | 0<br>( 0)  | 0<br>( 0) | 0<br>( 0)   | 0<br>( 0)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)    |
|                    | clear 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) | 0<br>( 0)   | 0<br>( 0)  | 0<br>( 0) | 0<br>( 0)   | 0<br>( 0)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)    |
|                    | basophilic cell focus    |                         | 14<br>( 28) | 8<br>( 16) | 0<br>( 0) | 0<br>( 0) | 7<br>( 14)  | 9<br>( 18) | 0<br>( 0)  | 0<br>( 0) | 4<br>( 8)   | 7<br>( 14) | 0<br>( 0) | 0<br>( 0) * | 3<br>( 6)   | 2<br>( 4) | 0<br>( 0) | 0<br>( 0) ** |

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 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 25

| Organ              | Findings               | Group Name<br>No. of Animals on Study<br>Grade | Control |      |      |      | 10 ppm |      |      |      | 30 ppm |      |      |      | 90 ppm |      |      |      |
|--------------------|------------------------|--|---------|------|------|------|--------|------|------|------|--------|------|------|------|--------|------|------|------|
|                    |                        |  | 50      |      |      |      | 50     |      |      |      | 50     |      |      |      | 50     |      |      |      |
|                    |                        |  | 1       | 2    | 3    | 4    | 1      | 2    | 3    | 4    | 1      | 2    | 3    | 4    | 1      | 2    | 3    | 4    |
|                    |                        |  | (%)     | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  |
| {Digestive system} |                        |  |         |      |      |      |        |      |      |      |        |      |      |      |        |      |      |      |
| liver              | bile duct hyperplasia  |  | <50>    |      |      |      | <50>   |      |      |      | <50>   |      |      |      | <50>   |      |      |      |
|                    |                        |  | 7       | 2    | 0    | 0    | 4      | 2    | 0    | 0    | 7      | 4    | 0    | 0    | 4      | 0    | 0    | 0    |
|                    |                        |  | ( 14)   | ( 4) | ( 0) | ( 0) | ( 8)   | ( 4) | ( 0) | ( 0) | ( 14)  | ( 8) | ( 0) | ( 0) | ( 8)   | ( 0) | ( 0) | ( 0) |
| pancreas           | atrophy                |  | <50>    |      |      |      | <50>   |      |      |      | <50>   |      |      |      | <50>   |      |      |      |
|                    |                        |  | 2       | 2    | 0    | 0    | 1      | 2    | 0    | 0    | 1      | 2    | 0    | 0    | 1      | 2    | 1    | 0    |
|                    |                        |  | ( 4)    | ( 4) | ( 0) | ( 0) | ( 2)   | ( 4) | ( 0) | ( 0) | ( 2)   | ( 4) | ( 0) | ( 0) | ( 2)   | ( 4) | ( 2) | ( 0) |
| {Urinary system}   |                        |  |         |      |      |      |        |      |      |      |        |      |      |      |        |      |      |      |
| kidney             | hyaline droplet        |  | <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) |
|                    | deposit of hemosiderin |  | 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) |
|                    | inflammatory cell nest |  | 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) |
|                    | chronic nephropathy    |  | 9       | 4    | 0    | 0    | 18     | 3    | 1    | 0    | 16     | 4    | 2    | 0    | 1      | 0    | 0    | 0 ** |
|                    |                        |  | ( 18)   | ( 8) | ( 0) | ( 0) | ( 36)  | ( 6) | ( 2) | ( 0) | ( 32)  | ( 8) | ( 4) | ( 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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

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

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| Organ              | Findings                                    | Group Name<br>No. of Animals on Study |       |       |       | Control |       |       |       | 10 ppm |       |       |       | 30 ppm |       |       |       | 90 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>   |       |       |       |
|                    | hydronephrosis                              | 0                                     | 1     | 0     | 0     | 0       | 0     | 0     | 0     | 1      | 1     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     |
|                    |   | ( 0 )                                 | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                    | mineralization:cortico-medullary junction   | 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 ) |
| urine bladder      | mineralization:papilla                      | 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 ) |
|                    | mineralization:pelvis                       | 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 ) |
|                    | mineralization:cortex                       | 0                                     | 0     | 0     | 0     | 1       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 2      | 0     | 0     | 0     |
|                    |   | ( 0 )                                 | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )  | ( 0 ) | ( 0 ) | ( 0 ) |
| urine bladder      |   | <50>                                  |       |       |       | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |       |       |       |
|                    | nodular hyperplasia:transitional epithelium | 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 ) |
| {Endocrine system} |   |                                       |       |       |       |         |       |       |       |        |       |       |       |        |       |       |       |        |       |       |       |
| pituitary          |   | <50>                                  |       |       |       | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |       |       |       |
|                    | angiectasis                                 | 0                                     | 0     | 0     | 0     | 2       | 1     | 0     | 0     | 0      | 1     | 0     | 0     | 0      | 1     | 0     | 0     | 0      | 1     | 0     | 0     |
|                    |   | ( 0 )                                 | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )   | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 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



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

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| Organ              | Findings                          | Group Name<br>No. of Animals on Study<br>Grade | Control     |            |            |             | 10 ppm      |              |            |             | 30 ppm      |             |            |            | 90 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>(%)   |
| {Endocrine system} |                                   |  |             |            |            |             |             |              |            |             |             |             |            |            |              |            |            |            |
| pituitary          | cyst                              |  | <50>        |            |            |             | <50>        |              |            |             | <50>        |             |            |            | <50>         |            |            |            |
|                    |                                   | 2<br>( 4 )                                     | 9<br>( 18 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )  | 5<br>( 10 ) | 0<br>( 0 )   | 0<br>( 0 ) | 1<br>( 2 )  | 9<br>( 18 ) | 0<br>( 0 )  | 0<br>( 0 ) | 0<br>( 0 ) | 10<br>( 20 ) | 0<br>( 0 ) | 0<br>( 0 ) |            |
|                    |                                   |  |             |            |            |             |             |              |            |             |             |             |            |            |              |            |            |            |
|                    | hyperplasia                       |  | 0<br>( 0 )  | 4<br>( 8 ) | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 )  | 11<br>( 22 ) | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 )  | 5<br>( 10 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )   | 4<br>( 8 ) | 0<br>( 0 ) | 0<br>( 0 ) |
|                    |                                   |  |             |            |            |             |             |              |            |             |             |             |            |            |              |            |            |            |
|                    |                                   |  |             |            |            |             |             |              |            |             |             |             |            |            |              |            |            |            |
|                    | Rathke pouch                      |  | 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 ) |
|                    |                                   |  |             |            |            |             |             |              |            |             |             |             |            |            |              |            |            |            |
|                    |                                   |  |             |            |            |             |             |              |            |             |             |             |            |            |              |            |            |            |
| thyroid            | C-cell hyperplasia                |  | <50>        |            |            |             | <50>        |              |            |             | <50>        |             |            |            | <50>         |            |            |            |
|                    |                                   | 6<br>( 12 )                                    | 4<br>( 8 )  | 0<br>( 0 ) | 0<br>( 0 ) | 7<br>( 14 ) | 2<br>( 4 )  | 0<br>( 0 )   | 0<br>( 0 ) | 7<br>( 14 ) | 4<br>( 8 )  | 0<br>( 0 )  | 0<br>( 0 ) | 1<br>( 2 ) | 2<br>( 4 )   | 0<br>( 0 ) | 0<br>( 0 ) |            |
|                    |                                   |  |             |            |            |             |             |              |            |             |             |             |            |            |              |            |            |            |
|                    | focal follicular cell hyperplasia |  | 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 )   | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |
|                    |                                   |  |             |            |            |             |             |              |            |             |             |             |            |            |              |            |            |            |
|                    |                                   |  |             |            |            |             |             |              |            |             |             |             |            |            |              |            |            |            |
| adrenal            | peliosis-like lesion              |  | <50>        |            |            |             | <50>        |              |            |             | <50>        |             |            |            | <50>         |            |            |            |
|                    |                                   | 0<br>( 0 )                                     | 2<br>( 4 )  | 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 ) | 5<br>( 10 )  | 0<br>( 0 ) | 0<br>( 0 ) |            |
|                    |                                   |  |             |            |            |             |             |              |            |             |             |             |            |            |              |            |            |            |
|                    | hyperplasia:cortical cell         |  | 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 ) |
|                    |                                   |  |             |            |            |             |             |              |            |             |             |             |            |            |              |            |            |            |
|                    |                                   |  |             |            |            |             |             |              |            |             |             |             |            |            |              |            |            |            |

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 < a > a : Number of animals examined at the site  
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 ( c ) c : b / a \* 100  
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ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
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SEX : FEMALE

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

PAGE : 28

| Organ                 | Findings                       | Group Name              | Control |        |       |       | 10 ppm |        |       |       | 30 ppm |       |       |       | 90 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     |
|                       |                                |                         | (%)     | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   |
| {Endocrine system}    |                                |                         |         |        |       |       |        |        |       |       |        |       |       |       |        |       |       |       |
| adrenal               |                                |                         | <50>    |        |       |       | <50>   |        |       |       | <50>   |       |       |       | <50>   |       |       |       |
|                       | hyperplasia:medulla            |                         | 0       | 2      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 1     | 0     | 0     |
|                       |                                |                         | ( 0 )   | ( 4 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) |       |
|                       | focal fatty change:cortex      |                         | 0       | 5      | 0     | 0     | 0      | 5      | 0     | 0     | 0      | 3     | 0     | 0     | 3      | 4     | 0     | 0     |
|                       |                                |                         | ( 0 )   | ( 10 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 10 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 6 ) | ( 0 ) | ( 0 ) | ( 6 )  | ( 8 ) | ( 0 ) | ( 0 ) |
| {Reproductive system} |                                |                         |         |        |       |       |        |        |       |       |        |       |       |       |        |       |       |       |
| uterus                |                                |                         | <50>    |        |       |       | <50>   |        |       |       | <50>   |       |       |       | <50>   |       |       |       |
|                       | hyperplasia:epithelium         |                         | 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 ) |       |
|                       | hyperplasia:gland              |                         | 0       | 0      | 0     | 0     | 0      | 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 ) |
|                       | cystic endometrial hyperplasia |                         | 1       | 0      | 0     | 0     | 2      | 1      | 0     | 0     | 0      | 0     | 0     | 0     | 2      | 2     | 0     | 0     |
|                       |                                |                         | ( 2 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 4 )  | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )  | ( 4 ) | ( 0 ) | ( 0 ) |
| mammary gl            |                                |                         | <50>    |        |       |       | <50>   |        |       |       | <50>   |       |       |       | <50>   |       |       |       |
|                       | hyperplasia                    |                         | 0       | 0      | 0     | 0     | 1      | 0      | 0     | 0     | 2      | 0     | 1     | 0     | 0      | 0     | 0     | 0     |
|                       |                                |                         | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 4 )  | ( 0 ) | ( 2 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |

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

PAGE : 29

|                                  |                           | Group Name              | Control |       |       |       | 10 ppm |       |       |       | 30 ppm |       |       |       | 90 ppm |       |       |       |
|----------------------------------|---------------------------|-------------------------|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
|                                  |                           | No. of Animals on Study | 50      |       |       |       | 50     |       |       |       | 50     |       |       |       | 50     |       |       |       |
| Organ                            | Findings                  | Grade                   | 1       | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     |
|                                  |                           |                         | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   |
| {Nervous system}                 |                           |                         |         |       |       |       |        |       |       |       |        |       |       |       |        |       |       |       |
| brain                            | hemorrhage                |                         | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |       |       |       |
|                                  |                           |                         | 2       | 0     | 0     | 0     | 0      | 1     | 0     | 0     | 0      | 0     | 0     | 0     | 2      | 0     | 0     | 0     |
|                                  |                           |                         | ( 4 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                                  | necrosis:focal            |                         | 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 )  | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 ) | ( 0 ) | ( 0 ) |
|                                  | inflammatory infiltration |                         | 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 ) |       |
| spinal cord                      | gliosis                   |                         | <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 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) |
| {Special sense organs/appendage} |                           |                         |         |       |       |       |        |       |       |       |        |       |       |       |        |       |       |       |
| eye                              | hemorrhage                |                         | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |       |       |       |
|                                  |                           |                         | 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 ) | ( 2 )  | ( 2 ) | ( 0 ) | ( 0 ) |
| inflammation                     |                           | 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 ) | ( 2 ) | ( 0 ) |

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ALL ANIMALS (0-105W)

PAGE : 30

|                                  |                           | Group Name              | Control |      |      |      | 10 ppm |      |      |      | 30 ppm |      |      |      | 90 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/>                            |                           |                         |         |      |      |      |        |      |      |      |        |      |      |      |        |       |      |      |
| {Special sense organs/appendage} |                           |                         |         |      |      |      |        |      |      |      |        |      |      |      |        |       |      |      |
| eye                              |                           |                         | <50>    |      |      |      | <50>   |      |      |      | <50>   |      |      |      | <50>   |       |      |      |
|                                  | cataract                  |                         | 2       | 2    | 0    | 0    | 1      | 3    | 0    | 0    | 0      | 2    | 0    | 0    | 0      | 2     | 0    | 0    |
|                                  |                           |                         | ( 4)    | ( 4) | ( 0) | ( 0) | ( 2)   | ( 6) | ( 0) | ( 0) | ( 0)   | ( 4) | ( 0) | ( 0) | ( 0)   | ( 4)  | ( 0) | ( 0) |
|                                  | retinal atrophy           |                         | 37      | 1    | 4    | 0    | 44     | 0    | 4    | 0    | 42     | 0    | 2    | 0    | 28     | 0     | 3    | 0    |
|                                  |                           |                         | ( 74)   | ( 2) | ( 8) | ( 0) | ( 88)  | ( 0) | ( 8) | ( 0) | ( 84)  | ( 0) | ( 4) | ( 0) | ( 56)  | ( 0)  | ( 6) | ( 0) |
|                                  | keratitis                 |                         | 1       | 1    | 0    | 0    | 0      | 0    | 0    | 0    | 1      | 0    | 0    | 0    | 10     | 12    | 1    | 2 ** |
|                                  |                           |                         | ( 2)    | ( 2) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 2)   | ( 0) | ( 0) | ( 0) | ( 20)  | ( 24) | ( 2) | ( 4) |
|                                  | iritis                    |                         | 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>   |      |      |      | <50>   |      |      |      | <50>   |       |      |      |
|                                  | degeneration              |                         | 3       | 0    | 0    | 0    | 2      | 1    | 0    | 0    | 2      | 0    | 0    | 0    | 0      | 1     | 0    | 0    |
|                                  |                           |                         | ( 6)    | ( 0) | ( 0) | ( 0) | ( 4)   | ( 2) | ( 0) | ( 0) | ( 4)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 2)  | ( 0) | ( 0) |
|                                  | inflammatory infiltration |                         | 0       | 0    | 0    | 0    | 2      | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 1      | 0     | 0    | 0    |
|                                  |                           |                         | ( 0)    | ( 0) | ( 0) | ( 0) | ( 4)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 2)   | ( 0)  | ( 0) | ( 0) |
|                                  | lymphocytic infiltration  |                         | 4       | 0    | 0    | 0    | 2      | 0    | 0    | 0    | 6      | 0    | 0    | 0    | 3      | 0     | 0    | 0    |
|                                  |                           |                         | ( 8)    | ( 0) | ( 0) | ( 0) | ( 4)   | ( 0) | ( 0) | ( 0) | ( 12)  | ( 0) | ( 0) | ( 0) | ( 6)   | ( 0)  | ( 0) | ( 0) |
|                                  | granulation               |                         | 3       | 0    | 0    | 0    | 5      | 0    | 0    | 0    | 3      | 0    | 0    | 0    | 1      | 0     | 0    | 0    |
|                                  |                           |                         | ( 6)    | ( 0) | ( 0) | ( 0) | ( 10)  | ( 0) | ( 0) | ( 0) | ( 6)   | ( 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 ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 31

| Organ | Findings | Group Name              | Control |     |     |     | 10 ppm |     |     |     | 30 ppm |     |     |     | 90 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   |
|       |          |                         | (%)     | (%) | (%) | (%) | (%)    | (%) | (%) | (%) | (%)    | (%) | (%) | (%) | (%)    | (%) | (%) | (%) |

{Special sense organs/appendage}

|            |              |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
|------------|--------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| nasolacr d | inflammation | <50>  |       |       |       | <50>  |       |       |       | <50>  |       |       |       | <50>  |       |       |       |
|            |              | 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 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) |

{Musculoskeletal system}

|      |                |        |       |       |       |       |       |       |       |        |       |       |       |        |       |       |       |
|------|----------------|--------|-------|-------|-------|-------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
| bone | osteosclerosis | <50>   |       |       |       | <50>  |       |       |       | <50>   |       |       |       | <50>   |       |       |       |
|      |                | 5      | 3     | 0     | 0     | 1     | 1     | 0     | 0     | 6      | 2     | 0     | 0     | 5      | 2     | 0     | 0     |
|      |                | ( 10 ) | ( 6 ) | ( 0 ) | ( 0 ) | ( 2 ) | ( 2 ) | ( 0 ) | ( 0 ) | ( 12 ) | ( 4 ) | ( 0 ) | ( 0 ) | ( 10 ) | ( 4 ) | ( 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. : 0437  
 ANIMAL : RAT F344/DuCrIj[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 15

|                      |   | Group Name              | Control |       |       |      | 10 ppm |       |      |      | 30 ppm |       |      |      | 90 ppm |       |      |      |
|----------------------|---|-------------------------|---------|-------|-------|------|--------|-------|------|------|--------|-------|------|------|--------|-------|------|------|
|                      |   | No. of Animals on Study | 10      |       |       |      | 5      |       |      |      | 9      |       |      |      | 35     |       |      |      |
| Organ                | Findings  | Grade                   | 1       | 2     | 3     | 4    | 1      | 2     | 3    | 4    | 1      | 2     | 3    | 4    | 1      | 2     | 3    | 4    |
|                      |   |                         | (%)     | (%)   | (%)   | (%)  | (%)    | (%)   | (%)  | (%)  | (%)    | (%)   | (%)  | (%)  | (%)    | (%)   | (%)  | (%)  |
| {Respiratory system} |   |                         |         |       |       |      |        |       |      |      |        |       |      |      |        |       |      |      |
| nasal cavit          |   |                         | <10>    |       |       |      | < 5>   |       |      |      | < 9>   |       |      |      | <35>   |       |      |      |
|                      | squamous cell hyperplasia with atypia           |                         | 0       | 0     | 0     | 0    | 0      | 0     | 0    | 0    | 0      | 0     | 0    | 0    | 5      | 21    | 0    | 0 ** |
|                      |   |                         | ( 0)    | ( 0)  | ( 0)  | ( 0) | ( 0)   | ( 0)  | ( 0) | ( 0) | ( 0)   | ( 0)  | ( 0) | ( 0) | ( 14)  | ( 60) | ( 0) | ( 0) |
|                      | eosinophilic change:olfactory epithelium        |                         | 1       | 7     | 1     | 0    | 1      | 4     | 0    | 0    | 2      | 7     | 0    | 0    | 7      | 13    | 0    | 0 *  |
|                      |   |                         | ( 10)   | ( 70) | ( 10) | ( 0) | ( 20)  | ( 80) | ( 0) | ( 0) | ( 22)  | ( 78) | ( 0) | ( 0) | ( 20)  | ( 37) | ( 0) | ( 0) |
|                      | eosinophilic change:respiratory epithelium      |                         | 2       | 0     | 0     | 0    | 1      | 0     | 0    | 0    | 0      | 0     | 0    | 0    | 0      | 0     | 0    | 0    |
|                      |   |                         | ( 20)   | ( 0)  | ( 0)  | ( 0) | ( 20)  | ( 0)  | ( 0) | ( 0) | ( 0)   | ( 0)  | ( 0) | ( 0) | ( 0)   | ( 0)  | ( 0) | ( 0) |
|                      | inflammation:foreign body                       |                         | 0       | 0     | 0     | 0    | 1      | 0     | 0    | 0    | 0      | 0     | 0    | 0    | 0      | 0     | 0    | 0    |
|                      |   |                         | ( 0)    | ( 0)  | ( 0)  | ( 0) | ( 20)  | ( 0)  | ( 0) | ( 0) | ( 0)   | ( 0)  | ( 0) | ( 0) | ( 0)   | ( 0)  | ( 0) | ( 0) |
|                      | inflammation:respiratory epithelium             |                         | 0       | 0     | 0     | 0    | 0      | 0     | 0    | 0    | 0      | 0     | 0    | 0    | 5      | 13    | 0    | 0 *  |
|                      |   |                         | ( 0)    | ( 0)  | ( 0)  | ( 0) | ( 0)   | ( 0)  | ( 0) | ( 0) | ( 0)   | ( 0)  | ( 0) | ( 0) | ( 14)  | ( 37) | ( 0) | ( 0) |
|                      | respiratory metaplasia:olfactory epithelium     |                         | 0       | 0     | 0     | 0    | 0      | 0     | 0    | 0    | 1      | 0     | 0    | 0    | 2      | 0     | 0    | 0    |
|                      |   |                         | ( 0)    | ( 0)  | ( 0)  | ( 0) | ( 0)   | ( 0)  | ( 0) | ( 0) | ( 11)  | ( 0)  | ( 0) | ( 0) | ( 6)   | ( 0)  | ( 0) | ( 0) |
|                      | respiratory metaplasia:gland                    |                         | 1       | 1     | 0     | 0    | 3      | 0     | 0    | 0    | 2      | 1     | 0    | 0    | 6      | 4     | 0    | 0    |
|                      |   |                         | ( 10)   | ( 10) | ( 0)  | ( 0) | ( 60)  | ( 0)  | ( 0) | ( 0) | ( 22)  | ( 11) | ( 0) | ( 0) | ( 17)  | ( 11) | ( 0) | ( 0) |
|                      | squamous cell metaplasia:respiratory epithelium |                         | 0       | 0     | 0     | 0    | 0      | 0     | 0    | 0    | 4      | 0     | 0    | 0    | 1      | 28    | 0    | 0 ** |
|                      |   |                         | ( 0)    | ( 0)  | ( 0)  | ( 0) | ( 0)   | ( 0)  | ( 0) | ( 0) | ( 44)  | ( 0)  | ( 0) | ( 0) | ( 3)   | ( 80) | ( 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. : 0437  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 16

|                        |   | Group Name              | Control |       |      |      | 10 ppm |      |      |      | 30 ppm |       |      |      | 90 ppm |       |      |      |
|------------------------|---|-------------------------|---------|-------|------|------|--------|------|------|------|--------|-------|------|------|--------|-------|------|------|
|                        |   | No. of Animals on Study | 10      |       |      |      | 5      |      |      |      | 9      |       |      |      | 35     |       |      |      |
| Organ                  | Findings                                      | Grade                   | 1       | 2     | 3    | 4    | 1      | 2    | 3    | 4    | 1      | 2     | 3    | 4    | 1      | 2     | 3    | 4    |
|                        |   |                         | (%)     | (%)   | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  | (%)    | (%)   | (%)  | (%)  | (%)    | (%)   | (%)  | (%)  |
| {Respiratory system}   |   |                         |         |       |      |      |        |      |      |      |        |       |      |      |        |       |      |      |
| nasal cavit            |   |                         | <10>    |       |      |      | < 5>   |      |      |      | < 9>   |       |      |      | <35>   |       |      |      |
|                        | squamous cell metaplasia:olfactory epithelium |                         | 0       | 0     | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0     | 0    | 0    | 7      | 0     | 0    | 0    |
|                        |   |                         | ( 0)    | ( 0)  | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0)  | ( 0) | ( 0) | ( 20)  | ( 0)  | ( 0) | ( 0) |
|                        | hyperplasia:transitional epithelium           |                         | 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) | ( 0)   | ( 0)  | ( 0) | ( 0) |
|                        | atrophy:olfactory epithelium                  |                         | 0       | 0     | 0    | 0    | 0      | 0    | 0    | 0    | 1      | 0     | 0    | 0    | 12     | 6     | 0    | 0 *  |
|                        |   |                         | ( 0)    | ( 0)  | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 11)  | ( 0)  | ( 0) | ( 0) | ( 34)  | ( 17) | ( 0) | ( 0) |
| lung                   |   |                         | <10>    |       |      |      | < 5>   |      |      |      | < 9>   |       |      |      | <35>   |       |      |      |
|                        | congestion                                    |                         | 0       | 1     | 0    | 0    | 0      | 0    | 0    | 0    | 1      | 0     | 0    | 0    | 0      | 2     | 0    | 0    |
|                        |   |                         | ( 0)    | ( 10) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 11)  | ( 0)  | ( 0) | ( 0) | ( 0)   | ( 6)  | ( 0) | ( 0) |
|                        | hemorrhage                                    |                         | 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) | ( 6)   | ( 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)   | ( 3)  | ( 0) | ( 0) |
|                        | inflammation:foreign body                     |                         | 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)   | ( 11) | ( 0) | ( 0) |
| {Hematopoietic system} |   |                         |         |       |      |      |        |      |      |      |        |       |      |      |        |       |      |      |
| bone marrow            |   |                         | <10>    |       |      |      | < 5>   |      |      |      | < 9>   |       |      |      | <35>   |       |      |      |
|                        | granulation                                   |                         | 1       | 0     | 0    | 0    | 1      | 0    | 0    | 0    | 0      | 1     | 0    | 0    | 4      | 0     | 0    | 0    |
|                        |   |                         | ( 10)   | ( 0)  | ( 0) | ( 0) | ( 20)  | ( 0) | ( 0) | ( 0) | ( 0)   | ( 11) | ( 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 ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square



STUDY NO. : 0437  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 17

| Organ                  | Findings                               | Group Name<br>No. of Animals on Study<br>Grade | Control |       |      |      | 10 ppm |       |       |      | 30 ppm |       |       |      | 90 ppm |       |      |      |
|------------------------|--|--|---------|-------|------|------|--------|-------|-------|------|--------|-------|-------|------|--------|-------|------|------|
|                        |  |  | 10      |       |      |      | 5      |       |       |      | 9      |       |       |      | 35     |       |      |      |
|                        |  |  | 1       | 2     | 3    | 4    | 1      | 2     | 3     | 4    | 1      | 2     | 3     | 4    | 1      | 2     | 3    | 4    |
|                        |  |  | (%)     | (%)   | (%)  | (%)  | (%)    | (%)   | (%)   | (%)  | (%)    | (%)   | (%)   | (%)  | (%)    | (%)   | (%)  | (%)  |
| {Hematopoietic system} |  |  |         |       |      |      |        |       |       |      |        |       |       |      |        |       |      |      |
| bone marrow            | increased hematopoiesis                |  | <10>    |       |      |      | < 5>   |       |       |      | < 9>   |       |       |      | <35>   |       |      |      |
|                        |  |  | 3       | 0     | 0    | 0    | 1      | 0     | 0     | 0    | 3      | 0     | 0     | 0    | 3      | 0     | 0    | 0    |
|                        |  |  | ( 30)   | ( 0)  | ( 0) | ( 0) | ( 20)  | ( 0)  | ( 0)  | ( 0) | ( 33)  | ( 0)  | ( 0)  | ( 0) | ( 9)   | ( 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)  | ( 0) | ( 3)   | ( 0)  | ( 0) | ( 0) |
| spleen                 | congestion                             |  | <10>    |       |      |      | < 5>   |       |       |      | < 9>   |       |       |      | <35>   |       |      |      |
|                        |  |  | 0       | 1     | 0    | 0    | 0      | 0     | 0     | 0    | 0      | 0     | 0     | 0    | 0      | 1     | 0    | 0    |
|                        |  |  | ( 0)    | ( 10) | ( 0) | ( 0) | ( 0)   | ( 0)  | ( 0)  | ( 0) | ( 0)   | ( 0)  | ( 0)  | ( 0) | ( 0)   | ( 3)  | ( 0) | ( 0) |
|                        | deposit of hemosiderin                 |  | 0       | 2     | 0    | 0    | 0      | 0     | 0     | 0    | 0      | 2     | 0     | 0    | 0      | 3     | 0    | 0    |
|                        |  |  | ( 0)    | ( 20) | ( 0) | ( 0) | ( 0)   | ( 0)  | ( 0)  | ( 0) | ( 0)   | ( 22) | ( 0)  | ( 0) | ( 0)   | ( 9)  | ( 0) | ( 0) |
|                        | increased extramedullary hematopoiesis |  | 0       | 1     | 0    | 0    | 0      | 2     | 1     | 0    | 0      | 1     | 2     | 0    | 0      | 4     | 0    | 0    |
|                        |  |  | ( 0)    | ( 10) | ( 0) | ( 0) | ( 0)   | ( 40) | ( 20) | ( 0) | ( 0)   | ( 11) | ( 22) | ( 0) | ( 0)   | ( 11) | ( 0) | ( 0) |
| {Circulatory system}   |  |  |         |       |      |      |        |       |       |      |        |       |       |      |        |       |      |      |
| heart                  | thrombus                               |  | <10>    |       |      |      | < 5>   |       |       |      | < 9>   |       |       |      | <35>   |       |      |      |
|                        |  |  | 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) |

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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 18

| Organ                | Findings               | Group Name<br>No. of Animals on Study<br>Grade | Control |       |      |      | 10 ppm |      |      |      | 30 ppm |      |      |      | 90 ppm |      |      |      |
|----------------------|------------------------|--|---------|-------|------|------|--------|------|------|------|--------|------|------|------|--------|------|------|------|
|                      |                        |  | 10      |       |      |      | 5      |      |      |      | 9      |      |      |      | 35     |      |      |      |
|                      |                        |  | 1       | 2     | 3    | 4    | 1      | 2    | 3    | 4    | 1      | 2    | 3    | 4    | 1      | 2    | 3    | 4    |
|                      |                        |  | (%)     | (%)   | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  |
| {Circulatory system} |                        |  |         |       |      |      |        |      |      |      |        |      |      |      |        |      |      |      |
| heart                |                        |  | <10>    |       |      |      | < 5>   |      |      |      | < 9>   |      |      |      | <35>   |      |      |      |
|                      | necrosis:focal         |  | 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) |
|                      | mineralization         |  | 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) |
|                      | 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) | ( 3)   | ( 0) | ( 0) | ( 0) |
|                      | inflammatory cell nest |  | 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) |
|                      | myocardial fibrosis    |  | 3       | 1     | 0    | 0    | 3      | 0    | 0    | 0    | 6      | 0    | 0    | 0    | 18     | 0    | 0    | 0    |
|                      |                        |  | ( 30)   | ( 10) | ( 0) | ( 0) | ( 60)  | ( 0) | ( 0) | ( 0) | ( 67)  | ( 0) | ( 0) | ( 0) | ( 51)  | ( 0) | ( 0) | ( 0) |

{Digestive system}

|         |                        |  |      |      |      |      |      |      |      |      |      |       |      |      |       |      |      |      |
|---------|------------------------|--|------|------|------|------|------|------|------|------|------|-------|------|------|-------|------|------|------|
| stomach |                        |  | <10> |      |      |      | < 5> |      |      |      | < 9> |       |      |      | <35>  |      |      |      |
|         | basal cell hyperplasia |  | 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) | ( 11) | ( 0) | ( 0) | ( 0) |
|         | erosion:forestomach    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1     | 0    | 0    | 3     | 0    | 0    | 0    |
|         |                        |  | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 9)  | ( 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. : 0437  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 19

| Organ              | Findings                  | Group Name              | Control |       |      |      | 10 ppm |       |       |      | 30 ppm |       |      |       | 90 ppm |      |      |      |
|--------------------|---------------------------|-------------------------|---------|-------|------|------|--------|-------|-------|------|--------|-------|------|-------|--------|------|------|------|
|                    |                           | No. of Animals on Study | 10      |       |      |      | 5      |       |       |      | 9      |       |      |       | 35     |      |      |      |
|                    |                           | Grade                   | 1       | 2     | 3    | 4    | 1      | 2     | 3     | 4    | 1      | 2     | 3    | 4     | 1      | 2    | 3    | 4    |
|                    |                           |                         | (%)     | (%)   | (%)  | (%)  | (%)    | (%)   | (%)   | (%)  | (%)    | (%)   | (%)  | (%)   | (%)    | (%)  | (%)  | (%)  |
| {Digestive system} |                           |                         |         |       |      |      |        |       |       |      |        |       |      |       |        |      |      |      |
| stomach            |                           |                         | <10>    |       |      |      | < 5>   |       |       |      | < 9>   |       |      |       | <35>   |      |      |      |
|                    | ulcer:forestomach         |                         | 0       | 2     | 0    | 0    | 0      | 1     | 1     | 0    | 0      | 2     | 0    | 0     | 2      | 3    | 0    | 0    |
|                    |                           |                         | ( 0)    | ( 20) | ( 0) | ( 0) | ( 0)   | ( 20) | ( 20) | ( 0) | ( 0)   | ( 22) | ( 0) | ( 0)  | ( 6)   | ( 9) | ( 0) | ( 0) |
|                    | hyperplasia:forestomach   |                         | 3       | 2     | 0    | 0    | 0      | 2     | 0     | 0    | 0      | 2     | 0    | 0     | 4      | 2    | 0    | 0    |
|                    |                           |                         | ( 30)   | ( 20) | ( 0) | ( 0) | ( 0)   | ( 40) | ( 0)  | ( 0) | ( 0)   | ( 22) | ( 0) | ( 0)  | ( 11)  | ( 6) | ( 0) | ( 0) |
|                    | erosion:glandular stomach |                         | 3       | 0     | 0    | 0    | 1      | 1     | 0     | 0    | 0      | 0     | 0    | 2     | 0      | 0    | 0    |      |
|                    |                           |                         | ( 30)   | ( 0)  | ( 0) | ( 0) | ( 20)  | ( 20) | ( 0)  | ( 0) | ( 0)   | ( 0)  | ( 0) | ( 6)  | ( 0)   | ( 0) | ( 0) |      |
|                    | ulcer:glandular stomach   |                         | 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) | ( 3)  | ( 3)   | ( 0) | ( 0) |      |
| small intes        |                           |                         | <10>    |       |      |      | < 5>   |       |       |      | < 9>   |       |      |       | <35>   |      |      |      |
|                    | erosion                   |                         | 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) |
| liver              |                           |                         | <10>    |       |      |      | < 5>   |       |       |      | < 9>   |       |      |       | <35>   |      |      |      |
|                    | herniation                |                         | 0       | 0     | 0    | 0    | 1      | 0     | 0     | 0    | 0      | 0     | 0    | 10    | 0      | 0    | 0    | 0    |
|                    |                           |                         | ( 0)    | ( 0)  | ( 0) | ( 0) | ( 20)  | ( 0)  | ( 0)  | ( 0) | ( 0)   | ( 0)  | ( 0) | ( 29) | ( 0)   | ( 0) | ( 0) | ( 0) |
|                    | necrosis:central          |                         | 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)  | ( 0)   | ( 0) | ( 0) | ( 0) |

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< 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

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REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 20

| Organ              | Findings                 | Group Name<br>No. of Animals on Study<br>Grade | Control |       |      |      | 10 ppm |      |      |      | 30 ppm |      |      |      | 90 ppm |      |      |      |
|--------------------|--------------------------|--|---------|-------|------|------|--------|------|------|------|--------|------|------|------|--------|------|------|------|
|                    |                          |  | 10      |       |      |      | 5      |      |      |      | 9      |      |      |      | 35     |      |      |      |
|                    |                          |  | 1       | 2     | 3    | 4    | 1      | 2    | 3    | 4    | 1      | 2    | 3    | 4    | 1      | 2    | 3    | 4    |
|                    |                          |  | (%)     | (%)   | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  |
| {Digestive system} |                          |  |         |       |      |      |        |      |      |      |        |      |      |      |        |      |      |      |
| liver              |                          |  |         |       |      |      |        |      |      |      |        |      |      |      |        |      |      |      |
|                    | fatty change:central     |  | <10>    |       |      |      | < 5>   |      |      |      | < 9>   |      |      |      | <35>   |      |      |      |
|                    |                          |  | 0       | 2     | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0    | 0    | 0    |
|                    |                          |  | ( 0)    | ( 20) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) |
|                    | lymphocytic 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)   | ( 3) | ( 0) | ( 0) |
|                    | granulation              |  | 1       | 1     | 0    | 0    | 0      | 0    | 0    | 0    | 2      | 0    | 0    | 0    | 0      | 0    | 1    | 0    |
|                    |                          |  | ( 10)   | ( 10) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 22)  | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 3) | ( 0) |
|                    | basophilic cell focus    |  | 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) | ( 3)   | ( 3) | ( 0) | ( 0) |
|                    | bile duct hyperplasia    |  | 2       | 0     | 0    | 0    | 0      | 0    | 0    | 0    | 1      | 0    | 0    | 0    | 1      | 0    | 0    | 0    |
|                    |                          |  | ( 20)   | ( 0)  | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 11)  | ( 0) | ( 0) | ( 0) | ( 3)   | ( 0) | ( 0) | ( 0) |
| pancreas           |                          |  |         |       |      |      |        |      |      |      |        |      |      |      |        |      |      |      |
|                    | atrophy                  |  | <10>    |       |      |      | < 5>   |      |      |      | < 9>   |      |      |      | <35>   |      |      |      |
|                    |                          |  | 1       | 0     | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 1    | 1    | 0    |
|                    |                          |  | ( 10)   | ( 0)  | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 3) | ( 3) | ( 0) |
| {Urinary system}   |                          |  |         |       |      |      |        |      |      |      |        |      |      |      |        |      |      |      |
| kidney             |                          |  |         |       |      |      |        |      |      |      |        |      |      |      |        |      |      |      |
|                    | inflammatory cell nest   |  | <10>    |       |      |      | < 5>   |      |      |      | < 9>   |      |      |      | <35>   |      |      |      |
|                    |                          |  | 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) |

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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 21

| Organ | Findings | Group Name<br>No. of Animals on Study<br>Grade | Control |     |     |     | 10 ppm |     |     |     | 30 ppm |     |     |     | 90 ppm |     |     |     |
|-------|----------|--|---------|-----|-----|-----|--------|-----|-----|-----|--------|-----|-----|-----|--------|-----|-----|-----|
|       |          |  | 10      |     |     |     | 5      |     |     |     | 9      |     |     |     | 35     |     |     |     |
|       |          |  | 1       | 2   | 3   | 4   | 1      | 2   | 3   | 4   | 1      | 2   | 3   | 4   | 1      | 2   | 3   | 4   |
|       |          |  | (%)     | (%) | (%) | (%) | (%)    | (%) | (%) | (%) | (%)    | (%) | (%) | (%) | (%)    | (%) | (%) | (%) |

{Urinary system}

|        |   |  |       |       |      |      |       |      |      |      |       |       |      |      |      |      |      |      |
|--------|---|--|-------|-------|------|------|-------|------|------|------|-------|-------|------|------|------|------|------|------|
| kidney |   |  | <10>  |       |      |      | < 5>  |      |      |      | < 9>  |       |      |      | <35> |      |      |      |
|        | chronic nephropathy                       |  | 1     | 2     | 0    | 0    | 2     | 0    | 0    | 0    | 0     | 1     | 0    | 0    | 1    | 0    | 0    | 0 *  |
|        |   |  | ( 10) | ( 20) | ( 0) | ( 0) | ( 40) | ( 0) | ( 0) | ( 0) | ( 0)  | ( 11) | ( 0) | ( 0) | ( 3) | ( 0) | ( 0) | ( 0) |
|        | hydronephrosis                            |  | 0     | 0     | 0    | 0    | 0     | 0    | 0    | 0    | 1     | 1     | 0    | 0    | 0    | 0    | 0    | 0    |
|        |   |  | ( 0)  | ( 0)  | ( 0) | ( 0) | ( 0)  | ( 0) | ( 0) | ( 0) | ( 11) | ( 11) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
|        | mineralization:cortico-medullary junction |  | 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) |
|        | mineralization:pelvis                     |  | 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) |
|        | mineralization:cortex                     |  | 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) | ( 6) | ( 0) | ( 0) | ( 0) |

{Endocrine system}

|           |             |  |      |      |      |      |      |      |      |      |      |       |      |      |      |       |      |      |
|-----------|-------------|--|------|------|------|------|------|------|------|------|------|-------|------|------|------|-------|------|------|
| pituitary |             |  | <10> |      |      |      | < 5> |      |      |      | < 9> |       |      |      | <35> |       |      |      |
|           | angiectasis |  | 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) |
|           | cyst        |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1     | 0    | 0    | 0    | 7     | 0    | 0    |
|           |             |  | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 11) | ( 0) | ( 0) | ( 0) | ( 20) | ( 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

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

PAGE : 22

|                       |                                   | Group Name              | Control |        |       |       | 10 ppm |        |       |       | 30 ppm |        |       |       | 90 ppm |        |       |       |
|-----------------------|-----------------------------------|-------------------------|---------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|
|                       |                                   | No. of Animals on Study | 10      |        |       |       | 5      |        |       |       | 9      |        |       |       | 35     |        |       |       |
|                       |                                   | Grade                   | 1       | 2      | 3     | 4     | 1      | 2      | 3     | 4     | 1      | 2      | 3     | 4     | 1      | 2      | 3     | 4     |
| Organ                 | Findings                          |                         | (%)     | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   |
| {Endocrine system}    |                                   |                         |         |        |       |       |        |        |       |       |        |        |       |       |        |        |       |       |
| pituitary             |                                   |                         | <10>    |        |       |       | < 5>   |        |       |       | < 9>   |        |       |       | <35>   |        |       |       |
|                       | hyperplasia                       |                         | 0       | 1      | 0     | 0     | 0      | 1      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 1      | 0     | 0     |
|                       |                                   |                         | ( 0 )   | ( 10 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 20 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 3 )  | ( 0 ) | ( 0 ) |
| thyroid               |                                   |                         | <10>    |        |       |       | < 5>   |        |       |       | < 9>   |        |       |       | <35>   |        |       |       |
|                       | C-cell hyperplasia                |                         | 1       | 0      | 0     | 0     | 0      | 1      | 0     | 0     | 0      | 1      | 0     | 0     | 0      | 0      | 0     | 0     |
|                       |                                   |                         | ( 10 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 20 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 11 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                       | focal follicular cell hyperplasia |                         | 0       | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 1      | 1      | 0     | 0     | 1      | 0      | 0     | 0     |
|                       |                                   |                         | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 11 ) | ( 11 ) | ( 0 ) | ( 0 ) | ( 3 )  | ( 0 )  | ( 0 ) | ( 0 ) |
| adrenal               |                                   |                         | <10>    |        |       |       | < 5>   |        |       |       | < 9>   |        |       |       | <35>   |        |       |       |
|                       | peliosis-like lesion              |                         | 0       | 1      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 1      | 0     | 0     | 0      | 5      | 0     | 0     |
|                       |                                   |                         | ( 0 )   | ( 10 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 11 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 14 ) | ( 0 ) | ( 0 ) |
|                       | focal fatty change:cortex         |                         | 0       | 1      | 0     | 0     | 0      | 0      | 0     | 0     | 1      | 0      | 0     | 2     | 3      | 0      | 0     |       |
|                       |                                   |                         | ( 0 )   | ( 10 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 11 ) | ( 0 )  | ( 0 ) | ( 6 ) | ( 9 )  | ( 0 )  | ( 0 ) |       |
| {Reproductive system} |                                   |                         |         |        |       |       |        |        |       |       |        |        |       |       |        |        |       |       |
| uterus                |                                   |                         | <10>    |        |       |       | < 5>   |        |       |       | < 9>   |        |       |       | <35>   |        |       |       |
|                       | cystic endometrial hyperplasia    |                         | 1       | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0     | 0     |
|                       |                                   |                         | ( 10 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |

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 < a > a : Number of animals examined at the site  
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DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 23

|                                  |                           | Group Name              | Control |      |      |      | 10 ppm |      |      |      | 30 ppm |       |      |      | 90 ppm |      |      |      |
|----------------------------------|---------------------------|-------------------------|---------|------|------|------|--------|------|------|------|--------|-------|------|------|--------|------|------|------|
|                                  |                           | No. of Animals on Study | 10      |      |      |      | 5      |      |      |      | 9      |       |      |      | 35     |      |      |      |
| Organ                            | Findings                  | Grade                   | 1       | 2    | 3    | 4    | 1      | 2    | 3    | 4    | 1      | 2     | 3    | 4    | 1      | 2    | 3    | 4    |
|                                  |                           |                         | (%)     | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  | (%)    | (%)   | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  |
| {Nervous system}                 |                           |                         |         |      |      |      |        |      |      |      |        |       |      |      |        |      |      |      |
| brain                            |                           |                         | <10>    |      |      |      | < 5>   |      |      |      | < 9>   |       |      |      | <35>   |      |      |      |
|                                  | hemorrhage                |                         | 2       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0     | 0    | 0    | 2      | 0    | 0    | 0    |
|                                  |                           |                         | ( 20)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0)  | ( 0) | ( 0) | ( 6)   | ( 0) | ( 0) | ( 0) |
|                                  | necrosis:focal            |                         | 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)   | ( 11) | ( 0) | ( 0) | ( 0)   | ( 3) | ( 0) | ( 0) |
|                                  | inflammatory infiltration |                         | 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) |
| {Special sense organs/appendage} |                           |                         |         |      |      |      |        |      |      |      |        |       |      |      |        |      |      |      |
| eye                              |                           |                         | <10>    |      |      |      | < 5>   |      |      |      | < 9>   |       |      |      | <35>   |      |      |      |
|                                  | hemorrhage                |                         | 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) | ( 3)   | ( 3) | ( 0) | ( 0) |
|                                  | inflammation              |                         | 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) |
|                                  | cataract                  |                         | 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) |
|                                  | retinal atrophy           |                         | 2       | 0    | 0    | 0    | 3      | 0    | 0    | 0    | 3      | 0     | 0    | 0    | 16     | 0    | 2    | 0    |
|                                  |                           |                         | ( 20)   | ( 0) | ( 0) | ( 0) | ( 60)  | ( 0) | ( 0) | ( 0) | ( 33)  | ( 0)  | ( 0) | ( 0) | ( 46)  | ( 0) | ( 6) | ( 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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 24

|                                  |                           | Group Name              | Control |        |       |       | 10 ppm |       |       |       | 30 ppm |        |       |       | 90 ppm |        |       |       |
|----------------------------------|---------------------------|-------------------------|---------|--------|-------|-------|--------|-------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|
|                                  |                           | No. of Animals on Study | 10      |        |       |       | 5      |       |       |       | 9      |        |       |       | 35     |        |       |       |
| Organ                            | Findings                  | Grade                   | 1       | 2      | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2      | 3     | 4     | 1      | 2      | 3     | 4     |
|                                  |                           |                         | (%)     | (%)    | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   |
| {Special sense organs/appendage} |                           |                         |         |        |       |       |        |       |       |       |        |        |       |       |        |        |       |       |
| eye                              |                           |                         | <10>    |        |       |       | < 5>   |       |       |       | < 9>   |        |       |       | <35>   |        |       |       |
|                                  | keratitis                 |                         | 0       | 1      | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0      | 0     | 0     | 10     | 10     | 1     | 2 *   |
|                                  |                           |                         | ( 0 )   | ( 10 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 29 ) | ( 29 ) | ( 3 ) | ( 6 ) |
| Harder gl                        |                           |                         | <10>    |        |       |       | < 5>   |       |       |       | < 9>   |        |       |       | <35>   |        |       |       |
|                                  | degeneration              |                         | 0       | 0      | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 1      | 0     | 0     |
|                                  |                           |                         | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 20 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 3 )  | ( 0 ) | ( 0 ) |
|                                  | inflammatory infiltration |                         | 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 ) |
|                                  | lymphocytic infiltration  |                         | 1       | 0      | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 0      | 0     | 0     | 0      | 0      | 0     | 0     |
|                                  |                           |                         | ( 10 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 11 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                                  | granulation               |                         | 0       | 0      | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0     | 0     |
|                                  |                           |                         | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 20 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |
| {Musculoskeletal system}         |                           |                         |         |        |       |       |        |       |       |       |        |        |       |       |        |        |       |       |
| bone                             |                           |                         | <10>    |        |       |       | < 5>   |       |       |       | < 9>   |        |       |       | <35>   |        |       |       |
|                                  | osteosclerosis            |                         | 0       | 1      | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 1      | 0     | 0     | 3      | 2      | 0     | 0     |
|                                  |                           |                         | ( 0 )   | ( 10 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 11 ) | ( 11 ) | ( 0 ) | ( 0 ) | ( 9 )  | ( 6 )  | ( 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 L 6

HISTOPATHOLOGICAL FINDINGS :  
NON-NEOPLASTIC LESIONS : FEMALE  
SACRIFICED ANIMALS

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 13

| Organ                            | Findings                                   | Control                 |        |        |       | 10 ppm |        |       |       | 30 ppm |        |       |       | 90 ppm |        |       |       |       |
|----------------------------------|--|-------------------------|--------|--------|-------|--------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|-------|
|                                  |  | No. of Animals on Study |        |        |       | 45     |        |       |       | 41     |        |       |       | 15     |        |       |       |       |
|                                  |  | Grade                   | 1      | 2      | 3     | 4      | 1      | 2     | 3     | 4      | 1      | 2     | 3     | 4      | 1      | 2     | 3     | 4     |
|                                  |  | (%)                     | (%)    | (%)    | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)   |
| {Integumentary system/appandage} |  |                         |        |        |       |        |        |       |       |        |        |       |       |        |        |       |       |       |
| skin/app                         |  | <40>                    |        |        |       | <45>   |        |       |       | <41>   |        |       |       | <15>   |        |       |       |       |
|                                  | angiectasis                                | 0                       | 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 ) |
|                                  | inflammation                               | 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 )  | ( 7 )  | ( 0 ) | ( 0 ) | ( 0 ) |
| {Respiratory system}             |  |                         |        |        |       |        |        |       |       |        |        |       |       |        |        |       |       |       |
| nasal cavit                      |  | <40>                    |        |        |       | <45>   |        |       |       | <41>   |        |       |       | <15>   |        |       |       |       |
|                                  | squamous cell hyperplasia with atypia      | 0                       | 0      | 0      | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 4      | 9      | 0     | 0 **  |       |
|                                  |  | ( 0 )                   | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 27 ) | ( 60 ) | ( 0 ) | ( 0 ) |       |
|                                  | eosinophilic change:olfactory epithelium   | 0                       | 28     | 12     | 0     | 1      | 42     | 2     | 0 **  | 1      | 39     | 1     | 0 **  | 3      | 12     | 0     | 0 **  |       |
|                                  |  | ( 0 )                   | ( 70 ) | ( 30 ) | ( 0 ) | ( 2 )  | ( 93 ) | ( 4 ) | ( 0 ) | ( 2 )  | ( 95 ) | ( 2 ) | ( 0 ) | ( 20 ) | ( 80 ) | ( 0 ) | ( 0 ) |       |
|                                  | eosinophilic change:respiratory epithelium | 20                      | 5      | 0      | 0     | 19     | 6      | 0     | 0     | 11     | 2      | 0     | 0 *   | 1      | 0      | 0     | 0 **  |       |
|                                  |  | ( 50 )                  | ( 13 ) | ( 0 )  | ( 0 ) | ( 42 ) | ( 13 ) | ( 0 ) | ( 0 ) | ( 27 ) | ( 5 )  | ( 0 ) | ( 0 ) | ( 7 )  | ( 0 )  | ( 0 ) | ( 0 ) |       |
|                                  | inflammation:foreign body                  | 3                       | 1      | 0      | 0     | 2      | 1      | 0     | 0     | 1      | 1      | 0     | 0     | 0      | 0      | 0     | 0     | 0     |
|                                  |  | ( 8 )                   | ( 3 )  | ( 0 )  | ( 0 ) | ( 4 )  | ( 2 )  | ( 0 ) | ( 0 ) | ( 2 )  | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                                  | inflammation:respiratory epithelium        | 0                       | 0      | 0      | 0     | 0      | 0      | 0     | 0     | 2      | 0      | 0     | 0     | 3      | 10     | 1     | 0 **  |       |
|                                  |  | ( 0 )                   | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 5 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 20 ) | ( 67 ) | ( 7 ) | ( 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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 14

|                      |   | Group Name              | Control |       |       |       | 10 ppm |       |       |       | 30 ppm |       |       |       | 90 ppm |        |       |       |
|----------------------|---|-------------------------|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|--------|-------|-------|
|                      |   | No. of Animals on Study | 40      |       |       |       | 45     |       |       |       | 41     |       |       |       | 15     |        |       |       |
| Organ                | Findings  | Grade                   | 1       | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2      | 3     | 4     |
|                      |   |                         | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   |
| {Respiratory system} |   |                         |         |       |       |       |        |       |       |       |        |       |       |       |        |        |       |       |
| nasal cavit          |   |                         | <40>    |       |       |       | <45>   |       |       |       | <41>   |       |       |       | <15>   |        |       |       |
|                      | inflammation:olfactory epithelium               |                         | 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 ) | ( 7 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                      | respiratory metaplasia:olfactory epithelium     |                         | 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 ) | ( 20 ) | ( 0 )  | ( 0 ) | ( 0 ) |
|                      | respiratory metaplasia:gland                    |                         | 15      | 2     | 0     | 0     | 21     | 1     | 0     | 0     | 19     | 0     | 0     | 0     | 8      | 1      | 0     | 0     |
|                      |   |                         | ( 38 )  | ( 5 ) | ( 0 ) | ( 0 ) | ( 47 ) | ( 2 ) | ( 0 ) | ( 0 ) | ( 46 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 53 ) | ( 7 )  | ( 0 ) | ( 0 ) |
|                      | squamous cell metaplasia:respiratory epithelium |                         | 0       | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 2      | 0     | 0     | 0     | 1      | 13     | 0     | 0 **  |
|                      |   |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 5 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 7 )  | ( 87 ) | ( 0 ) | ( 0 ) |
|                      | squamous cell metaplasia:olfactory epithelium   |                         | 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 ) | ( 7 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                      | hyperplasia:transitional epithelium             |                         | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 5      | 0     | 0     | 0     | 0      | 0      | 0     | 0     |
|                      |   |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 12 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                      | atrophy:olfactory epithelium                    |                         | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 9      | 2      | 0     | 0 **  |
|                      |   |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 60 ) | ( 13 ) | ( 0 ) | ( 0 ) |
| lung                 |   |                         | <40>    |       |       |       | <45>   |       |       |       | <41>   |       |       |       | <15>   |        |       |       |
|                      | inflammation                                    |                         | 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 )  | ( 7 )  | ( 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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 15

| Organ                  | Findings                              | Group Name<br>No. of Animals on Study<br>Grade | Control |       |       |       | 10 ppm |       |       |       | 30 ppm |       |       |       | 90 ppm |        |       |       |
|------------------------|---------------------------------------|--|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|--------|-------|-------|
|                        |                                       |  | 40      |       |       |       | 45     |       |       |       | 41     |       |       |       | 15     |        |       |       |
|                        |                                       |  | 1       | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2      | 3     | 4     |
|                        |                                       |  | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   |
| {Respiratory system}   |                                       |  |         |       |       |       |        |       |       |       |        |       |       |       |        |        |       |       |
| lung                   |                                       |  | <40>    |       |       |       | <45>   |       |       |       | <41>   |       |       |       | <15>   |        |       |       |
|                        | bronchiolar-alveolar cell hyperplasia |  | 0       | 1     | 0     | 0     | 1      | 1     | 0     | 0     | 1      | 2     | 0     | 0     | 1      | 0      | 0     | 0     |
|                        |                                       |  | ( 0 )   | ( 3 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 2 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 5 ) | ( 0 ) | ( 0 ) | ( 7 )  | ( 0 )  | ( 0 ) | ( 0 ) |
| {Hematopoietic system} |                                       |  |         |       |       |       |        |       |       |       |        |       |       |       |        |        |       |       |
| bone marrow            |                                       |  | <40>    |       |       |       | <45>   |       |       |       | <41>   |       |       |       | <15>   |        |       |       |
|                        | granulation                           |  | 13      | 1     | 0     | 0     | 14     | 4     | 0     | 0     | 15     | 2     | 0     | 0     | 6      | 0      | 0     | 0     |
|                        |                                       |  | ( 33 )  | ( 3 ) | ( 0 ) | ( 0 ) | ( 31 ) | ( 9 ) | ( 0 ) | ( 0 ) | ( 37 ) | ( 5 ) | ( 0 ) | ( 0 ) | ( 40 ) | ( 0 )  | ( 0 ) | ( 0 ) |
|                        | increased hematopoiesis               |  | 3       | 0     | 0     | 0     | 2      | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 2      | 0      | 0     | 0     |
|                        |                                       |  | ( 8 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 13 ) | ( 0 )  | ( 0 ) | ( 0 ) |
|                        | decreased hematopoiesis               |  | 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 ) | ( 0 ) |
| spleen                 |                                       |  | <40>    |       |       |       | <45>   |       |       |       | <40>   |       |       |       | <15>   |        |       |       |
|                        | congestion                            |  | 0       | 1     | 0     | 0     | 0      | 1     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0      | 0     | 0     |
|                        |                                       |  | ( 0 )   | ( 3 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                        | deposit of hemosiderin                |  | 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 )  | ( 3 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 13 ) | ( 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

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

PAGE : 16

|                        |  | Group Name              | Control |       |      |      | 10 ppm |      |      |      | 30 ppm |       |      |      | 90 ppm |       |      |      |
|------------------------|--|-------------------------|---------|-------|------|------|--------|------|------|------|--------|-------|------|------|--------|-------|------|------|
|                        |  | No. of Animals on Study | 40      |       |      |      | 45     |      |      |      | 41     |       |      |      | 15     |       |      |      |
| Organ                  | Findings                               | Grade                   | 1       | 2     | 3    | 4    | 1      | 2    | 3    | 4    | 1      | 2     | 3    | 4    | 1      | 2     | 3    | 4    |
|                        |  |                         | (%)     | (%)   | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  | (%)    | (%)   | (%)  | (%)  | (%)    | (%)   | (%)  | (%)  |
| {Hematopoietic system} |  |                         |         |       |      |      |        |      |      |      |        |       |      |      |        |       |      |      |
| spleen                 |  |                         | <40>    |       |      |      | <45>   |      |      |      | <40>   |       |      |      | <15>   |       |      |      |
|                        | granulation                            |                         | 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) |
|                        | fibrosis                               |                         | 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)   | ( 7)  | ( 0) | ( 0) |
|                        | increased extramedullary hematopoiesis |                         | 0       | 1     | 1    | 0    | 0      | 0    | 0    | 0    | 0      | 1     | 1    | 0    | 0      | 1     | 0    | 0    |
|                        |  |                         | ( 0)    | ( 3)  | ( 3) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 3)  | ( 3) | ( 0) | ( 0)   | ( 7)  | ( 0) | ( 0) |
| {Circulatory system}   |  |                         |         |       |      |      |        |      |      |      |        |       |      |      |        |       |      |      |
| heart                  |  |                         | <40>    |       |      |      | <45>   |      |      |      | <41>   |       |      |      | <15>   |       |      |      |
|                        | necrosis:focal                         |                         | 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) |
|                        | inflammatory cell nest                 |                         | 1       | 0     | 0    | 0    | 3      | 0    | 0    | 0    | 1      | 0     | 0    | 0    | 0      | 0     | 0    | 0    |
|                        |  |                         | ( 3)    | ( 0)  | ( 0) | ( 0) | ( 7)   | ( 0) | ( 0) | ( 0) | ( 2)   | ( 0)  | ( 0) | ( 0) | ( 0)   | ( 0)  | ( 0) | ( 0) |
|                        | myocardial fibrosis                    |                         | 27      | 4     | 0    | 0    | 28     | 3    | 0    | 0    | 28     | 5     | 0    | 0    | 7      | 2     | 0    | 0    |
|                        |  |                         | ( 68)   | ( 10) | ( 0) | ( 0) | ( 62)  | ( 7) | ( 0) | ( 0) | ( 68)  | ( 12) | ( 0) | ( 0) | ( 47)  | ( 13) | ( 0) | ( 0) |
|                        | subendocardial fibrosis                |                         | 1       | 0     | 0    | 0    | 3      | 0    | 0    | 0    | 2      | 0     | 0    | 0    | 0      | 0     | 0    | 0    |
|                        |  |                         | ( 3)    | ( 0)  | ( 0) | ( 0) | ( 7)   | ( 0) | ( 0) | ( 0) | ( 5)   | ( 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. : 0437  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 17

|                    |                           | Group Name              | Control |      |      |      | 10 ppm |      |      |      | 30 ppm |      |      |      | 90 ppm |      |      |      |
|--------------------|---------------------------|-------------------------|---------|------|------|------|--------|------|------|------|--------|------|------|------|--------|------|------|------|
|                    |                           | No. of Animals on Study | 40      |      |      |      | 45     |      |      |      | 41     |      |      |      | 15     |      |      |      |
| Organ              | Findings                  | Grade                   | 1       | 2    | 3    | 4    | 1      | 2    | 3    | 4    | 1      | 2    | 3    | 4    | 1      | 2    | 3    | 4    |
|                    |                           |                         | (%)     | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  |
| {Digestive system} |                           |                         |         |      |      |      |        |      |      |      |        |      |      |      |        |      |      |      |
| tongue             |                           |                         | <40>    |      |      |      | <45>   |      |      |      | <41>   |      |      |      | <15>   |      |      |      |
|                    | inflammatory infiltration |                         | 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) | ( 13)  | ( 0) | ( 0) | ( 0) |
|                    | arteritis                 |                         | 1       | 0    | 0    | 0    | 2      | 0    | 0    | 0    | 1      | 0    | 0    | 0    | 2      | 0    | 0    | 0    |
|                    |                           |                         | ( 3)    | ( 0) | ( 0) | ( 0) | ( 4)   | ( 0) | ( 0) | ( 0) | ( 2)   | ( 0) | ( 0) | ( 0) | ( 13)  | ( 0) | ( 0) | ( 0) |
| stomach            |                           |                         | <40>    |      |      |      | <45>   |      |      |      | <41>   |      |      |      | <15>   |      |      |      |
|                    | basal cell hyperplasia    |                         | 1       | 0    | 0    | 0    | 3      | 0    | 0    | 0    | 1      | 0    | 0    | 0    | 0      | 0    | 0    | 0    |
|                    |                           |                         | ( 3)    | ( 0) | ( 0) | ( 0) | ( 7)   | ( 0) | ( 0) | ( 0) | ( 2)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) |
|                    | erosion:forestomach       |                         | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 1      | 0    | 0    | 0    |
|                    |                           |                         | ( 0)    | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 7)   | ( 0) | ( 0) | ( 0) |
|                    | hyperplasia:forestomach   |                         | 1       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 2      | 0    | 0    | 0    |
|                    |                           |                         | ( 3)    | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 13)  | ( 0) | ( 0) | ( 0) |
|                    | erosion:glandular stomach |                         | 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) |
| liver              |                           |                         | <40>    |      |      |      | <45>   |      |      |      | <41>   |      |      |      | <15>   |      |      |      |
|                    | herniation                |                         | 9       | 0    | 0    | 0    | 9      | 0    | 0    | 0    | 6      | 0    | 0    | 0    | 2      | 0    | 0    | 0    |
|                    |                           |                         | ( 23)   | ( 0) | ( 0) | ( 0) | ( 20)  | ( 0) | ( 0) | ( 0) | ( 15)  | ( 0) | ( 0) | ( 0) | ( 13)  | ( 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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 18

| Organ              | Findings                 | Control                 |        |       |       | 10 ppm |        |        |       | 30 ppm |        |       |       | 90 ppm |       |       |       |
|--------------------|--------------------------|-------------------------|--------|-------|-------|--------|--------|--------|-------|--------|--------|-------|-------|--------|-------|-------|-------|
|                    |                          | No. of Animals on Study |        |       |       | Grade  |        |        |       | Grade  |        |       |       | Grade  |       |       |       |
|                    |                          | 1                       | 2      | 3     | 4     | 1      | 2      | 3      | 4     | 1      | 2      | 3     | 4     | 1      | 2     | 3     | 4     |
|                    |                          | (%)                     | (%)    | (%)   | (%)   | (%)    | (%)    | (%)    | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   |
| {Digestive system} |                          |                         |        |       |       |        |        |        |       |        |        |       |       |        |       |       |       |
| liver              |                          | <40>                    |        |       |       | <45>   |        |        |       | <41>   |        |       |       | <15>   |       |       |       |
|                    | fatty change:central     | 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 ) |
|                    | lymphocytic infiltration | 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 ) |
|                    | granulation              | 11                      | 6      | 2     | 0     | 14     | 8      | 6      | 0     | 11     | 8      | 3     | 0     | 4      | 1     | 0     | 0     |
|                    |                          | ( 28 )                  | ( 15 ) | ( 5 ) | ( 0 ) | ( 31 ) | ( 18 ) | ( 13 ) | ( 0 ) | ( 27 ) | ( 20 ) | ( 7 ) | ( 0 ) | ( 27 ) | ( 7 ) | ( 0 ) | ( 0 ) |
|                    | inflammatory cell nest   | 1                       | 3      | 0     | 0     | 0      | 1      | 0      | 0     | 3      | 0      | 0     | 0     | 0      | 0     | 0     | 0     |
|                    |                          | ( 3 )                   | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 )  | ( 0 )  | ( 0 ) | ( 7 )  | ( 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 ) | ( 2 )  | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                    | basophilic cell focus    | 14                      | 8      | 0     | 0     | 7      | 9      | 0      | 0     | 4      | 7      | 0     | 0 *   | 2      | 1     | 0     | 0     |
|                    |                          | ( 35 )                  | ( 20 ) | ( 0 ) | ( 0 ) | ( 16 ) | ( 20 ) | ( 0 )  | ( 0 ) | ( 10 ) | ( 17 ) | ( 0 ) | ( 0 ) | ( 13 ) | ( 7 ) | ( 0 ) | ( 0 ) |
|                    | bile duct hyperplasia    | 5                       | 2      | 0     | 0     | 4      | 2      | 0      | 0     | 6      | 4      | 0     | 0     | 3      | 0     | 0     | 0     |
|                    |                          | ( 13 )                  | ( 5 )  | ( 0 ) | ( 0 ) | ( 9 )  | ( 4 )  | ( 0 )  | ( 0 ) | ( 15 ) | ( 10 ) | ( 0 ) | ( 0 ) | ( 20 ) | ( 0 ) | ( 0 ) | ( 0 ) |
| pancreas           |                          | <40>                    |        |       |       | <45>   |        |        |       | <41>   |        |       |       | <15>   |       |       |       |
|                    | atrophy                  | 1                       | 2      | 0     | 0     | 1      | 2      | 0      | 0     | 1      | 2      | 0     | 0     | 1      | 1     | 0     | 0     |
|                    |                          | ( 3 )                   | ( 5 )  | ( 0 ) | ( 0 ) | ( 2 )  | ( 4 )  | ( 0 )  | ( 0 ) | ( 2 )  | ( 5 )  | ( 0 ) | ( 0 ) | ( 7 )  | ( 7 ) | ( 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

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

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|   |                        | Group Name              | Control |       |       |       | 10 ppm |       |       |       | 30 ppm |       |       |       | 90 ppm |       |       |       |
|---|------------------------|-------------------------|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
|   |                        | No. of Animals on Study | 40      |       |       |       | 45     |       |       |       | 41     |       |       |       | 15     |       |       |       |
|   |                        | Grade                   | 1       | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     |
| Organ                                       | Findings               |                         | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   |
| {Urinary system}                            |                        |                         |         |       |       |       |        |       |       |       |        |       |       |       |        |       |       |       |
| kidney                                      |                        |                         | <40>    |       |       |       | <45>   |       |       |       | <41>   |       |       |       | <15>   |       |       |       |
|   | hyaline droplet        |                         | 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 ) |
|   | deposit of hemosiderin |                         | 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 ) |
|   | chronic nephropathy    |                         | 8       | 2     | 0     | 0     | 16     | 3     | 1     | 0     | 16     | 3     | 2     | 0     | 0      | 0     | 0     | 0     |
|   |                        |                         | ( 20 )  | ( 5 ) | ( 0 ) | ( 0 ) | ( 36 ) | ( 7 ) | ( 2 ) | ( 0 ) | ( 39 ) | ( 7 ) | ( 5 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
| hydronephrosis                              |                        | 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 ) |       |
| mineralization:papilla                      |                        | 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:cortex                       |                        | 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 ) |       |
| urin bladd                                  |                        |                         | <40>    |       |       |       | <45>   |       |       |       | <41>   |       |       |       | <15>   |       |       |       |
| nodular hyperplasia:transitional epithelium |                        |                         | 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 ) | ( 0 ) |
| {Endocrine system}                          |                        |                         |         |       |       |       |        |       |       |       |        |       |       |       |        |       |       |       |
| pituitary                                   |                        |                         | <40>    |       |       |       | <45>   |       |       |       | <41>   |       |       |       | <15>   |       |       |       |
|   | angiectasis            |                         | 0       | 0     | 0     | 0     | 2      | 1     | 0     | 0     | 0      | 1     | 0     | 0     | 0      | 0     | 0     | 0     |
|   |                        | ( 0 )                   | ( 0 )   | ( 0 ) | ( 0 ) | ( 4 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 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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 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 SACRIFICED ANIMALS (105W)

PAGE : 20

| Organ              | Findings                  | Group Name              | Control |        |       |       | 10 ppm |        |       |       | 30 ppm |        |       |       | 90 ppm |        |       |       |
|--------------------|---------------------------|-------------------------|---------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|
|                    |                           | No. of Animals on Study | 40      |        |       |       | 45     |        |       |       | 41     |        |       |       | 15     |        |       |       |
|                    |                           | Grade                   | 1       | 2      | 3     | 4     | 1      | 2      | 3     | 4     | 1      | 2      | 3     | 4     | 1      | 2      | 3     | 4     |
|                    |                           |                         | (%)     | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   |
| {Endocrine system} |                           |                         |         |        |       |       |        |        |       |       |        |        |       |       |        |        |       |       |
| pituitary          |                           |                         | <40>    |        |       |       | <45>   |        |       |       | <41>   |        |       |       | <15>   |        |       |       |
|                    | cyst                      |                         | 2       | 9      | 0     | 0     | 0      | 5      | 0     | 0     | 1      | 8      | 0     | 0     | 0      | 3      | 0     | 0     |
|                    |                           |                         | ( 5 )   | ( 23 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 11 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 20 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 20 ) | ( 0 ) | ( 0 ) |
|                    | hyperplasia               |                         | 0       | 3      | 0     | 0     | 0      | 10     | 0     | 0     | 0      | 5      | 0     | 0     | 0      | 3      | 0     | 0     |
|                    |                           |                         | ( 0 )   | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 22 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 12 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 20 ) | ( 0 ) | ( 0 ) |
|                    | Rathke pouch              |                         | 1       | 0      | 0     | 0     | 1      | 0      | 0     | 0     | 1      | 0      | 0     | 0     | 0      | 0      | 0     | 0     |
|                    |                           |                         | ( 3 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |
| thyroid            |                           |                         | <40>    |        |       |       | <45>   |        |       |       | <41>   |        |       |       | <15>   |        |       |       |
|                    | C-cell hyperplasia        |                         | 5       | 4      | 0     | 0     | 7      | 1      | 0     | 0     | 7      | 3      | 0     | 0     | 1      | 2      | 0     | 0     |
|                    |                           |                         | ( 13 )  | ( 10 ) | ( 0 ) | ( 0 ) | ( 16 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 17 ) | ( 7 )  | ( 0 ) | ( 0 ) | ( 7 )  | ( 13 ) | ( 0 ) | ( 0 ) |
| adrenal            |                           |                         | <40>    |        |       |       | <45>   |        |       |       | <41>   |        |       |       | <15>   |        |       |       |
|                    | peliosis-like lesion      |                         | 0       | 1      | 0     | 0     | 0      | 1      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0     | 0     |
|                    |                           |                         | ( 0 )   | ( 3 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                    | hyperplasia:cortical cell |                         | 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 ) |
|                    | hyperplasia:medulla       |                         | 0       | 2      | 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 ) | ( 7 )  | ( 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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 21

|                       |                                | Group Name              | Control |        |       |       | 10 ppm |        |       |       | 30 ppm |       |       |       | 90 ppm |        |       |       |
|-----------------------|--------------------------------|-------------------------|---------|--------|-------|-------|--------|--------|-------|-------|--------|-------|-------|-------|--------|--------|-------|-------|
|                       |                                | No. of Animals on Study | 40      |        |       |       | 45     |        |       |       | 41     |       |       |       | 15     |        |       |       |
| Organ                 | Findings                       | Grade                   | 1       | 2      | 3     | 4     | 1      | 2      | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2      | 3     | 4     |
|                       |                                |                         | (%)     | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   |
| {Endocrine system}    |                                |                         |         |        |       |       |        |        |       |       |        |       |       |       |        |        |       |       |
| adrenal               |                                |                         | <40>    |        |       |       | <45>   |        |       |       | <41>   |       |       |       | <15>   |        |       |       |
|                       | focal fatty change:cortex      |                         | 0       | 4      | 0     | 0     | 0      | 5      | 0     | 0     | 0      | 2     | 0     | 0     | 1      | 1      | 0     | 0     |
|                       |                                |                         | ( 0 )   | ( 10 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 11 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 5 ) | ( 0 ) | ( 0 ) | ( 7 )  | ( 7 )  | ( 0 ) | ( 0 ) |
| {Reproductive system} |                                |                         |         |        |       |       |        |        |       |       |        |       |       |       |        |        |       |       |
| uterus                |                                |                         | <40>    |        |       |       | <45>   |        |       |       | <41>   |       |       |       | <15>   |        |       |       |
|                       | hyperplasia:epithelium         |                         | 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 ) |
|                       | hyperplasia:gland              |                         | 0       | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 1      | 0     | 0     | 0     | 1      | 0      | 0     | 0     |
|                       |                                |                         | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 7 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                       | cystic endometrial hyperplasia |                         | 0       | 0      | 0     | 0     | 2      | 1      | 0     | 0     | 0      | 0     | 0     | 0     | 2      | 2      | 0     | 0 **  |
|                       |                                |                         | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 4 )  | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 13 ) | ( 13 ) | ( 0 ) | ( 0 ) |
| mammary gl            |                                |                         | <40>    |        |       |       | <45>   |        |       |       | <41>   |       |       |       | <15>   |        |       |       |
|                       | hyperplasia                    |                         | 0       | 0      | 0     | 0     | 1      | 0      | 0     | 0     | 2      | 0     | 1     | 0     | 0      | 0      | 0     | 0     |
|                       |                                |                         | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 5 )  | ( 0 ) | ( 2 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |
| {Nervous system}      |                                |                         |         |        |       |       |        |        |       |       |        |       |       |       |        |        |       |       |
| brain                 |                                |                         | <40>    |        |       |       | <45>   |        |       |       | <41>   |       |       |       | <15>   |        |       |       |
|                       | hemorrhage                     |                         | 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 : Number of animals with lesion  
 ( c ) c : b / a \* 100  
 Significant difference ; \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 22

|                                  |                 | Group Name              | Control |       |        |       | 10 ppm |       |       |       | 30 ppm |       |       |       | 90 ppm |        |       |       |
|----------------------------------|-----------------|-------------------------|---------|-------|--------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|--------|-------|-------|
|                                  |                 | No. of Animals on Study | 40      |       |        |       | 45     |       |       |       | 41     |       |       |       | 15     |        |       |       |
| Organ                            | Findings        | Grade                   | 1       | 2     | 3      | 4     | 1      | 2     | 3     | 4     | 1      | 2     | 3     | 4     | 1      | 2      | 3     | 4     |
|                                  |                 |                         | (%)     | (%)   | (%)    | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   |
| {Nervous system}                 |                 |                         |         |       |        |       |        |       |       |       |        |       |       |       |        |        |       |       |
| spinal cord                      |                 |                         | <40>    |       |        |       | <45>   |       |       |       | <41>   |       |       |       | <15>   |        |       |       |
|                                  | gliosis         |                         | 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 ) | ( 7 )  | ( 0 )  | ( 0 ) | ( 0 ) |
| {Special sense organs/appendage} |                 |                         |         |       |        |       |        |       |       |       |        |       |       |       |        |        |       |       |
| eye                              |                 |                         | <40>    |       |        |       | <45>   |       |       |       | <41>   |       |       |       | <15>   |        |       |       |
|                                  | cataract        |                         | 2       | 2     | 0      | 0     | 1      | 3     | 0     | 0     | 0      | 2     | 0     | 0     | 0      | 1      | 0     | 0     |
|                                  |                 |                         | ( 5 )   | ( 5 ) | ( 0 )  | ( 0 ) | ( 2 )  | ( 7 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 5 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 7 )  | ( 0 ) | ( 0 ) |
|                                  | retinal atrophy |                         | 35      | 1     | 4      | 0     | 41     | 0     | 4     | 0     | 39     | 0     | 2     | 0     | 12     | 0      | 1     | 0     |
|                                  |                 |                         | ( 88 )  | ( 3 ) | ( 10 ) | ( 0 ) | ( 91 ) | ( 0 ) | ( 9 ) | ( 0 ) | ( 95 ) | ( 0 ) | ( 5 ) | ( 0 ) | ( 80 ) | ( 0 )  | ( 7 ) | ( 0 ) |
|                                  | keratitis       |                         | 1       | 0     | 0      | 0     | 0      | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 2      | 0     | 0     |
|                                  |                 |                         | ( 3 )   | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 13 ) | ( 0 ) | ( 0 ) |
|                                  | iritis          |                         | 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                        |                 |                         | <40>    |       |        |       | <45>   |       |       |       | <41>   |       |       |       | <15>   |        |       |       |
|                                  | degeneration    |                         | 3       | 0     | 0      | 0     | 1      | 1     | 0     | 0     | 2      | 0     | 0     | 0     | 0      | 0      | 0     | 0     |
|                                  |                 |                         | ( 8 )   | ( 0 ) | ( 0 )  | ( 0 ) | ( 2 )  | ( 2 ) | ( 0 ) | ( 0 ) | ( 5 )  | ( 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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 23

|                                  |                           | Group Name              | Control |      |      |      | 10 ppm |      |      |       | 30 ppm |      |      |       | 90 ppm |      |      |      |
|----------------------------------|---------------------------|-------------------------|---------|------|------|------|--------|------|------|-------|--------|------|------|-------|--------|------|------|------|
|                                  |                           | No. of Animals on Study | 40      |      |      |      | 45     |      |      |       | 41     |      |      |       | 15     |      |      |      |
|                                  |                           | Grade                   | 1       | 2    | 3    | 4    | 1      | 2    | 3    | 4     | 1      | 2    | 3    | 4     | 1      | 2    | 3    | 4    |
| Organ_____                       | Findings_____             |                         | (%)     | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)   | (%)    | (%)  | (%)  | (%)   | (%)    | (%)  | (%)  | (%)  |
| <hr/>                            |                           |                         |         |      |      |      |        |      |      |       |        |      |      |       |        |      |      |      |
| {Special sense organs/appendage} |                           |                         |         |      |      |      |        |      |      |       |        |      |      |       |        |      |      |      |
| Harder gl                        |                           |                         | <40>    |      |      |      | <45>   |      |      |       | <41>   |      |      |       | <15>   |      |      |      |
|                                  | inflammatory infiltration |                         | 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)  | ( 0)   | ( 0) | ( 0) | ( 0) |
|                                  | lymphocytic infiltration  |                         | 3       | 0    | 0    | 0    | 2      | 0    | 0    | 0     | 5      | 0    | 0    | 0     | 3      | 0    | 0    | 0    |
|                                  |                           |                         | ( 8)    | ( 0) | ( 0) | ( 0) | ( 4)   | ( 0) | ( 0) | ( 0)  | ( 12)  | ( 0) | ( 0) | ( 0)  | ( 20)  | ( 0) | ( 0) | ( 0) |
|                                  | granulation               |                         | 3       | 0    | 0    | 0    | 4      | 0    | 0    | 0     | 3      | 0    | 0    | 0     | 1      | 0    | 0    | 0    |
|                                  |                           | ( 8)                    | ( 0)    | ( 0) | ( 0) | ( 9) | ( 0)   | ( 0) | ( 0) | ( 7)  | ( 0)   | ( 0) | ( 0) | ( 7)  | ( 0)   | ( 0) | ( 0) |      |
| nasolacr d                       | inflammation              |                         | <40>    |      |      |      | <45>   |      |      |       | <41>   |      |      |       | <15>   |      |      |      |
|                                  |                           |                         | 0       | 1    | 0    | 0    | 0      | 1    | 0    | 0     | 0      | 0    | 0    | 0     | 0      | 0    | 0    | 0    |
|                                  |                           |                         | ( 0)    | ( 3) | ( 0) | ( 0) | ( 0)   | ( 2) | ( 0) | ( 0)  | ( 0)   | ( 0) | ( 0) | ( 0)  | ( 0)   | ( 0) | ( 0) | ( 0) |
| <hr/>                            |                           |                         |         |      |      |      |        |      |      |       |        |      |      |       |        |      |      |      |
| {Musculoskeletal system}         |                           |                         |         |      |      |      |        |      |      |       |        |      |      |       |        |      |      |      |
| bone                             | osteosclerosis            |                         | <40>    |      |      |      | <45>   |      |      |       | <41>   |      |      |       | <15>   |      |      |      |
|                                  |                           |                         | 5       | 2    | 0    | 0    | 1      | 1    | 0    | 0     | 5      | 1    | 0    | 0     | 2      | 0    | 0    | 0    |
|                                  |                           | ( 13)                   | ( 5)    | ( 0) | ( 0) | ( 2) | ( 2)   | ( 0) | ( 0) | ( 12) | ( 2)   | ( 0) | ( 0) | ( 13) | ( 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

## APPENDIX M 1

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

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
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 | 10 ppm | 30 ppm | 90 ppm |
|-----------------------|-------------------------------------|------------|---------|--------|--------|--------|
| 0 - 52                | NO. OF EXAMINED ANIMALS             |            | 0       | 0      | 1      | 1      |
|                       | NO. OF ANIMALS WITH TUMORS          |            | 0       | 0      | 0      | 0      |
|                       | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 0       | 0      | 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       | 0      | 0      | 0      |
|                       | NO. OF TOTAL TUMORS                 |            | 0       | 0      | 0      | 0      |
| 53 - 78               | NO. OF EXAMINED ANIMALS             |            | 0       | 2      | 3      | 6      |
|                       | NO. OF ANIMALS WITH TUMORS          |            | 0       | 2      | 2      | 6      |
|                       | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 0       | 2      | 2      | 4      |
|                       | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 0       | 0      | 0      | 2      |
|                       | NO. OF BENIGN TUMORS                |            | 0       | 0      | 0      | 2      |
|                       | NO. OF MALIGNANT TUMORS             |            | 0       | 2      | 2      | 6      |
|                       | NO. OF TOTAL TUMORS                 |            | 0       | 2      | 2      | 8      |
| 79 - 104              | NO. OF EXAMINED ANIMALS             |            | 12      | 10     | 8      | 32     |
|                       | NO. OF ANIMALS WITH TUMORS          |            | 11      | 10     | 7      | 31     |
|                       | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 4       | 3      | 3      | 13     |
|                       | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 7       | 7      | 4      | 18     |
|                       | NO. OF BENIGN TUMORS                |            | 14      | 11     | 8      | 28     |
|                       | NO. OF MALIGNANT TUMORS             |            | 7       | 8      | 5      | 33     |
|                       | NO. OF TOTAL TUMORS                 |            | 21      | 19     | 13     | 61     |
| 105 - 106             | NO. OF EXAMINED ANIMALS             |            | 38      | 38     | 38     | 11     |
|                       | NO. OF ANIMALS WITH TUMORS          |            | 38      | 38     | 38     | 11     |
|                       | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 9       | 8      | 5      | 3      |
|                       | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 29      | 30     | 33     | 8      |
|                       | NO. OF BENIGN TUMORS                |            | 74      | 70     | 72     | 12     |
|                       | NO. OF MALIGNANT TUMORS             |            | 9       | 16     | 27     | 10     |
|                       | NO. OF TOTAL TUMORS                 |            | 83      | 86     | 99     | 22     |

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
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 | 10 ppm | 30 ppm | 90 ppm |
|-----------------------|-------------------------------------|------------|---------|--------|--------|--------|
| 0 - 106               | NO. OF EXAMINED ANIMALS             |            | 50      | 50     | 50     | 50     |
|                       | NO. OF ANIMALS WITH TUMORS          |            | 49      | 50     | 47     | 48     |
|                       | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 13      | 13     | 10     | 20     |
|                       | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 36      | 37     | 37     | 28     |
|                       | NO. OF BENIGN TUMORS                |            | 88      | 81     | 80     | 42     |
|                       | NO. OF MALIGNANT TUMORS             |            | 16      | 26     | 34     | 49     |
|                       | NO. OF TOTAL TUMORS                 |            | 104     | 107    | 114    | 91     |

(HPT070)

BAIS4

## APPENDIX M 2

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



STUDY NO. : 0437  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
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 | 10 ppm | 30 ppm | 90 ppm |
|-----------------------|-------------------------------------|------------|---------|--------|--------|--------|
| 0 - 52                | NO. OF EXAMINED ANIMALS             |            | 0       | 0      | 0      | 0      |
|                       | NO. OF ANIMALS WITH TUMORS          |            | 0       | 0      | 0      | 0      |
|                       | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 0       | 0      | 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       | 0      | 0      | 0      |
|                       | NO. OF TOTAL TUMORS                 |            | 0       | 0      | 0      | 0      |
| 53 - 78               | NO. OF EXAMINED ANIMALS             |            | 3       | 0      | 3      | 5      |
|                       | NO. OF ANIMALS WITH TUMORS          |            | 3       | 0      | 3      | 4      |
|                       | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 2       | 0      | 1      | 2      |
|                       | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 1       | 0      | 2      | 2      |
|                       | NO. OF BENIGN TUMORS                |            | 4       | 0      | 4      | 2      |
|                       | NO. OF MALIGNANT TUMORS             |            | 2       | 0      | 1      | 4      |
|                       | NO. OF TOTAL TUMORS                 |            | 6       | 0      | 5      | 6      |
| 79 - 104              | NO. OF EXAMINED ANIMALS             |            | 7       | 5      | 6      | 30     |
|                       | NO. OF ANIMALS WITH TUMORS          |            | 7       | 5      | 6      | 27     |
|                       | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 4       | 1      | 3      | 15     |
|                       | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 3       | 4      | 3      | 12     |
|                       | NO. OF BENIGN TUMORS                |            | 7       | 7      | 5      | 12     |
|                       | NO. OF MALIGNANT TUMORS             |            | 4       | 3      | 4      | 31     |
|                       | NO. OF TOTAL TUMORS                 |            | 11      | 10     | 9      | 43     |
| 105 - 106             | NO. OF EXAMINED ANIMALS             |            | 40      | 45     | 41     | 15     |
|                       | NO. OF ANIMALS WITH TUMORS          |            | 26      | 34     | 32     | 15     |
|                       | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 20      | 20     | 20     | 9      |
|                       | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 6       | 14     | 12     | 6      |
|                       | NO. OF BENIGN TUMORS                |            | 25      | 40     | 40     | 12     |
|                       | NO. OF MALIGNANT TUMORS             |            | 8       | 11     | 7      | 12     |
|                       | NO. OF TOTAL TUMORS                 |            | 33      | 51     | 47     | 24     |

(HPT070)

BAIS4

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
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 | 10 ppm | 30 ppm | 90 ppm |
|-----------------------|-------------------------------------|------------|---------|--------|--------|--------|
| 0 - 106               | NO. OF EXAMINED ANIMALS             |            | 50      | 50     | 50     | 50     |
|                       | NO. OF ANIMALS WITH TUMORS          |            | 36      | 39     | 41     | 46     |
|                       | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 26      | 21     | 24     | 26     |
|                       | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 10      | 18     | 17     | 20     |
|                       | NO. OF BENIGN TUMORS                |            | 36      | 47     | 49     | 26     |
|                       | NO. OF MALIGNANT TUMORS             |            | 14      | 14     | 12     | 47     |
|                       | NO. OF TOTAL TUMORS                 |            | 50      | 61     | 61     | 73     |

(HPT070)

BAIS4

## APPENDIX N 1

HISTOPATHOLOGICAL FINDINGS :

NEOPLASTIC LESIONS : MALE

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 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 | 10 ppm<br>50 | 30 ppm<br>50 | 90 ppm<br>50 |
|----------------------------------|--------------------------------|---------------------------------------|---------------|--------------|--------------|--------------|
| {Integumentary system/appandage} |                                |                                       |               |              |              |              |
| skin/app                         |                                |                                       | <50>          | <50>         | <50>         | <50>         |
|                                  |                                |                                       | 2 ( 4%)       | 2 ( 4%)      | 3 ( 6%)      | 1 ( 2%)      |
|                                  | keratoacanthoma                |                                       | 0 ( 0%)       | 1 ( 2%)      | 0 ( 0%)      | 0 ( 0%)      |
|                                  | sebaceous adenoma              |                                       |               |              |              |              |
| subcutis                         |                                |                                       | <50>          | <50>         | <50>         | <50>         |
|                                  |                                |                                       | 8 ( 16%)      | 4 ( 8%)      | 6 ( 12%)     | 0 ( 0%)      |
|                                  | fibroma                        |                                       | 0 ( 0%)       | 0 ( 0%)      | 0 ( 0%)      | 1 ( 2%)      |
|                                  | leiomyoma                      |                                       | 2 ( 4%)       | 2 ( 4%)      | 0 ( 0%)      | 0 ( 0%)      |
|                                  | fibrosarcoma                   |                                       |               |              |              |              |
| {Respiratory system}             |                                |                                       |               |              |              |              |
| nasal cavit                      |                                |                                       | <50>          | <50>         | <50>         | <50>         |
|                                  |                                |                                       | 0 ( 0%)       | 0 ( 0%)      | 0 ( 0%)      | 1 ( 2%)      |
|                                  | squamous cell papilloma        |                                       | 0 ( 0%)       | 0 ( 0%)      | 5 ( 10%)     | 0 ( 0%)      |
|                                  | adenoma                        |                                       | 0 ( 0%)       | 0 ( 0%)      | 0 ( 0%)      | 35 ( 70%)    |
|                                  | squamous cell carcinoma        |                                       | 0 ( 0%)       | 0 ( 0%)      | 0 ( 0%)      | 1 ( 2%)      |
|                                  | ethesioneuroepithelioma        |                                       |               |              |              |              |
| lung                             |                                |                                       | <50>          | <50>         | <50>         | <50>         |
|                                  |                                |                                       | 5 ( 10%)      | 2 ( 4%)      | 1 ( 2%)      | 1 ( 2%)      |
|                                  | bronchiolar-alveolar adenoma   |                                       | 1 ( 2%)       | 0 ( 0%)      | 0 ( 0%)      | 0 ( 0%)      |
|                                  | bronchiolar-alveolar carcinoma |                                       |               |              |              |              |
| {Hematopoietic system}           |                                |                                       |               |              |              |              |
| spleen                           |                                |                                       | <50>          | <50>         | <50>         | <50>         |
|                                  |                                |                                       | 0 ( 0%)       | 1 ( 2%)      | 0 ( 0%)      | 0 ( 0%)      |
|                                  | histiocytic sarcoma            |                                       |               |              |              |              |

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

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 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     | 10 ppm<br>50      | 30 ppm<br>50      | 90 ppm<br>50     |
|------------------------|-----------------------------|---------------------------------------|-------------------|-------------------|-------------------|------------------|
| {Hematopoietic system} |                             |                                       |                   |                   |                   |                  |
| spleen                 | mononuclear cell leukemia   |                                       | <50><br>10 ( 20%) | <50><br>16 ( 32%) | <50><br>19 ( 38%) | <50><br>7 ( 14%) |
| {Digestive system}     |                             |                                       |                   |                   |                   |                  |
| oral cavity            | squamous cell papilloma     |                                       | <50><br>0 ( 0%)   | <50><br>1 ( 2%)   | <50><br>0 ( 0%)   | <50><br>0 ( 0%)  |
| tongue                 | squamous cell papilloma     |                                       | <50><br>1 ( 2%)   | <49><br>0 ( 0%)   | <50><br>0 ( 0%)   | <50><br>0 ( 0%)  |
| stomach                | squamous cell papilloma     |                                       | <50><br>0 ( 0%)   | <50><br>0 ( 0%)   | <50><br>1 ( 2%)   | <50><br>1 ( 2%)  |
| large intes            | adenocarcinoma              |                                       | <50><br>0 ( 0%)   | <50><br>0 ( 0%)   | <50><br>1 ( 2%)   | <50><br>0 ( 0%)  |
| liver                  | hepatocellular adenoma      |                                       | <50><br>0 ( 0%)   | <50><br>1 ( 2%)   | <50><br>1 ( 2%)   | <50><br>0 ( 0%)  |
|                        | histiocytic sarcoma         |                                       | <50><br>0 ( 0%)   | <50><br>0 ( 0%)   | <50><br>1 ( 2%)   | <50><br>0 ( 0%)  |
|                        | hepatocellular carcinoma    |                                       | <50><br>0 ( 0%)   | <50><br>1 ( 2%)   | <50><br>1 ( 2%)   | <50><br>1 ( 2%)  |
| pancreas               | islet cell adenoma          |                                       | <50><br>2 ( 4%)   | <50><br>3 ( 6%)   | <50><br>3 ( 6%)   | <50><br>1 ( 2%)  |
| {Urinary system}       |                             |                                       |                   |                   |                   |                  |
| urin bladd             | transitional cell papilloma |                                       | <50><br>0 ( 0%)   | <50><br>0 ( 0%)   | <50><br>0 ( 0%)   | <50><br>1 ( 2%)  |
| {Endocrine system}     |                             |                                       |                   |                   |                   |                  |
| pituitary              | adenoma                     |                                       | <50><br>8 ( 16%)  | <50><br>14 ( 28%) | <50><br>7 ( 14%)  | <50><br>2 ( 4%)  |

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

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 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 | 10 ppm<br>50 | 30 ppm<br>50 | 90 ppm<br>50 |
|-----------------------|----------------------------|---------------------------------------|---------------|--------------|--------------|--------------|
| {Endocrine system}    |                            |                                       |               |              |              |              |
| thyroid               |                            |                                       | <50>          | <49>         | <50>         | <50>         |
|                       | C-cell adenoma             |                                       | 7 ( 14%)      | 4 ( 8%)      | 7 ( 14%)     | 4 ( 8%)      |
|                       | follicular adenoma         |                                       | 0 ( 0%)       | 0 ( 0%)      | 1 ( 2%)      | 0 ( 0%)      |
|                       | C-cell carcinoma           |                                       | 1 ( 2%)       | 1 ( 2%)      | 1 ( 2%)      | 1 ( 2%)      |
|                       | follicular adenocarcinoma  |                                       | 0 ( 0%)       | 0 ( 0%)      | 3 ( 6%)      | 0 ( 0%)      |
| adrenal               |                            |                                       | <50>          | <50>         | <50>         | <50>         |
|                       | pheochromocytoma           |                                       | 4 ( 8%)       | 6 ( 12%)     | 2 ( 4%)      | 1 ( 2%)      |
|                       | pheochromocytoma:malignant |                                       | 2 ( 4%)       | 1 ( 2%)      | 0 ( 0%)      | 1 ( 2%)      |
|                       | ganglioneuroma:malignant   |                                       | 0 ( 0%)       | 0 ( 0%)      | 1 ( 2%)      | 0 ( 0%)      |
| {Reproductive system} |                            |                                       |               |              |              |              |
| testis                |                            |                                       | <50>          | <50>         | <50>         | <50>         |
|                       | interstitial cell tumor    |                                       | 47 ( 94%)     | 38 ( 76%)    | 40 ( 80%)    | 24 ( 48%)    |
|                       | rete testis adenoma        |                                       | 0 ( 0%)       | 0 ( 0%)      | 0 ( 0%)      | 1 ( 2%)      |
| mammary gl            |                            |                                       | <50>          | <50>         | <50>         | <50>         |
|                       | fibroadenoma               |                                       | 2 ( 4%)       | 0 ( 0%)      | 0 ( 0%)      | 0 ( 0%)      |
| prep/cli gl           |                            |                                       | <50>          | <50>         | <50>         | <50>         |
|                       | adenoma                    |                                       | 1 ( 2%)       | 1 ( 2%)      | 1 ( 2%)      | 3 ( 6%)      |
| {Nervous system}      |                            |                                       |               |              |              |              |
| brain                 |                            |                                       | <50>          | <50>         | <50>         | <50>         |
|                       | meningioma:benign          |                                       | 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. : 0437  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
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   | 10 ppm<br>50    | 30 ppm<br>50    | 90 ppm<br>50    |
|----------------------------------|--------------------------|---------------------------------------|-----------------|-----------------|-----------------|-----------------|
| (Nervous system)                 |                          |                                       |                 |                 |                 |                 |
| brain                            | glioma                   |                                       | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>1 ( 2%) | <50><br>1 ( 2%) |
| periph nerv                      | schwannoma:malignant     |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>2 ( 4%) | <50><br>0 ( 0%) |
| (Special sense organs/appendage) |                          |                                       |                 |                 |                 |                 |
| Zymbal gl                        | Zmbal gland tumor:benign |                                       | <50><br>0 ( 0%) | <50><br>2 ( 4%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) |
| (Musculoskeletal system)         |                          |                                       |                 |                 |                 |                 |
| bone                             | osteosarcoma             |                                       | <50><br>0 ( 0%) | <50><br>2 ( 4%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) |
| (Body cavities)                  |                          |                                       |                 |                 |                 |                 |
| mediastinum                      | sarcoma:NOS              |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) |
| peritoneum                       | fibroma                  |                                       | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) |
|                                  | mesothelioma             |                                       | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>3 ( 6%) | <50><br>1 ( 2%) |
| retroperit                       | schwannoma:malignant     |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) |
| adipose                          | lipoma                   |                                       | <50><br>1 ( 2%) | <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

## APPENDIX N 2

HISTOPATHOLOGICAL FINDINGS :

NEOPLASTIC LESIONS : FEMALE



STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 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    | 10 ppm<br>50     | 30 ppm<br>50     | 90 ppm<br>50      |
|----------------------------------|------------------------------|---------------------------------------|------------------|------------------|------------------|-------------------|
| {Integumentary system/appandage} |                              |                                       |                  |                  |                  |                   |
| skin/app                         | squamous cell carcinoma      |                                       | <50><br>1 ( 2%)  | <50><br>0 ( 0%)  | <50><br>0 ( 0%)  | <50><br>0 ( 0%)   |
| subcutis                         | fibroma                      |                                       | <50><br>0 ( 0%)  | <50><br>1 ( 2%)  | <50><br>0 ( 0%)  | <50><br>0 ( 0%)   |
|                                  | leiomyoma                    |                                       | 1 ( 2%)          | 0 ( 0%)          | 0 ( 0%)          | 0 ( 0%)           |
| {Respiratory system}             |                              |                                       |                  |                  |                  |                   |
| nasal cavit                      | adenoma                      |                                       | <50><br>1 ( 2%)  | <50><br>1 ( 2%)  | <50><br>2 ( 4%)  | <50><br>0 ( 0%)   |
|                                  | chondroma                    |                                       | 0 ( 0%)          | 0 ( 0%)          | 1 ( 2%)          | 0 ( 0%)           |
|                                  | squamous cell carcinoma      |                                       | 0 ( 0%)          | 0 ( 0%)          | 0 ( 0%)          | 28 ( 56%)         |
|                                  | sarcoma:NOS                  |                                       | 0 ( 0%)          | 0 ( 0%)          | 0 ( 0%)          | 1 ( 2%)           |
|                                  | adenosquamous carcinoma      |                                       | 0 ( 0%)          | 0 ( 0%)          | 0 ( 0%)          | 1 ( 2%)           |
|                                  | ethesioneuroepithelioma      |                                       | 0 ( 0%)          | 0 ( 0%)          | 0 ( 0%)          | 2 ( 4%)           |
| lung                             | bronchiolar-alveolar adenoma |                                       | <50><br>1 ( 2%)  | <50><br>2 ( 4%)  | <50><br>1 ( 2%)  | <50><br>1 ( 2%)   |
| {Hematopoietic system}           |                              |                                       |                  |                  |                  |                   |
| spleen                           | mononuclear cell leukemia    |                                       | <50><br>7 ( 14%) | <50><br>8 ( 16%) | <49><br>5 ( 10%) | <50><br>13 ( 26%) |

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

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 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     | 10 ppm<br>50      | 30 ppm<br>50      | 90 ppm<br>50     |
|--------------------|-----------------------------|---------------------------------------|-------------------|-------------------|-------------------|------------------|
| {Digestive system} |                             |                                       |                   |                   |                   |                  |
| stomach            | squamous cell papilloma     |                                       | <50><br>0 ( 0%)   | <50><br>0 ( 0%)   | <50><br>1 ( 2%)   | <50><br>0 ( 0%)  |
| small intes        | fibroma                     |                                       | <50><br>0 ( 0%)   | <50><br>1 ( 2%)   | <50><br>0 ( 0%)   | <50><br>0 ( 0%)  |
| large intes        | adenocarcinoma              |                                       | <50><br>0 ( 0%)   | <50><br>0 ( 0%)   | <50><br>1 ( 2%)   | <50><br>0 ( 0%)  |
| pancreas           | islet cell adenoma          |                                       | <50><br>0 ( 0%)   | <50><br>1 ( 2%)   | <50><br>0 ( 0%)   | <50><br>0 ( 0%)  |
| {Urinary system}   |                             |                                       |                   |                   |                   |                  |
| kidney             | mesenchymoma                |                                       | <50><br>0 ( 0%)   | <50><br>1 ( 2%)   | <50><br>0 ( 0%)   | <50><br>0 ( 0%)  |
| urin bladd         | transitional cell papilloma |                                       | <50><br>0 ( 0%)   | <50><br>0 ( 0%)   | <50><br>1 ( 2%)   | <50><br>1 ( 2%)  |
| {Endocrine system} |                             |                                       |                   |                   |                   |                  |
| pituitary          | adenoma                     |                                       | <50><br>15 ( 30%) | <50><br>16 ( 32%) | <50><br>14 ( 28%) | <50><br>5 ( 10%) |
|                    | adenocarcinoma              |                                       | 0 ( 0%)           | 1 ( 2%)           | 1 ( 2%)           | 0 ( 0%)          |
| thyroid            | C-cell adenoma              |                                       | <50><br>4 ( 8%)   | <50><br>7 ( 14%)  | <50><br>9 ( 18%)  | <50><br>4 ( 8%)  |
|                    | follicular adenoma          |                                       | 0 ( 0%)           | 0 ( 0%)           | 2 ( 4%)           | 0 ( 0%)          |
|                    | C-cell carcinoma            |                                       | 1 ( 2%)           | 0 ( 0%)           | 2 ( 4%)           | 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. : 0437  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
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   | 10 ppm<br>50    | 30 ppm<br>50    | 90 ppm<br>50    |
|-----------------------|-----------------------------|---------------------------------------|-----------------|-----------------|-----------------|-----------------|
| {Endocrine system}    |                             |                                       |                 |                 |                 |                 |
| adrenal               | pheochromocytoma            |                                       | <50><br>1 ( 2%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) |
|                       | cortical adenoma            |                                       | 0 ( 0%)         | 0 ( 0%)         | 1 ( 2%)         | 0 ( 0%)         |
| {Reproductive system} |                             |                                       |                 |                 |                 |                 |
| ovary                 | granulosa-theca cell tumor  |                                       | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>1 ( 2%) | <50><br>1 ( 2%) |
|                       |                             |                                       |                 |                 |                 |                 |
| uterus                | adenoma                     |                                       | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) |
|                       | leiomyoma                   |                                       | 1 ( 2%)         | 0 ( 0%)         | 1 ( 2%)         | 2 ( 4%)         |
|                       | endometrial stromal polyp   |                                       | 7 ( 14%)        | 6 ( 12%)        | 6 ( 12%)        | 7 ( 14%)        |
|                       | squamous cell carcinoma     |                                       | 0 ( 0%)         | 1 ( 2%)         | 0 ( 0%)         | 0 ( 0%)         |
|                       | adenocarcinoma              |                                       | 0 ( 0%)         | 0 ( 0%)         | 1 ( 2%)         | 0 ( 0%)         |
|                       | endometrial stromal sarcoma |                                       | 2 ( 4%)         | 1 ( 2%)         | 2 ( 4%)         | 2 ( 4%)         |
| mammary gl            | adenoma                     |                                       | <50><br>1 ( 2%) | <50><br>3 ( 6%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) |
|                       | fibroma                     |                                       | 0 ( 0%)         | 0 ( 0%)         | 0 ( 0%)         | 1 ( 2%)         |
|                       | fibroadenoma                |                                       | 4 ( 8%)         | 5 ( 10%)        | 5 ( 10%)        | 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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 9

| Organ                            | Findings                 | Group Name<br>No. of animals on Study | Control<br>50 | 10 ppm<br>50 | 30 ppm<br>50 | 90 ppm<br>50 |
|----------------------------------|--------------------------|---------------------------------------|---------------|--------------|--------------|--------------|
| {Reproductive system}            |                          |                                       |               |              |              |              |
| mammary gl                       |                          |                                       | <50>          | <50>         | <50>         | <50>         |
|                                  | adenocarcinoma           |                                       | 0 ( 0%)       | 2 ( 4%)      | 0 ( 0%)      | 0 ( 0%)      |
| prep/cli gl                      |                          |                                       | <50>          | <50>         | <50>         | <50>         |
|                                  | adenoma                  |                                       | 0 ( 0%)       | 0 ( 0%)      | 2 ( 4%)      | 1 ( 2%)      |
| {Nervous system}                 |                          |                                       |               |              |              |              |
| spinal cord                      |                          |                                       | <50>          | <50>         | <50>         | <50>         |
|                                  | glioma                   |                                       | 1 ( 2%)       | 1 ( 2%)      | 0 ( 0%)      | 0 ( 0%)      |
| {Special sense organs/appendage} |                          |                                       |               |              |              |              |
| Zymbal gl                        |                          |                                       | <50>          | <50>         | <50>         | <50>         |
|                                  | Zmbal gland tumor:benign |                                       | 0 ( 0%)       | 0 ( 0%)      | 1 ( 2%)      | 0 ( 0%)      |
| {Musculoskeletal system}         |                          |                                       |               |              |              |              |
| bone                             |                          |                                       | <50>          | <50>         | <50>         | <50>         |
|                                  | osteoma                  |                                       | 0 ( 0%)       | 0 ( 0%)      | 0 ( 0%)      | 1 ( 2%)      |
| vertebra                         |                          |                                       | <50>          | <50>         | <50>         | <50>         |
|                                  | chordoma:malignant       |                                       | 1 ( 2%)       | 0 ( 0%)      | 0 ( 0%)      | 0 ( 0%)      |
| {Body cavities}                  |                          |                                       |               |              |              |              |
| peritoneum                       |                          |                                       | <50>          | <50>         | <50>         | <50>         |
|                                  | sarcoma:NOS              |                                       | 1 ( 2%)       | 0 ( 0%)      | 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 O 1

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

STUDY No. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 1

| Group Name                                       | Control      | 10 ppm      | 30 ppm      | 90 ppm       |
|--|--------------|-------------|-------------|--------------|
| SITE : skin/appendage<br>TUMOR : keratoacanthoma |              |             |             |              |
| Tumor rate                                       |              |             |             |              |
| Overall rates(a)                                 | 2/50( 4.0)   | 2/50( 4.0)  | 3/50( 6.0)  | 1/50( 2.0)   |
| Adjusted rates(b)                                | 5.26         | 5.26        | 7.89        | 4.00         |
| Terminal rates(c)                                | 2/38( 5.3)   | 2/38( 5.3)  | 3/38( 7.9)  | 0/11( 0.0)   |
| Statistical analysis                             |              |             |             |              |
| Peto test  |              |             |             |              |
| Standard method(d)                               | P = -----    |             |             |              |
| Prevalence method(d)                             | P = 0.3525   |             |             |              |
| Combined analysis(d)                             | P = -----    |             |             |              |
| Cochran-Armitage test(e)                         | P = 0.5351   |             |             |              |
| Fisher Exact test(e)                             |              | P = 0.6913  | P = 0.5000  | P = 0.5000   |
| SITE : subcutis<br>TUMOR : fibroma               |              |             |             |              |
| Tumor rate                                       |              |             |             |              |
| Overall rates(a)                                 | 8/50( 16.0)  | 4/50( 8.0)  | 6/50( 12.0) | 0/50( 0.0)   |
| Adjusted rates(b)                                | 19.51        | 10.53       | 13.16       | 0.0          |
| Terminal rates(c)                                | 7/38( 18.4)  | 4/38( 10.5) | 5/38( 13.2) | 0/11( 0.0)   |
| Statistical analysis                             |              |             |             |              |
| Peto test  |              |             |             |              |
| Standard method(d)                               | P = 0.2731   |             |             |              |
| Prevalence method(d)                             | P = 0.9671   |             |             |              |
| Combined analysis(d)                             | P = 0.9529   |             |             |              |
| Cochran-Armitage test(e)                         | P = 0.0098** |             |             |              |
| Fisher Exact test(e)                             |              | P = 0.1783  | P = 0.3871  | P = 0.0029** |
| SITE : subcutis<br>TUMOR : fibroma, fibrosarcoma |              |             |             |              |
| Tumor rate                                       |              |             |             |              |
| Overall rates(a)                                 | 10/50( 20.0) | 6/50( 12.0) | 6/50( 12.0) | 0/50( 0.0)   |
| Adjusted rates(b)                                | 20.00        | 13.16       | 13.16       | 0.0          |
| Terminal rates(c)                                | 7/38( 18.4)  | 5/38( 13.2) | 5/38( 13.2) | 0/11( 0.0)   |
| Statistical analysis                             |              |             |             |              |
| Peto test  |              |             |             |              |
| Standard method(d)                               | P = 0.8122   |             |             |              |
| Prevalence method(d)                             | P = 0.9741   |             |             |              |
| Combined analysis(d)                             | P = 0.9869   |             |             |              |
| Cochran-Armitage test(e)                         | P = 0.0021** |             |             |              |
| Fisher Exact test(e)                             |              | P = 0.2070  | P = 0.2070  | P = 0.0006** |

STUDY No. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 2

| Group Name  | Control       | 10 ppm     | 30 ppm      | 90 ppm       |
|---|---------------|------------|-------------|--------------|
| SITE : nasal cavity<br>TUMOR : adenoma  |               |            |             |              |
| Tumor rate  |               |            |             |              |
| Overall rates(a)  | 0/50( 0.0)    | 0/50( 0.0) | 5/50( 10.0) | 0/50( 0.0)   |
| Adjusted rates(b)   | 0.0           | 0.0        | 13.16       | 0.0          |
| Terminal rates(c)   | 0/38( 0.0)    | 0/38( 0.0) | 5/38( 13.2) | 0/11( 0.0)   |
| Statistical analysis  |               |            |             |              |
| Peto test   |               |            |             |              |
| Standard method(d)  | P = -----     |            |             |              |
| Prevalence method(d)  | P = 0.1624    |            |             |              |
| Combined analysis(d)  | P = -----     |            |             |              |
| Cochran-Armitage test(e)  | P = 0.8712    |            |             |              |
| Fisher Exact test(e)  |               | P = N. C.  | P = 0.0281* | P = N. C.    |
| SITE : nasal cavity<br>TUMOR : squamous cell carcinoma                          |               |            |             |              |
| Tumor rate  |               |            |             |              |
| Overall rates(a)  | 0/50( 0.0)    | 0/50( 0.0) | 0/50( 0.0)  | 35/50( 70.0) |
| Adjusted rates(b)   | 0.0           | 0.0        | 0.0         | 50.00        |
| Terminal rates(c)   | 0/38( 0.0)    | 0/38( 0.0) | 0/38( 0.0)  | 5/11( 45.5)  |
| Statistical analysis  |               |            |             |              |
| Peto test   |               |            |             |              |
| Standard method(d)  | P < 0.0001**? |            |             |              |
| Prevalence method(d)  | P < 0.0001**? |            |             |              |
| Combined analysis(d)  | P < 0.0001**? |            |             |              |
| Cochran-Armitage test(e)  | P < 0.0001**  |            |             |              |
| Fisher Exact test(e)  |               | P = N. C.  | P = N. C.   | P < 0.0001** |
| SITE : nasal cavity<br>TUMOR : squamous cell papilloma, squamous cell carcinoma |               |            |             |              |
| Tumor rate  |               |            |             |              |
| Overall rates(a)  | 0/50( 0.0)    | 0/50( 0.0) | 0/50( 0.0)  | 36/50( 72.0) |
| Adjusted rates(b)   | 0.0           | 0.0        | 0.0         | 50.00        |
| Terminal rates(c)   | 0/38( 0.0)    | 0/38( 0.0) | 0/38( 0.0)  | 5/11( 45.5)  |
| Statistical analysis  |               |            |             |              |
| Peto test   |               |            |             |              |
| Standard method(d)  | P < 0.0001**? |            |             |              |
| Prevalence method(d)  | P < 0.0001**? |            |             |              |
| Combined analysis(d)  | P < 0.0001**? |            |             |              |
| Cochran-Armitage test(e)  | P < 0.0001**  |            |             |              |
| Fisher Exact test(e)  |               | P = N. C.  | P = N. C.   | P < 0.0001** |

STUDY No. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 3

| Group Name  | Control      | 10 ppm       | 30 ppm       | 90 ppm      |
|---|--------------|--------------|--------------|-------------|
| SITE : lung<br>TUMOR : bronchiolar-alveolar adenoma                                 |              |              |              |             |
| Tumor rate  |              |              |              |             |
| Overall rates(a)  | 5/50( 10.0)  | 2/50( 4.0)   | 1/50( 2.0)   | 1/50( 2.0)  |
| Adjusted rates(b)   | 11.90        | 5.26         | 2.63         | 2.78        |
| Terminal rates(c)   | 4/38( 10.5)  | 2/38( 5.3)   | 1/38( 2.6)   | 0/11( 0.0)  |
| Statistical analysis  |              |              |              |             |
| Peto test   |              |              |              |             |
| Standard method(d)  | P = -----    |              |              |             |
| Prevalence method(d)  | P = 0.8692   |              |              |             |
| Combined analysis(d)  | P = -----    |              |              |             |
| Cochran-Armitage test(e)  | P = 0.1362   |              |              |             |
| Fisher Exact test(e)  |              | P = 0.2180   | P = 0.1022   | P = 0.1022  |
| SITE : lung<br>TUMOR : bronchiolar-alveolar adenoma, bronchiolar-alveolar carcinoma |              |              |              |             |
| Tumor rate  |              |              |              |             |
| Overall rates(a)  | 6/50( 12.0)  | 2/50( 4.0)   | 1/50( 2.0)   | 1/50( 2.0)  |
| Adjusted rates(b)   | 14.29        | 5.26         | 2.63         | 2.78        |
| Terminal rates(c)   | 5/38( 13.2)  | 2/38( 5.3)   | 1/38( 2.6)   | 0/11( 0.0)  |
| Statistical analysis  |              |              |              |             |
| Peto test   |              |              |              |             |
| Standard method(d)  | P = -----    |              |              |             |
| Prevalence method(d)  | P = 0.9092   |              |              |             |
| Combined analysis(d)  | P = -----    |              |              |             |
| Cochran-Armitage test(e)  | P = 0.0856   |              |              |             |
| Fisher Exact test(e)  |              | P = 0.1343   | P = 0.0559   | P = 0.0559  |
| SITE : spleen<br>TUMOR : mononuclear cell leukemia                                  |              |              |              |             |
| Tumor rate  |              |              |              |             |
| Overall rates(a)  | 10/50( 20.0) | 16/50( 32.0) | 19/50( 38.0) | 7/50( 14.0) |
| Adjusted rates(b)   | 18.42        | 30.77        | 42.11        | 30.00       |
| Terminal rates(c)   | 7/38( 18.4)  | 11/38( 28.9) | 16/38( 42.1) | 3/11( 27.3) |
| Statistical analysis  |              |              |              |             |
| Peto test   |              |              |              |             |
| Standard method(d)  | P = 0.1180   |              |              |             |
| Prevalence method(d)  | P = 0.1830   |              |              |             |
| Combined analysis(d)  | P = 0.0729   |              |              |             |
| Cochran-Armitage test(e)  | P = 0.1275   |              |              |             |
| Fisher Exact test(e)  |              | P = 0.1271   | P = 0.0385*  | P = 0.2977  |



STUDY No. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 4

| Group Name                                    | Control      | 10 ppm       | 30 ppm      | 90 ppm      |
|---|--------------|--------------|-------------|-------------|
| SITE : pancreas<br>TUMOR : islet cell adenoma |              |              |             |             |
| Tumor rate                                    |              |              |             |             |
| Overall rates(a)                              | 2/50( 4.0)   | 3/50( 6.0)   | 3/50( 6.0)  | 1/50( 2.0)  |
| Adjusted rates(b)                             | 5.26         | 7.89         | 7.89        | 2.50        |
| Terminal rates(c)                             | 2/38( 5.3)   | 3/38( 7.9)   | 3/38( 7.9)  | 0/11( 0.0)  |
| Statistical analysis                          |              |              |             |             |
| Peto test                                     |              |              |             |             |
| Standard method(d)                            | P = -----    |              |             |             |
| Prevalence method(d)                          | P = 0.4582   |              |             |             |
| Combined analysis(d)                          | P = -----    |              |             |             |
| Cochran-Armitage test(e)                      | P = 0.4202   |              |             |             |
| Fisher Exact test(e)                          |              | P = 0.5000   | P = 0.5000  | P = 0.5000  |
| SITE : pituitary gland<br>TUMOR : adenoma     |              |              |             |             |
| Tumor rate                                    |              |              |             |             |
| Overall rates(a)                              | 8/50( 16.0)  | 14/50( 28.0) | 7/50( 14.0) | 2/50( 4.0)  |
| Adjusted rates(b)                             | 18.42        | 26.32        | 15.79       | 10.00       |
| Terminal rates(c)                             | 7/38( 18.4)  | 10/38( 26.3) | 6/38( 15.8) | 1/11( 9.1)  |
| Statistical analysis                          |              |              |             |             |
| Peto test                                     |              |              |             |             |
| Standard method(d)                            | P = 0.3914   |              |             |             |
| Prevalence method(d)                          | P = 0.8854   |              |             |             |
| Combined analysis(d)                          | P = 0.8215   |              |             |             |
| Cochran-Armitage test(e)                      | P = 0.0075** |              |             |             |
| Fisher Exact test(e)                          |              | P = 0.1135   | P = 0.5000  | P = 0.0458* |
| SITE : thyroid<br>TUMOR : C-cell adenoma      |              |              |             |             |
| Tumor rate                                    |              |              |             |             |
| Overall rates(a)                              | 7/50( 14.0)  | 4/49( 8.2)   | 7/50( 14.0) | 4/50( 8.0)  |
| Adjusted rates(b)                             | 18.42        | 8.51         | 16.28       | 9.52        |
| Terminal rates(c)                             | 7/38( 18.4)  | 3/37( 8.1)   | 6/38( 15.8) | 0/11( 0.0)  |
| Statistical analysis                          |              |              |             |             |
| Peto test                                     |              |              |             |             |
| Standard method(d)                            | P = -----    |              |             |             |
| Prevalence method(d)                          | P = 0.5544   |              |             |             |
| Combined analysis(d)                          | P = -----    |              |             |             |
| Cochran-Armitage test(e)                      | P = 0.4870   |              |             |             |
| Fisher Exact test(e)                          |              | P = 0.2740   | P = 0.6129  | P = 0.2623  |

STUDY No. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 5

| Group Name  | Control     | 10 ppm      | 30 ppm      | 90 ppm      |
|---|-------------|-------------|-------------|-------------|
| SITE : thyroid<br>TUMOR : follicular adenocarcinoma                     |             |             |             |             |
| Tumor rate  |             |             |             |             |
| Overall rates(a)  | 0/50( 0.0)  | 0/49( 0.0)  | 3/50( 6.0)  | 0/50( 0.0)  |
| Adjusted rates(b)   | 0.0         | 0.0         | 7.89        | 0.0         |
| Terminal rates(c)   | 0/38( 0.0)  | 0/37( 0.0)  | 3/38( 7.9)  | 0/11( 0.0)  |
| Statistical analysis  |             |             |             |             |
| Peto test   |             |             |             |             |
| Standard method(d)  | P = -----   |             |             |             |
| Prevalence method(d)  | P = 0.2050  |             |             |             |
| Combined analysis(d)  | P = -----   |             |             |             |
| Cochran-Armitage test(e)  | P = 0.8962  |             |             |             |
| Fisher Exact test(e)  |             | P = N. C.   | P = 0.1212  | P = N. C.   |
| SITE : thyroid<br>TUMOR : C-cell adenoma, C-cell carcinoma              |             |             |             |             |
| Tumor rate  |             |             |             |             |
| Overall rates(a)  | 8/50( 16.0) | 5/49( 10.2) | 8/50( 16.0) | 5/50( 10.0) |
| Adjusted rates(b)   | 18.42       | 10.64       | 18.60       | 9.52        |
| Terminal rates(c)   | 7/38( 18.4) | 3/37( 8.1)  | 7/38( 18.4) | 0/11( 0.0)  |
| Statistical analysis  |             |             |             |             |
| Peto test   |             |             |             |             |
| Standard method(d)  | P = 0.1663  |             |             |             |
| Prevalence method(d)  | P = 0.6139  |             |             |             |
| Combined analysis(d)  | P = 0.4918  |             |             |             |
| Cochran-Armitage test(e)  | P = 0.5161  |             |             |             |
| Fisher Exact test(e)  |             | P = 0.2900  | P = 0.6071  | P = 0.2768  |
| SITE : thyroid<br>TUMOR : follicular adenoma, follicular adenocarcinoma |             |             |             |             |
| Tumor rate  |             |             |             |             |
| Overall rates(a)  | 0/50( 0.0)  | 0/49( 0.0)  | 4/50( 8.0)  | 0/50( 0.0)  |
| Adjusted rates(b)   | 0.0         | 0.0         | 10.53       | 0.0         |
| Terminal rates(c)   | 0/38( 0.0)  | 0/37( 0.0)  | 4/38( 10.5) | 0/11( 0.0)  |
| Statistical analysis  |             |             |             |             |
| Peto test   |             |             |             |             |
| Standard method(d)  | P = -----   |             |             |             |
| Prevalence method(d)  | P = 0.1842  |             |             |             |
| Combined analysis(d)  | P = -----   |             |             |             |
| Cochran-Armitage test(e)  | P = 0.8800  |             |             |             |
| Fisher Exact test(e)  |             | P = N. C.   | P = 0.0587  | P = N. C.   |

STUDY No. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 6

| Group Name   | Control      | 10 ppm       | 30 ppm       | 90 ppm       |
|--|--------------|--------------|--------------|--------------|
| SITE : adrenal gland<br>TUMOR : pheochromocytoma                             |              |              |              |              |
| Tumor rate   |              |              |              |              |
| Overall rates(a)   | 4/50( 8.0)   | 6/50( 12.0)  | 2/50( 4.0)   | 1/50( 2.0)   |
| Adjusted rates(b)  | 10.53        | 15.79        | 4.76         | 3.13         |
| Terminal rates(c)  | 4/38( 10.5)  | 6/38( 15.8)  | 1/38( 2.6)   | 0/11( 0.0)   |
| Statistical analysis   |              |              |              |              |
| Peto test  |              |              |              |              |
| Standard method(d)   | P = -----    |              |              |              |
| Prevalence method(d)   | P = 0.8466   |              |              |              |
| Combined analysis(d)   | P = -----    |              |              |              |
| Cochran-Armitage test(e)   | P = 0.0808   |              |              |              |
| Fisher Exact test(e)   |              | P = 0.3703   | P = 0.3389   | P = 0.1811   |
| SITE : adrenal gland<br>TUMOR : pheochromocytoma, pheochromocytoma:malignant |              |              |              |              |
| Tumor rate   |              |              |              |              |
| Overall rates(a)   | 6/50( 12.0)  | 7/50( 14.0)  | 2/50( 4.0)   | 2/50( 4.0)   |
| Adjusted rates(b)  | 13.16        | 15.79        | 4.76         | 3.23         |
| Terminal rates(c)  | 5/38( 13.2)  | 6/38( 15.8)  | 1/38( 2.6)   | 0/11( 0.0)   |
| Statistical analysis   |              |              |              |              |
| Peto test  |              |              |              |              |
| Standard method(d)   | P = 0.3217   |              |              |              |
| Prevalence method(d)   | P = 0.8894   |              |              |              |
| Combined analysis(d)   | P = 0.8045   |              |              |              |
| Cochran-Armitage test(e)   | P = 0.0782   |              |              |              |
| Fisher Exact test(e)   |              | P = 0.5000   | P = 0.1343   | P = 0.1343   |
| SITE : testis<br>TUMOR : interstitial cell tumor                             |              |              |              |              |
| Tumor rate   |              |              |              |              |
| Overall rates(a)   | 47/50( 94.0) | 38/50( 76.0) | 40/50( 80.0) | 24/50( 48.0) |
| Adjusted rates(b)  | 97.44        | 86.84        | 94.74        | 100.00       |
| Terminal rates(c)  | 37/38( 97.4) | 33/38( 86.8) | 36/38( 94.7) | 11/11(100.0) |
| Statistical analysis   |              |              |              |              |
| Peto test  |              |              |              |              |
| Standard method(d)   | P = -----    |              |              |              |
| Prevalence method(d)   | P = 0.3458   |              |              |              |
| Combined analysis(d)   | P = -----    |              |              |              |
| Cochran-Armitage test(e)   | P < 0.0001** |              |              |              |
| Fisher Exact test(e)   |              | P = 0.0113*  | P = 0.0357*  | P < 0.0001** |

STUDY No. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 SEX : MALE

# NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 7

| Group Name   | Control    | 10 ppm     | 30 ppm     | 90 ppm     |
|--|------------|------------|------------|------------|
| SITE : preputial/clitoral gland<br>TUMOR : adenoma |            |            |            |            |
| Tumor rate   |            |            |            |            |
| Overall rates(a)                                   | 1/50( 2.0) | 1/50( 2.0) | 1/50( 2.0) | 3/50( 6.0) |
| Adjusted rates(b)                                  | 2.63       | 2.63       | 2.63       | 4.76       |
| Terminal rates(c)                                  | 1/38( 2.6) | 1/38( 2.6) | 1/38( 2.6) | 0/11( 0.0) |
| Statistical analysis                               |            |            |            |            |
| Peto test  |            |            |            |            |
| Standard method(d)                                 | P = 0.1077 |            |            |            |
| Prevalence method(d)                               | P = 0.1861 |            |            |            |
| Combined analysis(d)                               | P = 0.0710 |            |            |            |
| Cochran-Armitage test(e)                           | P = 0.1721 |            |            |            |
| Fisher Exact test(e)                               |            | P = 0.7525 | P = 0.7525 | P = 0.3087 |
| SITE : peritoneum<br>TUMOR : mesothelioma          |            |            |            |            |
| Tumor rate   |            |            |            |            |
| Overall rates(a)                                   | 0/50( 0.0) | 1/50( 2.0) | 3/50( 6.0) | 1/50( 2.0) |
| Adjusted rates(b)                                  | 0.0        | 2.63       | 7.89       | 7.69       |
| Terminal rates(c)                                  | 0/38( 0.0) | 1/38( 2.6) | 3/38( 7.9) | 0/11( 0.0) |
| Statistical analysis                               |            |            |            |            |
| Peto test  |            |            |            |            |
| Standard method(d)                                 | P = -----  |            |            |            |
| Prevalence method(d)                               | P = 0.0845 |            |            |            |
| Combined analysis(d)                               | P = -----  |            |            |            |
| Cochran-Armitage test(e)                           | P = 0.7213 |            |            |            |
| Fisher Exact test(e)                               |            | P = 0.5000 | 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.

## APPENDIX O 2

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

STUDY No. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name  | Control       | 10 ppm      | 30 ppm      | 90 ppm       |
|---|---------------|-------------|-------------|--------------|
| SITE : nasal cavity<br>TUMOR : squamous cell carcinoma                          |               |             |             |              |
| Tumor rate  |               |             |             |              |
| Overall rates(a)  | 0/50( 0.0)    | 0/50( 0.0)  | 0/50( 0.0)  | 28/50( 56.0) |
| Adjusted rates(b)   | 0.0           | 0.0         | 0.0         | 37.50        |
| Terminal rates(c)   | 0/40( 0.0)    | 0/45( 0.0)  | 0/41( 0.0)  | 5/15( 33.3)  |
| Statistical analysis  |               |             |             |              |
| Peto test   |               |             |             |              |
| Standard method(d)  | P < 0.0001**? |             |             |              |
| Prevalence method(d)  | P < 0.0001**? |             |             |              |
| Combined analysis(d)  | P < 0.0001**? |             |             |              |
| Cochran-Armitage test(e)  | P < 0.0001**  |             |             |              |
| Fisher Exact test(e)  |               | P = N. C.   | P = N. C.   | P < 0.0001** |
| SITE : nasal cavity<br>TUMOR : squamous cell papilloma, squamous cell carcinoma |               |             |             |              |
| Tumor rate  |               |             |             |              |
| Overall rates(a)  | 0/50( 0.0)    | 0/50( 0.0)  | 0/50( 0.0)  | 28/50( 56.0) |
| Adjusted rates(b)   | 0.0           | 0.0         | 0.0         | 37.50        |
| Terminal rates(c)   | 0/40( 0.0)    | 0/45( 0.0)  | 0/41( 0.0)  | 5/15( 33.3)  |
| Statistical analysis  |               |             |             |              |
| Peto test   |               |             |             |              |
| Standard method(d)  | P < 0.0001**? |             |             |              |
| Prevalence method(d)  | P < 0.0001**? |             |             |              |
| Combined analysis(d)  | P < 0.0001**? |             |             |              |
| Cochran-Armitage test(e)  | P < 0.0001**  |             |             |              |
| Fisher Exact test(e)  |               | P = N. C.   | P = N. C.   | P < 0.0001** |
| SITE : spleen<br>TUMOR : mononuclear cell leukemia                              |               |             |             |              |
| Tumor rate  |               |             |             |              |
| Overall rates(a)  | 7/50( 14.0)   | 8/50( 16.0) | 5/49( 10.2) | 13/50( 26.0) |
| Adjusted rates(b)   | 12.50         | 15.56       | 10.00       | 41.18        |
| Terminal rates(c)   | 5/40( 12.5)   | 7/45( 15.6) | 4/40( 10.0) | 6/15( 40.0)  |
| Statistical analysis  |               |             |             |              |
| Peto test   |               |             |             |              |
| Standard method(d)  | P = 0.1084    |             |             |              |
| Prevalence method(d)  | P = 0.0050**  |             |             |              |
| Combined analysis(d)  | P = 0.0023**  |             |             |              |
| Cochran-Armitage test(e)  | P = 0.0749    |             |             |              |
| Fisher Exact test(e)  |               | P = 0.5000  | P = 0.3942  | P = 0.1054   |

STUDY No. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name  | Control      | 10 ppm       | 30 ppm       | 90 ppm      |
|---|--------------|--------------|--------------|-------------|
| SITE : pituitary gland<br>TUMOR : adenoma                 |              |              |              |             |
| Tumor rate  |              |              |              |             |
| Overall rates(a)  | 15/50( 30.0) | 16/50( 32.0) | 14/50( 28.0) | 5/50( 10.0) |
| Adjusted rates(b)   | 25.58        | 29.79        | 26.83        | 18.52       |
| Terminal rates(c)   | 10/40( 25.0) | 13/45( 28.9) | 11/41( 26.8) | 2/15( 13.3) |
| Statistical analysis                                      |              |              |              |             |
| Peto test   |              |              |              |             |
| Standard method(d)  | P = 0.8906   |              |              |             |
| Prevalence method(d)                                      | P = 0.9538   |              |              |             |
| Combined analysis(d)                                      | P = 0.9815   |              |              |             |
| Cochran-Armitage test(e)                                  | P = 0.0054** |              |              |             |
| Fisher Exact test(e)                                      |              | P = 0.5000   | P = 0.5000   | P = 0.0114* |
| SITE : pituitary gland<br>TUMOR : adenoma, adenocarcinoma |              |              |              |             |
| Tumor rate  |              |              |              |             |
| Overall rates(a)  | 15/50( 30.0) | 17/50( 34.0) | 15/50( 30.0) | 5/50( 10.0) |
| Adjusted rates(b)   | 25.58        | 31.91        | 26.83        | 18.52       |
| Terminal rates(c)   | 10/40( 25.0) | 14/45( 31.1) | 11/41( 26.8) | 2/15( 13.3) |
| Statistical analysis                                      |              |              |              |             |
| Peto test   |              |              |              |             |
| Standard method(d)  | P = 0.8717   |              |              |             |
| Prevalence method(d)                                      | P = 0.9601   |              |              |             |
| Combined analysis(d)                                      | P = 0.9828   |              |              |             |
| Cochran-Armitage test(e)                                  | P = 0.0042** |              |              |             |
| Fisher Exact test(e)                                      |              | P = 0.4152   | P = 0.5862   | P = 0.0114* |
| SITE : thyroid<br>TUMOR : C-cell adenoma                  |              |              |              |             |
| Tumor rate  |              |              |              |             |
| Overall rates(a)  | 4/50( 8.0)   | 7/50( 14.0)  | 9/50( 18.0)  | 4/50( 8.0)  |
| Adjusted rates(b)   | 8.89         | 14.00        | 20.00        | 13.33       |
| Terminal rates(c)   | 2/40( 5.0)   | 6/45( 13.3)  | 8/41( 19.5)  | 2/15( 13.3) |
| Statistical analysis                                      |              |              |              |             |
| Peto test   |              |              |              |             |
| Standard method(d)  | P = -----    |              |              |             |
| Prevalence method(d)                                      | P = 0.5749   |              |              |             |
| Combined analysis(d)                                      | P = -----    |              |              |             |
| Cochran-Armitage test(e)                                  | P = 0.6180   |              |              |             |
| Fisher Exact test(e)                                      |              | P = 0.2623   | P = 0.1168   | P = 0.6425  |

STUDY No. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 11

| Group Name   | Control     | 10 ppm      | 30 ppm       | 90 ppm      |
|--|-------------|-------------|--------------|-------------|
| SITE : thyroid<br>TUMOR : C-cell adenoma, C-cell carcinoma |             |             |              |             |
| Tumor rate   |             |             |              |             |
| Overall rates(a)   | 5/50( 10.0) | 7/50( 14.0) | 11/50( 22.0) | 4/50( 8.0)  |
| Adjusted rates(b)  | 11.11       | 14.00       | 24.44        | 13.33       |
| Terminal rates(c)  | 3/40( 7.5)  | 6/45( 13.3) | 10/41( 24.4) | 2/15( 13.3) |
| Statistical analysis                                       |             |             |              |             |
| Peto test  |             |             |              |             |
| Standard method(d)   | P = -----   |             |              |             |
| Prevalence method(d)                                       | P = 0.6298  |             |              |             |
| Combined analysis(d)                                       | P = -----   |             |              |             |
| Cochran-Armitage test(e)                                   | P = 0.4861  |             |              |             |
| Fisher Exact test(e)                                       |             | P = 0.3798  | P = 0.0857   | P = 0.5000  |
| SITE : uterus<br>TUMOR : endometrial stromal polyp         |             |             |              |             |
| Tumor rate   |             |             |              |             |
| Overall rates(a)   | 7/50( 14.0) | 6/50( 12.0) | 6/50( 12.0)  | 7/50( 14.0) |
| Adjusted rates(b)  | 14.00       | 13.33       | 14.63        | 20.00       |
| Terminal rates(c)  | 5/40( 12.5) | 6/45( 13.3) | 6/41( 14.6)  | 3/15( 20.0) |
| Statistical analysis                                       |             |             |              |             |
| Peto test  |             |             |              |             |
| Standard method(d)   | P = -----   |             |              |             |
| Prevalence method(d)                                       | P = 0.2599  |             |              |             |
| Combined analysis(d)                                       | P = -----   |             |              |             |
| Cochran-Armitage test(e)                                   | P = 0.8803  |             |              |             |
| Fisher Exact test(e)                                       |             | P = 0.5000  | P = 0.5000   | P = 0.6129  |
| SITE : mammary gland<br>TUMOR : adenoma                    |             |             |              |             |
| Tumor rate   |             |             |              |             |
| Overall rates(a)   | 1/50( 2.0)  | 3/50( 6.0)  | 1/50( 2.0)   | 0/50( 0.0)  |
| Adjusted rates(b)  | 2.27        | 6.38        | 2.38         | 0.0         |
| Terminal rates(c)  | 0/40( 0.0)  | 2/45( 4.4)  | 0/41( 0.0)   | 0/15( 0.0)  |
| Statistical analysis                                       |             |             |              |             |
| Peto test  |             |             |              |             |
| Standard method(d)   | P = -----   |             |              |             |
| Prevalence method(d)                                       | P = 0.8551  |             |              |             |
| Combined analysis(d)                                       | P = -----   |             |              |             |
| Cochran-Armitage test(e)                                   | P = 0.1836  |             |              |             |
| Fisher Exact test(e)                                       |             | P = 0.3087  | P = 0.7525   | P = 0.5000  |



STUDY No. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 12

| Group Name   | Control     | 10 ppm      | 30 ppm      | 90 ppm     |
|--|-------------|-------------|-------------|------------|
| SITE : mammary gland<br>TUMOR : fibroadenoma                   |             |             |             |            |
| Tumor rate   |             |             |             |            |
| Overall rates(a)   | 4/50( 8.0)  | 5/50( 10.0) | 5/50( 10.0) | 1/50( 2.0) |
| Adjusted rates(b)  | 10.00       | 10.42       | 10.20       | 4.55       |
| Terminal rates(c)  | 4/40( 10.0) | 4/45( 8.9)  | 4/41( 9.8)  | 0/15( 0.0) |
| Statistical analysis   |             |             |             |            |
| Peto test  |             |             |             |            |
| Standard method(d)   | P = -----   |             |             |            |
| Prevalence method(d)   | P = 0.8358  |             |             |            |
| Combined analysis(d)   | P = -----   |             |             |            |
| Cochran-Armitage test(e)                                       | P = 0.1288  |             |             |            |
| Fisher Exact test(e)   |             | P = 0.5000  | P = 0.5000  | P = 0.1811 |
| SITE : mammary gland<br>TUMOR : adenoma, fibroma, fibroadenoma |             |             |             |            |
| Tumor rate   |             |             |             |            |
| Overall rates(a)   | 5/50( 10.0) | 8/50( 16.0) | 6/50( 12.0) | 2/50( 4.0) |
| Adjusted rates(b)  | 11.36       | 16.67       | 12.24       | 4.55       |
| Terminal rates(c)  | 4/40( 10.0) | 6/45( 13.3) | 4/41( 9.8)  | 0/15( 0.0) |
| Statistical analysis   |             |             |             |            |
| Peto test  |             |             |             |            |
| Standard method(d)   | P = -----   |             |             |            |
| Prevalence method(d)   | P = 0.9177  |             |             |            |
| Combined analysis(d)   | P = -----   |             |             |            |
| Cochran-Armitage test(e)                                       | P = 0.1091  |             |             |            |
| Fisher Exact test(e)   |             | P = 0.2768  | P = 0.5000  | P = 0.2180 |

(HPT360A)

BAIS4

STUDY No. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 13

| Group Name   | Control     | 10 ppm       | 30 ppm      | 90 ppm     |
|--|-------------|--------------|-------------|------------|
| SITE : mammary gland                                   |             |              |             |            |
| TUMOR : adenoma, adenocarcinoma, fibroma, fibroadenoma |             |              |             |            |
| Tumor rate   |             |              |             |            |
| Overall rates(a)                                       | 5/50( 10.0) | 10/50( 20.0) | 6/50( 12.0) | 2/50( 4.0) |
| Adjusted rates(b)                                      | 11.96       | 19.15        | 12.24       | 4.55       |
| Terminal rates(c)                                      | 4/40( 10.0) | 7/45( 15.6)  | 4/41( 9.8)  | 0/15( 0.0) |
| Statistical analysis                                   |             |              |             |            |
| Peto test  |             |              |             |            |
| Standard method(d)                                     | P = 0.4769  |              |             |            |
| Prevalence method(d)                                   | P = 0.9316  |              |             |            |
| Combined analysis(d)                                   | P = 0.9395  |              |             |            |
| Cochran-Armitage test(e)                               | P = 0.0679  |              |             |            |
| Fisher Exact test(e)                                   |             | P = 0.1312   | P = 0.5000  | P = 0.2180 |

(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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 1

|                                  |                              | Group Name              | Control | 10 ppm | 30 ppm | 90 ppm |
|----------------------------------|------------------------------|-------------------------|---------|--------|--------|--------|
|                                  |                              | No. of Animals on Study | 50      | 50     | 50     | 50     |
| Organ                            | Findings                     |                         |         |        |        |        |
| {Integumentary system/appandage} |                              |                         |         |        |        |        |
| skin/app                         |                              |                         | <50>    | <50>   | <50>   | <50>   |
|                                  | leukemic cell infiltration   |                         | 0       | 1      | 0      | 0      |
| {Respiratory system}             |                              |                         |         |        |        |        |
| trachea                          |                              |                         | <50>    | <50>   | <50>   | <50>   |
|                                  | metastasis:thyroid tumor     |                         | 1       | 0      | 0      | 0      |
| lung                             |                              |                         | <50>    | <50>   | <50>   | <50>   |
|                                  | leukemic cell infiltration   |                         | 4       | 4      | 4      | 5      |
|                                  | metastasis:liver tumor       |                         | 0       | 0      | 1      | 0      |
|                                  | metastasis:thyroid tumor     |                         | 1       | 0      | 1      | 0      |
|                                  | metastasis:subcutis tumor    |                         | 0       | 2      | 0      | 0      |
|                                  | metastasis:bone tumor        |                         | 0       | 1      | 0      | 0      |
|                                  | metastasis:nasal tumor       |                         | 0       | 0      | 0      | 2      |
|                                  | metastasis:mediastinum tumor |                         | 0       | 0      | 0      | 1      |
| {Hematopoietic system}           |                              |                         |         |        |        |        |
| bone marrow                      |                              |                         | <50>    | <50>   | <50>   | <50>   |
|                                  | leukemic cell infiltration   |                         | 2       | 1      | 1      | 2      |
|                                  | metastasis:liver tumor       |                         | 0       | 0      | 1      | 0      |
|                                  | metastasis:spleen tumor      |                         | 0       | 1      | 0      | 0      |
| lymph node                       |                              |                         | <50>    | <50>   | <50>   | <50>   |
|                                  | leukemic cell infiltration   |                         | 3       | 3      | 1      | 0      |

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

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 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 | 10 ppm<br>50 | 30 ppm<br>50 | 90 ppm<br>50 |
|--|----------------------------|---------------|--------------|--------------|--------------|
| Organ  | Findings                   |               |              |              |              |
| {Hematopoietic system}                           |                            |               |              |              |              |
| lymph node                                       | metastasis:spleen tumor    | <50><br>0     | <50><br>1    | <50><br>0    | <50><br>0    |
|  | metastasis:nasal tumor     | 0             | 0            | 0            | 3            |
| {Circulatory system}                             |                            |               |              |              |              |
| heart  | leukemic cell infiltration | <50><br>1     | <50><br>0    | <50><br>0    | <50><br>0    |
|  |                            |               |              |              |              |
| {Digestive system}                               |                            |               |              |              |              |
| stomach  | leukemic cell infiltration | <50><br>0     | <50><br>0    | <50><br>1    | <50><br>0    |
|  |                            |               |              |              |              |
| liver  | leukemic cell infiltration | <50><br>4     | <50><br>5    | <50><br>6    | <50><br>4    |
|  | metastasis:bone tumor      | 0             | 1            | 0            | 0            |
| pancreas   | leukemic cell infiltration | <50><br>1     | <50><br>1    | <50><br>1    | <50><br>0    |
|  |                            |               |              |              |              |
| {Urinary system}                                 |                            |               |              |              |              |
| kidney   | leukemic cell infiltration | <50><br>2     | <50><br>2    | <50><br>1    | <50><br>0    |
|  |                            |               |              |              |              |
| urin bladd                                       | leukemic cell infiltration | <50><br>0     | <50><br>0    | <50><br>1    | <50><br>0    |
|  |                            |               |              |              |              |
| {Endocrine system}                               |                            |               |              |              |              |
| pituitary  | leukemic cell infiltration | <50><br>0     | <50><br>1    | <50><br>1    | <50><br>0    |
|  |                            |               |              |              |              |
| < a > a : Number of animals examined at the site |                            |               |              |              |              |
| b b : Number of animals with lesion              |                            |               |              |              |              |

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 3

|                                  |                            | Group Name              | Control   | 10 ppm    | 30 ppm    | 90 ppm    |
|----------------------------------|----------------------------|-------------------------|-----------|-----------|-----------|-----------|
|                                  |                            | No. of Animals on Study | 50        | 50        | 50        | 50        |
| Organ                            | Findings                   |                         |           |           |           |           |
| {Endocrine system}               |                            |                         |           |           |           |           |
| adrenal                          | leukemic cell infiltration |                         | <50><br>0 | <50><br>1 | <50><br>1 | <50><br>0 |
| {Reproductive system}            |                            |                         |           |           |           |           |
| prostate                         | leukemic cell infiltration |                         | <50><br>1 | <50><br>1 | <50><br>0 | <50><br>0 |
| {Nervous system}                 |                            |                         |           |           |           |           |
| brain                            | leukemic cell infiltration |                         | <50><br>2 | <50><br>2 | <50><br>2 | <50><br>2 |
|                                  | metastasis: nasal tumor    |                         | 0         | 0         | 0         | 2         |
| spinal cord                      | leukemic cell infiltration |                         | <50><br>2 | <50><br>0 | <50><br>0 | <50><br>0 |
| {Special sense organs/appendage} |                            |                         |           |           |           |           |
| Harder gl                        | metastasis: nasal tumor    |                         | <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

(JPT150)

BAIS4

## APPENDIX P 2

HISTOPATHOLOGICAL FINDINGS :

METASTASIS OF TUMOR :

MALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 1

|                                  |                              | Group Name              | Control   | 10 ppm    | 30 ppm    | 90 ppm    |
|----------------------------------|------------------------------|-------------------------|-----------|-----------|-----------|-----------|
|                                  |                              | No. of Animals on Study | 12        | 12        | 12        | 39        |
| Organ                            | Findings                     |                         |           |           |           |           |
| {Integumentary system/appandage} |                              |                         |           |           |           |           |
| skin/app                         | leukemic cell infiltration   |                         | <12><br>0 | <12><br>1 | <12><br>0 | <39><br>0 |
| {Respiratory system}             |                              |                         |           |           |           |           |
| trachea                          | metastasis:thyroid tumor     |                         | <12><br>1 | <12><br>0 | <12><br>0 | <39><br>0 |
| lung                             | leukemic cell infiltration   |                         | <12><br>3 | <12><br>3 | <12><br>3 | <39><br>4 |
|                                  | metastasis:thyroid tumor     |                         | 1         | 0         | 0         | 0         |
|                                  | metastasis:subcutis tumor    |                         | 0         | 1         | 0         | 0         |
|                                  | metastasis:nasal tumor       |                         | 0         | 0         | 0         | 2         |
|                                  | metastasis:mediastinum tumor |                         | 0         | 0         | 0         | 1         |
| {Hematopoietic system}           |                              |                         |           |           |           |           |
| bone marrow                      | leukemic cell infiltration   |                         | <12><br>2 | <12><br>1 | <12><br>1 | <39><br>2 |
|                                  | metastasis:spleen tumor      |                         | 0         | 1         | 0         | 0         |
| lymph node                       | leukemic cell infiltration   |                         | <12><br>2 | <12><br>1 | <12><br>0 | <39><br>0 |
|                                  | metastasis:spleen tumor      |                         | 0         | 1         | 0         | 0         |
|                                  | metastasis:nasal tumor       |                         | 0         | 0         | 0         | 3         |
| {Circulatory system}             |                              |                         |           |           |           |           |
| heart                            | leukemic cell infiltration   |                         | <12><br>1 | <12><br>0 | <12><br>0 | <39><br>0 |

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



STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 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>12 | 10 ppm<br>12 | 30 ppm<br>12 | 90 ppm<br>39 |
|-----------------------|----------------------------|---------------------------------------|---------------|--------------|--------------|--------------|
| Organ                 | Findings                   |                                       |               |              |              |              |
| {Digestive system}    |                            |                                       |               |              |              |              |
| stomach               | leukemic cell infiltration |                                       | <12><br>0     | <12><br>0    | <12><br>1    | <39><br>0    |
| liver                 | leukemic cell infiltration |                                       | <12><br>3     | <12><br>4    | <12><br>3    | <39><br>3    |
| pancreas              | leukemic cell infiltration |                                       | <12><br>1     | <12><br>1    | <12><br>1    | <39><br>0    |
| {Urinary system}      |                            |                                       |               |              |              |              |
| kidney                | leukemic cell infiltration |                                       | <12><br>2     | <12><br>2    | <12><br>1    | <39><br>0    |
| urin bladd            | leukemic cell infiltration |                                       | <12><br>0     | <12><br>0    | <12><br>1    | <39><br>0    |
| {Endocrine system}    |                            |                                       |               |              |              |              |
| pituitary             | leukemic cell infiltration |                                       | <12><br>0     | <12><br>0    | <12><br>1    | <39><br>0    |
| adrenal               | leukemic cell infiltration |                                       | <12><br>0     | <12><br>1    | <12><br>1    | <39><br>0    |
| {Reproductive system} |                            |                                       |               |              |              |              |
| prostate              | leukemic cell infiltration |                                       | <12><br>1     | <12><br>1    | <12><br>0    | <39><br>0    |
| {Nervous system}      |                            |                                       |               |              |              |              |
| brain                 | leukemic cell infiltration |                                       | <12><br>2     | <12><br>2    | <12><br>2    | <39><br>2    |

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

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : MALE

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

PAGE : 3

|                                  |                            | Group Name                                 | Control | 10 ppm | 30 ppm | 90 ppm |
|----------------------------------|----------------------------|--|---------|--------|--------|--------|
|                                  |                            | No. of Animals on Study                    | 12      | 12     | 12     | 39     |
| Organ                            | Findings                   |  |         |        |        |        |
| {Nervous system}                 |                            |  |         |        |        |        |
| brain                            |                            |  | <12>    | <12>   | <12>   | <39>   |
|                                  | metastasis: nasal tumor    |  | 0       | 0      | 0      | 2      |
| spinal cord                      |                            |  | <12>    | <12>   | <12>   | <39>   |
|                                  | leukemic cell infiltration |  | 2       | 0      | 0      | 0      |
| {Special sense organs/appendage} |                            |  |         |        |        |        |
| Harder gl                        |                            |  | <12>    | <12>   | <12>   | <39>   |
|                                  | metastasis: nasal tumor    |  | 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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

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

PAGE : 1

|                        |                            | Group Name<br>No. of Animals on Study | Control<br>38 | 10 ppm<br>38 | 30 ppm<br>38 | 90 ppm<br>11 |
|------------------------|----------------------------|---------------------------------------|---------------|--------------|--------------|--------------|
| Organ                  | Findings                   |                                       |               |              |              |              |
| {Respiratory system}   |                            |                                       |               |              |              |              |
| lung                   |                            |                                       | <38>          | <38>         | <38>         | <11>         |
|                        | leukemic cell infiltration |                                       | 1             | 1            | 1            | 1            |
|                        | metastasis:liver tumor     |                                       | 0             | 0            | 1            | 0            |
|                        | metastasis:thyroid tumor   |                                       | 0             | 0            | 1            | 0            |
|                        | metastasis:subcutis tumor  |                                       | 0             | 1            | 0            | 0            |
|                        | metastasis:bone tumor      |                                       | 0             | 1            | 0            | 0            |
| {Hematopoietic system} |                            |                                       |               |              |              |              |
| bone marrow            |                            |                                       | <38>          | <38>         | <38>         | <11>         |
|                        | metastasis:liver tumor     |                                       | 0             | 0            | 1            | 0            |
| lymph node             |                            |                                       | <38>          | <38>         | <38>         | <11>         |
|                        | leukemic cell infiltration |                                       | 1             | 2            | 1            | 0            |
| {Digestive system}     |                            |                                       |               |              |              |              |
| liver                  |                            |                                       | <38>          | <38>         | <38>         | <11>         |
|                        | leukemic cell infiltration |                                       | 1             | 1            | 3            | 1            |
|                        | metastasis:bone tumor      |                                       | 0             | 1            | 0            | 0            |
| {Endocrine system}     |                            |                                       |               |              |              |              |
| pituitary              |                            |                                       | <38>          | <38>         | <38>         | <11>         |
|                        | leukemic cell infiltration |                                       | 0             | 1            | 0            | 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. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 4

|                        |  | Group Name<br>No. of Animals on Study | Control<br>50 | 10 ppm<br>50 | 30 ppm<br>50 | 90 ppm<br>50 |
|------------------------|--|---------------------------------------|---------------|--------------|--------------|--------------|
| Organ                  | Findings                                   |                                       |               |              |              |              |
| {Respiratory system}   |  |                                       |               |              |              |              |
| larynx                 |  |                                       | <50>          | <50>         | <50>         | <50>         |
|                        | metastasis:vertebra tumor                  |                                       | 1             | 0            | 0            | 0            |
| lung                   |  |                                       | <50>          | <50>         | <50>         | <50>         |
|                        | leukemic cell infiltration                 |                                       | 3             | 4            | 4            | 5            |
|                        | metastasis:uterus tumor                    |                                       | 0             | 1            | 0            | 0            |
|                        | metastasis:mammary gland tumor             |                                       | 0             | 1            | 0            | 0            |
|                        | metastasis:vertebra tumor                  |                                       | 1             | 0            | 0            | 0            |
| {Hematopoietic system} |  |                                       |               |              |              |              |
| bone marrow            |  |                                       | <50>          | <50>         | <50>         | <50>         |
|                        | leukemic cell infiltration                 |                                       | 0             | 0            | 1            | 3            |
| lymph node             |  |                                       | <50>          | <50>         | <50>         | <50>         |
|                        | leukemic cell infiltration                 |                                       | 0             | 2            | 0            | 5            |
|                        | metastasis:vertebra tumor                  |                                       | 1             | 0            | 0            | 0            |
|                        | metastasis:skin/appendage tumor            |                                       | 1             | 0            | 0            | 0            |
|                        | metastasis:large intestine tumor           |                                       | 0             | 0            | 1            | 0            |
| thymus                 |  |                                       | <50>          | <50>         | <50>         | <50>         |
|                        | metastasis:vertebra tumor                  |                                       | 1             | 0            | 0            | 0            |
| spleen                 |  |                                       | <50>          | <50>         | <50>         | <50>         |
|                        | metastasis:peritoneum tumor                |                                       | 1             | 0            | 0            | 0            |
| {Circulatory system}   |  |                                       |               |              |              |              |
| heart                  |  |                                       | <50>          | <50>         | <50>         | <50>         |
|                        | leukemic cell infiltration                 |                                       | 0             | 0            | 1            | 1            |
| < a >                  | a : Number of animals examined at the site |                                       |               |              |              |              |
| b                      | b : Number of animals with lesion          |                                       |               |              |              |              |

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 5

|                       |                                  | Group Name<br>No. of Animals on Study | Control<br>50 | 10 ppm<br>50 | 30 ppm<br>50 | 90 ppm<br>50 |
|-----------------------|----------------------------------|---------------------------------------|---------------|--------------|--------------|--------------|
| Organ                 | Findings                         |                                       |               |              |              |              |
| {Digestive system}    |                                  |                                       |               |              |              |              |
| liver                 |                                  |                                       | <50>          | <50>         | <50>         | <50>         |
|                       | leukemic cell infiltration       |                                       | 4             | 6            | 4            | 6            |
|                       | metastasis:uterus tumor          |                                       | 0             | 1            | 0            | 0            |
|                       | metastasis:large intestine tumor |                                       | 0             | 0            | 1            | 0            |
| pancreas              |                                  |                                       | <50>          | <50>         | <50>         | <50>         |
|                       | leukemic cell infiltration       |                                       | 0             | 0            | 0            | 1            |
|                       | metastasis:uterus tumor          |                                       | 0             | 1            | 0            | 0            |
| {Urinary system}      |                                  |                                       |               |              |              |              |
| kidney                |                                  |                                       | <50>          | <50>         | <50>         | <50>         |
|                       | leukemic cell infiltration       |                                       | 0             | 0            | 1            | 0            |
| {Endocrine system}    |                                  |                                       |               |              |              |              |
| pituitary             |                                  |                                       | <50>          | <50>         | <50>         | <50>         |
|                       | leukemic cell infiltration       |                                       | 0             | 1            | 0            | 3            |
| thyroid               |                                  |                                       | <50>          | <50>         | <50>         | <50>         |
|                       | metastasis:vertebra tumor        |                                       | 1             | 0            | 0            | 0            |
| adrenal               |                                  |                                       | <50>          | <50>         | <50>         | <50>         |
|                       | leukemic cell infiltration       |                                       | 0             | 1            | 0            | 2            |
| {Reproductive system} |                                  |                                       |               |              |              |              |
| ovary                 |                                  |                                       | <50>          | <50>         | <50>         | <50>         |
|                       | metastasis:uterus tumor          |                                       | 0             | 1            | 0            | 0            |

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

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 6

|  |                                  | Group Name<br>No. of Animals on Study | Control<br>50 | 10 ppm<br>50 | 30 ppm<br>50 | 90 ppm<br>50 |
|--|----------------------------------|---------------------------------------|---------------|--------------|--------------|--------------|
| Organ  | Findings                         |                                       |               |              |              |              |
| {Reproductive system}                            |                                  |                                       |               |              |              |              |
| ovary  |                                  |                                       | <50>          | <50>         | <50>         | <50>         |
|  | metastasis:large intestine tumor |                                       | 0             | 0            | 1            | 0            |
| {Nervous system}                                 |                                  |                                       |               |              |              |              |
| brain  |                                  |                                       | <50>          | <50>         | <50>         | <50>         |
|  | leukemic cell infiltration       |                                       | 0             | 0            | 1            | 0            |
|  | metastasis:pituitary tumor       |                                       | 0             | 1            | 1            | 0            |
|  | metastasis:nasal tumor           |                                       | 0             | 0            | 0            | 1            |
|  | metastasis:vertebra tumor        |                                       | 1             | 0            | 0            | 0            |
| spinal cord                                      |                                  |                                       | <50>          | <50>         | <50>         | <50>         |
|  | metastasis:vertebra tumor        |                                       | 1             | 0            | 0            | 0            |
| {Special sense organs/appendage}                 |                                  |                                       |               |              |              |              |
| eye  |                                  |                                       | <50>          | <50>         | <50>         | <50>         |
|  | metastasis:skin/appendage tumor  |                                       | 1             | 0            | 0            | 0            |
| Harder gl  |                                  |                                       | <50>          | <50>         | <50>         | <50>         |
|  | metastasis:nasal tumor           |                                       | 0             | 0            | 0            | 1            |
| {Body cavities}                                  |                                  |                                       |               |              |              |              |
| peritoneum                                       |                                  |                                       | <50>          | <50>         | <50>         | <50>         |
|  | metastasis:uterus tumor          |                                       | 1             | 0            | 0            | 0            |
| retroperit                                       |                                  |                                       | <50>          | <50>         | <50>         | <50>         |
|  | metastasis:uterus tumor          |                                       | 0             | 1            | 0            | 0            |
| < a > a : Number of animals examined at the site |                                  |                                       |               |              |              |              |
| b b : Number of animals with lesion              |                                  |                                       |               |              |              |              |



STUDY NO. : 0437  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 7

|                 |                                  | Group Name              | Control   | 10 ppm    | 30 ppm    | 90 ppm    |
|-----------------|----------------------------------|-------------------------|-----------|-----------|-----------|-----------|
|                 |                                  | No. of Animals on Study | 50        | 50        | 50        | 50        |
| Organ           | Findings                         |                         |           |           |           |           |
| {Body cavities} |                                  |                         |           |           |           |           |
| retroperit      | metastasis:large intestine tumor |                         | <50><br>0 | <50><br>0 | <50><br>1 | <50><br>0 |

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

(JPT150)

BAIS4

## APPENDIX P 5

HISTOPATHOLOGICAL FINDINGS :

METASTASIS OF TUMOR :

FEMALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 4

|                        |                                  | Group Name<br>No. of Animals on Study | Control<br>10 | 10 ppm<br>5 | 30 ppm<br>9 | 90 ppm<br>35 |
|------------------------|----------------------------------|---------------------------------------|---------------|-------------|-------------|--------------|
| Organ                  | Findings                         |                                       |               |             |             |              |
| {Respiratory system}   |                                  |                                       |               |             |             |              |
| larynx                 |                                  |                                       | <10>          | < 5>        | < 9>        | <35>         |
|                        | metastasis:vertebra tumor        |                                       | 1             | 0           | 0           | 0            |
| lung                   |                                  |                                       | <10>          | < 5>        | < 9>        | <35>         |
|                        | leukemic cell infiltration       |                                       | 2             | 1           | 1           | 4            |
|                        | metastasis:uterus tumor          |                                       | 0             | 1           | 0           | 0            |
|                        | metastasis:mammary gland tumor   |                                       | 0             | 1           | 0           | 0            |
|                        | metastasis:vertebra tumor        |                                       | 1             | 0           | 0           | 0            |
| {Hematopoietic system} |                                  |                                       |               |             |             |              |
| bone marrow            |                                  |                                       | <10>          | < 5>        | < 9>        | <35>         |
|                        | leukemic cell infiltration       |                                       | 0             | 0           | 1           | 3            |
| lymph node             |                                  |                                       | <10>          | < 5>        | < 9>        | <35>         |
|                        | leukemic cell infiltration       |                                       | 0             | 1           | 0           | 3            |
|                        | metastasis:vertebra tumor        |                                       | 1             | 0           | 0           | 0            |
|                        | metastasis:skin/appendage tumor  |                                       | 1             | 0           | 0           | 0            |
|                        | metastasis:large intestine tumor |                                       | 0             | 0           | 1           | 0            |
| thymus                 |                                  |                                       | <10>          | < 5>        | < 9>        | <35>         |
|                        | metastasis:vertebra tumor        |                                       | 1             | 0           | 0           | 0            |
| {Circulatory system}   |                                  |                                       |               |             |             |              |
| heart                  |                                  |                                       | <10>          | < 5>        | < 9>        | <35>         |
|                        | leukemic cell infiltration       |                                       | 0             | 0           | 0           | 1            |

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

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

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

PAGE : 5

|                       |                                  | Group Name<br>No. of Animals on Study | Control<br>10 | 10 ppm<br>5 | 30 ppm<br>9 | 90 ppm<br>35 |
|-----------------------|----------------------------------|---------------------------------------|---------------|-------------|-------------|--------------|
| Organ                 | Findings                         |                                       |               |             |             |              |
| {Digestive system}    |                                  |                                       |               |             |             |              |
| liver                 |                                  |                                       | <10>          | < 5>        | < 9>        | <35>         |
|                       | leukemic cell infiltration       |                                       | 1             | 1           | 1           | 5            |
|                       | metastasis:uterus tumor          |                                       | 0             | 1           | 0           | 0            |
|                       | metastasis:large intestine tumor |                                       | 0             | 0           | 1           | 0            |
| pancreas              |                                  |                                       | <10>          | < 5>        | < 9>        | <35>         |
|                       | leukemic cell infiltration       |                                       | 0             | 0           | 0           | 1            |
|                       | metastasis:uterus tumor          |                                       | 0             | 1           | 0           | 0            |
| {Urinary system}      |                                  |                                       |               |             |             |              |
| kidney                |                                  |                                       | <10>          | < 5>        | < 9>        | <35>         |
|                       | leukemic cell infiltration       |                                       | 0             | 0           | 1           | 0            |
| {Endocrine system}    |                                  |                                       |               |             |             |              |
| pituitary             |                                  |                                       | <10>          | < 5>        | < 9>        | <35>         |
|                       | leukemic cell infiltration       |                                       | 0             | 0           | 0           | 3            |
| thyroid               |                                  |                                       | <10>          | < 5>        | < 9>        | <35>         |
|                       | metastasis:vertebra tumor        |                                       | 1             | 0           | 0           | 0            |
| adrenal               |                                  |                                       | <10>          | < 5>        | < 9>        | <35>         |
|                       | leukemic cell infiltration       |                                       | 0             | 0           | 0           | 2            |
| {Reproductive system} |                                  |                                       |               |             |             |              |
| ovary                 |                                  |                                       | <10>          | < 5>        | < 9>        | <35>         |
|                       | metastasis:uterus tumor          |                                       | 0             | 1           | 0           | 0            |

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

STUDY NO. : 0437  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 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>10 | 10 ppm<br>5 | 30 ppm<br>9 | 90 ppm<br>35 |
|---------------------------------------|--|---------------|-------------|-------------|--------------|
| Organ                                 | Findings                                   |               |             |             |              |
| {Reproductive system}                 |  |               |             |             |              |
| ovary                                 | metastasis:large intestine tumor           | <10><br>0     | < 5><br>0   | < 9><br>1   | <35><br>0    |
| {Nervous system}                      |  |               |             |             |              |
| brain                                 | leukemic cell infiltration                 | <10><br>0     | < 5><br>0   | < 9><br>1   | <35><br>0    |
|                                       | metastasis:pituitary tumor                 | 0             | 0           | 1           | 0            |
|                                       | metastasis:nasal tumor                     | 0             | 0           | 0           | 1            |
|                                       | metastasis:vertebra tumor                  | 1             | 0           | 0           | 0            |
| spinal cord                           | metastasis:vertebra tumor                  | <10><br>1     | < 5><br>0   | < 9><br>0   | <35><br>0    |
| {Special sense organs/appendage}      |  |               |             |             |              |
| eye                                   | metastasis:skin/appendage tumor            | <10><br>1     | < 5><br>0   | < 9><br>0   | <35><br>0    |
| Harder gl                             | metastasis:nasal tumor                     | <10><br>0     | < 5><br>0   | < 9><br>0   | <35><br>1    |
| {Body cavities}                       |  |               |             |             |              |
| retroperit                            | metastasis:uterus tumor                    | <10><br>0     | < 5><br>1   | < 9><br>0   | <35><br>0    |
|                                       | metastasis:large intestine tumor           | 0             | 0           | 1           | 0            |
| < 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. : 0437  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 2

|                        |                             | Group Name<br>No. of Animals on Study | Control<br>40 | 10 ppm<br>45 | 30 ppm<br>41 | 90 ppm<br>15 |
|------------------------|-----------------------------|---------------------------------------|---------------|--------------|--------------|--------------|
| Organ                  | Findings                    |                                       |               |              |              |              |
| {Respiratory system}   |                             |                                       |               |              |              |              |
| lung                   | leukemic cell infiltration  |                                       | <40><br>1     | <45><br>3    | <41><br>3    | <15><br>1    |
| {Hematopoietic system} |                             |                                       |               |              |              |              |
| lymph node             | leukemic cell infiltration  |                                       | <40><br>0     | <45><br>1    | <41><br>0    | <15><br>2    |
| spleen                 | metastasis:peritoneum tumor |                                       | <40><br>1     | <45><br>0    | <41><br>0    | <15><br>0    |
| {Circulatory system}   |                             |                                       |               |              |              |              |
| heart                  | leukemic cell infiltration  |                                       | <40><br>0     | <45><br>0    | <41><br>1    | <15><br>0    |
| {Digestive system}     |                             |                                       |               |              |              |              |
| liver                  | leukemic cell infiltration  |                                       | <40><br>3     | <45><br>5    | <41><br>3    | <15><br>1    |
| {Endocrine system}     |                             |                                       |               |              |              |              |
| pituitary              | leukemic cell infiltration  |                                       | <40><br>0     | <45><br>1    | <41><br>0    | <15><br>0    |
| adrenal                | leukemic cell infiltration  |                                       | <40><br>0     | <45><br>1    | <41><br>0    | <15><br>0    |
| {Nervous system}       |                             |                                       |               |              |              |              |
| brain                  | metastasis:pituitary tumor  |                                       | <40><br>0     | <45><br>1    | <41><br>0    | <15><br>0    |

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

STUDY NO. : 0437  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : FEMALE

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

PAGE : 3

|  |                         | Group Name              | Control   | 10 ppm    | 30 ppm    | 90 ppm    |
|--|-------------------------|-------------------------|-----------|-----------|-----------|-----------|
|  |                         | No. of Animals on Study | 40        | 45        | 41        | 15        |
| Organ  | Findings                |                         |           |           |           |           |
| {Body cavities}                                  |                         |                         |           |           |           |           |
| peritoneum                                       | metastasis:uterus tumor |                         | <40><br>1 | <45><br>0 | <41><br>0 | <15><br>0 |
| < a > a : Number of animals examined at the site |                         |                         |           |           |           |           |
| b b : Number of animals with lesion              |                         |                         |           |           |           |           |

(JPT150)

BAIS4



## APPENDIX Q

METHODS, UNITS AND DECIMAL PLACE FOR  
HEMATOLOGY AND BIOCHEMISTRY IN THE 2-YEAR  
INHALATION STUDY OF BUTYL 2,3-EPOXYPROPYL ETHER

METHODS, UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY  
IN THE 2-YEAR INHALATION STUDY OF BUTYL 2,3-EPOXYPROPYL ETHER

| 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             |
| Creatinine   | Jaffe method <sup>3)</sup>  | mg/dL                     | 1             |
| Sodium   | Ion selective electrode method <sup>3)</sup>                      | mEq/L                     | 0             |
| Potassium  | Ion selective electrode method <sup>3)</sup>                      | mEq/L                     | 1             |
| Chloride   | Ion selective electrode method <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 7070 : Hitachi,Ltd.)