

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

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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

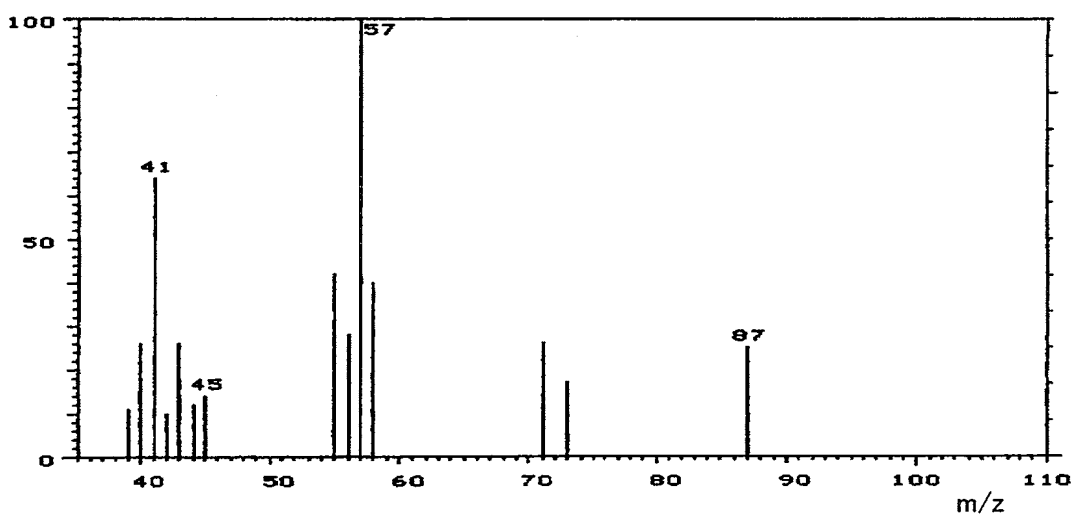
1. Spectral Data

Mass Spectrometry

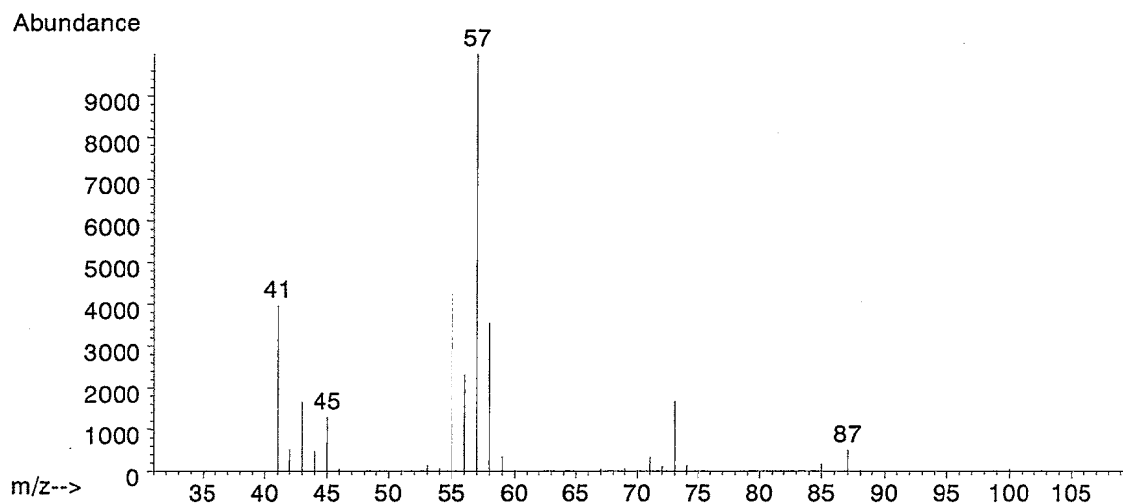
Instrument : Hitachi M-80B Mass Spectrometer

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.

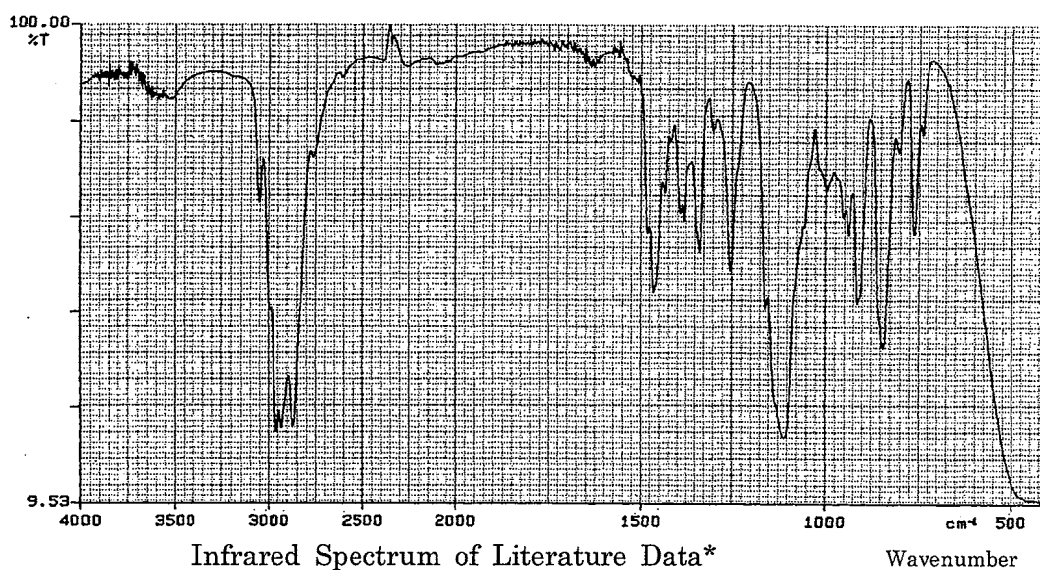
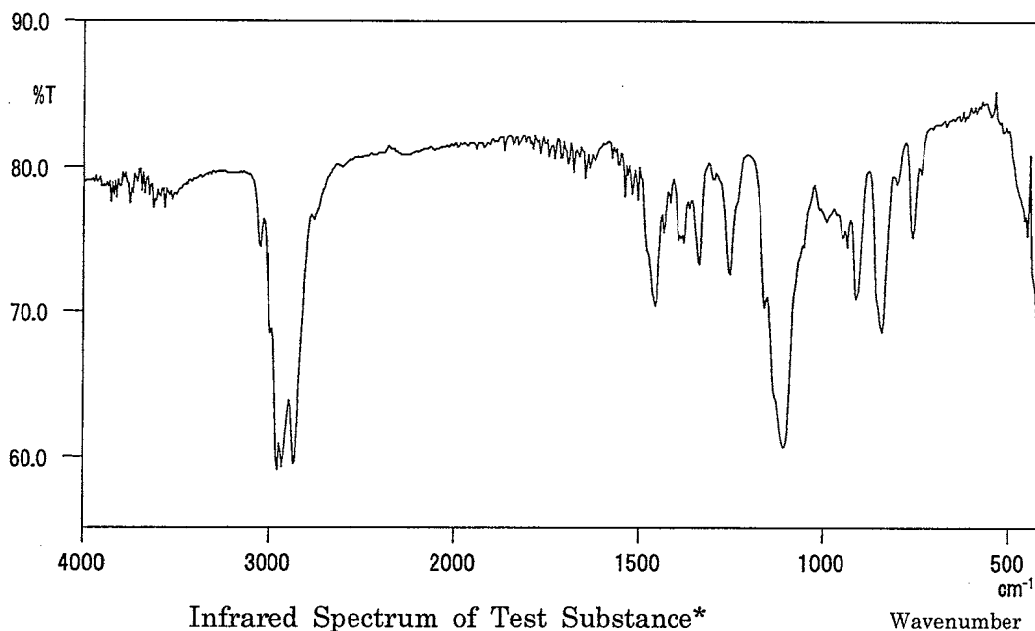
(*McLafferty FW, ed. 1994. Wiley Registry of Mass Spectral Data. 6th ed. New York, NY:John Wiley and Sons.)

Infrared Spectrometry

Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 4 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

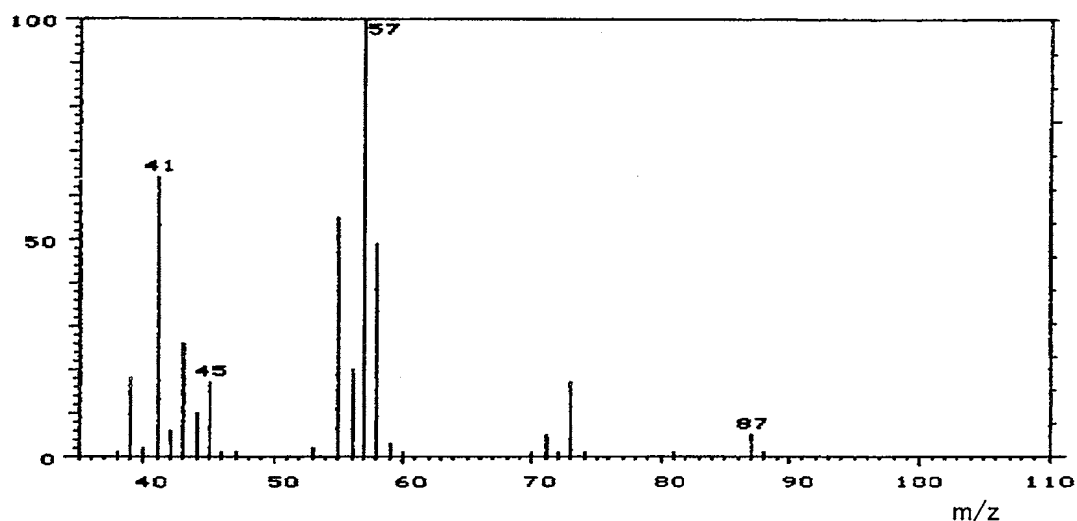
1. Spectral Data

Mass Spectrometry

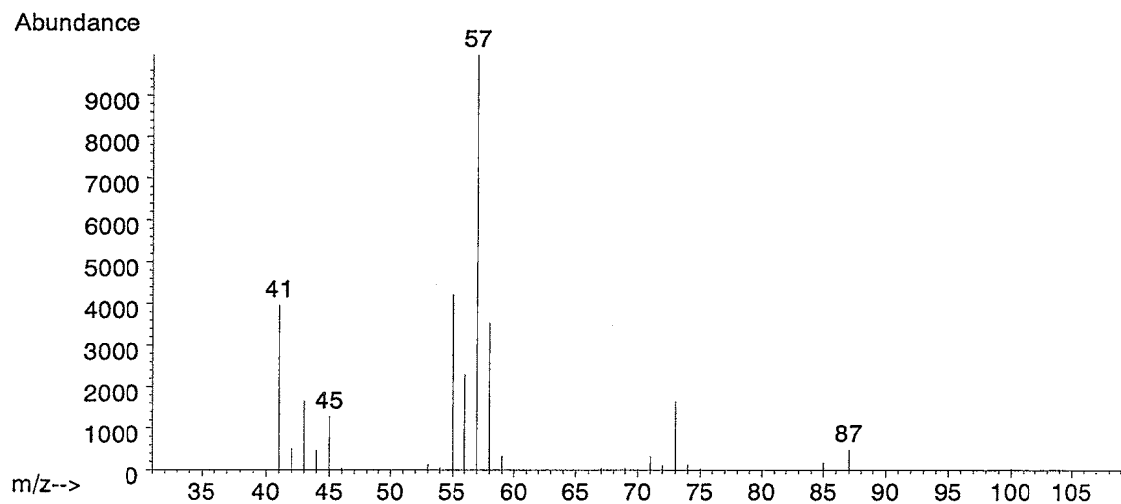
Instrument : Hitachi M-80B Mass Spectrometer

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.

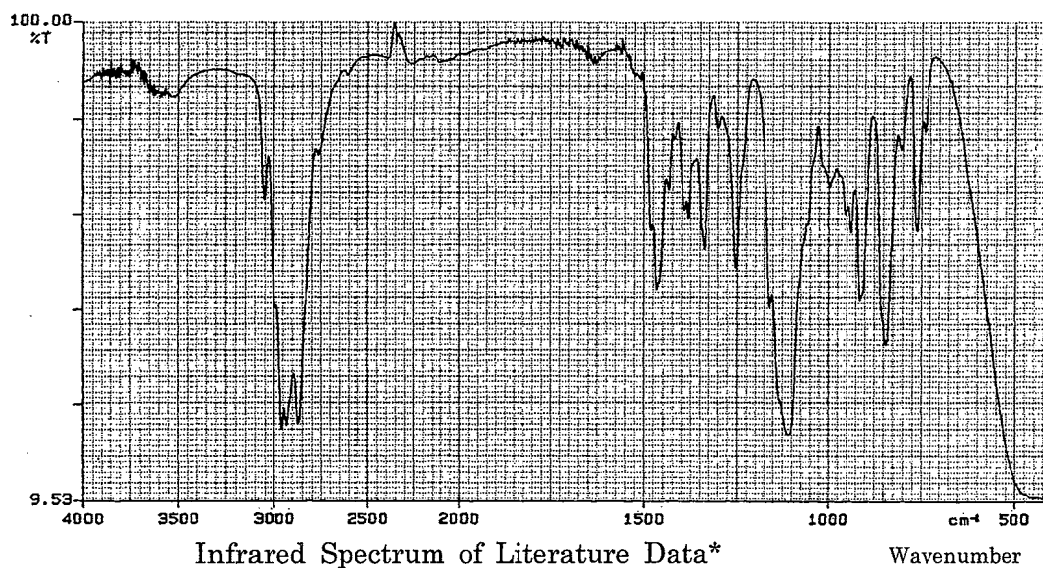
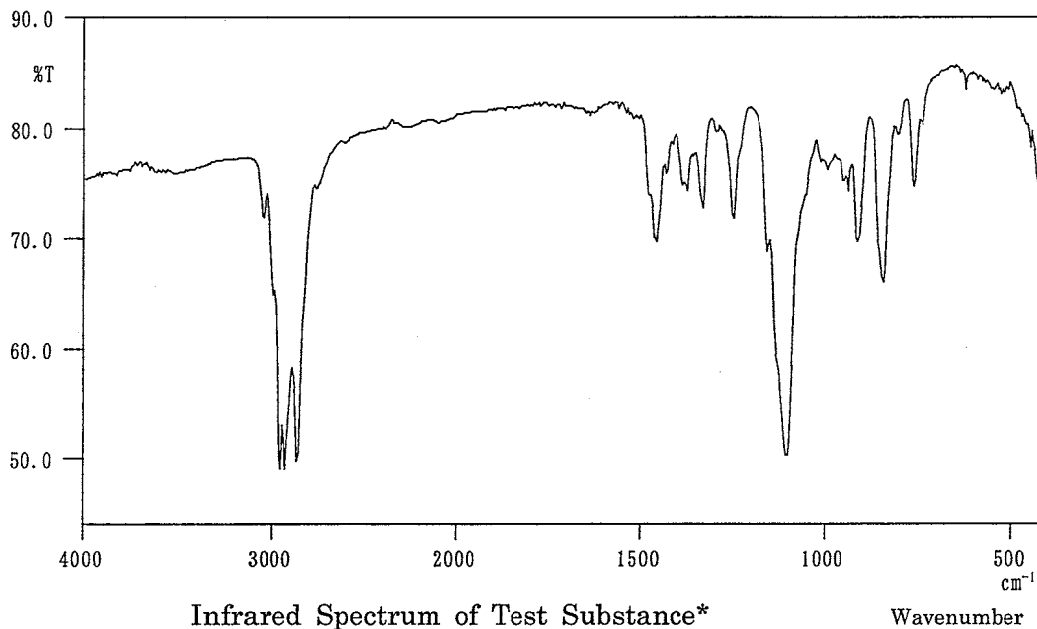
(*McLafferty FW, ed. 1994. Wiley Registry of Mass Spectral Data. 6th ed. New York, NY:John Wiley and Sons.)

Infrared Spectrometry

Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 4 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

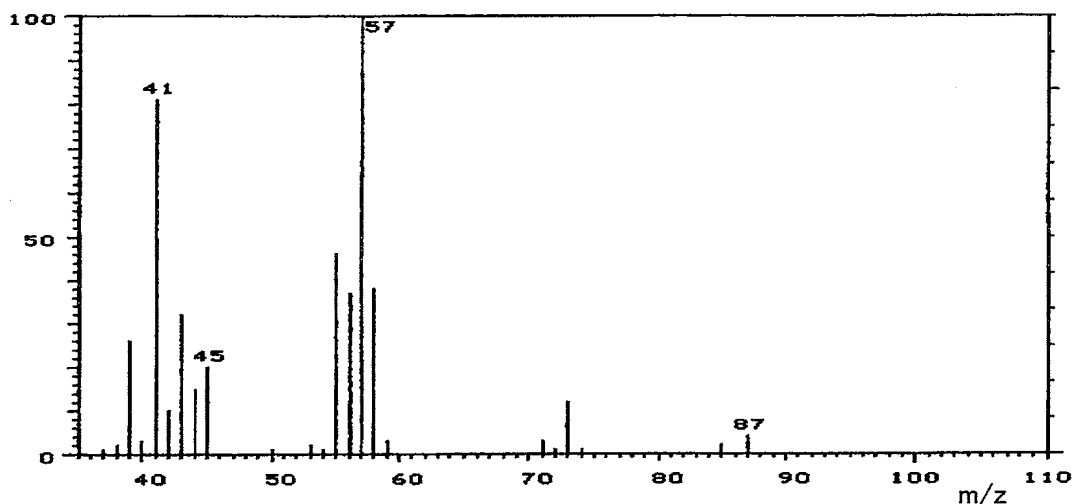
1. Spectral Data

Mass Spectrometry

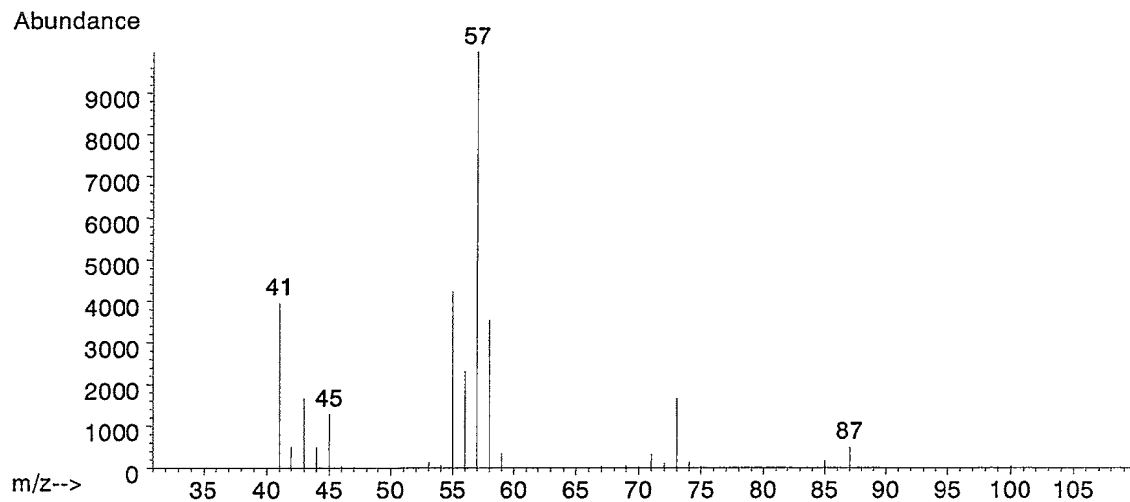
Instrument : Hitachi M-80B Mass Spectrometer

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.

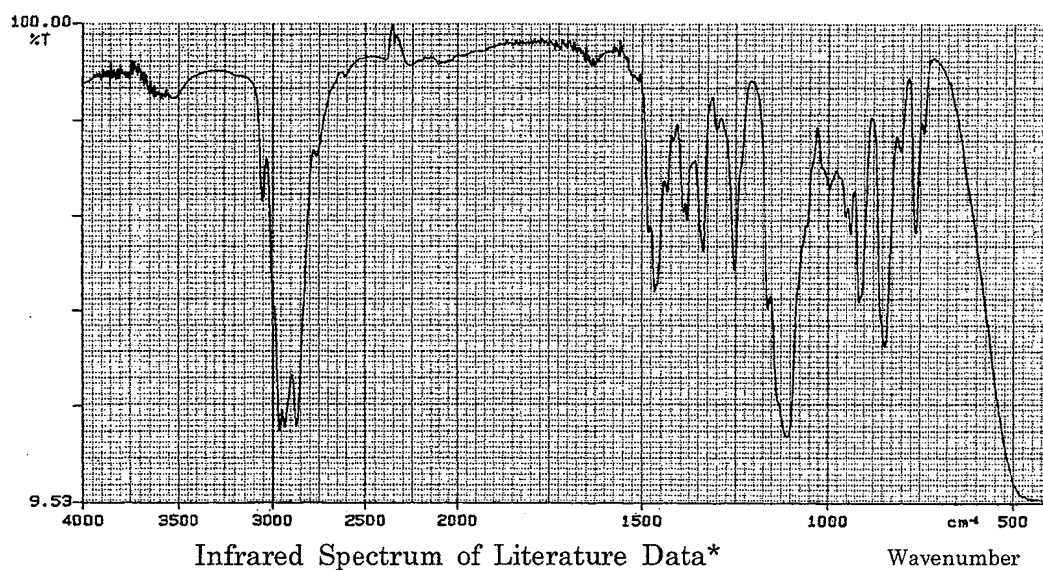
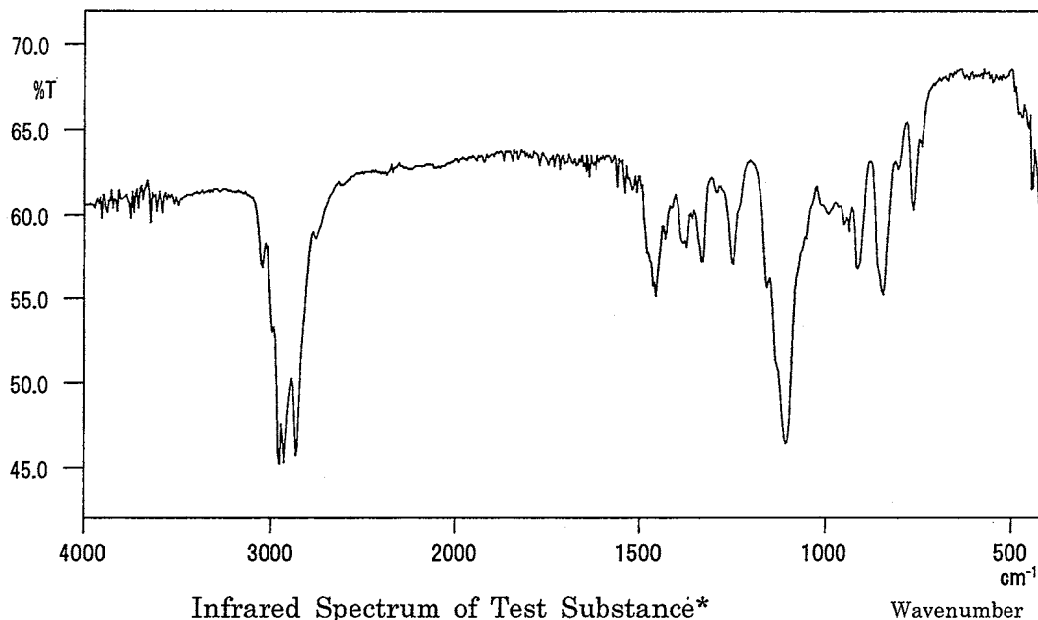
(*McLafferty FW, ed. 1994. Wiley Registry of Mass Spectral Data. 6th ed. New York, NY:John Wiley and Sons.)

Infrared Spectrometry

Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 4 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

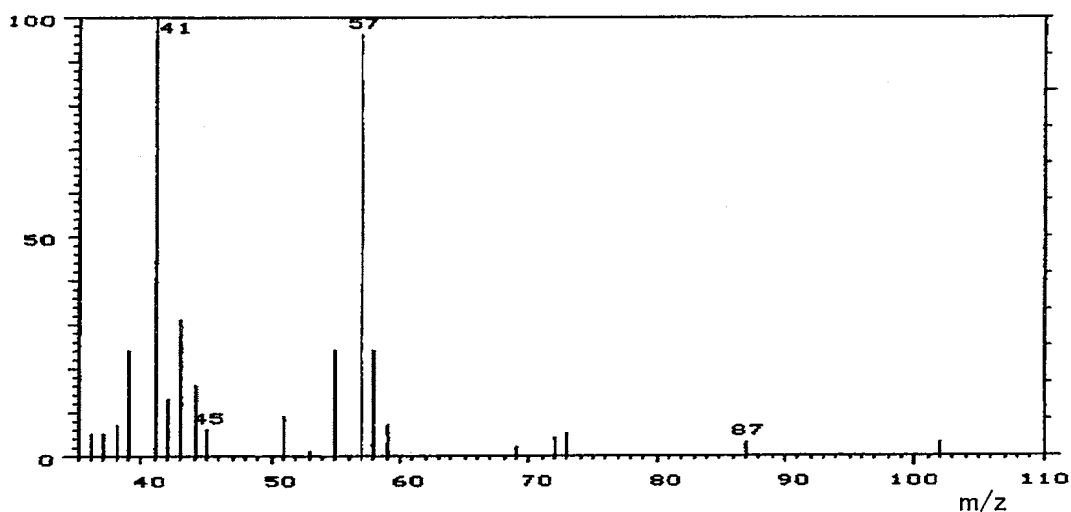
1. Spectral Data

Mass Spectrometry

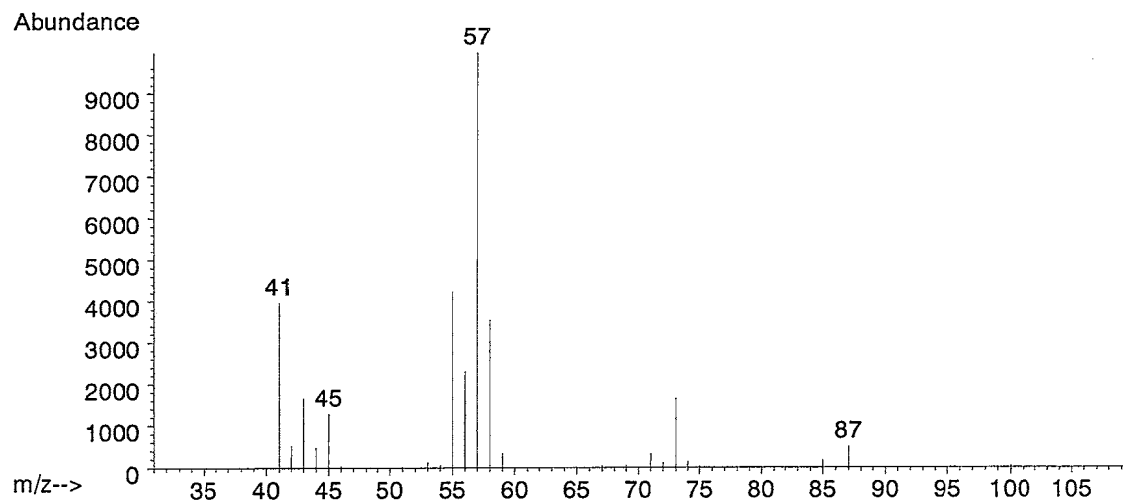
Instrument : Hitachi M-80B Mass Spectrometer

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.

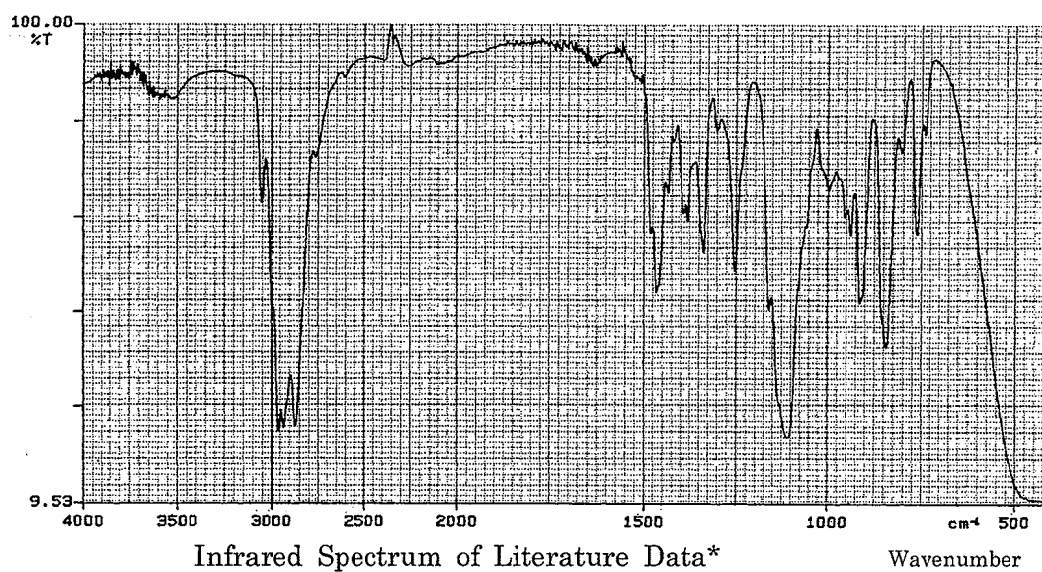
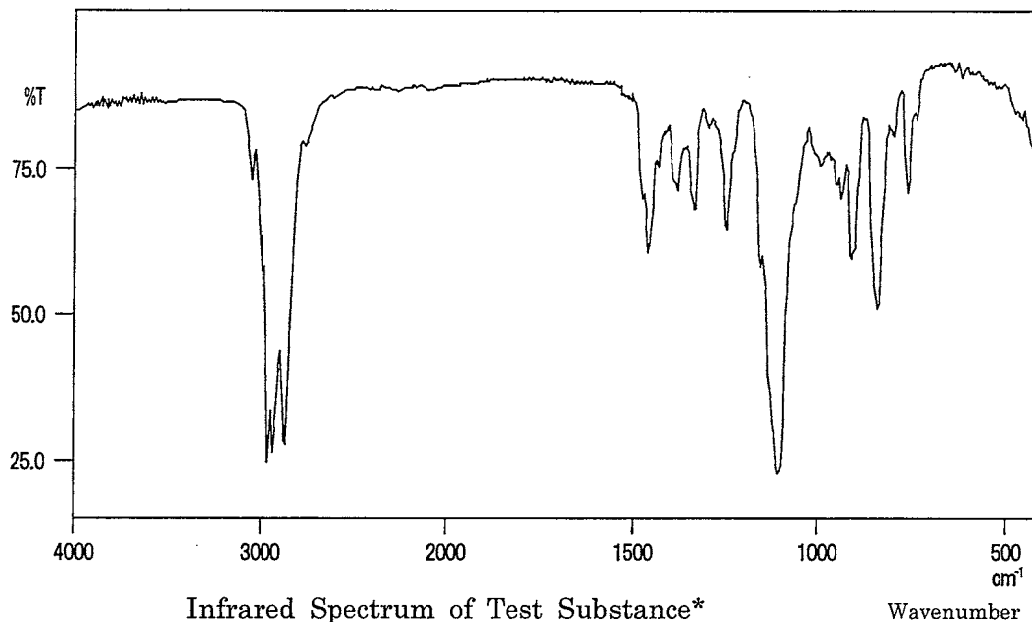
(*McLafferty FW, ed. 1994. Wiley Registry of Mass Spectral Data. 6th ed. New York, NY:John Wiley and Sons.)

Infrared Spectrometry

Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 4 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 ϕ \times 60 m)

Column Temperature: 160° C

Flow Rate : 20 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μ L

| Date (date analyzed) | Peak No. | Retention Time (min) | Area (%) |
|-------------------------|----------|-------------------------|-------------|
| 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 ϕ \times 60 m)

Column Temperature: 160° C

Flow Rate : 20 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μ L

| Date (date analyzed) | Peak No. | Retention Time (min) | Area (%) |
|-------------------------|----------|-------------------------|-------------|
| 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 ϕ \times 60 m)

Column Temperature: 160° C

Flow Rate : 20 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μ L

| Date (date analyzed) | Peak No. | Retention Time (min) | Area (%) |
|-------------------------|----------|-------------------------|-------------|
| 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 ϕ \times 60 m)

Column Temperature: 160° C

Flow Rate : 20 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μ L

| Date (date analyzed) | Peak No. | Retention Time (min) | Area (%) |
|-------------------------|----------|-------------------------|-------------|
| 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 (°C) | Humidity (%) | Ventilation Rate (L/min) | | Air Change (time/h) | |
|------------|---------------------|-----------------|-----------------------------|---------------------------|------------------------|--------------------|
| | Mean ± S.D. | Mean ± S.D. | Mean ± S.D.* ¹ | Mean ± S.D.* ² | Mean* ¹ | Mean* ² |
| 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 |

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 | | | 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 |

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 |
| 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 |

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 |
| 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 |

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 | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 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 |

STUDY NO. : 0437
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 | | | 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 |

STUDY NO. : 0437
 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 | | | | | |
|-------------------------|------------|-------------------------|-------|-------|-------|-------|-------|
| | | 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 |

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

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 |
| 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 | 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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 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

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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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ANIMAL : RAT F344/DuCrj
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 |
|-----------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 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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| 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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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 |
| 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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ANIMAL : RAT F344/DuCrj
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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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 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

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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)
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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 |
| 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 | 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 |

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

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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 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

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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 |

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

CLINICAL OBSERVATION (SUMMARY)
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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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 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 |
| 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
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
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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 |

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 | | | | | | | | | | | | | |
|--------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 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 |

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 | | | | 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 |

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 |
| 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 |

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 | | | | | | | | | | | | | |
|---------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|------|
| | | 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 |

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 | | | | | | | | | | | | | |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 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 |

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 | | | | | | | | | | | | | |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 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 |

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 |
| 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

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

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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 |

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

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

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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 |

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 | | | | | | | | | | | | | |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 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 |

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 |
| 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 |

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

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 |
| 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 |

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

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 |
| 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 |

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 | | | | | | | | | | | | | |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 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 |

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 |
| 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 |

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 |
| 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 |

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 | | | | | | | | | | | | | |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 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 |

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 | | | | | | | | | | | | | |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 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 |

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 |
| 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 |

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 | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|------|
| | | 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

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : MALE

PAGE : 42

| 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 |

(HAN190)

BAIS 4

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

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : MALE

PAGE : 43

| 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

PAGE : 44

| 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 |

(HAN190)

BAIS 4

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

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : MALE

PAGE : 45

| 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 |

(HAN190)

BAIS 4

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

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : MALE

PAGE : 46

| 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 |

(HAN190)

BAIS 4

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

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : MALE

PAGE : 47

| 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 |

(HAN190)

BAIS 4

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

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

PAGE : 48

| 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 |

(HAN190)

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

PAGE : 49

| 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 |

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 | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 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 |

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 | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 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 |

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 | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 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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ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

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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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ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
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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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 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

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| Clinical sign | Group Name | Administration Week-day | | | | | |
|-------------------------|------------|-------------------------|-------|-------|-------|-------|-------|
| | | 99-7 | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| DEATH | Control | 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 |

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 |
| 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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ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

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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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ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

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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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ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

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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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ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
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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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ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
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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 |

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 | | | | | | | | | | | | | |
|--------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 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 |

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 | | | | | |
|--------------------------|------------|-------------------------|-------|-------|-------|-------|-------|
| | | 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 |

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 | | | | | | | | | | | | | |
|---------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|------|
| | | 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 |

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 |
| 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 |

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 | | | | | | | | | | | | | |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 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 |

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 | | | | | | | | | | | | | |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 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 |

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 | | | | | | | | | | | | | |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 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 |

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 | | | | | | | | | | | | | |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 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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 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 | | | | | | | | | | | | | |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 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 |

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 | | | | | |
|---------------------|------------|-------------------------|-------|-------|-------|-------|-------|
| | | 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 |

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 |
| 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 |

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

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

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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 |

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 | | | | | | | | | | | | | |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 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 |

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 | | | | | | | | | | | | | |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 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 |

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 | | | | | | | | | | | | | |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 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 |

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 | | | | | | | | | | | | | |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 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 |

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 | | | | | | | | | | | | | |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 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 |

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 | | | | | |
|---------------------|------------|-------------------------|-------|-------|-------|-------|-------|
| | | 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 |

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 |
| 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

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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 | | 13-7 | |
| Control | 159± | 9 | 162± | 8 | 168± | 9 | 171± | 9 | 176± | 10 | 178± | 10 | 180± | 10 |
| 10 ppm | 158± | 10 | 160± | 9 | 165± | 10 | 168± | 10 | 172± | 11 | 176± | 11 | 178± | 11 |
| 30 ppm | 153± | 8** | 156± | 7** | 161± | 7** | 165± | 8** | 169± | 8** | 173± | 9* | 174± | 9** |
| 90 ppm | 148± | 8** | 151± | 8** | 155± | 8** | 157± | 9** | 162± | 9** | 168± | 9** | 166± | 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 8-7(7) | week-day(effective) 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 74-7(7) | week-day(effective) 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

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 Animals | RED BLOOD CELL 10 ⁶ /μl | | HEMOGLOBIN g/dl | | HEMATOCRIT % | | MCV fl | | MCH pg | | MCHC g/dl | | PLATELET 10 ³ /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 Animals | WBC 10 ³ /μl | | Differential N-BAND | | WBC (%) 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 Animals | RED BLOOD CELL 10 ⁶ /μl | | HEMOGLOBIN g/dl | | HEMATOCRIT % | | MCV fl | | MCH pg | | MCHC g/dl | | PLATELET 10 ³ /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

REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
 ALL ANIMALS (105W)

PAGE : 4

| Group Name | NO. of Animals | WBC 10 ³ /μl | | Differential N-BAND | | WBC (%) 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 Animals | TOTAL PROTEIN g/dl | | ALBUMIN g/dl | | A/G RATIO | | T-BILIRUBIN mg/dl | | GLUCOSE mg/dl | | T-CHOLESTEROL mg/dl | | TRIGLYCERIDE mg/dl | |
|------------|-------------------|-----------------------|-----|-----------------|-------|-----------|-----|----------------------|------|------------------|----|------------------------|------|-----------------------|------|
| Control | 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 Animals | PHOSPHOLIPID mg/dl | | AST IU/l | | ALT IU/l | | LDH IU/l | | ALP IU/l | | G-GTP IU/l | | CK 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 mg/dl | | CREATININE mg/dl | | SODIUM mEq/l | | POTASSIUM mEq/l | | CHLORIDE mEq/l | | CALCIUM mg/dl | | INORGANIC PHOSPHORUS 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 Animals | TOTAL PROTEIN g/dl | | ALBUMIN g/dl | | A/G RATIO | | T-BILIRUBIN mg/dl | | GLUCOSE mg/dl | | T-CHOLESTEROL mg/dl | | TRIGLYCERIDE mg/dl | |
|------------|-------------------|-----------------------|-------|-----------------|------|-----------|-----|----------------------|------|------------------|----|------------------------|------|-----------------------|-----|
| Control | 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 Animals | PHOSPHOLIPID mg/dl | | AST IU/l | | ALT IU/l | | LDH IU/l | | ALP IU/l | | G-GTP IU/l | | CK 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 Animals | UREA NITROGEN mg/dl | | CREATININE mg/dl | | SODIUM mEq/l | | POTASSIUM mEq/l | | CHLORIDE mEq/l | | CALCIUM mg/dl | | INORGANIC PHOSPHORUS 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 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 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 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 Animals | Occult blood | | | | | CHI | Urobilinogen | | | | | CHI |
|------------|-------------------|--------------|---|---|----|----|-----|--------------|---|----|----|----|-----|
| | | - | ± | + | 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 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 NO. of Animals | Control | | 10 ppm | | 30 ppm | | 90 ppm | |
|-------------|------------------------|------------------------------|---------|------|--------|-------|--------|-------|--------|-------|
| | | | 50 | (%) | 50 | (%) | 50 | (%) | 50 | (%) |
| stomach | gas | | 0 | (0) | 0 | (0) | 0 | (0) | 10 | (20) |
| small intes | nodule | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |
| | gas | | 0 | (0) | 0 | (0) | 0 | (0) | 14 | (28) |
| cecum | gas | | 0 | (0) | 0 | (0) | 0 | (0) | 2 | (4) |
| large intes | gas | | 0 | (0) | 0 | (0) | 0 | (0) | 9 | (18) |
| liver | enlarged | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |
| | pale | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (2) |
| | yellow | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |
| | white zone | | 0 | (0) | 1 | (2) | 0 | (0) | 0 | (0) |
| | red zone | | 0 | (0) | 0 | (0) | 1 | (2) | 0 | (0) |
| | nodule | | 0 | (0) | 2 | (4) | 5 | (10) | 1 | (2) |
| | cyst | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (2) |
| | 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) |
| | 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) |
| | 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 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 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 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 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 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 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 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 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 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 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 NO. of Animals | Control 10 (%) | 10 ppm 5 (%) | 30 ppm 9 (%) | 90 ppm 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 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 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 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 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 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 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 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 Animals | Body Weight (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 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 Animals | Body Weight (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 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

| | | 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 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Integumentary system/appandage} | | | | | | | | | | | | | | | | | | |
| skin/app | | | <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) | (2) | (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) | (2) | (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 | 0 | 0 | 0 |
| | | | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) |
| subcutis | | | <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) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| {Respiratory system} | | | | | | | | | | | | | | | | | | |
| nasal cavit | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | exudate | | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (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 | 30 | 1 | 0 ** |
| | | | (0) | (0) | (0) | (0) | (0) | (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 (36) | 23 (46) | 1 (2) | 0 (0) | 20 (40) | 20 (40) | 1 (2) | 0 (0) | 11 (22) | 22 (44) | 1 (2) | 0 (0) | 9 (18) | 6 (12) | 0 (0) | 0 ** (0) |
| | eosinophilic change:respiratory epithelium | | 2 (4) | 3 (6) | 0 (0) | 0 (0) | 4 (8) | 0 (0) | 0 (0) | 0 (0) | 2 (4) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | inflammation:foreign body | | 7 (14) | 17 (34) | 0 (0) | 0 (0) | 8 (16) | 15 (30) | 0 (0) | 0 (0) | 6 (12) | 23 (46) | 0 (0) | 0 (0) | 2 (4) | 7 (14) | 0 (0) | 0 ** (0) |
| | inflammation:respiratory epithelium | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 2 (4) | 0 (0) | 0 (0) | 4 (8) | 17 (34) | 1 (2) | 0 ** (0) |
| | respiratory metaplasia:olfactory epithelium | | 3 (6) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 4 (8) | 1 (2) | 0 (0) | 0 (0) | 2 (4) | 6 (12) | 0 (0) | 0 * (0) |
| | respiratory metaplasia:gland | | 5 (10) | 14 (28) | 0 (0) | 0 (0) | 9 (18) | 10 (20) | 0 (0) | 0 (0) | 5 (10) | 12 (24) | 0 (0) | 0 (0) | 3 (6) | 17 (34) | 1 (2) | 0 (0) |
| | squamous cell metaplasia:respiratory epithelium | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 1 (2) | 0 (0) | 0 (0) | 4 (8) | 6 (12) | 0 (0) | 0 ** (0) | 4 (8) | 38 (76) | 0 (0) | 0 ** (0) |
| | squamous cell metaplasia:olfactory epithelium | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 5 (10) | 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)

PAGE : 3

| | | 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} | | | | | | | | | | | | | | | | | | |
| nasal cavit | | | <50> | | | | <50> | | | | <50> | | | | <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) | (2) | (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) | (6) | (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) | (10) | (6) | (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) | (2) | (0) | (0) | (14) | (4) | (0) | (0) | (20) | (28) | (0) | (0) |
| lung | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | congestion | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) |
| | 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) |
| | inflammatory infiltration | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | |
| | | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | |
| | accumulation of foamy cells | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| | | | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | |

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

| | | 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 | | | | 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 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Hematopoietic system} | | | | | | | | | | | | | | | | | | | | | |
| spleen | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | congestion | 0 | 6 | 0 | 0 | 1 | 3 | 0 | 0 | 1 | 3 | 0 | 0 | 1 | 3 | 0 | 0 | 0 | 0 | 0 | 0 * |
| | | (0) | (12) | (0) | (0) | (2) | (6) | (0) | (0) | (2) | (6) | (0) | (0) | (2) | (6) | (0) | (0) | (0) | (0) | (0) | (0) |
| | deposit of hemosiderin | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) |
| | inflammatory cell nest | 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) | (2) | (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 | 1 | 1 | 0 | 0 | 2 | 0 | 0 |
| | | (2) | (6) | (0) | (0) | (0) | (8) | (0) | (0) | (4) | (2) | (2) | (0) | (4) | (2) | (2) | (0) | (0) | (4) | (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 | 0 | 0 | 2 | 0 |
| | | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) |
| | necrosis:focal | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 1 | 0 | 0 |
| | | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (2) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b : 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 : 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
 < 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 : 7

| Organ | Findings | Group Name 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
 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 : 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) |

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 : 9

| | | 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 | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Digestive system} | | | | | | | | | | | | | | | | | | |
| liver | | | | | | | | | | | | | | | | | | |
| | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | fatty change:central | | 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) |

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

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) | |

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 : 11

| 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} | | | | | | | | | | | | | | | | | | | | | |
| 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 | 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) |
| | 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) |

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 : 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 | hemorrhage | <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) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| | simple hyperplasia:transitional epithelium | <50> | | | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) |
| {Endocrine system} | | | | | | | | | | | | | | | | | | | | | |
| pituitary | cyst | <50> | | | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (4) | (0) | (0) |
| | hyperplasia | <50> | | | | 2 | 6 | 0 | 0 | 0 | 8 | 0 | 0 | 1 | 4 | 0 | 0 | 0 | 2 | 0 | 0 |
| | | (4) | (12) | (0) | (0) | (0) | (16) | (0) | (0) | (0) | (16) | (0) | (0) | (2) | (8) | (0) | (0) | (0) | (4) | (0) | (0) |
| | Rathke pouch | <50> | | | | 1 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 0 | 3 | 0 | 0 |
| | | (2) | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (2) | (0) | (0) | (0) | (6) | (0) | (0) |
| thyroid | cyst | <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) | (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)

PAGE : 13

| | | 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]
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 14

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

PAGE : 15

| | | 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 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) |
| | dilatation:cerebral ventricle | | 0 | 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) |
| 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 | 1 | 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 : MALE

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

PAGE : 16

| Organ | Findings | Group Name 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 (6) | 5 (10) | 0 (0) | 0 (0) | 3 (6) | 3 (6) | 0 (0) | 0 (0) | 0 (0) | 5 (10) | 0 (0) | 0 (0) | 0 (0) | 5 (10) | 0 (0) | 0 (0) | 0 (0) | 2 (4) | 0 (0) | 0 (0) |
| | retinal atrophy | 32 (64) | 0 (0) | 8 (16) | 0 (0) | 36 (72) | 0 (0) | 5 (10) | 0 (0) | 40 (80) | 0 (0) | 5 (10) | 0 (0) | 18 (36) | 0 (0) | 2 (4) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | keratitis | 3 (6) | 0 (0) | 0 (0) | 0 (0) | 3 (6) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 10 (20) | 13 (26) | 3 (6) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| Harder gl | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | degeneration | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 1 (2) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | inflammatory infiltration | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | lymphocytic infiltration | 3 (6) | 0 (0) | 0 (0) | 0 (0) | 3 (6) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| {Musculoskeletal system} | | | | | | | | | | | | | | | | | | | | | |
| muscle | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | mineralization | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |

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

STUDY NO. : 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 | Control | | | | 10 ppm | | | | 30 ppm | | | | 90 ppm | | | |
|-------|----------|-------------------------|-----|-----|-----|--------|-----|-----|-----|--------|-----|-----|-----|--------|-----|-----|-----|
| | | No. of Animals on Study | | | | 50 | | | | 50 | | | | 50 | | | |
| | | Grade | | | | 1 | | | | 1 | | | | 1 | | | |
| | | 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) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |

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

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

b b : Number of animals with lesion

(c) c : b / a * 100

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

(HPT150)

BAIS4

APPENDIX L 2

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

STUDY NO. : 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

| Organ | Findings | Group Name No. of Animals on Study Grade | Control | | | | 10 ppm | | | | 30 ppm | | | | 90 ppm | | | |
|----------------------------------|--|--|---------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|
| | | | 12 | | | | 12 | | | | 12 | | | | 39 | | | |
| | | | 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

| 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 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {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) | (8) | (0) | (0) | (0) | (0) | (3) | (0) | (0) |
| | inflammation:foreign body | | 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) | (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 | 1 | 0 | 0 | |
| | | | (0) | (8) | (0) | (0) | (8) | (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 | 1 | 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 No. of Animals on Study Grade | Control | | | | 10 ppm | | | | 30 ppm | | | | 90 ppm | | | |
|----------------------|---------------------------|--|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| | | | 12 | | | | 12 | | | | 12 | | | | 39 | | | |
| | | | 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 (0) | 0 (0) | 0 (0) | 1 (8) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 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 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) |
| tooth | | | <12> | | | | <12> | | | | <12> | | | | <39> | | | |
| | inflammation | | 0 (0) | 1 (8) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 2 (5) | 0 (0) | 0 (0) |
| tongue | | | <12> | | | | <12> | | | | <12> | | | | <39> | | | |
| | inflammatory infiltration | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) |
| stomach | | | <12> | | | | <12> | | | | <12> | | | | <39> | | | |
| | mineralization | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (8) | 1 (8) | 0 (0) | 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) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (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)
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 6

| | | 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} | | | | | | | | | | | | | | | | | | |
| stomach | | | <12> | | | | <12> | | | | <12> | | | | <39> | | | |
| | atrophy:glandular mucosa | | 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) |
| | erosion:forestomach | | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 4 | 0 | 0 | 0 |
| | | | (17) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (8) | (0) | (0) | (10) | (0) | (0) | (0) |
| | ulcer:forestomach | | 0 | 2 | 0 | 0 | 1 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 * |
| | | (0) | (17) | (0) | (0) | (8) | (25) | (0) | (0) | (0) | (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 ** |
| | | | (0) | (33) | (0) | (0) | (8) | (25) | (0) | (0) | (8) | (17) | (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 |
| | | | (17) | (8) | (0) | (0) | (8) | (0) | (0) | (0) | (17) | (0) | (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) | (8) | (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 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (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) | (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 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
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 : 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) | (3) | (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) | (0) | (3) | (0) | (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) | (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) | (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 : 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 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| Organ | Findings | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {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

| | | 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 | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Reproductive system} | | | | | | | | | | | | | | | | | | |
| testis | | | <12> | | | | <12> | | | | <12> | | | | <39> | | | |
| | mineralization | | 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) | (25) | (0) | (0) | (0) | (26) | (0) | (0) | (0) |
| prostate | | | <12> | | | | <12> | | | | <12> | | | | <39> | | | |
| | inflammation | | 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) |
| {Nervous system} | | | | | | | | | | | | | | | | | | |
| brain | | | <12> | | | | <12> | | | | <12> | | | | <39> | | | |
| | hemorrhage | | 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) |

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 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) | (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 | Control | | | | 10 ppm | | | | 30 ppm | | | | 90 ppm | | | |
|-----------------|--------------|-------------------------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
| | | No. of Animals on Study | | | | 12 | | | | 12 | | | | 39 | | | |
| | | Grade | | | | 12 | | | | 12 | | | | 39 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {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)

PAGE : 1

| | | 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 | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| <hr/> | | | | | | | | | | | | | | | | | | |
| {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)

PAGE : 2

| 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 | 0 |
| | | (5) | (5) | (0) | (0) | (8) | (0) | (0) | (0) | (5) | (0) | (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 | 0 |
| | | (18) | (34) | (0) | (0) | (16) | (32) | (0) | (0) | (16) | (50) | (0) | (0) | (0) | (45) | (0) | (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

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

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

PAGE : 3

| | | 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) |
| | 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) |
| | 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) |
| | 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) |
| | 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) |

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)

PAGE : 4

| | | 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 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (3) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) |
| | increased hematopoiesis | | 1 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 5 | 0 | 0 | 0 ** |
| | | | (3) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (45) | (0) | (0) | (0) |
| spleen | | | <38> | | | | <38> | | | | <38> | | | | <11> | | | |
| | congestion | | 0 | 6 | 0 | 0 | 1 | 3 | 0 | 0 | 1 | 3 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (16) | (0) | (0) | (3) | (8) | (0) | (0) | (3) | (8) | (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) | (9) | (0) | (0) |
| | fibrosis | | 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) | |
| | increased extramedullary hematopoiesis | | 1 | 1 | 0 | 0 | 0 | 3 | 0 | 0 | 2 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| | | | (3) | (3) | (0) | (0) | (0) | (8) | (0) | (0) | (5) | (0) | (3) | (0) | (0) | (0) | (0) | (0) |
| {Circulatory system} | | | | | | | | | | | | | | | | | | |
| heart | | | <38> | | | | <38> | | | | <38> | | | | <11> | | | |
| | inflammatory cell nest | | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (8) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 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 : 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 | | | | | | | | | | | | | | | | | | |
| | myocardial fibrosis | | <38> | | | | <38> | | | | <38> | | | | <11> | | | |
| | | | 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 | | | | | | | | | | | | | | | | | | |
| | inflammation | | <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) |
| stomach | | | | | | | | | | | | | | | | | | |
| | erosion:forestomach | | <38> | | | | <38> | | | | <38> | | | | <11> | | | |
| | | | 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 ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square

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

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 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 hepatis | | 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
 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 : 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) | (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 : 9

| 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 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Endocrine system} | | | | | | | | | | | | | | | | | | |
| thyroid | | | <38> | | | | <37> | | | | <38> | | | | <11> | | | |
| | C-cell hyperplasia | | 5 (13) | 1 (3) | 0 (0) | 0 (0) | 4 (11) | 4 (11) | 0 (0) | 0 (0) | 3 (8) | 4 (11) | 0 (0) | 0 (0) | 2 (18) | 0 (0) | 0 (0) | 0 (0) |
| | focal follicular cell hyperplasia | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | |
| adrenal | | | <38> | | | | <38> | | | | <38> | | | | <11> | | | |
| | hyperplasia:cortical cell | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | |
| | hyperplasia:medulla | | 2 (5) | 4 (11) | 0 (0) | 0 (0) | 1 (3) | 2 (5) | 0 (0) | 0 (0) | 0 (0) | 4 (11) | 0 (0) | 0 (0) | 0 (0) | 1 (9) | 0 (0) | 0 (0) |
| | focal fatty change:cortex | | 0 (0) | 2 (5) | 0 (0) | 0 (0) | 0 (0) | 2 (5) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| {Reproductive system} | | | | | | | | | | | | | | | | | | |
| testis | | | <38> | | | | <38> | | | | <38> | | | | <11> | | | |
| | atrophy | | 0 (0) | 1 (3) | 36 (95) | 0 (0) | 0 (0) | 0 (0) | 38 (100) | 0 (0) | 0 (0) | 0 (0) | 38 (100) | 0 (0) | 0 (0) | 0 (0) | 11 (100) | 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 : 10

| | | 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 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) |

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 : 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) |

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)
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
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(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)

PAGE : 21

| Organ | Findings | Group Name 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 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 | 34 | 5 | 0 | 0 | 25 | 2 | 0 | 0 |
| | | (60) | (10) | (0) | (0) | (62) | (6) | (0) | (0) | (68) | (10) | (0) | (0) | (68) | (10) | (0) | (0) | (50) | (4) | (0) | (0) |
| | subendocardial fibrosis | 1 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (2) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (4) | (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) |

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 : 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) | (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) | (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) | (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) | (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) | (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
 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 : 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 (18) | 0 (0) | 0 (0) | 0 (0) | 10 (20) | 0 (0) | 0 (0) | 0 (0) | 6 (12) | 0 (0) | 0 (0) | 0 (0) | 12 (24) | 0 (0) | 0 (0) | 0 (0) |
| | necrosis:central | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | fatty change:central | | 0 (0) | 3 (6) | 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) |
| | lymphocytic infiltration | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) |
| | granulation | | 12 (24) | 7 (14) | 2 (4) | 0 (0) | 14 (28) | 8 (16) | 6 (12) | 0 (0) | 13 (26) | 8 (16) | 3 (6) | 0 (0) | 4 (8) | 1 (2) | 1 (2) | 0 ** (0) |
| | inflammatory cell nest | | 1 (2) | 3 (6) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 3 (6) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | clear cell focus | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | basophilic cell focus | | 14 (28) | 8 (16) | 0 (0) | 0 (0) | 7 (14) | 9 (18) | 0 (0) | 0 (0) | 4 (8) | 7 (14) | 0 (0) | 0 * (0) | 3 (6) | 2 (4) | 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
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 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 25

| Organ | Findings | Group Name No. of Animals on Study 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 | | <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) |
| | inflammatory cell nest | | <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) |
| | chronic nephropathy | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | | 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
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 ALL ANIMALS (0-105W)

PAGE : 26

| | | 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 | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Urinary system} | | | | | | | | | | | | | | | | | | |
| kidney | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | hydronephrosis | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (2) | (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) | (2) | (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: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) | (2) | (0) | (0) | (0) |
| | mineralization:cortex | | 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) | (4) | (0) | (0) | (0) |
| urin bladd | | | <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) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| {Endocrine system} | | | | | | | | | | | | | | | | | | |
| pituitary | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | angiectasis | | 0 | 0 | 0 | 0 | 2 | 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) |

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)

PAGE : 27

| 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} | | | | | | | | | | | | | | | | | | |
| pituitary | cyst | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 2 | 9 | 0 | 0 | 0 | 5 | 0 | 0 | 1 | 9 | 0 | 0 | 0 | 10 | 0 | 0 | |
| | | (4) | (18) | (0) | (0) | (0) | (10) | (0) | (0) | (2) | (18) | (0) | (0) | (0) | (20) | (0) | (0) | |
| | hyperplasia | 0 | 4 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 4 | 0 | 0 | |
| | | (0) | (8) | (0) | (0) | (0) | (22) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (8) | (0) | (0) | |
| | | | | | | | | | | | | | | | | | | |
| | Rathke pouch | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| | | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | |
| | | | | | | | | | | | | | | | | | | |
| thyroid | C-cell hyperplasia | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 6 | 4 | 0 | 0 | 7 | 2 | 0 | 0 | 7 | 4 | 0 | 0 | 1 | 2 | 0 | 0 | |
| | | (12) | (8) | (0) | (0) | (14) | (4) | (0) | (0) | (14) | (8) | (0) | (0) | (2) | (4) | (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) | (2) | (2) | (0) | (0) | (2) | (0) | (0) | (0) | |
| | | | | | | | | | | | | | | | | | | |
| adrenal | peliosis-like lesion | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 5 | 0 | 0 | |
| | | (0) | (4) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (10) | (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) | |
| | | | | | | | | | | | | | | | | | | |

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 < a > a : Number of animals examined at the site
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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) | (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) | (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) |

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

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REPORT TYPE : A1
SEX : FEMALE

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 | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | hemorrhage | | 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 | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | 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) | (2) | (0) | (0) | (0) |
| {Special sense organs/appendage} | | | | | | | | | | | | | | | | | | |
| eye | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | 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) | (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) | (2) | (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)

PAGE : 30

| 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} | | | | | | | | | | | | | | | | | | |
| 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 | 1 | 0 | 0 | 0 | 10 | 12 | 1 | 2 ** | |
| | | | (2) | (2) | (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) | (2) | (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 | Control | | | | 10 ppm | | | | 30 ppm | | | | 90 ppm | | | |
|-------|----------|-------------------------|-----|-----|-----|--------|-----|-----|-----|--------|-----|-----|-----|--------|-----|-----|-----|
| | | No. of Animals on Study | | | | 50 | | | | 50 | | | | 50 | | | |
| | | Grade | | | | 1 | | | | 1 | | | | 1 | | | |
| | | 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 | 1 | 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 | 4 | 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 No. of Animals on Study 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 No. of Animals on Study 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) | (20) | (0) | (0) | (0) | (0) | (0) | (0) | (29) | (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) | (11) | (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)
 DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 20

| Organ | Findings | Group Name No. of Animals on Study 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 No. of Animals on Study 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

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 : 22

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

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 : 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/DuCrjCrj[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 | | | | Grade | | | | Grade | | | | 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 (0) | 1 (3) | 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) |
| | inflammation | 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) | 1 (7) | 0 (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) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 4 (27) | 9 (60) | 0 (0) |
| | eosinophilic change:olfactory epithelium | 0 (0) | 28 (70) | 12 (30) | 0 (0) | 1 (2) | 42 (93) | 2 (4) | 0 ** (0) | 1 (2) | 39 (95) | 1 (2) | 0 ** (0) | 3 (20) | 12 (80) | 0 (0) | 0 ** (0) |
| | eosinophilic change:respiratory epithelium | 20 (50) | 5 (13) | 0 (0) | 0 (0) | 19 (42) | 6 (13) | 0 (0) | 0 (0) | 11 (27) | 2 (5) | 0 (0) | 0 * (0) | 1 (7) | 0 (0) | 0 (0) | 0 ** (0) |
| | inflammation:foreign body | 3 (8) | 1 (3) | 0 (0) | 0 (0) | 2 (4) | 1 (2) | 0 (0) | 0 (0) | 1 (2) | 1 (2) | 0 (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) | 0 (0) | 0 (0) | 2 (5) | 0 (0) | 0 (0) | 0 (0) | 3 (20) | 10 (67) | 1 (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

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 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 No. of Animals on Study 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

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

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

| | | 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} | | | | | | | | | | | | | | | | | | |
| 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

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

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

PAGE : 19

| 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 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {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) |

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 : 20

| | | 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} | | | | | | | | | | | | | | | | | | |
| 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 | 0 | 1 | 0 | 0 |
| | | | (0) | (5) | (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 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 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 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 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 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 |

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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 No. of animals on Study | Control 50 | 10 ppm 50 | 30 ppm 50 | 90 ppm 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 No. of animals on Study | Control 50 | 10 ppm 50 | 30 ppm 50 | 90 ppm 50 |
|------------------------|-----------------------------|---------------------------------------|-------------------|-------------------|-------------------|------------------|
| {Hematopoietic system} | | | | | | |
| spleen | mononuclear cell leukemia | | <50> 10 (20%) | <50> 16 (32%) | <50> 19 (38%) | <50> 7 (14%) |
| {Digestive system} | | | | | | |
| oral cavity | squamous cell papilloma | | <50> 0 (0%) | <50> 1 (2%) | <50> 0 (0%) | <50> 0 (0%) |
| tongue | squamous cell papilloma | | <50> 1 (2%) | <49> 0 (0%) | <50> 0 (0%) | <50> 0 (0%) |
| stomach | squamous cell papilloma | | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) | <50> 1 (2%) |
| large intes | adenocarcinoma | | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) | <50> 0 (0%) |
| liver | hepatocellular adenoma | | <50> 0 (0%) | <50> 1 (2%) | <50> 1 (2%) | <50> 0 (0%) |
| | histiocytic sarcoma | | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) | <50> 0 (0%) |
| | hepatocellular carcinoma | | <50> 0 (0%) | <50> 1 (2%) | <50> 1 (2%) | <50> 1 (2%) |
| pancreas | islet cell adenoma | | <50> 2 (4%) | <50> 3 (6%) | <50> 3 (6%) | <50> 1 (2%) |
| {Urinary system} | | | | | | |
| urin bladd | transitional cell papilloma | | <50> 0 (0%) | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) |
| {Endocrine system} | | | | | | |
| pituitary | adenoma | | <50> 8 (16%) | <50> 14 (28%) | <50> 7 (14%) | <50> 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 No. of animals on Study | Control 50 | 10 ppm 50 | 30 ppm 50 | 90 ppm 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 No. of animals on Study | Control 50 | 10 ppm 50 | 30 ppm 50 | 90 ppm 50 |
|----------------------------------|--------------------------|---------------------------------------|-----------------|-----------------|-----------------|-----------------|
| (Nervous system) | | | | | | |
| brain | glioma | | <50> 0 (0%) | <50> 1 (2%) | <50> 1 (2%) | <50> 1 (2%) |
| periph nerv | schwannoma:malignant | | <50> 0 (0%) | <50> 0 (0%) | <50> 2 (4%) | <50> 0 (0%) |
| (Special sense organs/appendage) | | | | | | |
| Zymbal gl | Zmbal gland tumor:benign | | <50> 0 (0%) | <50> 2 (4%) | <50> 0 (0%) | <50> 0 (0%) |
| (Musculoskeletal system) | | | | | | |
| bone | osteosarcoma | | <50> 0 (0%) | <50> 2 (4%) | <50> 0 (0%) | <50> 0 (0%) |
| (Body cavities) | | | | | | |
| mediastinum | sarcoma:NOS | | <50> 0 (0%) | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) |
| peritoneum | fibroma | | <50> 0 (0%) | <50> 1 (2%) | <50> 1 (2%) | <50> 0 (0%) |
| | mesothelioma | | <50> 0 (0%) | <50> 1 (2%) | <50> 3 (6%) | <50> 1 (2%) |
| retroperit | schwannoma:malignant | | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) | <50> 0 (0%) |
| adipose | lipoma | | <50> 1 (2%) | <50> 1 (2%) | <50> 0 (0%) | <50> 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 No. of animals on Study | Control 50 | 10 ppm 50 | 30 ppm 50 | 90 ppm 50 |
|----------------------------------|------------------------------|---------------------------------------|------------------|------------------|------------------|-------------------|
| {Integumentary system/appandage} | | | | | | |
| skin/app | squamous cell carcinoma | | <50> 1 (2%) | <50> 0 (0%) | <50> 0 (0%) | <50> 0 (0%) |
| subcutis | fibroma | | <50> 0 (0%) | <50> 1 (2%) | <50> 0 (0%) | <50> 0 (0%) |
| | leiomyoma | | 1 (2%) | 0 (0%) | 0 (0%) | 0 (0%) |
| {Respiratory system} | | | | | | |
| nasal cavit | adenoma | | <50> 1 (2%) | <50> 1 (2%) | <50> 2 (4%) | <50> 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> 1 (2%) | <50> 2 (4%) | <50> 1 (2%) | <50> 1 (2%) |
| {Hematopoietic system} | | | | | | |
| spleen | mononuclear cell leukemia | | <50> 7 (14%) | <50> 8 (16%) | <49> 5 (10%) | <50> 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 No. of animals on Study | Control 50 | 10 ppm 50 | 30 ppm 50 | 90 ppm 50 |
|--------------------|-----------------------------|---------------------------------------|-------------------|-------------------|-------------------|------------------|
| {Digestive system} | | | | | | |
| stomach | squamous cell papilloma | | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) | <50> 0 (0%) |
| small intes | fibroma | | <50> 0 (0%) | <50> 1 (2%) | <50> 0 (0%) | <50> 0 (0%) |
| large intes | adenocarcinoma | | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) | <50> 0 (0%) |
| pancreas | islet cell adenoma | | <50> 0 (0%) | <50> 1 (2%) | <50> 0 (0%) | <50> 0 (0%) |
| {Urinary system} | | | | | | |
| kidney | mesenchymoma | | <50> 0 (0%) | <50> 1 (2%) | <50> 0 (0%) | <50> 0 (0%) |
| urin bladd | transitional cell papilloma | | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) | <50> 1 (2%) |
| {Endocrine system} | | | | | | |
| pituitary | adenoma | | <50> 15 (30%) | <50> 16 (32%) | <50> 14 (28%) | <50> 5 (10%) |
| | adenocarcinoma | | 0 (0%) | 1 (2%) | 1 (2%) | 0 (0%) |
| thyroid | C-cell adenoma | | <50> 4 (8%) | <50> 7 (14%) | <50> 9 (18%) | <50> 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 No. of animals on Study | Control 50 | 10 ppm 50 | 30 ppm 50 | 90 ppm 50 |
|-----------------------|-----------------------------|---------------------------------------|-----------------|-----------------|-----------------|-----------------|
| {Endocrine system} | | | | | | |
| adrenal | pheochromocytoma | | <50> 1 (2%) | <50> 1 (2%) | <50> 0 (0%) | <50> 1 (2%) |
| | cortical adenoma | | 0 (0%) | 0 (0%) | 1 (2%) | 0 (0%) |
| {Reproductive system} | | | | | | |
| ovary | granulosa-theca cell tumor | | <50> 0 (0%) | <50> 1 (2%) | <50> 1 (2%) | <50> 1 (2%) |
| | | | | | | |
| uterus | adenoma | | <50> 0 (0%) | <50> 1 (2%) | <50> 0 (0%) | <50> 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> 1 (2%) | <50> 3 (6%) | <50> 1 (2%) | <50> 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 No. of animals on Study | Control 50 | 10 ppm 50 | 30 ppm 50 | 90 ppm 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 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 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 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 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 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 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 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 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 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 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 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 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 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 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 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 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 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 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 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 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

PAGE : 9

| Group Name | Control | 10 ppm | 30 ppm | 90 ppm |
|---|---------------|-------------|-------------|--------------|
| SITE : nasal cavity 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 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 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

PAGE : 10

| Group Name | Control | 10 ppm | 30 ppm | 90 ppm |
|---|--------------|--------------|--------------|-------------|
| SITE : pituitary gland 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 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 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 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 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 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 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 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

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

| Organ | Findings | Group Name | Control | 10 ppm | 30 ppm | 90 ppm |
|------------------------|--|-------------------------|---------|--------|--------|--------|
| | | No. of Animals on Study | 50 | 50 | 50 | 50 |
| {Hematopoietic system} | | | | | | |
| lymph node | | | <50> | <50> | <50> | <50> |
| | metastasis:spleen tumor | | 0 | 1 | 0 | 0 |
| | metastasis:nasal tumor | | 0 | 0 | 0 | 3 |
| {Circulatory system} | | | | | | |
| heart | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 1 | 0 | 0 | 0 |
| {Digestive system} | | | | | | |
| stomach | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 0 | 0 | 1 | 0 |
| liver | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 4 | 5 | 6 | 4 |
| | metastasis:bone tumor | | 0 | 1 | 0 | 0 |
| pancreas | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 1 | 1 | 1 | 0 |
| {Urinary system} | | | | | | |
| kidney | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 2 | 2 | 1 | 0 |
| urin bladd | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 0 | 0 | 1 | 0 |
| {Endocrine system} | | | | | | |
| pituitary | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 0 | 1 | 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 : 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> 0 | <50> 1 | <50> 1 | <50> 0 |
| {Reproductive system} | | | | | | |
| prostate | leukemic cell infiltration | | <50> 1 | <50> 1 | <50> 0 | <50> 0 |
| {Nervous system} | | | | | | |
| brain | leukemic cell infiltration | | <50> 2 | <50> 2 | <50> 2 | <50> 2 |
| | metastasis: nasal tumor | | 0 | 0 | 0 | 2 |
| spinal cord | leukemic cell infiltration | | <50> 2 | <50> 0 | <50> 0 | <50> 0 |
| {Special sense organs/appendage} | | | | | | |
| Harder gl | metastasis: nasal tumor | | <50> 0 | <50> 0 | <50> 0 | <50> 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> 0 | <12> 1 | <12> 0 | <39> 0 |
| {Respiratory system} | | | | | | |
| trachea | metastasis:thyroid tumor | | <12> 1 | <12> 0 | <12> 0 | <39> 0 |
| lung | leukemic cell infiltration | | <12> 3 | <12> 3 | <12> 3 | <39> 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> 2 | <12> 1 | <12> 1 | <39> 2 |
| | metastasis:spleen tumor | | 0 | 1 | 0 | 0 |
| lymph node | leukemic cell infiltration | | <12> 2 | <12> 1 | <12> 0 | <39> 0 |
| | metastasis:spleen tumor | | 0 | 1 | 0 | 0 |
| | metastasis:nasal tumor | | 0 | 0 | 0 | 3 |
| {Circulatory system} | | | | | | |
| heart | leukemic cell infiltration | | <12> 1 | <12> 0 | <12> 0 | <39> 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 No. of Animals on Study | Control 12 | 10 ppm 12 | 30 ppm 12 | 90 ppm 39 |
|-----------------------|----------------------------|---------------------------------------|---------------|--------------|--------------|--------------|
| Organ | Findings | | | | | |
| {Digestive system} | | | | | | |
| stomach | leukemic cell infiltration | | <12> 0 | <12> 0 | <12> 1 | <39> 0 |
| liver | leukemic cell infiltration | | <12> 3 | <12> 4 | <12> 3 | <39> 3 |
| pancreas | leukemic cell infiltration | | <12> 1 | <12> 1 | <12> 1 | <39> 0 |
| {Urinary system} | | | | | | |
| kidney | leukemic cell infiltration | | <12> 2 | <12> 2 | <12> 1 | <39> 0 |
| urin bladd | leukemic cell infiltration | | <12> 0 | <12> 0 | <12> 1 | <39> 0 |
| {Endocrine system} | | | | | | |
| pituitary | leukemic cell infiltration | | <12> 0 | <12> 0 | <12> 1 | <39> 0 |
| adrenal | leukemic cell infiltration | | <12> 0 | <12> 1 | <12> 1 | <39> 0 |
| {Reproductive system} | | | | | | |
| prostate | leukemic cell infiltration | | <12> 1 | <12> 1 | <12> 0 | <39> 0 |
| {Nervous system} | | | | | | |
| brain | leukemic cell infiltration | | <12> 2 | <12> 2 | <12> 2 | <39> 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)

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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 No. of Animals on Study | Control 38 | 10 ppm 38 | 30 ppm 38 | 90 ppm 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 No. of Animals on Study | Control 50 | 10 ppm 50 | 30 ppm 50 | 90 ppm 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 No. of Animals on Study | Control 50 | 10 ppm 50 | 30 ppm 50 | 90 ppm 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 | Control | 10 ppm | 30 ppm | 90 ppm |
|--|----------------------------------|-------------------------|---------|--------|--------|--------|
| | | No. of Animals on Study | 50 | 50 | 50 | 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> 0 | <50> 0 | <50> 1 | <50> 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 No. of Animals on Study | Control 10 | 10 ppm 5 | 30 ppm 9 | 90 ppm 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 No. of Animals on Study | Control 10 | 10 ppm 5 | 30 ppm 9 | 90 ppm 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 No. of Animals on Study | | Control 10 | 10 ppm 5 | 30 ppm 9 | 90 ppm 35 |
|---------------------------------------|--|---------------|-------------|-------------|--------------|
| Organ | Findings | | | | |
| {Reproductive system} | | | | | |
| ovary | metastasis:large intestine tumor | <10> 0 | < 5> 0 | < 9> 1 | <35> 0 |
| {Nervous system} | | | | | |
| brain | leukemic cell infiltration | <10> 0 | < 5> 0 | < 9> 1 | <35> 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> 1 | < 5> 0 | < 9> 0 | <35> 0 |
| {Special sense organs/appendage} | | | | | |
| eye | metastasis:skin/appendage tumor | <10> 1 | < 5> 0 | < 9> 0 | <35> 0 |
| Harder gl | metastasis:nasal tumor | <10> 0 | < 5> 0 | < 9> 0 | <35> 1 |
| {Body cavities} | | | | | |
| retroperit | metastasis:uterus tumor | <10> 0 | < 5> 1 | < 9> 0 | <35> 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 No. of Animals on Study | Control 40 | 10 ppm 45 | 30 ppm 41 | 90 ppm 15 |
|------------------------|-----------------------------|---------------------------------------|---------------|--------------|--------------|--------------|
| Organ | Findings | | | | | |
| {Respiratory system} | | | | | | |
| lung | leukemic cell infiltration | | <40> 1 | <45> 3 | <41> 3 | <15> 1 |
| {Hematopoietic system} | | | | | | |
| lymph node | leukemic cell infiltration | | <40> 0 | <45> 1 | <41> 0 | <15> 2 |
| spleen | metastasis:peritoneum tumor | | <40> 1 | <45> 0 | <41> 0 | <15> 0 |
| {Circulatory system} | | | | | | |
| heart | leukemic cell infiltration | | <40> 0 | <45> 0 | <41> 1 | <15> 0 |
| {Digestive system} | | | | | | |
| liver | leukemic cell infiltration | | <40> 3 | <45> 5 | <41> 3 | <15> 1 |
| {Endocrine system} | | | | | | |
| pituitary | leukemic cell infiltration | | <40> 0 | <45> 1 | <41> 0 | <15> 0 |
| adrenal | leukemic cell infiltration | | <40> 0 | <45> 1 | <41> 0 | <15> 0 |
| {Nervous system} | | | | | | |
| brain | metastasis:pituitary tumor | | <40> 0 | <45> 1 | <41> 0 | <15> 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> 1 | <45> 0 | <41> 0 | <15> 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 |
|--|---|---------------------------|---------------|
| Hematology | | | |
| Red blood cell (RBC) | Light scattering method ¹⁾ | $\times 10^6/\mu\text{L}$ | 2 |
| Hemoglobin(Hgb) | Cyanmethemoglobin method ¹⁾ | g/dL | 1 |
| Hematocrit(Hct) | Calculated as $\text{RBC} \times \text{MCV}/10$ ¹⁾ | % | 1 |
| Mean corpuscular volume(MCV) | Light scattering method ¹⁾ | fL | 1 |
| Mean corpuscular hemoglobin(MCH) | Calculated as $\text{Hgb}/\text{RBC} \times 10$ ¹⁾ | pg | 1 |
| Mean corpuscular hemoglobin concentration (MCHC) | Calculated as $\text{Hgb}/\text{Hct} \times 100$ ¹⁾ | g/dL | 1 |
| Platelet | Light scattering method ¹⁾ | $\times 10^3/\mu\text{L}$ | 0 |
| White blood cell(WBC) | Light scattering method ¹⁾ | $\times 10^3/\mu\text{L}$ | 2 |
| Differential WBC | Pattern recognition method ²⁾ (Wright staining) | % | 0 |
| Biochemistry | | | |
| Total protein(TP) | Biuret method ³⁾ | g/dL | 1 |
| Albumin (Alb) | BCG method ³⁾ | g/dL | 1 |
| A/G ratio | Calculated as $\text{Alb}/(\text{TP} - \text{Alb})$ ³⁾ | — | 1 |
| T-bilirubin | Alkaline azobilirubin method ³⁾ | mg/dL | 2 |
| Glucose | GlcK·G-6-PDH method ³⁾ | mg/dL | 0 |
| T-cholesterol | CE·COD·POD method ³⁾ | mg/dL | 0 |
| Triglyceride | LPL·GK·GPO·POD method ³⁾ | mg/dL | 0 |
| Phospholipid | PLD·ChOD·POD method ³⁾ | mg/dL | 0 |
| Aspartate aminotransferase (AST) | JSCC method ³⁾ | IU/L | 0 |
| Alanine aminotransferase (ALT) | JSCC method ³⁾ | IU/L | 0 |
| Lactate dehydrogenase (LDH) | SFBC method ³⁾ | IU/L | 0 |
| Alkaline phosphatase (ALP) | GSCC method ³⁾ | IU/L | 0 |
| γ -Glutamyl transpeptidase (γ -GTP) | JSCC method ³⁾ | IU/L | 0 |
| Creatine kinase (CK) | JSCC method ³⁾ | IU/L | 0 |
| Urea nitrogen | Urease·GLDH method ³⁾ | mg/dL | 1 |
| Creatinine | Jaffe method ³⁾ | mg/dL | 1 |
| Sodium | Ion selective electrode method ³⁾ | mEq/L | 0 |
| Potassium | Ion selective electrode method ³⁾ | mEq/L | 1 |
| Chloride | Ion selective electrode method ³⁾ | mEq/L | 0 |
| Calcium | OCPC method ³⁾ | mg/dL | 1 |
| Inorganic phosphorus | PNP·XOD·POD method ³⁾ | mg/dL | 1 |

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

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

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