

1-ブロモ-3-クロロプロバンのラットを用いた
吸入によるがん原性試験報告書

試験番号：0417

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OF 1-BROMO-3-CHLOROPROPANE

APPENDIX A 1

IDENTITY AND IMPURITY OF 1-BROMO-3-CHLOROPROPANEIN THE 2-YEAR INHALATION STUDY

IDENTITY AND IMPURITY OF 1-BROMO-3-CHLOROPROPANE IN THE 2-YEAR
INHALATION STUDY

Test Substance : 1-Bromo-3-chloropropane (Wako Pure Chemical Industries, Ltd.)

A. Lot No. : SEJ4084

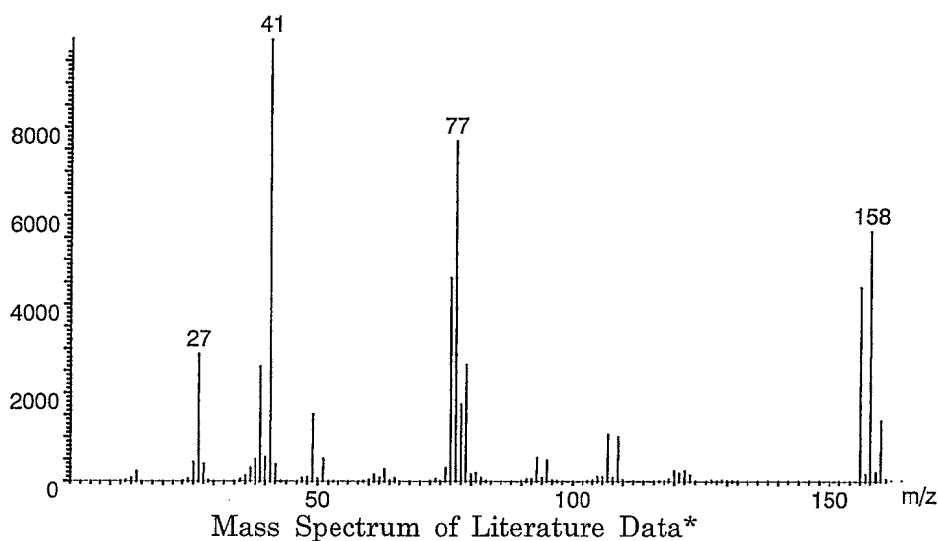
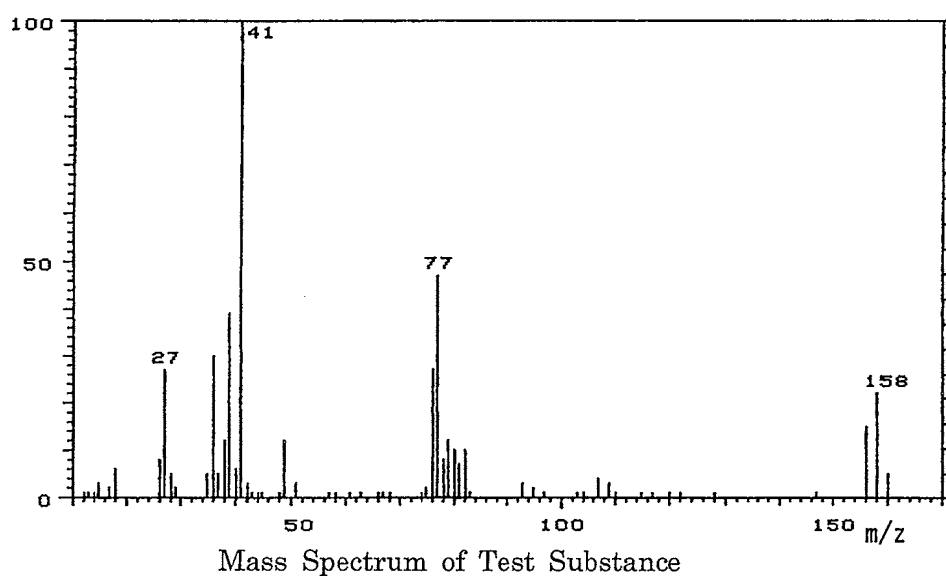
1. Spectral Data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Result: The mass spectrum was consistent with literature spectrum.

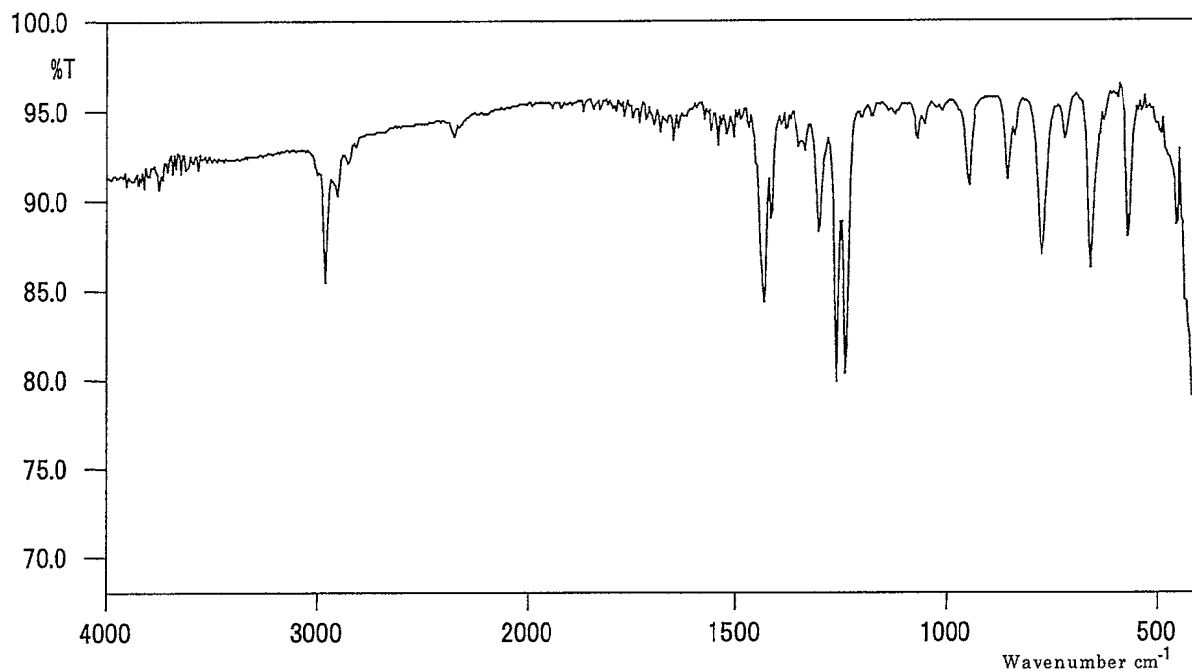
(*McLafferty FW, ed. 1994. Wiley Registry of Mass Spectral Data. 6th ed.
New York, NY:John Wiley and Sons.)

Infrared Spectrometry

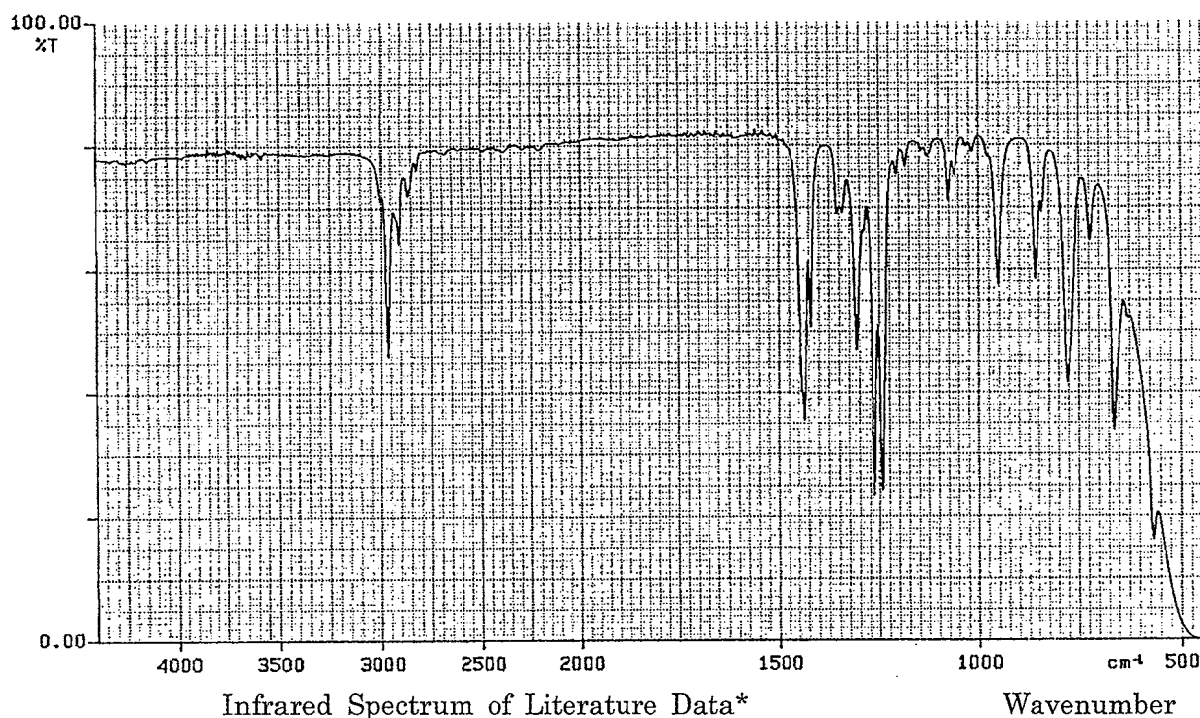
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 4 cm^{-1}



Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data*

Result: The infrared spectrum was consistent with literature spectrum.

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

2. Impurity

Instrument : Hewlett Packard 5890A Gas Chromatograph
Column : Methyl Silicone (0.53 mm ϕ \times 60 m)
Column Temperature : 100° C
Flow Rate : 20 mL/min
Detector : FID (Flame Ionization Detector)
Injection Volume : 1 μ L

| Sample Name | Peak No. | Area (%) | Peak Name |
|----------------|----------|----------|-------------------------|
| Test Substance | 1 | 0.046 | 1,2-Epoxybutane |
| | 2 | 99.954 | 1-Bromo-3-chloropropane |

Result: Gas chromatography indicated one major peak (peak No. 2) and one impurity. It was identified by comparing GC-MS with that of 1,2-Epoxybutane (peak No. 1) in the 1-bromo-3-chloropropane. The amount in the test substance was 0.046%(The quantity value by the standard sample was 0.045%.) with a gas chromatograph.

3. Conclusion: The test substance was identified as 1-bromo-3-chloropropane by mass spectrum and infrared spectrum. Gas chromatography indicated one major peak(1-bromo-3-chloropropane) and one impurity. The impurity was 1,2-epoxybutane in the test substance.

B. Lot No. : LDK4248

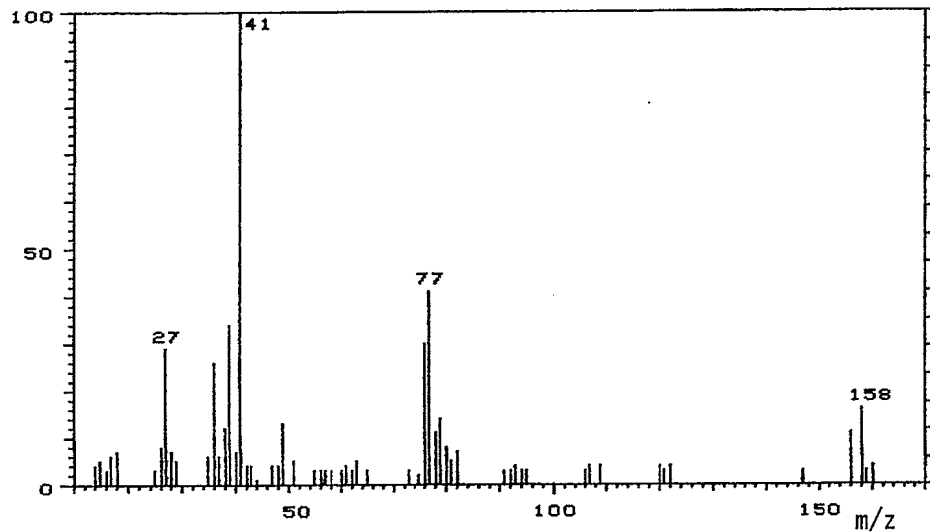
1. Spectral Data

Mass Spectrometry

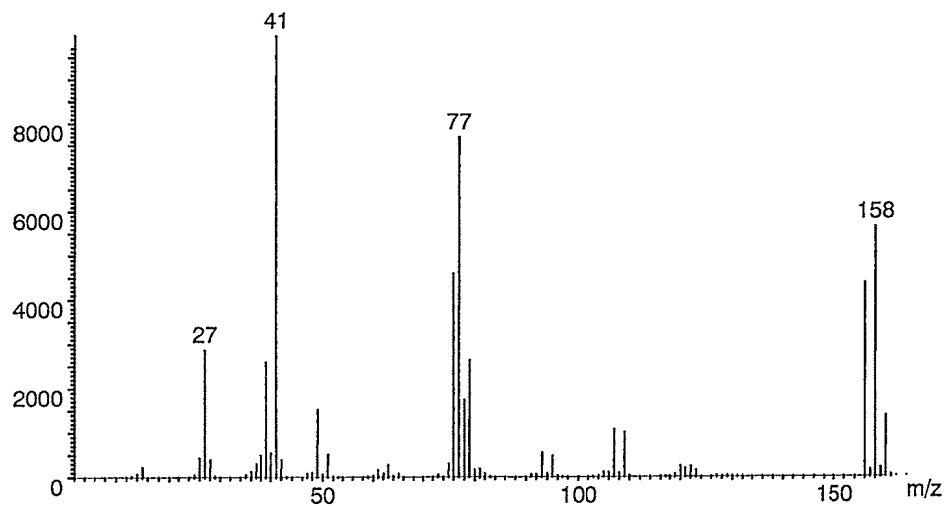
Instrument : Hitachi M-80B Mass Spectrometer

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.

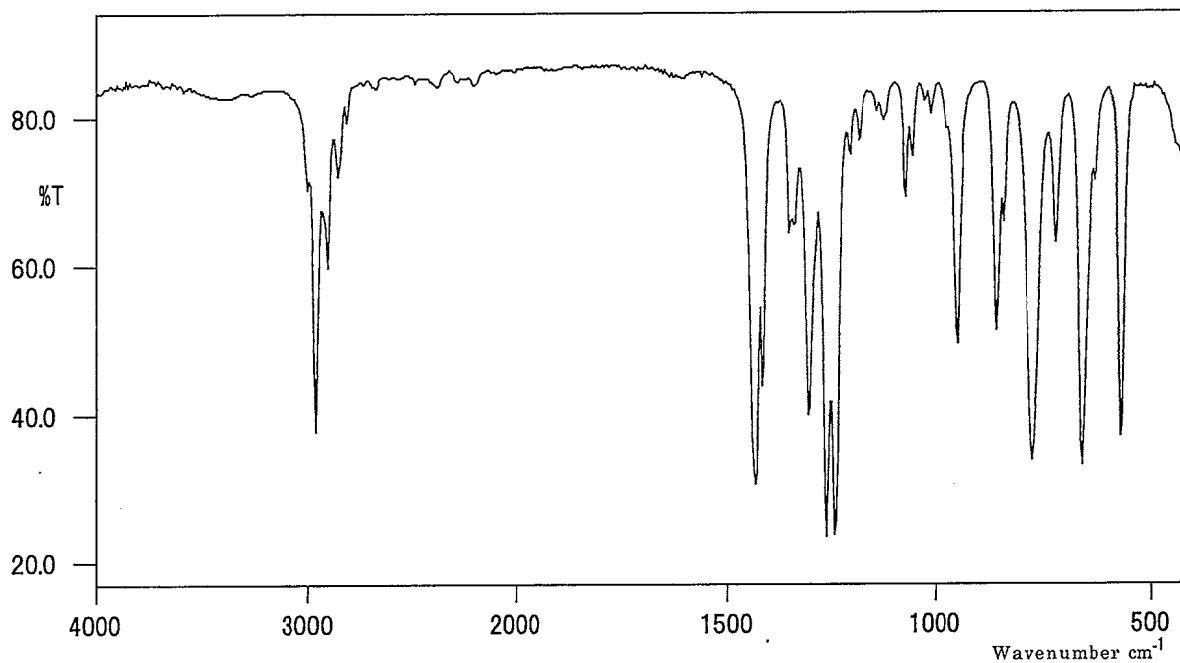
(*McLafferty FW, ed. 1994. Wiley Registry of Mass Spectral Data. 6th ed.
New York, NY:John Wiley and Sons.)

Infrared Spectrometry

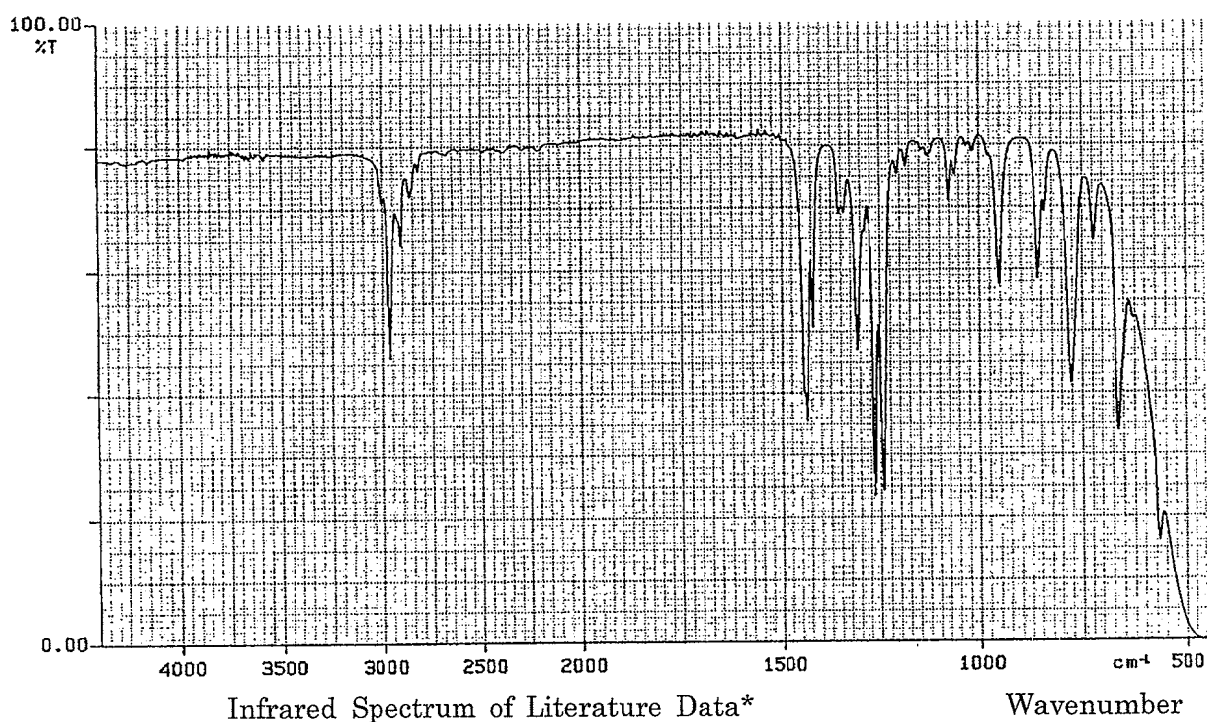
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 4 cm^{-1}



Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data*

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

2. Impurity

Instrument : Hewlett Packard 5890A Gas Chromatograph
Column : Methyl Silicone (0.53 mm ϕ \times 60 m)
Column Temperature : 100° C
Flow Rate : 20 mL/min
Detector : FID (Flame Ionization Detector)
Injection Volume : 1 μ L

| Sample Name | Peak No. | Area (%) | Peak Name |
|----------------|----------|----------|-------------------------|
| Test Substance | 1 | 0.046 | 1,2-Epoxybutane |
| | 2 | 99.954 | 1-Bromo-3-chloropropane |

Result: Gas chromatography indicated one major peak (peak No. 2) and one impurity. It was identified by comparing GC-MS with that of 1,2-Epoxybutane (peak No. 1) in the 1-bromo-3-chloropropane. The amount in the test substance was 0.046%(The quantity value by the standard sample was 0.045%.) with a gas chromatograph.

3. Conclusion: The test substance was identified as 1-bromo-3-chloropropane by mass spectrum and infrared spectrum. Gas chromatography indicated one major peak(1-bromo-3-chloropropane) and one impurity. The impurity was 1,2-epoxybutane in the test substance.

C. Lot No. : WAN5724

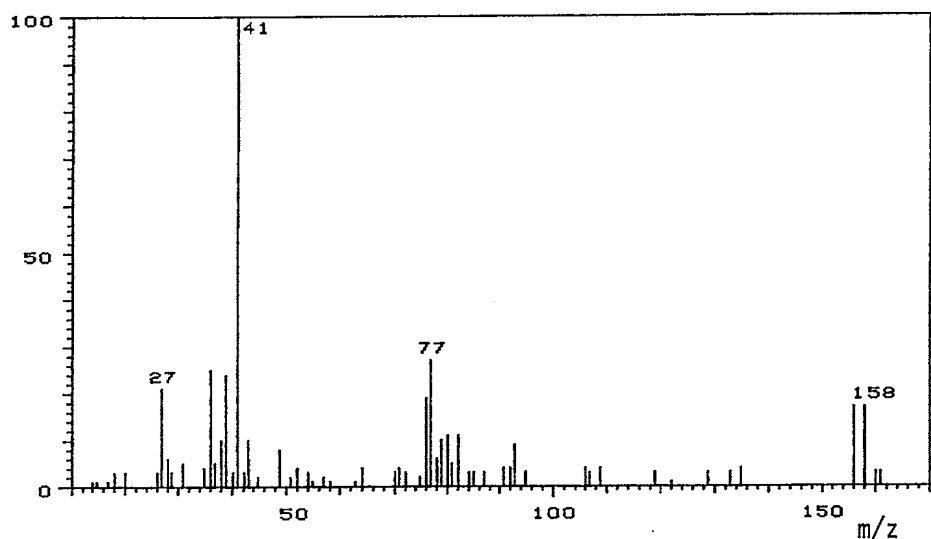
1. Spectral Data

Mass Spectrometry

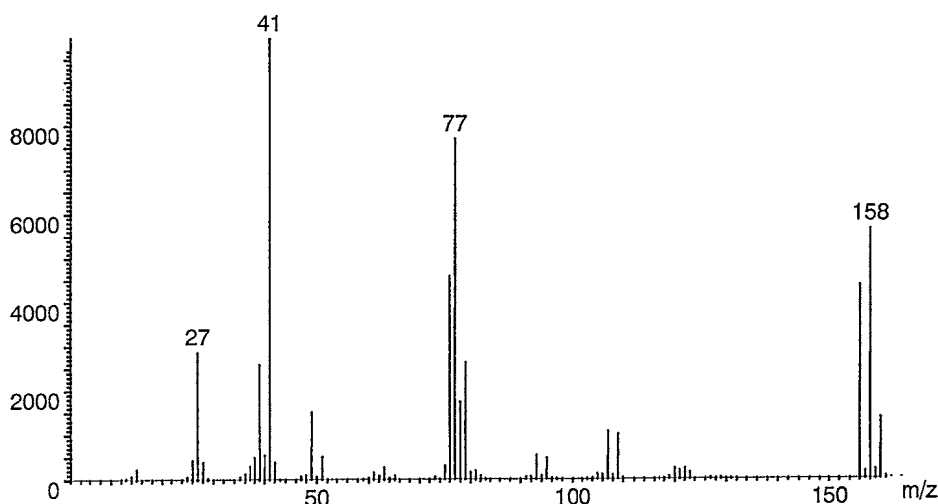
Instrument : Hitachi M-80B Mass Spectrometer

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.

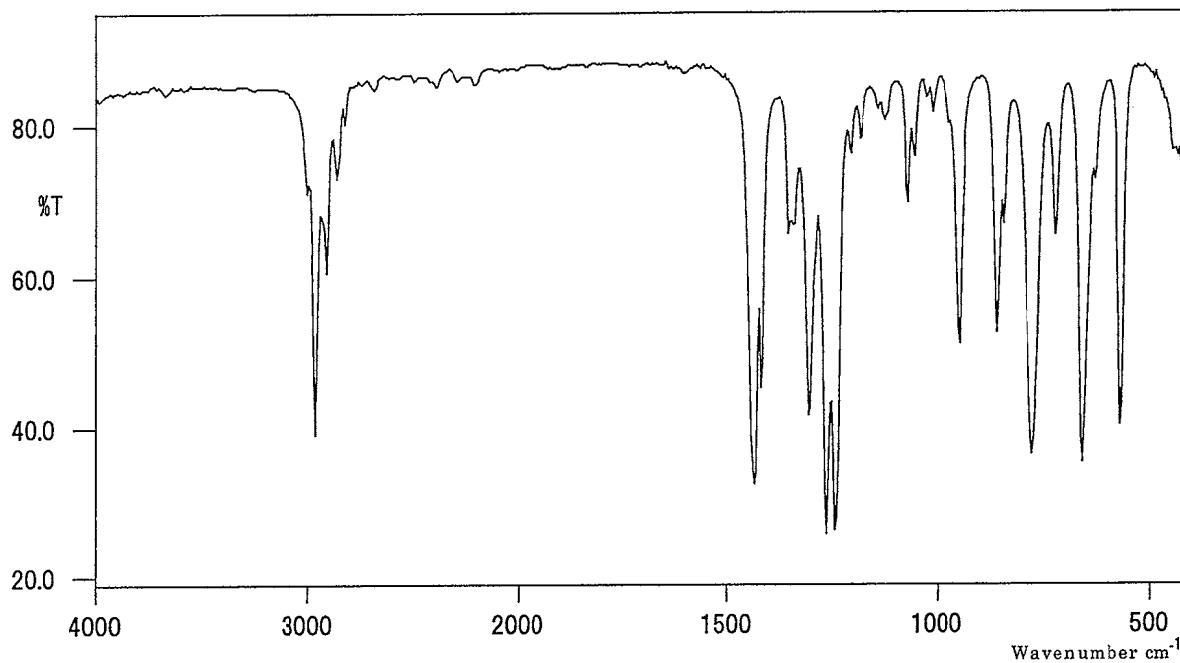
(*McLafferty FW, ed. 1994. Wiley Registry of Mass Spectral Data. 6th ed.
New York, NY:John Wiley and Sons.)

Infrared Spectrometry

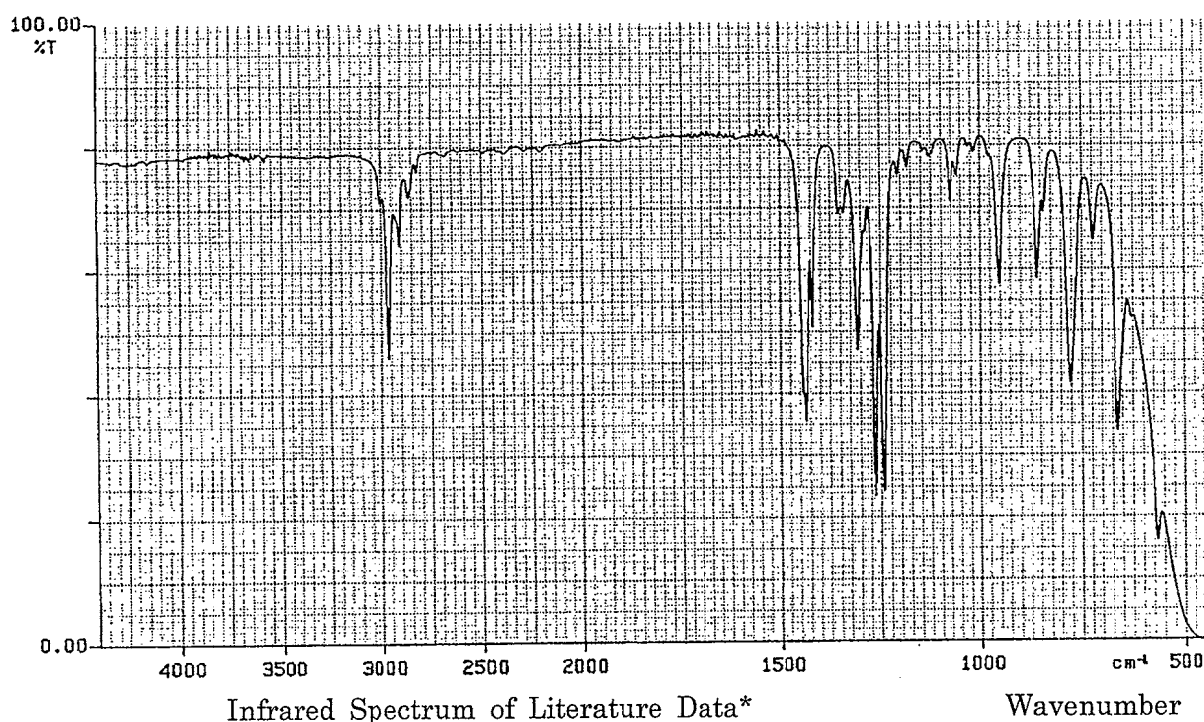
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 4 cm^{-1}



Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data*

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

2. Impurity

Instrument : Hewlett Packard 5890A Gas Chromatograph
Column : Methyl Silicone (0.53 mm ϕ \times 60 m)
Column Temperature : 100° C
Flow Rate : 20 mL/min
Detector : FID (Flame Ionization Detector)
Injection Volume : 1 μ L

| Sample Name | Peak No. | Area (%) | Peak Name |
|----------------|----------|----------|-------------------------|
| Test Substance | 1 | 0.041 | 1,2-Epoxybutane |
| | 2 | 99.959 | 1-Bromo-3-chloropropane |

Result: Gas chromatography indicated one major peak (peak No. 2) and one impurity. It was identified by comparing GC-MS with that of 1,2-Epoxybutane (peak No. 1) in the 1-bromo-3-chloropropane. The amount in the test substance was 0.041%(The quantity value by the standard sample was 0.041%.) with a gas chromatograph.

3. Conclusion: The test substance was identified as 1-bromo-3-chloropropane by mass spectrum and infrared spectrum. Gas chromatography indicated one major peak(1-bromo-3-chloropropane) and one impurity. The impurity was 1,2-epoxybutane in the test substance.

APPENDIX A 2

STABILITY OF 1-BROMO-3-CHLOROPROPANE IN THE 2-YEAR INHALATION STUDY

STABILITY OF 1-BROMO-3-CHLOROPROPANE IN THE 2-YEAR INHALATION STUDY

Test Substance : 1-Bromo-3-chloropropane (Wako Pure Chemical Industries, Ltd.)

A. Lot No. : SEJ4084

1. Sample : This lot was used from 2000.11.7 to 2001.9.28. 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 : 100° 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 (%) |
|-------------------------|----------|-------------------------|-------------|
| 2000.11.06 | 1 | 1.828 | 0.046 |
| | 2 | 6.667 | 99.954 |
| 2001.10.02 | 1 | 1.827 | 0.059 |
| | 2 | 6.659 | 99.941 |

Result: Gas chromatography indicated one major peak (peak No. 2) and one impurity (peak No. 1 < 0.1% of total area) analyzed on 2000.11.6 and one major peak (peak No. 2) and one impurity (peak No. 1 < 0.1% of total area) analyzed on 2001.10.2. No new trace impurity peak in the test substance analyzed on 2001.10.2 was detected.

3. Conclusion: The test substance was stable for about 11 months in a dark place at room temperature.

B. Lot No. : LDK4248

1. Sample : This lot was used from 2001.10.1 to 2002.7.9. 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 : 100° 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 (%) |
|-------------------------|----------|-------------------------|-------------|
| 2001.09.27 | 1 | 1.828 | 0.046 |
| | 2 | 6.665 | 99.954 |
| 2002.07.10 | 1 | 1.805 | 0.045 |
| | 2 | 6.611 | 99.955 |

Result: Gas chromatography indicated one major peak (peak No. 2) and one impurity (peak No. 1 < 0.1% of total area) analyzed on 2001.9.27 and one major peak (peak No. 2) and one impurity (peak No. 1 < 0.1% of total area) analyzed on 2002.7.10. No new trace impurity peak in the test substance analyzed on 2001.7.10 was detected.

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

C. Lot No. : WAN5724

1. Sample : This lot was used from 2002.7.10 to 2002.11.1. 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 : 100° 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 (%) |
|-------------------------|----------|-------------------------|-------------|
| 2002.07.09 | 1 | 1.806 | 0.041 |
| | 2 | 6.618 | 99.959 |
| 2002.12.10 | 1 | 1.806 | 0.041 |
| | 2 | 6.625 | 99.959 |

Result: Gas chromatography indicated one major peak (peak No. 2) and one impurity (peak No. 1 < 0.1% of total area) analyzed on 2002.7.9 and one major peak (peak No. 2) and one impurity (peak No. 1 < 0.1% of total area) analyzed on 2002.12.10. No new trace impurity peak in the test substance analyzed on 2002.12.10 was detected.

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

APPENDIX B 1

CONCENTRATION OF 1-BROMO-3-CHLOROPROPANE IN THE INHALATION CHAMBER OF THE 2-YEAR INHALATION STUDY

CONCENTRATION OF 1-BROMO-3-CHLOROPROPANE IN THE
INHALATION CHAMBER OF THE 2-YEAR INHALATION STUDY

| Group Name | Concentration(ppm) |
|------------|--------------------|
| | Mean \pm S.D. |
| Control | 0.0 \pm 0.0 |
| 25 ppm | 25.2 \pm 0.4 |
| 100 ppm | 100.4 \pm 0.9 |
| 400 ppm | 400.1 \pm 3.6 |

APPENDIX B 2

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 2-YEAR INHALATION STUDY OF 1-BROMO-3-CHLOROPROPANE

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 2-YEAR
INHALATION STUDY OF 1-BROMO-3-CHLOROPROPANE

| 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 ± 0.1 | 57.2 ± 0.8 | 766.0 ± 4.4 | 1514.8 ± 21.8 | 6.0 | 12.0 |
| 25 ppm | 23.2 ± 0.2 | 56.6 ± 1.5 | 765.1 ± 5.6 | 1526.7 ± 24.5 | 6.0 | 12.1 |
| 100 ppm | 23.1 ± 0.2 | 57.2 ± 0.8 | 765.6 ± 3.1 | 1525.8 ± 19.7 | 6.0 | 12.0 |
| 400 ppm | 23.0 ± 0.1 | 56.5 ± 0.8 | 761.5 ± 2.9 | 1516.3 ± 20.3 | 6.0 | 12.0 |

* 1: Exposure period * 2: After exposure period

APPENDIX C 1

CLINICAL OBSERVATION : SUMMARY,

RAT : MALE

(2-YEAR STUDY)

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| DEATH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| DEATH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PILORECTION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| DEATH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 |
| | 400ppm | 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 |
| | 25ppm | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| SOILED | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| DEATH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 2 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 400ppm | 1 | 2 | 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 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 1 | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| DEATH | Control | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 400ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 |
| MORIBUND SACRIFICE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PILOERECTIO | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| DEATH | Control | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 5 | 5 | 5 | 6 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 400ppm | 3 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 5 |
| MORIBUND SACRIFICE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| | 25ppm | 1 | 1 | 2 | 2 | 2 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| LOCOMOTOR MOVEMENT DECR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | Control | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 |
| | 25ppm | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| SOILED | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PILOBRECTION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| DEATH | Control | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 7 | 7 | 7 |
| | 25ppm | 1 | 1 | 1 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 |
| | 100ppm | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 |
| | 400ppm | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 6 | 6 | 6 | 6 | 8 |
| MORIBUND SACRIFICE | Control | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 25ppm | 4 | 5 | 5 | 5 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 |
| | 400ppm | 1 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 |
| LOCOMOTOR MOVEMENT DECR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 2 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 |
| | 400ppm | 1 | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 |
| DEATH | Control | 7 | 7 | 7 | 9 | 9 | 9 |
| | 25ppm | 6 | 7 | 8 | 8 | 8 | 8 |
| | 100ppm | 6 | 6 | 7 | 7 | 8 | 8 |
| | 400ppm | 8 | 8 | 8 | 8 | 9 | 10 |
| MORIBUND SACRIFICE | Control | 1 | 1 | 1 | 1 | 1 | 1 |
| | 25ppm | 7 | 7 | 7 | 7 | 7 | 7 |
| | 100ppm | 3 | 4 | 4 | 4 | 4 | 4 |
| | 400ppm | 4 | 5 | 6 | 7 | 10 | 10 |
| LOCOMOTOR MOVEMENT DECR | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| LATERAL | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| PARALYTIC GAIT | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| PILOERRECTION | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| FROG BELLY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PROLAPSE OF ANUS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| MYDRIASIS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| FROG BELLY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PROLAPSE OF ANUS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| MYDRIASIS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| FROG BELLY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PROLAPSE OF ANUS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| MYDRIASIS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| FROG BELLY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PROLAPSE OF ANUS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| EXOPHTHALMOS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 3 | 4 | 4 | 4 | 4 | 4 |
| | 400ppm | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| MYDRIASIS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| FROG BELLY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PROLAPSE OF ANUS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXOPHTHALMOS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CATARACT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 5 | 5 | 5 | 6 | 6 | 6 |
| | 400ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| MYDRIASIS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| FROG BELLY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PROLAPSE OF ANUS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 |
| | 400ppm | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 |
| EXOPHTHALMOS | Control | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 25ppm | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 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 |
| | 25ppm | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CATARACT | Control | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 1 |
| | 25ppm | 0 | 0 | 0 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 100ppm | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 5 | 5 |
| | 400ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| MYDRIASIS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| FROG BELLY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PROLAPSE OF ANUS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| | 400ppm | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| EXOPHTHALMOS | Control | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 2 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| CATARACT | Control | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 2 | 2 |
| | 25ppm | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| | 100ppm | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| | 400ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| MYDRIASIS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 | 1 | 1 | 1 | 1 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 |
| FROG BELLY | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 1 | 1 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| PROLAPSE OF ANUS | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 1 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 1 | 1 |
| SOILED PERI-GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 1 | 1 | 1 | 1 | 1 | 2 |
| EXOPHTHALMOS | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 1 | 1 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| EYE OPACITY | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| CATARACT | Control | 2 | 2 | 2 | 2 | 2 | 2 |
| | 25ppm | 2 | 2 | 2 | 2 | 2 | 3 |
| | 100ppm | 5 | 5 | 5 | 5 | 5 | 5 |
| | 400ppm | 2 | 2 | 2 | 2 | 2 | 2 |
| MYDRIASIS | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| ANTERIOR CHAMBER OPACITY | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| EXTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. EYE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. MANDIBULAR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. EAR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| EXTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. EYE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. MANDIBULAR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. EAR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| EXTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| | 25ppm | 0 | 0 | 1 | 2 | 1 | 2 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 | 1 | 1 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. EYE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 1 | 1 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. MANDIBULAR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. EAR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| EXTERNAL MASS | Control | 1 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| | 25ppm | 1 | 1 | 1 | 2 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 3 | 3 | 3 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 2 | 2 | 2 | 2 |
| INTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. NOSE | Control | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. EYE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 |
| M. MANDIBULAR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. EAR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| EXTERNAL MASS | Control | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 2 | 2 | 2 | 3 | 3 |
| | 25ppm | 4 | 4 | 4 | 4 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 8 |
| | 100ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 |
| | 400ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| INTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. NOSE | Control | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. EYE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. MANDIBULAR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. EAR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| EXTERNAL MASS | Control | 3 | 4 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | 5 | 5 |
| | 25ppm | 8 | 7 | 6 | 6 | 7 | 6 | 6 | 7 | 7 | 7 | 8 | 8 | 8 | 8 |
| | 100ppm | 2 | 3 | 4 | 4 | 4 | 5 | 5 | 6 | 6 | 6 | 6 | 6 | 5 | 5 |
| | 400ppm | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 |
| INTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. NOSE | Control | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. EYE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 |
| | 400ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. MANDIBULAR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. EAR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 0 | 0 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| EXTERNAL MASS | Control | 6 | 6 | 6 | 6 | 6 | 6 | 8 | 8 | 8 | 8 | 7 | 6 | 6 | 7 |
| | 25ppm | 8 | 7 | 7 | 7 | 6 | 5 | 5 | 5 | 6 | 6 | 6 | 6 | 5 | 5 |
| | 100ppm | 5 | 6 | 7 | 8 | 8 | 8 | 8 | 10 | 10 | 10 | 10 | 11 | 11 | 11 |
| | 400ppm | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 |
| INTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. NOSE | Control | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. EYE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 0 | 0 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. MANDIBULAR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. EAR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 0 | 0 |
| | 100ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 |
| EXTERNAL MASS | Control | 7 | 8 | 8 | 8 | 8 | 9 |
| | 25ppm | 4 | 5 | 5 | 7 | 7 | 10 |
| | 100ppm | 11 | 11 | 11 | 11 | 11 | 11 |
| | 400ppm | 4 | 4 | 3 | 5 | 4 | 4 |
| INTERNAL MASS | Control | 0 | 0 | 1 | 2 | 2 | 2 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| M. NOSE | Control | 2 | 2 | 2 | 2 | 2 | 2 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| M. EYE | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 2 | 2 | 2 | 2 | 2 | 2 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| M. PERI-MOUTH | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 1 | 1 | 1 | 2 | 2 | 2 |
| M. MANDIBULAR | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| M. EAR | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| M. PERI EAR | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 2 | 2 | 2 | 2 | 2 | 2 |
| | 400ppm | 0 | 0 | 0 | 1 | 1 | 1 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. FORELIMB | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. INTERSCAPULUM | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. FORELIMB | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. INTERSCAPULUM | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. FORELIMB | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. INTERSCAPULUM | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. FORELIMB | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. INTERSCAPULUM | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. SCROTUM | Control | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. FORELIMB | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 |
| | 400ppm | 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 | 1 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. INTERSCAPULUM | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 | 1 | 1 |
| | 25ppm | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. FORELIMB | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. ABDOMEN | Control | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| M. ANTERIOR. DORSUM | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. INTERSCAPULUM | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. POSTERIOR DORSUM | Control | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. SCROTUM | Control | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. FORELIMB | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 2 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. ABDOMEN | Control | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| | 400ppm | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. ANTERIOR. DORSUM | Control | 2 | 2 | 2 | 2 | 2 | 2 | 4 | 4 | 4 | 4 | 3 | 3 | 3 | 3 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. INTERSCAPULUM | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. POSTERIOR DORSUM | Control | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 3 | 3 | 3 |
| | 400ppm | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| M. GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. SCROTUM | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

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| Clinical sign | Group Name | Administration Week-day | | | | | |
|---------------------|------------|-------------------------|-------|-------|-------|-------|-------|
| | | 99-7 | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| | | 1 | 1 | 1 | 1 | 1 | 1 |
| M. FORELIMB | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| M. BREAST | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| M. ABDOMEN | Control | 1 | 2 | 2 | 2 | 2 | 2 |
| | 25ppm | 0 | 0 | 0 | 2 | 2 | 4 |
| | 100ppm | 3 | 3 | 3 | 3 | 3 | 3 |
| | 400ppm | 0 | 0 | 0 | 0 | 1 | 1 |
| M. ANTERIOR. DORSUM | Control | 3 | 3 | 3 | 3 | 3 | 3 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| M. INTERSCAPULUM | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| M. POSTERIOR DORSUM | Control | 1 | 1 | 1 | 1 | 1 | 1 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 2 |
| | 100ppm | 3 | 3 | 3 | 3 | 3 | 3 |
| | 400ppm | 2 | 2 | 1 | 1 | 0 | 0 |
| M. GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 1 | 1 | 1 | 1 | 0 | 0 |
| M. SCROTUM | Control | 0 | 0 | 0 | 0 | 0 | 1 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| ANEMIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRATION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| ANEMIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRATION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| ANEMIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| ABNORMAL RESPIRATION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|----------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 43-7 | 44-7 | 45-7 | 46-7 | 47-7 | 48-7 | 49-7 | 50-7 | 51-7 | 52-7 | 53-7 | 54-7 | 55-7 | 56-7 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| ANEMIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRATION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

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 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| ANEMIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRATION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|----------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 71-7 | 72-7 | 73-7 | 74-7 | 75-7 | 76-7 | 77-7 | 78-7 | 79-7 | 80-7 | 81-7 | 82-7 | 83-7 | 84-7 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| ANEMIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRATION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 1 | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 |

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|----------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 85-7 | 86-7 | 87-7 | 88-7 | 89-7 | 90-7 | 91-7 | 92-7 | 93-7 | 94-7 | 95-7 | 96-7 | 97-7 | 98-7 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| ANEMIA | Control | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| CRUSTA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 1 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRATION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : MALE

PAGE : 40

| Clinical sign | Group Name | Administration Week-day | | | | | |
|----------------------|------------|-------------------------|-------|-------|-------|-------|-------|
| | | 99-7 | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| | | 1 | 1 | 1 | 1 | 1 | 1 |
| ANEMIA | Control | 0 | 0 | 0 | 0 | 1 | 1 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 1 |
| | 400ppm | 0 | 1 | 1 | 1 | 0 | 0 |
| CRUSTA | Control | 1 | 1 | 1 | 1 | 1 | 1 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| HEMORRHAGE | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 1 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 1 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| PROLAPSE OF PENIS | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 1 | 0 | 0 |
| IRREGULAR BREATHING | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRATION | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| TACHYPNEA | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| DEEP BREATHING | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

PAGE : 41

| 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| ABNORMAL RESPIRA. SOUND | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

(HAN190)

BAIS 4

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| ABNORMAL RESPIRA. SOUND | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

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BAIS 4

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| ABNORMAL RESPIRA. SOUND | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

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BATS 4

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| ABNORMAL RESPIRA. SOUND | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

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BAIS 4

STUDY NO. : 0417
 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| ABNORMAL RESPIRA. SOUND | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

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BAIS 4

STUDY NO. : 0417
 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| ABNORMAL RESPIRA. SOUND | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| SUBNORMAL TEMP | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

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BAIS 4

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| ABNORMAL RESPIRA. SOUND | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

(HAN190)

BAIS 4

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 |
| ABNORMAL RESPIRA. SOUND | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| SUBNORMAL TEMP | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |

(HAN190)

BAIS 4

APPENDIX C 2

CLINICAL OBSERVATION : SUMMARY,

RAT : FEMALE

(2-YEAR STUDY)

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| DEATH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PILOBRECTION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PROLAPSE OF ANUS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| DEATH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PROLAPSE OF ANUS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| DEATH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PROLAPSE OF ANUS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 | 1 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| DEATH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PROLAPSE OF ANUS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED PERI-GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |

STUDY NO. : 0417
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 | | | | | | | | | | | | | |
|-----------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| DEATH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 2 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PILOBRECTION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PROLAPSE OF ANUS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| DEATH | Control | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 6 | 6 | 6 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| MORIBUND SACRIFICE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 3 | 3 | 4 | 4 |
| PARALYTIC GAIT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PILOBRECTION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PROLAPSE OF ANUS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| SOILED PERI-GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| DEATH | Control | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 7 | 7 |
| | 25ppm | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | 4 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 400ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 4 | 4 | 5 |
| MORIBUND SACRIFICE | Control | 0 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 1 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| | 400ppm | 4 | 5 | 5 | 5 | 6 | 6 | 7 | 8 | 10 | 10 | 11 | 12 | 12 | 12 |
| PARALYTIC GAIT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | Control | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 2 | 1 | 1 | 1 | 1 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 1 |
| SOILED | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PILOERECTION | Control | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PROLAPSE OF ANUS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 2 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 |
| SOILED PERI-GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 2 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 |
| DEATH | Control | 7 | 7 | 7 | 7 | 7 | 7 |
| | 25ppm | 4 | 4 | 4 | 4 | 4 | 4 |
| | 100ppm | 2 | 2 | 3 | 3 | 4 | 4 |
| | 400ppm | 6 | 8 | 9 | 9 | 9 | 9 |
| MORIBUND SACRIFICE | Control | 4 | 4 | 4 | 5 | 5 | 5 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 3 | 4 | 4 | 4 | 5 | 7 |
| | 400ppm | 12 | 12 | 12 | 13 | 14 | 15 |
| PARALYTIC GAIT | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | Control | 0 | 0 | 0 | 0 | 0 | 1 |
| | 25ppm | 1 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 1 | 1 | 1 | 2 | 0 |
| | 400ppm | 1 | 1 | 2 | 3 | 2 | 1 |
| SOILED | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 1 | 0 | 0 |
| PILORECTION | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| PROLAPSE OF ANUS | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 1 | 2 | 0 | 1 | 1 | 1 |
| SOILED PERI-GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 1 | 1 | 0 |
| | 400ppm | 1 | 1 | 2 | 1 | 1 | 1 |

STUDY NO. : 0417
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 |
| | | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| MYDRIASIS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL GROWTH OF TEETH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
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SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|--------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 15-7 | 16-7 | 17-7 | 18-7 | 19-7 | 20-7 | 21-7 | 22-7 | 23-7 | 24-7 | 25-7 | 26-7 | 27-7 | 28-7 |
| | | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 |
| | 400ppm | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| MYDRIASIS | Control | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL GROWTH OF TEETH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| MYDRIASIS | Control | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL GROWTH OF TEETH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CATARACT | Control | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| MYDRIASIS | Control | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL GROWTH OF TEETH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| MYDRIASIS | Control | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL GROWTH OF TEETH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| EXTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 2 | 1 | 1 | 1 | 1 | 1 |
| INTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 400ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| MYDRIASIS | Control | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL GROWTH OF TEETH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 1 | 1 | 1 | 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 | 1 | 1 |
| | 25ppm | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 4 |
| | 400ppm | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 4 | 6 | 6 |
| INTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 |
| M. NOSE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| EYE OPACITY | Control | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 4 | 4 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| | 100ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 400ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| MYDRIASIS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 | 1 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL GROWTH OF TEETH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXTERNAL MASS | Control | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 3 | 3 | 2 | 2 | 4 | 5 |
| | 25ppm | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 4 | 4 | 5 | 5 | 5 | 5 | 5 |
| | 100ppm | 3 | 3 | 3 | 3 | 4 | 4 | 5 | 4 | 5 | 5 | 6 | 8 | 9 | 9 |
| | 400ppm | 6 | 7 | 7 | 8 | 8 | 10 | 9 | 9 | 6 | 6 | 6 | 7 | 7 | 7 |
| INTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 1 | 2 | 2 | 2 | 1 | 1 | 2 | 1 | 1 | 0 |
| M. NOSE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 |
| EYE OPACITY | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| CATARACT | Control | 2 | 2 | 2 | 2 | 2 | 2 |
| | 25ppm | 5 | 5 | 5 | 5 | 5 | 5 |
| | 100ppm | 2 | 2 | 2 | 2 | 2 | 2 |
| | 400ppm | 1 | 1 | 1 | 0 | 0 | 0 |
| MYDRIASIS | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| ANTERIOR CHAMBER OPACITY | Control | 1 | 1 | 1 | 1 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL GROWTH OF TEETH | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| EXTERNAL MASS | Control | 5 | 6 | 6 | 7 | 7 | 8 |
| | 25ppm | 6 | 6 | 6 | 8 | 8 | 9 |
| | 100ppm | 9 | 9 | 9 | 9 | 9 | 9 |
| | 400ppm | 7 | 7 | 7 | 7 | 6 | 6 |
| INTERNAL MASS | Control | 0 | 0 | 1 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 1 | 1 |
| | 400ppm | 1 | 1 | 1 | 0 | 0 | 0 |
| M. NOSE | Control | 1 | 1 | 1 | 1 | 1 | 1 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. PERI-MOUTH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. MANDIBULAR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. PERI-MOUTH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. MANDIBULAR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. PERI-MOUTH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. MANDIBULAR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. PERI-MOUTH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. MANDIBULAR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. PERI-MOUTH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| M. MANDIBULAR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. ANTERIOR. DORSUM | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. PERI-MOUTH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. MANDIBULAR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| M. ABDOMEN | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| | 25ppm | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 |
| M. ANTERIOR. DORSUM | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 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 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 2 | 2 | 2 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. PERI-MOUTH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| M. MANDIBULAR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 1 | 1 | 1 | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 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 | 1 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 2 | 2 | 2 | 2 |
| | 400ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M. ABDOMEN | Control | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 |
| | 400ppm | 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 | 1 | 1 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 | 1 | 1 |
| | 25ppm | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 |
| | 100ppm | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 4 | 4 |
| | 400ppm | 2 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 2 | 2 | 2 | 3 | 3 | 3 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 |
| M. PERI-MOUTH | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 1 | 1 | 1 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| M. MANDIBULAR | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| M. NECK | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| | 400ppm | 0 | 1 | 1 | 1 | 0 | 0 |
| M. BREAST | Control | 1 | 1 | 1 | 1 | 1 | 1 |
| | 25ppm | 1 | 1 | 1 | 2 | 2 | 4 |
| | 100ppm | 2 | 2 | 2 | 2 | 2 | 2 |
| | 400ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| M. ABDOMEN | Control | 1 | 1 | 1 | 1 | 1 | 1 |
| | 25ppm | 3 | 3 | 3 | 3 | 3 | 3 |
| | 100ppm | 1 | 1 | 1 | 1 | 2 | 2 |
| | 400ppm | 2 | 2 | 2 | 2 | 2 | 2 |
| M. ANTERIOR. DORSUM | Control | 1 | 1 | 1 | 1 | 1 | 1 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| M. POSTERIOR DORSUM | Control | 0 | 0 | 0 | 0 | 0 | 1 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| M. GENITALIA | Control | 1 | 2 | 2 | 3 | 3 | 4 |
| | 25ppm | 2 | 2 | 2 | 3 | 3 | 3 |
| | 100ppm | 4 | 4 | 4 | 4 | 4 | 4 |
| | 400ppm | 3 | 2 | 2 | 2 | 2 | 2 |

STUDY NO. : 0417
 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| ANEMIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| RESPIRATORY SOUND ABNOR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| ANEMIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| RESPIRATORY SOUND ABNOR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| ANEMIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| RESPIRATORY SOUND ABNOR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

PAGE : 76

| 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| ANEMIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| RESPIRATORY SOUND ABNOR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

PAGE : 77

| 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| ANEMIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| RESPIRATORY SOUND ABNOR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : FEMALE

PAGE : 78

| 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| ANEMIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 1 | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| CRUSTA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 |
| IRREGULAR BREATHING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| RESPIRATORY SOUND ABNOR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

(HAN190)

BAIS 4

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

PAGE : 79

| 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| ANEMIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 25ppm | 1 | 1 | 0 | 0 | 0 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 1 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 |
| JAUNDICE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 2 | 1 | 1 | 1 | 0 | 0 | 0 |
| CRUSTA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 2 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| HEMORRHAGE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| IRREGULAR BREATHING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| RESPIRATORY SOUND ABNOR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 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 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

(HAN190)

BAIS 4

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : FEMALE

PAGE : 80

| Clinical sign | Group Name | Administration Week-day | | | | | |
|-------------------------|------------|-------------------------|-------|-------|-------|-------|-------|
| | | 99-7 | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| | | 1 | 1 | 1 | 1 | 1 | 1 |
| ANEMIA | Control | 0 | 0 | 1 | 0 | 0 | 1 |
| | 25ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| | 100ppm | 3 | 1 | 0 | 0 | 1 | 1 |
| | 400ppm | 0 | 1 | 1 | 1 | 0 | 0 |
| JAUNDICE | Control | 0 | 0 | 0 | 0 | 0 | 1 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| CRUSTA | Control | 2 | 2 | 2 | 2 | 2 | 2 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 1 | 0 | 0 | 0 | 0 | 0 |
| HEMORRHAGE | Control | 0 | 0 | 0 | 0 | 0 | 1 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| IRREGULAR BREATHING | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 1 | 1 | 1 | 0 | 0 | 0 |
| RESPIRATORY SOUND ABNOR | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400ppm | 0 | 1 | 1 | 1 | 1 | 0 |
| DEEP BREATHING | Control | 0 | 0 | 0 | 0 | 0 | 0 |
| | 25ppm | 0 | 0 | 0 | 0 | 0 | 0 |
| | 100ppm | 1 | 1 | 1 | 1 | 1 | 0 |
| | 400ppm | 1 | 1 | 1 | 1 | 1 | 0 |

(HAN190)

BAIS 4

APPENDIX D 1

BODY WEIGHT CHANGES : SUMMARY,

RAT : MALE

(2-YEAR STUDY)

STUDY NO. : 0417
 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 | 112± | 4 | 142± | 7 | 176± | 10 | 202± | 12 | 227± | 12 | 245± | 14 |
| 25ppm | 112± | 4 | 141± | 7 | 176± | 10 | 204± | 10 | 228± | 11 | 246± | 12 |
| 100ppm | 112± | 5 | 140± | 7 | 175± | 9 | 203± | 10 | 227± | 11 | 246± | 12 |
| 400ppm | 112± | 4 | 131± | 6** | 158± | 7** | 179± | 7** | 195± | 8** | 209± | 8** |

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

Test of Dunnett

(HAN260)

BAIS 4

STUDY NO. : 0417
 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 | |
| Control | 273± | 16 | 284± | 17 | 294± | 18 | 301± | 18 | 309± | 18 | 315± | 19 |
| 25ppm | 275± | 14 | 286± | 15 | 296± | 15 | 306± | 16 | 312± | 16 | 318± | 17 |
| 100ppm | 276± | 13 | 288± | 14 | 299± | 15 | 307± | 15 | 314± | 17 | 322± | 17 |
| 400ppm | 230± | 8** | 239± | 9** | 251± | 9** | 257± | 9** | 260± | 9** | 266± | 9** |
| | | | | | | | | | | | | |
| Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett | | | | | | | | | | | | |

(HAN260)

BAIS 4

STUDY NO. : 0417
 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 | 327± | 21 | 344± | 23 | 359± | 25 | 372± | 26 | 377± | 27 | 389± | 30 |
| 25ppm | 331± | 17 | 348± | 18 | 365± | 19 | 376± | 20 | 382± | 20 | 395± | 22 |
| 100ppm | 335± | 18 | 352± | 20 | 369± | 22 | 381± | 25 | 390± | 18 | 401± | 19 |
| 400ppm | 277± | 10** | 292± | 10** | 305± | 11** | 320± | 12** | 327± | 12** | 342± | 14** |
| Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett | | | | | | | | | | | | |

(HAN260)

BAIS 4

STUDY NO. : 0417
 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 | 403± | 31 | 412± | 32 | 415± | 33 | 414± | 34 | 421± | 34 | 425± | 33 |
| 25ppm | 407± | 22 | 418± | 23 | 421± | 23 | 423± | 23 | 427± | 22 | 429± | 24 |
| 100ppm | 415± | 21 | 422± | 21 | 425± | 21 | 425± | 21 | 431± | 23 | 433± | 23 |
| 400ppm | 349± | 18** | 339± | 14** | 345± | 15** | 347± | 15** | 351± | 17** | 355± | 18** |

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

Test of Dunnett

(HAN260)

BAIS 4

STUDY NO. : 0417
 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 | 428± | 34 | 424± | 38 | 427± | 41 | 424± | 43 | 427± | 30 | 429± | 32 |
| 25ppm | 434± | 25 | 432± | 30 | 435± | 29 | 436± | 38 | 428± | 30 | 430± | 23 |
| 100ppm | 439± | 22 | 436± | 23 | 436± | 28 | 434± | 36 | 435± | 21 | 435± | 22 |
| 400ppm | 352± | 16** | 349± | 16** | 347± | 17** | 339± | 20** | 338± | 17** | 334± | 17** |
| Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett | | | | | | | | | | | | |

(HAN260)

BAIS 4

STUDY NO. : 0417
 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 | 420± | 31 | 414± | 28 | 408± | 31 |
| 25ppm | 416± | 27 | 412± | 29 | 405± | 31 |
| 100ppm | 414± | 49 | 420± | 35 | 412± | 44 |
| 400ppm | 324± | 19** | 313± | 26** | 305± | 28** |

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

(HAN260)

BATS 4

APPENDIX D 2

BODY WEIGHT CHANGES : SUMMARY,

RAT : FEMALE

(2-YEAR STUDY)

STUDY NO. : 0417
 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 | 91± | 3 | 106± | 4 | 121± | 5 | 133± | 6 | 142± | 7 | 148± | 8 |
| 25ppm | 91± | 3 | 107± | 4 | 121± | 4 | 132± | 6 | 143± | 6 | 150± | 6 |
| 100ppm | 91± | 3 | 107± | 4 | 123± | 5 | 133± | 7 | 145± | 7 | 153± | 7** |
| 400ppm | 91± | 3 | 103± | 4** | 115± | 4** | 124± | 5** | 133± | 5** | 140± | 5** |

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

Test of Dunnett

(HAN260)

BAIS 4

STUDY NO. : 0417
 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 | 160± | 9 | 164± | 10 | 169± | 10 | 173± | 10 | 176± | 11 | 178± | 11 | 181± | 11 |
| 25ppm | 162± | 9 | 166± | 9 | 170± | 10 | 175± | 10 | 179± | 11 | 180± | 11 | 183± | 11 |
| 100ppm | 165± | 9* | 169± | 9* | 173± | 10 | 177± | 10 | 182± | 11* | 185± | 11** | 187± | 11* |
| 400ppm | 151± | 6** | 155± | 6** | 158± | 7** | 163± | 7** | 166± | 7** | 168± | 7** | 171± | 7** |
| Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ | | | | | | | | | | | | | | |

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

Test of Dunnett

(HAN260)

BAIS 4

STUDY NO. : 0417
 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 | 183± | 11 | 189± | 12 | 197± | 13 | 203± | 14 | 206± | 13 | 212± | 14 |
| 25ppm | 185± | 11 | 191± | 12 | 199± | 13 | 205± | 13 | 209± | 14 | 215± | 15 |
| 100ppm | 190± | 12* | 196± | 12* | 204± | 13* | 208± | 15 | 214± | 15* | 221± | 15* |
| 400ppm | 173± | 8** | 180± | 8** | 187± | 9** | 194± | 9** | 199± | 10* | 206± | 10 |

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

Test of Dunnett

(HAN260)

BAIS 4

STUDY NO. : 0417
 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 | 220± | 17 | 227± | 18 | 227± | 18 | 230± | 20 | 234± | 20 | 236± | 22 |
| 25ppm | 222± | 17 | 228± | 18 | 231± | 20 | 236± | 21 | 243± | 22 | 244± | 23 |
| 100ppm | 231± | 16** | 238± | 18* | 239± | 18* | 245± | 20** | 251± | 22** | 253± | 24** |
| 400ppm | 213± | 11* | 209± | 12** | 210± | 11** | 215± | 12** | 220± | 12** | 220± | 14** |
| Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett | | | | | | | | | | | | |

(HAN260)

BAIS 4

STUDY NO. : 0417
 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 | 247± | 24 | 252± | 21 | 255± | 22 | 259± | 21 | 259± | 25 | 269± | 23 |
| 25ppm | 256± | 26 | 259± | 26 | 266± | 27 | 268± | 28 | 270± | 29 | 278± | 28 |
| 100ppm | 265± | 26** | 270± | 26** | 275± | 27** | 279± | 29** | 281± | 29** | 290± | 28** |
| 400ppm | 227± | 15** | 229± | 15** | 230± | 15** | 229± | 16** | 229± | 16** | 230± | 19** |

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

Test of Dunnett

(HAN260)

BAIS 4

STUDY NO. : 0417
 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 | 273± | 25 | 274± | 26 | 272± | 27 |
| 25ppm | 284± | 28 | 282± | 31 | 280± | 30 |
| 100ppm | 293± | 30** | 289± | 39 | 295± | 24** |
| 400ppm | 228± | 22** | 218± | 29** | 218± | 28** |

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

Test of Dunnett

(HAN260)

BAIS 4

APPENDIX E 1

FOOD CONSUMPTION CHANGES : SUMMARY,

RAT : MALE

(2-YEAR STUDY)

STUDY NO. : 0417
 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 (6) | 2-7 (7) | 3-7 (7) | 4-7 (7) | 5-7 (7) | 6-7 (7) | 7-7 (7) |
| Control | 14.5± 1.0 | 15.9± 1.2 | 17.3± 1.4 | 17.5± 1.2 | 17.5± 1.4 | 17.1± 1.2 | 17.2± 1.2 |
| 25ppm | 14.3± 0.9 | 16.1± 1.1 | 17.5± 1.1 | 17.6± 1.1 | 17.5± 1.0 | 17.4± 1.0 | 17.3± 1.1 |
| 100ppm | 14.1± 1.1 | 16.2± 1.3 | 18.1± 1.6* | 18.2± 1.6* | 17.9± 1.5 | 18.1± 1.3** | 17.8± 1.4 |
| 400ppm | 12.6± 0.9** | 15.0± 1.0** | 16.7± 1.4 | 17.2± 1.5 | 17.3± 1.4 | 17.6± 1.6 | 17.4± 1.4 |

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

Test of Dunnett

(HAN260)

BAIS 4

STUDY NO. : 0417
 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 | 16.6± 1.3 | 17.2± 1.4 | 16.9± 1.4 | 16.8± 1.2 | 16.9± 1.2 | 16.8± 1.5 | 16.8± 1.4 |
| 25ppm | 16.8± 1.1 | 17.4± 1.0 | 17.3± 1.1 | 17.1± 1.1 | 17.0± 1.0 | 16.9± 1.0 | 16.9± 1.0 |
| 100ppm | 17.5± 1.2** | 17.7± 1.2 | 17.7± 1.3** | 17.4± 1.3* | 17.4± 1.1 | 17.3± 1.2 | 17.4± 1.2 |
| 400ppm | 17.5± 1.4** | 17.6± 1.2 | 17.4± 1.3 | 17.4± 1.3* | 17.7± 1.4** | 17.8± 1.3** | 17.9± 1.3** |

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

Test of Dunnett

(HAN260)

BAIS 4

STUDY NO. : 0417
 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) | | 26-7(7) | 30-7(7) | 34-7(7) | 38-7(7) | 42-7(7) |
|------------|----------------|--|---------------------|--|------------|-------------|-------------|------------|-----------|
| | 18-7(7) | | 22-7(7) | | | | | | |
| Control | 16.4± 1.4 | | 17.0± 1.4 | | 16.8± 1.4 | 16.2± 1.3 | 17.1± 1.5 | 16.6± 1.2 | 16.6± 1.4 |
| 25ppm | 16.6± 0.9 | | 17.0± 1.0 | | 16.7± 1.3 | 16.2± 0.9 | 17.5± 1.1 | 16.3± 1.1 | 16.6± 0.9 |
| 100ppm | 16.9± 1.0* | | 17.3± 1.1 | | 16.8± 1.2 | 16.7± 0.9 | 17.4± 1.1 | 16.7± 1.2 | 17.0± 1.0 |
| 400ppm | 17.5± 1.5** | | 18.0± 1.5** | | 17.6± 1.3* | 17.3± 1.5** | 17.9± 1.4** | 17.1± 1.0* | 16.2± 1.9 |

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

Test of Dunnett

(HAN260)

BAIS 4

STUDY NO. : 0417
 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 | 17.2± 1.4 | 17.1± 1.4 | 16.5± 1.4 | 17.1± 1.4 | 17.5± 1.5 | 17.4± 1.5 | 17.0± 1.4 |
| 25ppm | 17.2± 0.9 | 17.2± 0.9 | 17.0± 0.9 | 16.9± 0.9 | 17.1± 1.1 | 17.4± 1.2 | 17.0± 1.2 |
| 100ppm | 17.1± 0.8 | 17.2± 0.8 | 17.2± 0.9 | 17.2± 0.9 | 17.2± 0.9 | 17.4± 0.9 | 17.3± 0.9 |
| 400ppm | 17.8± 1.9 | 17.7± 1.2 | 17.6± 1.5** | 17.4± 1.4 | 17.0± 1.3 | 16.9± 1.7 | 17.2± 1.5 |

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

Test of Dunnett

(HAN260)

BAIS 4

STUDY NO. : 0417
 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± 1.3 | 17.6± 1.5 | 16.8± 2.7 | 17.2± 1.3 | 17.5± 1.5 | 16.8± 1.4 | 17.2± 1.4 |
| 25ppm | 17.0± 1.6 | 17.4± 1.1 | 17.3± 1.4 | 16.9± 1.8 | 17.1± 1.1 | 16.7± 1.0 | 16.8± 1.4 |
| 100ppm | 17.2± 1.0 | 17.5± 1.1 | 17.5± 1.5 | 17.1± 1.2 | 17.4± 1.7 | 17.0± 1.8 | 16.1± 4.1 |
| 400ppm | 17.0± 1.4 | 17.2± 1.7 | 16.9± 2.0 | 16.6± 1.5 | 16.7± 1.6 | 16.5± 1.7 | 17.2± 2.0 |

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

Test of Dunnett

(HAN260)

BAIS 4

STUDY NO. : 0417
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 | 17.6± | 1.5 | 17.2± | 1.9 |
| 25ppm | 16.8± | 1.1 | 16.3± | 1.2** |
| 100ppm | 17.3± | 2.4 | 17.0± | 2.2 |
| 400ppm | 16.8± | 2.0 | 16.7± | 3.8 |
| Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett | | | | |

(HAN260)

BAIS 4

APPENDIX E 2

FOOD CONSUMPTION CHANGES : SUMMARY,

RAT : FEMALE

(2-YEAR STUDY)

STUDY NO. : 0417
 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(6) | 2-7(7) | 3-7(7) | 4-7(7) | 5-7(7) | 6-7(7) | 7-7(7) |
| Control | 10.8± 0.6 | 11.0± 0.8 | 11.4± 0.9 | 11.5± 0.8 | 11.3± 0.9 | 11.2± 0.9 | 11.1± 1.0 |
| 25ppm | 10.7± 0.6 | 11.4± 0.6* | 11.6± 0.8 | 11.7± 0.8 | 11.6± 0.8 | 11.5± 0.9 | 11.4± 0.9 |
| 100ppm | 10.9± 0.8 | 11.9± 1.0** | 12.3± 1.2** | 12.4± 1.1** | 12.7± 1.0** | 12.1± 0.9** | 11.9± 1.1** |
| 400ppm | 9.8± 0.6** | 11.2± 0.8 | 11.5± 0.7 | 11.9± 0.9 | 12.2± 0.8** | 12.1± 0.8** | 12.2± 0.9** |
| Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett | | | | | | | |

(HAN260)

BAIS 4

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 8

| 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 | 10.8± 0.8 | 11.2± 1.0 | 11.0± 1.0 | 11.0± 0.9 | 11.3± 0.9 | 11.1± 0.8 | 11.3± 0.9 |
| 25ppm | 10.8± 0.9 | 11.2± 0.9 | 11.0± 0.9 | 11.5± 1.0* | 11.3± 1.0 | 11.3± 0.7 | 11.5± 1.0 |
| 100ppm | 11.4± 1.0** | 11.4± 1.0 | 11.4± 0.8* | 12.0± 1.2** | 12.1± 1.2** | 11.9± 1.1** | 12.2± 1.3** |
| 400ppm | 12.2± 0.9** | 12.0± 0.8** | 12.0± 0.8** | 12.4± 0.9** | 12.6± 0.9** | 12.7± 0.9** | 12.8± 1.0** |

(HAN260)

BAIS 4

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 9

| Group Name | Administration 18-7(7) | week-day(effective) 22-7(7) | 26-7(7) | 30-7(7) | 34-7(7) | 38-7(7) | 42-7(7) |
|------------|---------------------------|--------------------------------|-------------|-------------|-------------|-------------|-------------|
| Control | 10.8± 0.9 | 11.3± 1.1 | 11.0± 1.0 | 10.9± 0.9 | 10.9± 1.0 | 11.3± 1.0 | 11.2± 1.0 |
| 25ppm | 11.2± 0.9 | 11.6± 1.1 | 11.0± 0.9 | 10.9± 1.1 | 11.5± 0.9** | 11.3± 1.0 | 11.2± 1.0 |
| 100ppm | 11.4± 1.0** | 11.7± 1.0 | 11.1± 1.3 | 11.4± 0.8 | 12.0± 1.1** | 11.8± 1.1* | 12.2± 1.0** |
| 400ppm | 12.6± 1.0** | 12.6± 1.0** | 12.3± 0.8** | 12.4± 1.0** | 12.6± 0.9** | 12.3± 0.8** | 11.7± 0.9* |

(HAN260)

BAIS 4

STUDY NO. : 0417
 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) | | 54-7(7) | 58-7(7) | 62-7(7) | 66-7(7) | 70-7(7) |
|------------|----------------|--|---------------------|--|-------------|-------------|-----------|-------------|-------------|
| | 46-7(7) | | 50-7(7) | | | | | | |
| Control | 11.7± 1.1 | | 10.9± 0.9 | | 11.6± 1.0 | 11.5± 0.9 | 11.6± 1.1 | 12.0± 1.2 | 12.0± 1.1 |
| 25ppm | 11.5± 1.0 | | 11.4± 1.1* | | 11.9± 1.2 | 11.7± 1.1 | 11.5± 1.0 | 12.0± 1.2 | 12.0± 1.1 |
| 100ppm | 12.0± 1.0 | | 11.7± 0.9** | | 12.6± 1.1** | 12.2± 1.2** | 11.9± 1.1 | 12.7± 1.0** | 12.6± 0.9** |
| 400ppm | 12.4± 1.1** | | 12.5± 1.1** | | 13.0± 1.1** | 12.7± 0.9** | 12.1± 1.1 | 12.9± 1.0** | 12.6± 1.0* |

(HAN260)

BAIS 4

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 11

| 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 | 12.1± 1.0 | 12.3± 1.1 | 12.2± 0.9 | 12.0± 1.4 | 12.8± 1.4 | 12.1± 1.9 | 12.6± 1.3 |
| 25ppm | 12.0± 0.9 | 12.6± 1.2 | 12.2± 1.1 | 12.4± 1.4 | 12.5± 2.1 | 12.7± 1.0 | 13.0± 1.3 |
| 100ppm | 12.5± 1.2 | 13.0± 1.1* | 12.9± 1.2** | 12.8± 1.1** | 13.5± 1.3* | 13.2± 1.3** | 13.2± 1.9* |
| 400ppm | 12.4± 1.1 | 12.7± 1.2 | 12.8± 1.1* | 13.1± 1.9** | 13.1± 1.9 | 12.8± 1.7 | 13.8± 2.0* |
| Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett | | | | | | | |

(HAN260)

BAIS 4

STUDY NO. : 0417
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 | 12.4± 1.5 | 12.2± 1.9 |
| 25ppm | 12.6± 1.4 | 12.7± 1.3 |
| 100ppm | 12.8± 2.4 | 12.9± 2.0 |
| 400ppm | 13.2± 2.7 | 13.3± 3.4 |
| Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett | | |

(HAN260)

BAIS 4

APPENDIX F 1

HEMATOLOGY : SUMMARY,

RAT : MALE

(2-YEAR STUDY)

STUDY NO. : 0417
 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 | 40 | 8.44± | 1.51 | 13.9± | 2.6 | 42.8± | 6.7 | 51.1± | 3.8 | 16.5± | 1.2 | 32.3± | 1.8 | 929± | 241 |
| 25ppm | 35 | 8.52± | 1.50 | 13.8± | 2.5 | 42.9± | 6.4 | 51.0± | 4.4 | 16.3± | 1.1 | 32.0± | 1.9 | 1004± | 326 |
| 100ppm | 38 | 7.96± | 1.59 | 13.1± | 2.5 | 40.5± | 6.6 | 51.6± | 4.6 | 16.5± | 0.9 | 32.0± | 1.5 | 1117± | 241** |
| 400ppm | 29 | 8.50± | 1.73 | 13.4± | 2.8 | 41.9± | 7.4 | 49.9± | 4.6 | 15.8± | 0.9* | 31.8± | 1.9 | 1045± | 204 |

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 4

STUDY NO. : 0417
 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 | 40 | 6.50± | 3.30 | 1± | 2 | 47± | 11 | 2± | 1 | 0± | 0 | 5± | 2 | 42± | 11 | 3± | 12 |
| 25ppm | 35 | 5.91± | 2.10 | 1± | 1 | 49± | 8 | 2± | 1 | 0± | 0 | 5± | 2 | 43± | 9 | 1± | 1 |
| 100ppm | 38 | 6.79± | 2.61 | 1± | 1 | 51± | 9 | 2± | 1 | 0± | 0 | 5± | 1 | 41± | 9 | 1± | 1 |
| 400ppm | 29 | 6.42± | 1.97 | 1± | 1 | 45± | 8 | 1± | 1 | 0± | 0 | 5± | 2 | 46± | 7 | 2± | 3 |

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 4

APPENDIX F 2

HEMATOLOGY : SUMMARY,

RAT : FEMALE

(2-YEAR STUDY)

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : FEMALE

HEMATOLOGY (SUMMARY)
 ALL ANIMALS (105W)

REPORT TYPE : A1

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 | 36 | 7.98± | 1.35 | 14.5± | 2.4 | 42.6± | 6.3 | 53.9± | 3.3 | 18.2± | 0.8 | 33.9± | 1.9 | 658± | 92 |
| 25ppm | 45 | 8.11± | 1.24 | 14.4± | 2.3 | 42.8± | 6.0 | 53.1± | 3.0 | 17.8± | 1.0 | 33.5± | 2.0 | 716± | 208 |
| 100ppm | 37 | 8.05± | 1.45 | 14.5± | 2.2 | 43.1± | 5.7 | 54.9± | 8.7 | 18.3± | 1.9 | 33.6± | 1.7 | 721± | 168 |
| 400ppm | 26 | 7.89± | 1.25 | 13.2± | 1.6 | 40.7± | 4.7 | 52.1± | 4.2** | 16.9± | 1.3** | 32.4± | 1.1** | 1041± | 284** |

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 4

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : FEMALE

HEMATOLOGY (SUMMARY)
 ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 4

| Group Name | NO. of Animals | WBC 10 ³ /μl | | Differential N-BAND | | WBC (%) N-SEG | | EOSINO | | BASO | | MONO | | LYMPHO | | OTHER | |
|------------|-------------------|----------------------------|---------|------------------------|---|------------------|----|--------|---|------|---|------|---|--------|----|-------|----|
| Control | 36 | 12.46± | 57.20 | 1± | 1 | 39± | 11 | 2± | 1 | 0± | 0 | 4± | 2 | 49± | 13 | 6± | 21 |
| 25ppm | 45 | 2.98± | 1.48 | 1± | 1 | 41± | 11 | 2± | 1 | 0± | 0 | 4± | 2 | 50± | 12 | 2± | 10 |
| 100ppm | 37 | 3.21± | 3.38 | 1± | 1 | 39± | 12 | 2± | 1 | 0± | 0 | 4± | 2 | 52± | 14 | 2± | 12 |
| 400ppm | 26 | 11.62± | 20.13** | 1± | 1 | 39± | 14 | 1± | 1 | 0± | 0 | 5± | 2 | 43± | 17 | 11± | 28 |

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 4

APPENDIX G 1

BIOCHEMISTRY : SUMMARY,

RAT : MALE

(2-YEAR STUDY)

STUDY NO. : 0417
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 | 40 | 6.5± | 0.6 | 2.9± | 0.4 | 0.8± | 0.1 | 0.17± | 0.08 | 166± | 29 | 200± | 78 | 144± | 150 |
| 25ppm | 35 | 6.6± | 0.3 | 2.9± | 0.2 | 0.8± | 0.1 | 0.14± | 0.02 | 173± | 17 | 189± | 61 | 108± | 62 |
| 100ppm | 38 | 6.6± | 0.3 | 2.8± | 0.2 | 0.7± | 0.1** | 0.15± | 0.03 | 170± | 27 | 241± | 65* | 190± | 132* |
| 400ppm | 29 | 6.5± | 0.4 | 2.7± | 0.2** | 0.7± | 0.1* | 0.19± | 0.13 | 164± | 14 | 249± | 56** | 205± | 130** |

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 4

STUDY NO. : 0417
 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 | | GOT IU/l | | GPT IU/l | | LDH IU/l | | ALP IU/l | | G-GTP IU/l | | CPK IU/l | |
|------------|-------------------|-----------------------|------|-------------|-----|-------------|-----|-------------|-----|-------------|------|---------------|----|-------------|------|
| Control | 40 | 284± | 108 | 89± | 69 | 39± | 15 | 189± | 53 | 214± | 93 | 6± | 4 | 109± | 86 |
| 25ppm | 35 | 271± | 73 | 71± | 22 | 35± | 10 | 170± | 38 | 194± | 43 | 5± | 3 | 92± | 11 |
| 100ppm | 38 | 333± | 81** | 73± | 37 | 34± | 20* | 177± | 61 | 176± | 82** | 7± | 4 | 93± | 18 |
| 400ppm | 29 | 352± | 66** | 121± | 139 | 58± | 54 | 198± | 144 | 175± | 66** | 11± | 8* | 99± | 55** |

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 4

STUDY NO. : 0417
 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 | 40 | 24.2± | 12.8 | 0.6± | 0.2 | 142± | 2 | 3.8± | 0.4 | 106± | 2 | 10.4± | 0.5 | 4.3± | 0.8 |
| 25ppm | 35 | 21.0± | 4.4 | 0.6± | 0.1 | 142± | 1 | 3.5± | 0.3* | 106± | 1 | 10.4± | 0.4 | 4.2± | 0.5 |
| 100ppm | 38 | 26.8± | 12.2* | 0.7± | 0.3 | 142± | 2 | 3.6± | 0.3 | 107± | 2 | 10.8± | 0.7** | 4.8± | 1.4 |
| 400ppm | 29 | 38.8± | 70.5** | 0.7± | 0.7 | 142± | 4 | 3.8± | 0.7 | 111± | 4** | 10.7± | 0.8 | 5.1± | 2.7 |

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 4

APPENDIX G 2

BIOCHEMISTRY : SUMMARY,

RAT : FEMALE

(2-YEAR STUDY)

STUDY NO. : 0417
 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 | 37 | 6.8± | 0.5 | 3.6± | 0.3 | 1.1± | 0.1 | 0.14± | 0.07 | 155± | 15 | 124± | 25 | 53± | 56 |
| 25ppm | 45 | 7.0± | 0.5 | 3.6± | 0.2 | 1.1± | 0.1 | 0.14± | 0.04 | 159± | 18 | 162± | 67** | 114± | 146** |
| 100ppm | 38 | 7.0± | 0.4 | 3.5± | 0.3 | 1.0± | 0.1* | 0.23± | 0.60 | 163± | 20 | 187± | 55** | 118± | 104** |
| 400ppm | 26 | 6.8± | 0.8 | 3.1± | 0.4** | 0.9± | 0.1** | 0.20± | 0.07** | 136± | 22** | 288± | 85** | 159± | 107** |

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 4

STUDY NO. : 0417
 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 | | GOT IU/l | | GPT IU/l | | LDH IU/l | | ALP IU/l | | G-GTP IU/l | | CPK IU/l | |
|------------|-------------------|-----------------------|-------|-------------|--------|-------------|-------|-------------|-------|-------------|-------|---------------|------|-------------|-----|
| Control | 37 | 227± | 46 | 186± | 194 | 75± | 38 | 361± | 667 | 144± | 61 | 2± | 1 | 125± | 182 |
| 25ppm | 45 | 287± | 110** | 138± | 68 | 87± | 35 | 243± | 104 | 116± | 53** | 2± | 1 | 92± | 30 |
| 100ppm | 38 | 321± | 86** | 143± | 191 | 63± | 35 | 236± | 110 | 109± | 64** | 2± | 2 | 91± | 23 |
| 400ppm | 26 | 437± | 116** | 1015± | 1144** | 421± | 622** | 618± | 759** | 384± | 284** | 26± | 27** | 145± | 168 |

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 4

STUDY NO. : 0417
 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 | 37 | 20.0± | 13.7 | 0.5± | 0.0 | 141± | 1 | 3.4± | 0.4 | 104± | 2 | 10.3± | 0.4 | 4.1± | 0.9 |
| 25ppm | 45 | 18.1± | 2.6 | 0.5± | 0.1 | 141± | 2 | 3.3± | 0.4 | 104± | 3 | 10.4± | 0.3 | 4.0± | 0.6 |
| 100ppm | 38 | 17.7± | 2.8 | 0.5± | 0.1 | 141± | 1 | 3.3± | 0.4 | 106± | 2 | 10.5± | 0.4 | 3.8± | 0.8 |
| 400ppm | 26 | 22.2± | 5.2** | 0.4± | 0.1** | 141± | 2 | 3.4± | 0.6 | 109± | 5** | 10.6± | 0.5** | 4.3± | 0.9 |

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 4

APPENDIX H 1

URINALYSIS : SUMMARY,

RAT : MALE

(2-YEAR STUDY)

STUDY NO. : 0417
 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 | 40 | 0 | 0 | 4 | 7 | 17 | 12 | 0 | | 0 | 0 | 0 | 0 | 12 | 28 | | 40 | 0 | 0 | 0 | 0 | 0 | 0 | | 39 | 1 | 0 | 0 | 0 | 0 | | 40 | 0 | 0 | 0 |
| 25ppm | 35 | 0 | 0 | 2 | 3 | 18 | 12 | 0 | | 0 | 0 | 0 | 1 | 15 | 19 | | 35 | 0 | 0 | 0 | 0 | 0 | 0 | | 34 | 1 | 0 | 0 | 0 | 0 | | 35 | 0 | 0 | 0 |
| 100ppm | 38 | 0 | 0 | 3 | 5 | 16 | 14 | 0 | | 0 | 0 | 0 | 0 | 4 | 34 | * | 38 | 0 | 0 | 0 | 0 | 0 | 0 | | 38 | 0 | 0 | 0 | 0 | 0 | | 38 | 0 | 0 | 0 |
| 400ppm | 31 | 0 | 0 | 8 | 11 | 11 | 1 | 0 | ** | 0 | 0 | 0 | 0 | 5 | 26 | | 31 | 0 | 0 | 0 | 0 | 0 | 0 | | 29 | 1 | 1 | 0 | 0 | 0 | | 31 | 0 | 0 | 0 |

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

Test of CHI SQUARE

(HCL101)

BAIS 4

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE

URINALYSIS

REPORT TYPE : A1

PAGE : 2

| Group Name | NO. of Animals | Occult blood | | | | | Urobilinogen | | | | | | |
|------------|-------------------|--------------|---|---|----|----|--------------|----|---|----|----|----|-----|
| | | - | ± | + | 2+ | 3+ | CHI | ± | + | 2+ | 3+ | 4+ | CHI |
| Control | 40 | 38 | 0 | 1 | 0 | 1 | | 40 | 0 | 0 | 0 | 0 | |
| 25ppm | 35 | 34 | 0 | 0 | 0 | 1 | | 35 | 0 | 0 | 0 | 0 | |
| 100ppm | 38 | 38 | 0 | 0 | 0 | 0 | | 38 | 0 | 0 | 0 | 0 | |
| 400ppm | 31 | 30 | 0 | 0 | 0 | 1 | | 31 | 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 : SUMMARY,

RAT : FEMALE

(2-YEAR STUDY)

STUDY NO. : 0417
 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 | 38 | 0 | 0 | 2 | 7 | 8 | 17 | 4 | | 1 | 2 | 7 | 13 | 9 | 6 | | 38 | 0 | 0 | 0 | 0 | 0 | | 24 | 14 | 0 | 0 | 0 | 0 | | 37 | 0 | 0 | 1 | |
| 25ppm | 45 | 0 | 0 | 4 | 7 | 11 | 19 | 4 | | 0 | 1 | 13 | 10 | 10 | 11 | | 45 | 0 | 0 | 0 | 0 | 0 | | 27 | 16 | 2 | 0 | 0 | 0 | | 45 | 0 | 0 | 0 | |
| 100ppm | 41 | 0 | 2 | 1 | 5 | 10 | 19 | 4 | | 0 | 0 | 1 | 6 | 18 | 16 | ** | 41 | 0 | 0 | 0 | 0 | 0 | | 22 | 17 | 2 | 0 | 0 | 0 | | 41 | 0 | 0 | 0 | |
| 400ppm | 27 | 0 | 0 | 6 | 11 | 5 | 4 | 1 | * | 0 | 0 | 0 | 1 | 8 | 18 | ** | 27 | 0 | 0 | 0 | 0 | 0 | | 14 | 12 | 0 | 1 | 0 | 0 | | 27 | 0 | 0 | 0 | |

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

Test of CHI SQUARE

(HCL101)

BAIS4

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE

URINALYSIS

REPORT TYPE : A1

PAGE : 4

| Group Name | NO. of Animals | Occult blood | | | | | Urobilinogen | | | | | | |
|------------|-------------------|--------------|---|---|----|----|--------------|----|---|----|----|----|-----|
| | | — | ± | + | 2+ | 3+ | CHI | ± | + | 2+ | 3+ | 4+ | CHI |
| Control | 38 | 38 | 0 | 0 | 0 | 0 | | 38 | 0 | 0 | 0 | 0 | |
| 25ppm | 45 | 43 | 0 | 0 | 0 | 2 | | 45 | 0 | 0 | 0 | 0 | |
| 100ppm | 41 | 39 | 0 | 0 | 1 | 1 | | 41 | 0 | 0 | 0 | 0 | |
| 400ppm | 27 | 27 | 0 | 0 | 0 | 0 | | 27 | 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 : SUMMARY,

RAT : MALE

ALL ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 1

| Organ | Findings | Group Name NO. of Animals | Control | | 25ppm | | 100ppm | | 400ppm | |
|-------------|------------|------------------------------|---------|-------|-------|-------|--------|-------|--------|-------|
| | | | 50 | (%) | 50 | (%) | 50 | (%) | 50 | (%) |
| skin/app | hemorrhage | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (2) |
| | nodule | | 3 | (6) | 5 | (10) | 5 | (10) | 5 | (10) |
| subcutis | jaundice | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |
| | mass | | 5 | (10) | 11 | (22) | 8 | (16) | 4 | (8) |
| | abscess | | 0 | (0) | 1 | (2) | 0 | (0) | 0 | (0) |
| nasal cavit | red | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (2) |
| lung | red | | 2 | (4) | 0 | (0) | 0 | (0) | 2 | (4) |
| | white zone | | 1 | (2) | 0 | (0) | 0 | (0) | 1 | (2) |
| | red zone | | 1 | (2) | 1 | (2) | 2 | (4) | 1 | (2) |
| | nodule | | 2 | (4) | 3 | (6) | 1 | (2) | 7 | (14) |
| | voluminus | | 0 | (0) | 0 | (0) | 1 | (2) | 1 | (2) |
| lymph node | enlarged | | 2 | (4) | 2 | (4) | 2 | (4) | 1 | (2) |
| thymus | red zone | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (2) |
| spleen | enlarged | | 5 | (10) | 4 | (8) | 5 | (10) | 4 | (8) |
| | white zone | | 0 | (0) | 1 | (2) | 1 | (2) | 0 | (0) |
| | nodule | | 1 | (2) | 0 | (0) | 0 | (0) | 3 | (6) |
| | deformed | | 0 | (0) | 0 | (0) | 1 | (2) | 0 | (0) |
| heart | enlarged | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (2) |
| | white zone | | 2 | (4) | 1 | (2) | 0 | (0) | 1 | (2) |
| | nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (2) |
| vein | nodule | | 0 | (0) | 0 | (0) | 1 | (2) | 0 | (0) |
| oral cavity | nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (2) |

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 2

| Organ | Findings | Group Name NO. of Animals | Control | | 25ppm | | 100ppm | | 400ppm | |
|-------------|------------------------|------------------------------|---------|-------|-------|-------|--------|-------|--------|-------|
| | | | 50 | (%) | 50 | (%) | 50 | (%) | 50 | (%) |
| tongue | nodule | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |
| forestomach | ulcer | | 0 | (0) | 0 | (0) | 3 | (6) | 1 | (2) |
| | erosion | | 0 | (0) | 0 | (0) | 1 | (2) | 0 | (0) |
| gl stomach | red zone | | 0 | (0) | 0 | (0) | 1 | (2) | 0 | (0) |
| | ulcer | | 0 | (0) | 1 | (2) | 0 | (0) | 1 | (2) |
| | erosion | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (2) |
| small intes | nodule | | 0 | (0) | 0 | (0) | 2 | (4) | 0 | (0) |
| large intes | nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 4 | (8) |
| liver | enlarged | | 1 | (2) | 3 | (6) | 1 | (2) | 1 | (2) |
| | pale | | 0 | (0) | 0 | (0) | 1 | (2) | 0 | (0) |
| | white zone | | 0 | (0) | 0 | (0) | 1 | (2) | 5 | (10) |
| | nodule | | 2 | (4) | 1 | (2) | 5 | (10) | 9 | (18) |
| | herniation | | 8 | (16) | 6 | (12) | 4 | (8) | 3 | (6) |
| kidney | enlarged | | 0 | (0) | 1 | (2) | 0 | (0) | 0 | (0) |
| | white zone | | 0 | (0) | 1 | (2) | 0 | (0) | 0 | (0) |
| | granular | | 8 | (16) | 4 | (8) | 14 | (28) | 20 | (40) |
| urin bladd | dilated | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (2) |
| | urine:marked retention | | 0 | (0) | 0 | (0) | 0 | (0) | 5 | (10) |
| pituitary | enlarged | | 5 | (10) | 4 | (8) | 5 | (10) | 1 | (2) |
| | atrophic | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |
| | red zone | | 3 | (6) | 4 | (8) | 1 | (2) | 1 | (2) |
| | brown zone | | 0 | (0) | 0 | (0) | 1 | (2) | 0 | (0) |

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 3

| Organ | Findings | Group Name NO. of Animals | Control | | 25ppm | | 100ppm | | 400ppm | |
|-------------|-------------|------------------------------|---------|-------|-------|-------|--------|-------|--------|-------|
| | | | 50 | (%) | 50 | (%) | 50 | (%) | 50 | (%) |
| pituitary | black zone | | 1 | (2) | 2 | (4) | 2 | (4) | 1 | (2) |
| | nodule | | 3 | (6) | 0 | (0) | 0 | (0) | 2 | (4) |
| | cyst | | 0 | (0) | 1 | (2) | 1 | (2) | 0 | (0) |
| thyroid | enlarged | | 2 | (4) | 4 | (8) | 5 | (10) | 3 | (6) |
| adrenal | enlarged | | 4 | (8) | 4 | (8) | 2 | (4) | 1 | (2) |
| testis | atrophic | | 3 | (6) | 2 | (4) | 1 | (2) | 2 | (4) |
| | nodule | | 43 | (86) | 40 | (80) | 37 | (74) | 43 | (86) |
| epididymis | nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (2) |
| prep/cli gl | nodule | | 2 | (4) | 1 | (2) | 1 | (2) | 1 | (2) |
| brain | red zone | | 0 | (0) | 1 | (2) | 2 | (4) | 0 | (0) |
| | yellow zone | | 0 | (0) | 0 | (0) | 1 | (2) | 0 | (0) |
| | nodule | | 0 | (0) | 1 | (2) | 0 | (0) | 0 | (0) |
| | deformed | | 0 | (0) | 0 | (0) | 1 | (2) | 0 | (0) |
| | adhesion | | 0 | (0) | 1 | (2) | 0 | (0) | 0 | (0) |
| spinal cord | red zone | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |
| eye | turbid | | 0 | (0) | 1 | (2) | 0 | (0) | 0 | (0) |
| | white | | 3 | (6) | 3 | (6) | 5 | (10) | 1 | (2) |
| | red | | 0 | (0) | 0 | (0) | 1 | (2) | 2 | (4) |
| Zymbal gl | nodule | | 0 | (0) | 1 | (2) | 0 | (0) | 1 | (2) |
| bone | nodule | | 0 | (0) | 0 | (0) | 1 | (2) | 0 | (0) |
| mediastinum | nodule | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |
| peritoneum | nodule | | 0 | (0) | 1 | (2) | 6 | (12) | 2 | (4) |

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 4

| Organ | Findings | Group Name NO. of Animals | Control | | 25ppm | | 100ppm | | 400ppm | |
|-------------|------------------|------------------------------|---------|------|-------|------|--------|------|--------|------|
| | | | 50 | (%) | 50 | (%) | 50 | (%) | 50 | (%) |
| peritoneum | mass | | 0 | (0) | 0 | (0) | 1 | (2) | 0 | (0) |
| retroperit | mass | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (2) |
| abdominal c | hemorrhage | | 0 | (0) | 1 | (2) | 1 | (2) | 0 | (0) |
| | ascites | | 1 | (2) | 2 | (4) | 2 | (4) | 1 | (2) |
| thoracic ca | hemorrhage | | 1 | (2) | 0 | (0) | 1 | (2) | 0 | (0) |
| | mass | | 0 | (0) | 0 | (0) | 1 | (2) | 0 | (0) |
| | pleural fluid | | 1 | (2) | 0 | (0) | 2 | (4) | 2 | (4) |
| other | eye lid:nodule | | 0 | (0) | 0 | (0) | 1 | (2) | 0 | (0) |
| | ear:nodule | | 0 | (0) | 1 | (2) | 0 | (0) | 0 | (0) |
| | upper jaw:nodule | | 0 | (0) | 0 | (0) | 1 | (2) | 1 | (2) |
| | nose:nodule | | 2 | (4) | 0 | (0) | 0 | (0) | 0 | (0) |
| whole body | anemic | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (2) |

(HPT080)

BAIS 4

APPENDIX I 2

GROSS FINDINGS : SUMMARY,

RAT : MALE

DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0417
ANIMAL : RAT 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 | | 25ppm | | 100ppm | | 400ppm | |
|-------------|------------|------------------------------|---------|-------|-------|-------|--------|-------|--------|-------|
| | | | 10 | (%) | 15 | (%) | 12 | (%) | 20 | (%) |
| skin/app | hemorrhage | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (5) |
| | nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 2 | (10) |
| subcutis | jaundice | | 1 | (10) | 0 | (0) | 0 | (0) | 0 | (0) |
| | mass | | 0 | (0) | 6 | (40) | 1 | (8) | 1 | (5) |
| | abscess | | 0 | (0) | 1 | (7) | 0 | (0) | 0 | (0) |
| nasal cavit | red | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (5) |
| lung | red | | 2 | (20) | 0 | (0) | 0 | (0) | 2 | (10) |
| | red zone | | 1 | (10) | 1 | (7) | 2 | (17) | 1 | (5) |
| | nodule | | 0 | (0) | 1 | (7) | 0 | (0) | 3 | (15) |
| | voluminus | | 0 | (0) | 0 | (0) | 1 | (8) | 1 | (5) |
| lymph node | enlarged | | 1 | (10) | 2 | (13) | 1 | (8) | 1 | (5) |
| thymus | red zone | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (5) |
| spleen | enlarged | | 2 | (20) | 4 | (27) | 4 | (33) | 2 | (10) |
| | white zone | | 0 | (0) | 1 | (7) | 0 | (0) | 0 | (0) |
| | nodule | | 1 | (10) | 0 | (0) | 0 | (0) | 1 | (5) |
| heart | enlarged | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (5) |
| | white zone | | 0 | (0) | 1 | (7) | 0 | (0) | 1 | (5) |
| | nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (5) |
| oral cavity | nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (5) |
| forestomach | ulcer | | 0 | (0) | 0 | (0) | 2 | (17) | 1 | (5) |
| | erosion | | 0 | (0) | 0 | (0) | 1 | (8) | 0 | (0) |
| gl stomach | red zone | | 0 | (0) | 0 | (0) | 1 | (8) | 0 | (0) |

STUDY NO. : 0417
ANIMAL : RAT 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 | | 25ppm | | 100ppm | | 400ppm | |
|-------------|------------------------|------------------------------|---------|-------|-------|-------|--------|-------|--------|-------|
| | | | 10 | (%) | 15 | (%) | 12 | (%) | 20 | (%) |
| gl stomach | ulcer | | 0 | (0) | 1 | (7) | 0 | (0) | 1 | (5) |
| small intes | nodule | | 0 | (0) | 0 | (0) | 2 | (17) | 0 | (0) |
| large intes | nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (5) |
| liver | enlarged | | 0 | (0) | 3 | (20) | 1 | (8) | 0 | (0) |
| | pale | | 0 | (0) | 0 | (0) | 1 | (8) | 0 | (0) |
| | white zone | | 0 | (0) | 0 | (0) | 1 | (8) | 1 | (5) |
| | nodule | | 1 | (10) | 0 | (0) | 2 | (17) | 4 | (20) |
| | herniation | | 3 | (30) | 2 | (13) | 0 | (0) | 3 | (15) |
| kidney | enlarged | | 0 | (0) | 1 | (7) | 0 | (0) | 0 | (0) |
| | white zone | | 0 | (0) | 1 | (7) | 0 | (0) | 0 | (0) |
| | granular | | 1 | (10) | 2 | (13) | 4 | (33) | 6 | (30) |
| urin bladd | dilated | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (5) |
| | urine:marked retention | | 0 | (0) | 0 | (0) | 0 | (0) | 3 | (15) |
| pituitary | enlarged | | 3 | (30) | 4 | (27) | 3 | (25) | 1 | (5) |
| | red zone | | 1 | (10) | 1 | (7) | 0 | (0) | 0 | (0) |
| | black zone | | 0 | (0) | 0 | (0) | 1 | (8) | 0 | (0) |
| | nodule | | 1 | (10) | 0 | (0) | 0 | (0) | 2 | (10) |
| thyroid | enlarged | | 0 | (0) | 1 | (7) | 1 | (8) | 1 | (5) |
| adrenal | enlarged | | 2 | (20) | 2 | (13) | 0 | (0) | 1 | (5) |
| testis | atrophic | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (5) |
| | nodule | | 4 | (40) | 7 | (47) | 5 | (42) | 14 | (70) |
| epididymis | nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (5) |

STUDY NO. : 0417
 ANIMAL : RAT 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 | | 25ppm | | 100ppm | | 400ppm | |
|-------------|------------------|------------------------------|---------|-------|-------|------|--------|-------|--------|-------|
| | | | 10 | (%) | 15 | (%) | 12 | (%) | 20 | (%) |
| brain | red zone | | 0 | (0) | 1 | (7) | 1 | (8) | 0 | (0) |
| | yellow zone | | 0 | (0) | 0 | (0) | 1 | (8) | 0 | (0) |
| | nodule | | 0 | (0) | 1 | (7) | 0 | (0) | 0 | (0) |
| | adhesion | | 0 | (0) | 1 | (7) | 0 | (0) | 0 | (0) |
| spinal cord | red zone | | 1 | (10) | 0 | (0) | 0 | (0) | 0 | (0) |
| eye | turbid | | 0 | (0) | 1 | (7) | 0 | (0) | 0 | (0) |
| | white | | 1 | (10) | 0 | (0) | 0 | (0) | 0 | (0) |
| | red | | 0 | (0) | 0 | (0) | 1 | (8) | 1 | (5) |
| Zymbal gl | nodule | | 0 | (0) | 1 | (7) | 0 | (0) | 0 | (0) |
| mediastinum | nodule | | 1 | (10) | 0 | (0) | 0 | (0) | 0 | (0) |
| peritoneum | nodule | | 0 | (0) | 0 | (0) | 2 | (17) | 1 | (5) |
| retroperit | mass | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (5) |
| abdominal c | hemorrhage | | 0 | (0) | 1 | (7) | 1 | (8) | 0 | (0) |
| | ascites | | 1 | (10) | 1 | (7) | 0 | (0) | 0 | (0) |
| thoracic ca | hemorrhage | | 1 | (10) | 0 | (0) | 1 | (8) | 0 | (0) |
| | mass | | 0 | (0) | 0 | (0) | 1 | (8) | 0 | (0) |
| | pleural fluid | | 0 | (0) | 0 | (0) | 2 | (17) | 2 | (10) |
| other | upper jaw:nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (5) |
| whole body | anemic | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (5) |

APPENDIX I 3

GROSS FINDINGS : SUMMARY,

RAT : MALE

SACRIFICED ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

GROSS FINDINGS (SUMMARY)
 SACRIFICED ANIMALS (105W)

PAGE : 1

| Organ | Findings | Group Name NO. of Animals | Control | | 25ppm | | 100ppm | | 400ppm | |
|-------------|------------------------|------------------------------|---------|-------|-------|-------|--------|-------|--------|-------|
| | | | 40 | (%) | 35 | (%) | 38 | (%) | 30 | (%) |
| skin/app | nodule | | 3 | (8) | 5 | (14) | 5 | (13) | 3 | (10) |
| subcutis | mass | | 5 | (13) | 5 | (14) | 7 | (18) | 3 | (10) |
| lung | white zone | | 1 | (3) | 0 | (0) | 0 | (0) | 1 | (3) |
| | nodule | | 2 | (5) | 2 | (6) | 1 | (3) | 4 | (13) |
| lymph node | enlarged | | 1 | (3) | 0 | (0) | 1 | (3) | 0 | (0) |
| spleen | enlarged | | 3 | (8) | 0 | (0) | 1 | (3) | 2 | (7) |
| | white zone | | 0 | (0) | 0 | (0) | 1 | (3) | 0 | (0) |
| | nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 2 | (7) |
| | deformed | | 0 | (0) | 0 | (0) | 1 | (3) | 0 | (0) |
| heart | white zone | | 2 | (5) | 0 | (0) | 0 | (0) | 0 | (0) |
| vein | nodule | | 0 | (0) | 0 | (0) | 1 | (3) | 0 | (0) |
| tongue | nodule | | 1 | (3) | 0 | (0) | 0 | (0) | 0 | (0) |
| forestomach | ulcer | | 0 | (0) | 0 | (0) | 1 | (3) | 0 | (0) |
| gl stomach | erosion | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (3) |
| large intes | nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 3 | (10) |
| liver | enlarged | | 1 | (3) | 0 | (0) | 0 | (0) | 1 | (3) |
| | white zone | | 0 | (0) | 0 | (0) | 0 | (0) | 4 | (13) |
| | nodule | | 1 | (3) | 1 | (3) | 3 | (8) | 5 | (17) |
| | herniation | | 5 | (13) | 4 | (11) | 4 | (11) | 0 | (0) |
| kidney | granular | | 7 | (18) | 2 | (6) | 10 | (26) | 14 | (47) |
| urin bladd | urine:marked retention | | 0 | (0) | 0 | (0) | 0 | (0) | 2 | (7) |
| pituitary | enlarged | | 2 | (5) | 0 | (0) | 2 | (5) | 0 | (0) |

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

GROSS FINDINGS (SUMMARY)
 SACRIFICED ANIMALS (105W)

PAGE : 2

| Organ | Findings | Group Name NO. of Animals | Control | | 25ppm | | 100ppm | | 400ppm | |
|-------------|----------------|------------------------------|---------|-------|-------|-------|--------|-------|--------|-------|
| | | | 40 | (%) | 35 | (%) | 38 | (%) | 30 | (%) |
| pituitary | atrophic | | 1 | (3) | 0 | (0) | 0 | (0) | 0 | (0) |
| | red zone | | 2 | (5) | 3 | (9) | 1 | (3) | 1 | (3) |
| | brown zone | | 0 | (0) | 0 | (0) | 1 | (3) | 0 | (0) |
| | black zone | | 1 | (3) | 2 | (6) | 1 | (3) | 1 | (3) |
| | nodule | | 2 | (5) | 0 | (0) | 0 | (0) | 0 | (0) |
| | cyst | | 0 | (0) | 1 | (3) | 1 | (3) | 0 | (0) |
| thyroid | enlarged | | 2 | (5) | 3 | (9) | 4 | (11) | 2 | (7) |
| adrenal | enlarged | | 2 | (5) | 2 | (6) | 2 | (5) | 0 | (0) |
| testis | atrophic | | 3 | (8) | 2 | (6) | 1 | (3) | 1 | (3) |
| | nodule | | 39 | (98) | 33 | (94) | 32 | (84) | 29 | (97) |
| prep/cli gl | nodule | | 2 | (5) | 1 | (3) | 1 | (3) | 1 | (3) |
| brain | red zone | | 0 | (0) | 0 | (0) | 1 | (3) | 0 | (0) |
| | deformed | | 0 | (0) | 0 | (0) | 1 | (3) | 0 | (0) |
| eye | white | | 2 | (5) | 3 | (9) | 5 | (13) | 1 | (3) |
| | red | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (3) |
| Zymbal gl | nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (3) |
| bone | nodule | | 0 | (0) | 0 | (0) | 1 | (3) | 0 | (0) |
| peritoneum | nodule | | 0 | (0) | 1 | (3) | 4 | (11) | 1 | (3) |
| | mass | | 0 | (0) | 0 | (0) | 1 | (3) | 0 | (0) |
| abdominal c | ascites | | 0 | (0) | 1 | (3) | 2 | (5) | 1 | (3) |
| thoracic ca | pleural fluid | | 1 | (3) | 0 | (0) | 0 | (0) | 0 | (0) |
| other | eye lid:nodule | | 0 | (0) | 0 | (0) | 1 | (3) | 0 | (0) |

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (105W)

PAGE : 3

| Organ | Findings | Group Name | | Control | | 25ppm | | 100ppm | | 400ppm | |
|-------|------------------|----------------|--|---------|------|-------|------|--------|------|--------|------|
| | | NO. of Animals | | 40 | (%) | 35 | (%) | 38 | (%) | 30 | (%) |
| other | ear:nodule | | | 0 | (0) | 1 | (3) | 0 | (0) | 0 | (0) |
| | upper jaw:nodule | | | 0 | (0) | 0 | (0) | 1 | (3) | 0 | (0) |
| | nose:nodule | | | 2 | (5) | 0 | (0) | 0 | (0) | 0 | (0) |

(HPT080)

BAIS 4

APPENDIX I 4

GROSS FINDINGS : SUMMARY,

RAT : FEMALE

ALL ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 5

| Organ | Findings | Group Name NO. of Animals | Control | 25ppm | 100ppm | 400ppm |
|-------------|-------------|------------------------------|---------|----------|----------|----------|
| | | | 50 (%) | 50 (%) | 50 (%) | 50 (%) |
| skin/app | nodule | | 1 (2) | 1 (2) | 2 (4) | 3 (6) |
| | scab | | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| subcutis | jaundice | | 2 (4) | 0 (0) | 1 (2) | 4 (8) |
| | mass | | 6 (12) | 10 (20) | 11 (22) | 8 (16) |
| lung | red | | 0 (0) | 0 (0) | 0 (0) | 1 (2) |
| | white zone | | 0 (0) | 0 (0) | 1 (2) | 2 (4) |
| | red zone | | 1 (2) | 0 (0) | 0 (0) | 2 (4) |
| | nodule | | 1 (2) | 0 (0) | 1 (2) | 4 (8) |
| | voluminus | | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| lymph node | enlarged | | 1 (2) | 0 (0) | 1 (2) | 0 (0) |
| spleen | enlarged | | 7 (14) | 2 (4) | 6 (12) | 13 (26) |
| | white zone | | 0 (0) | 0 (0) | 1 (2) | 0 (0) |
| | nodule | | 1 (2) | 0 (0) | 0 (0) | 1 (2) |
| | adhesion | | 0 (0) | 0 (0) | 1 (2) | 0 (0) |
| heart | white zone | | 0 (0) | 1 (2) | 2 (4) | 0 (0) |
| | hypertrophy | | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| tongue | nodule | | 0 (0) | 0 (0) | 2 (4) | 4 (8) |
| forestomach | nodule | | 0 (0) | 0 (0) | 0 (0) | 1 (2) |
| | ulcer | | 0 (0) | 0 (0) | 1 (2) | 0 (0) |
| gl stomach | nodule | | 0 (0) | 1 (2) | 0 (0) | 0 (0) |
| | ulcer | | 1 (2) | 0 (0) | 0 (0) | 1 (2) |
| duodenum | thick | | 0 (0) | 0 (0) | 0 (0) | 1 (2) |

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 6

| Organ | Findings | Group Name NO. of Animals | Control | | 25ppm | | 100ppm | | 400ppm | |
|-------------|-------------|------------------------------|---------|-------|-------|-------|--------|-------|--------|-------|
| | | | 50 | (%) | 50 | (%) | 50 | (%) | 50 | (%) |
| large intes | nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 2 | (4) |
| liver | enlarged | | 1 | (2) | 0 | (0) | 1 | (2) | 3 | (6) |
| | white patch | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (2) |
| | white zone | | 1 | (2) | 0 | (0) | 0 | (0) | 5 | (10) |
| | nodule | | 1 | (2) | 0 | (0) | 2 | (4) | 41 | (82) |
| | cyst | | 1 | (2) | 0 | (0) | 0 | (0) | 1 | (2) |
| | deformed | | 0 | (0) | 0 | (0) | 1 | (2) | 0 | (0) |
| | rough | | 2 | (4) | 0 | (0) | 4 | (8) | 5 | (10) |
| | nodular | | 0 | (0) | 0 | (0) | 0 | (0) | 2 | (4) |
| | herniation | | 9 | (18) | 9 | (18) | 8 | (16) | 6 | (12) |
| | white zone | | 0 | (0) | 0 | (0) | 1 | (2) | 0 | (0) |
| kidney | granular | | 1 | (2) | 5 | (10) | 3 | (6) | 5 | (10) |
| | enlarged | | 10 | (20) | 8 | (16) | 8 | (16) | 5 | (10) |
| pituitary | red zone | | 6 | (12) | 9 | (18) | 7 | (14) | 4 | (8) |
| | black zone | | 7 | (14) | 4 | (8) | 1 | (2) | 3 | (6) |
| | nodule | | 2 | (4) | 4 | (8) | 3 | (6) | 1 | (2) |
| | enlarged | | 2 | (4) | 1 | (2) | 2 | (4) | 4 | (8) |
| thyroid | nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (2) |
| | enlarged | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (2) |
| adrenal | enlarged | | 0 | (0) | 1 | (2) | 0 | (0) | 1 | (2) |
| | cyst | | 0 | (0) | 0 | (0) | 1 | (2) | 1 | (2) |
| ovary | enlarged | | 0 | (0) | 0 | (0) | 0 | (0) | 0 | (0) |
| | enlarged | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |
| uterus | enlarged | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 7

| Organ | Findings | Group Name NO. of Animals | Control | | 25ppm | | 100ppm | | 400ppm | |
|-------------|------------------|------------------------------|---------|-------|-------|-------|--------|-------|--------|-------|
| | | | 50 | (%) | 50 | (%) | 50 | (%) | 50 | (%) |
| uterus | nodule | | 6 | (12) | 5 | (10) | 5 | (10) | 3 | (6) |
| | cyst | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (2) |
| | invagination | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |
| | fluid:red | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |
| vagina | fluid:red | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |
| prep/cli gl | nodule | | 2 | (4) | 3 | (6) | 5 | (10) | 4 | (8) |
| brain | red zone | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |
| | nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (2) |
| spinal cord | brown zone | | 0 | (0) | 0 | (0) | 1 | (2) | 0 | (0) |
| eye | turbid | | 1 | (2) | 0 | (0) | 1 | (2) | 1 | (2) |
| | white | | 2 | (4) | 5 | (10) | 2 | (4) | 1 | (2) |
| peritoneum | white zone | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |
| abdominal c | hemorrhage | | 0 | (0) | 0 | (0) | 0 | (0) | 7 | (14) |
| | nodule | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |
| | ascites | | 1 | (2) | 0 | (0) | 0 | (0) | 2 | (4) |
| thoracic ca | hemorrhage | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (2) |
| | pleural fluid | | 1 | (2) | 1 | (2) | 0 | (0) | 1 | (2) |
| other | lower jaw:nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (2) |
| | nose:nodule | | 1 | (2) | 0 | (0) | 0 | (0) | 0 | (0) |
| whole body | anemic | | 2 | (4) | 0 | (0) | 0 | (0) | 2 | (4) |

APPENDIX I 5

GROSS FINDINGS : SUMMARY,

RAT : FEMALE

DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0417
 ANIMAL : RAT 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 | 25ppm | 100ppm | 400ppm |
|-------------|-------------|------------------------------|---------|---------|---------|----------|
| | | | 12 (%) | 5 (%) | 11 (%) | 24 (%) |
| skin/app | nodule | | 0 (0) | 0 (0) | 1 (9) | 1 (4) |
| subcutis | jaundice | | 1 (8) | 0 (0) | 1 (9) | 4 (17) |
| | mass | | 1 (8) | 0 (0) | 3 (27) | 4 (17) |
| lung | red | | 0 (0) | 0 (0) | 0 (0) | 1 (4) |
| | red zone | | 1 (8) | 0 (0) | 0 (0) | 2 (8) |
| | nodule | | 0 (0) | 0 (0) | 0 (0) | 3 (13) |
| | voluminus | | 1 (8) | 0 (0) | 0 (0) | 0 (0) |
| lymph node | enlarged | | 1 (8) | 0 (0) | 1 (9) | 0 (0) |
| spleen | enlarged | | 3 (25) | 1 (20) | 4 (36) | 10 (42) |
| | nodule | | 1 (8) | 0 (0) | 0 (0) | 1 (4) |
| heart | white zone | | 0 (0) | 0 (0) | 1 (9) | 0 (0) |
| | hypertrophy | | 1 (8) | 0 (0) | 0 (0) | 0 (0) |
| forestomach | nodule | | 0 (0) | 0 (0) | 0 (0) | 1 (4) |
| | ulcer | | 0 (0) | 0 (0) | 1 (9) | 0 (0) |
| gl stomach | ulcer | | 1 (8) | 0 (0) | 0 (0) | 0 (0) |
| duodenum | thick | | 0 (0) | 0 (0) | 0 (0) | 1 (4) |
| large intes | nodule | | 0 (0) | 0 (0) | 0 (0) | 2 (8) |
| liver | enlarged | | 1 (8) | 0 (0) | 1 (9) | 1 (4) |
| | white patch | | 0 (0) | 0 (0) | 0 (0) | 1 (4) |
| | white zone | | 1 (8) | 0 (0) | 0 (0) | 3 (13) |
| | nodule | | 0 (0) | 0 (0) | 0 (0) | 17 (71) |
| | cyst | | 0 (0) | 0 (0) | 0 (0) | 1 (4) |

STUDY NO. : 0417
ANIMAL : RAT 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 | | 25ppm | | 100ppm | | 400ppm | |
|-------------|------------|------------------------------|---------|-------|-------|-------|--------|-------|--------|-------|
| | | | 12 | (%) | 5 | (%) | 11 | (%) | 24 | (%) |
| liver | deformed | | 0 | (0) | 0 | (0) | 1 | (9) | 0 | (0) |
| | rough | | 1 | (8) | 0 | (0) | 3 | (27) | 5 | (21) |
| | nodular | | 0 | (0) | 0 | (0) | 0 | (0) | 2 | (8) |
| | herniation | | 2 | (17) | 1 | (20) | 1 | (9) | 3 | (13) |
| kidney | white zone | | 0 | (0) | 0 | (0) | 1 | (9) | 0 | (0) |
| | granular | | 1 | (8) | 0 | (0) | 2 | (18) | 1 | (4) |
| pituitary | enlarged | | 5 | (42) | 0 | (0) | 5 | (45) | 2 | (8) |
| | red zone | | 0 | (0) | 0 | (0) | 2 | (18) | 1 | (4) |
| | black zone | | 1 | (8) | 0 | (0) | 0 | (0) | 2 | (8) |
| | nodule | | 0 | (0) | 1 | (20) | 0 | (0) | 0 | (0) |
| thyroid | enlarged | | 0 | (0) | 0 | (0) | 1 | (9) | 2 | (8) |
| | nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (4) |
| ovary | enlarged | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (4) |
| uterus | nodule | | 1 | (8) | 1 | (20) | 0 | (0) | 2 | (8) |
| | cyst | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (4) |
| | fluid:red | | 1 | (8) | 0 | (0) | 0 | (0) | 0 | (0) |
| vagina | fluid:red | | 1 | (8) | 0 | (0) | 0 | (0) | 0 | (0) |
| prep/cli gl | nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (4) |
| brain | red zone | | 1 | (8) | 0 | (0) | 0 | (0) | 0 | (0) |
| | nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (4) |
| spinal cord | brown zone | | 0 | (0) | 0 | (0) | 1 | (9) | 0 | (0) |
| eye | turbid | | 1 | (8) | 0 | (0) | 1 | (9) | 1 | (4) |

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 6

| Organ | Findings | Group Name NO. of Animals | Control | | 25ppm | | 100ppm | | 400ppm | |
|-------------|---------------|------------------------------|---------|-------|-------|-------|--------|------|--------|-------|
| | | | 12 | (%) | 5 | (%) | 11 | (%) | 24 | (%) |
| eye | white | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (4) |
| peritoneum | white zone | | 1 | (8) | 0 | (0) | 0 | (0) | 0 | (0) |
| abdominal c | hemorrhage | | 0 | (0) | 0 | (0) | 0 | (0) | 5 | (21) |
| | ascites | | 1 | (8) | 0 | (0) | 0 | (0) | 2 | (8) |
| thoracic ca | hemorrhage | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (4) |
| | pleural fluid | | 1 | (8) | 1 | (20) | 0 | (0) | 1 | (4) |
| whole body | anemic | | 2 | (17) | 0 | (0) | 0 | (0) | 2 | (8) |

(HPT080)

BAIS 4

APPENDIX I 6

GROSS FINDINGS : SUMMARY,

RAT : FEMALE

SACRIFICED ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (105W)

PAGE : 4

| Organ | Findings | Group Name NO. of Animals | Control | | 25ppm | | 100ppm | | 400ppm | |
|------------|------------|------------------------------|---------|-------|-------|-------|--------|-------|--------|-------|
| | | | 38 | (%) | 45 | (%) | 39 | (%) | 26 | (%) |
| skin/app | nodule | | 1 | (3) | 1 | (2) | 1 | (3) | 2 | (8) |
| | scab | | 1 | (3) | 0 | (0) | 0 | (0) | 0 | (0) |
| subcutis | jaundice | | 1 | (3) | 0 | (0) | 0 | (0) | 0 | (0) |
| | mass | | 5 | (13) | 10 | (22) | 8 | (21) | 4 | (15) |
| lung | white zone | | 0 | (0) | 0 | (0) | 1 | (3) | 2 | (8) |
| | nodule | | 1 | (3) | 0 | (0) | 1 | (3) | 1 | (4) |
| spleen | enlarged | | 4 | (11) | 1 | (2) | 2 | (5) | 3 | (12) |
| | white zone | | 0 | (0) | 0 | (0) | 1 | (3) | 0 | (0) |
| | adhesion | | 0 | (0) | 0 | (0) | 1 | (3) | 0 | (0) |
| heart | white zone | | 0 | (0) | 1 | (2) | 1 | (3) | 0 | (0) |
| tongue | nodule | | 0 | (0) | 0 | (0) | 2 | (5) | 4 | (15) |
| gl stomach | nodule | | 0 | (0) | 1 | (2) | 0 | (0) | 0 | (0) |
| | ulcer | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (4) |
| liver | enlarged | | 0 | (0) | 0 | (0) | 0 | (0) | 2 | (8) |
| | white zone | | 0 | (0) | 0 | (0) | 0 | (0) | 2 | (8) |
| | nodule | | 1 | (3) | 0 | (0) | 2 | (5) | 24 | (92) |
| | cyst | | 1 | (3) | 0 | (0) | 0 | (0) | 0 | (0) |
| | rough | | 1 | (3) | 0 | (0) | 1 | (3) | 0 | (0) |
| | herniation | | 7 | (18) | 8 | (18) | 7 | (18) | 3 | (12) |
| | granular | | 0 | (0) | 5 | (11) | 1 | (3) | 4 | (15) |
| pituitary | enlarged | | 5 | (13) | 8 | (18) | 3 | (8) | 3 | (12) |
| | red zone | | 6 | (16) | 9 | (20) | 5 | (13) | 3 | (12) |

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (105W)

PAGE : 5

| Organ | Findings | Group Name NO. of Animals | Control | | 25ppm | | 100ppm | | 400ppm | |
|-------------|------------------|------------------------------|---------|-------|-------|-------|--------|-------|--------|-------|
| | | | 38 | (%) | 45 | (%) | 39 | (%) | 26 | (%) |
| pituitary | black zone | | 6 | (16) | 4 | (9) | 1 | (3) | 1 | (4) |
| | nodule | | 2 | (5) | 3 | (7) | 3 | (8) | 1 | (4) |
| thyroid | enlarged | | 2 | (5) | 1 | (2) | 1 | (3) | 2 | (8) |
| adrenal | enlarged | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (4) |
| ovary | enlarged | | 0 | (0) | 1 | (2) | 0 | (0) | 0 | (0) |
| | cyst | | 0 | (0) | 0 | (0) | 1 | (3) | 1 | (4) |
| uterus | enlarged | | 1 | (3) | 0 | (0) | 0 | (0) | 0 | (0) |
| | nodule | | 5 | (13) | 4 | (9) | 5 | (13) | 1 | (4) |
| | invagination | | 1 | (3) | 0 | (0) | 0 | (0) | 0 | (0) |
| prep/cli gl | nodule | | 2 | (5) | 3 | (7) | 5 | (13) | 3 | (12) |
| eye | white | | 2 | (5) | 5 | (11) | 2 | (5) | 0 | (0) |
| abdominal c | hemorrhage | | 0 | (0) | 0 | (0) | 0 | (0) | 2 | (8) |
| | nodule | | 1 | (3) | 0 | (0) | 0 | (0) | 0 | (0) |
| other | lower jaw:nodule | | 0 | (0) | 0 | (0) | 0 | (0) | 1 | (4) |
| | nose:nodule | | 1 | (3) | 0 | (0) | 0 | (0) | 0 | (0) |

(HPT080)

BAIS 4

APPENDIX J 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY,

RAT : MALE

(2-YEAR STUDY)

STUDY NO. : 0417
 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 | 40 | 381± | 30 | 0.103± | 0.154 | 3.787± | 1.532 | 1.251± | 0.114 | 1.421± | 0.102 | 2.772± | 0.284 |
| 25ppm | 35 | 378± | 31 | 0.106± | 0.188 | 3.685± | 1.441 | 1.227± | 0.099 | 1.405± | 0.128 | 2.732± | 0.235 |
| 100ppm | 38 | 384± | 45 | 0.163± | 0.528 | 3.437± | 1.460 | 1.282± | 0.103 | 1.462± | 0.272 | 2.991± | 0.321** |
| 400ppm | 30 | 279± | 32** | 0.065± | 0.010** | 4.229± | 1.223 | 1.148± | 0.100** | 1.375± | 0.146* | 2.834± | 0.261 |
| Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett | | | | | | | | | | | | | |
| (HCL040) | | | | | | | | | | | | BAIS 4 | |

STUDY NO. : 0417
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 | 40 | 1.271± | 2.224 | 11.401± | 2.455 | 2.056± | 0.058 |
| 25ppm | 35 | 0.930± | 0.230 | 11.149± | 1.059 | 2.060± | 0.045 |
| 100ppm | 38 | 0.989± | 0.250 | 13.099± | 1.687** | 2.050± | 0.052 |
| 400ppm | 30 | 0.968± | 0.625 | 13.581± | 2.917** | 1.958± | 0.054** |
| Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett | | | | | | | |

(HCL040)

BAIS 4

APPENDIX J 2

ORGAN WEIGHT, ABSOLUTE : SUMMARY,

RAT : FEMALE

(2-YEAR STUDY)

STUDY NO. : 0417
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 | 38 | 253± 26 | 0.076± 0.015 | 0.131± 0.027 | 0.890± 0.084 | 1.034± 0.205 | 1.738± 0.174 |
| 25ppm | 45 | 260± 29 | 0.076± 0.021 | 0.199± 0.494 | 0.888± 0.099 | 0.991± 0.072 | 1.776± 0.229 |
| 100ppm | 39 | 275± 24** | 0.073± 0.008 | 0.131± 0.026 | 0.936± 0.119 | 1.059± 0.326 | 1.862± 0.204* |
| 400ppm | 26 | 199± 28** | 0.094± 0.090 | 0.104± 0.035** | 0.880± 0.081 | 1.156± 0.387* | 2.071± 0.167** |

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

Test of Dunnett

(HCL040)

BAIS 4

STUDY NO. : 0417
 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 | 38 | 0.798± | 1.043 | 6.543± | 1.056 | 1.866± | 0.053 |
| 25ppm | 45 | 0.646± | 0.608 | 7.019± | 0.902 | 1.855± | 0.054 |
| 100ppm | 39 | 0.869± | 1.957 | 7.937± | 1.032** | 1.848± | 0.048 |
| 400ppm | 26 | 0.943± | 1.020 | 15.357± | 4.930** | 1.798± | 0.049** |
| Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett | | | | | | | |
| (HCL040) | | | | | | | |

BALS 4

APPENDIX K 1

ORGAN WEIGHT, RELATIVE : SUMMARY,

RAT : MALE

(2-YEAR STUDY)

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE
 UNIT: %

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

PAGE : 1

| Group Name | NO. of Animals | Body Weight (g) | ADRENALS | TESTES | HEART | LUNGS | KIDNEYS |
|---|-------------------|--------------------|----------------|----------------|----------------|----------------|----------------|
| Control | 40 | 381± 30 | 0.030± 0.056 | 0.992± 0.395 | 0.331± 0.040 | 0.375± 0.037 | 0.731± 0.086 |
| 25ppm | 35 | 378± 31 | 0.029± 0.051 | 0.979± 0.401 | 0.327± 0.049 | 0.373± 0.035 | 0.729± 0.107 |
| 100ppm | 38 | 384± 45 | 0.041± 0.129 | 0.895± 0.367 | 0.337± 0.033 | 0.387± 0.101 | 0.789± 0.130* |
| 400ppm | 30 | 279± 32** | 0.024± 0.006** | 1.527± 0.416** | 0.416± 0.050** | 0.498± 0.069** | 1.023± 0.100** |
| Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett | | | | | | | |
| (HCL042) | | | | | | | |

BAIS 4

STUDY NO. : 0417
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 | 40 | 0.332± 0.575 | 2.993± 0.600 | 0.543± 0.044 |
| 25ppm | 35 | 0.247± 0.066 | 2.965± 0.361 | 0.549± 0.050 |
| 100ppm | 38 | 0.262± 0.083 | 3.442± 0.509** | 0.540± 0.051 |
| 400ppm | 30 | 0.342± 0.207** | 4.877± 1.039** | 0.711± 0.092** |
| Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett | | | | |
| (HCL042) | | | | BAIS 4 |

APPENDIX K 2

ORGAN WEIGHT, RELATIVE : SUMMARY,

RAT : FEMALE

(2-YEAR STUDY)

STUDY NO. : 0417
 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 | 38 | 253± 26 | 0.030± 0.007 | 0.052± 0.011 | 0.355± 0.052 | 0.415± 0.111 | 0.694± 0.107 |
| 25ppm | 45 | 260± 29 | 0.030± 0.014 | 0.077± 0.189 | 0.346± 0.065 | 0.386± 0.058 | 0.692± 0.149 |
| 100ppm | 39 | 275± 24** | 0.027± 0.003 | 0.048± 0.010 | 0.342± 0.040 | 0.390± 0.147 | 0.682± 0.093 |
| 400ppm | 26 | 199± 28** | 0.047± 0.040** | 0.052± 0.016 | 0.448± 0.060** | 0.601± 0.281** | 1.055± 0.151** |

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

Test of Dunnett

(HCL042)

BAIS 4

STUDY NO. : 0417
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 | 38 | 0.336± 0.506 | 2.612± 0.541 | 0.745± 0.079 |
| 25ppm | 45 | 0.263± 0.304 | 2.714± 0.342 | 0.722± 0.089 |
| 100ppm | 39 | 0.337± 0.839 | 2.899± 0.378** | 0.678± 0.064** |
| 400ppm | 26 | 0.481± 0.522** | 7.969± 3.238** | 0.918± 0.127** |

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

Test of Dunnett

(HCL042)

BAIS 4

APPENDIX L 1

HISTOPATHOLOGICAL FINDINGS :
NON-NEOPLASTIC LESIONS : SUMMARY,
RAT : MALE :
ALL ANIMALS
(2-YEAR STUDY)

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 1

| Organ | Findings | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|----------------------------------|--|-------------------------|---------|--------|-------|-------|--------|--------|-------|-------|--------|--------|--------|-------|--------|--------|-------|-------|
| | | No. of Animals on Study | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Integumentary system/appandage} | | | | | | | | | | | | | | | | | | |
| skin/app | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | squamous cell hyperplasia | | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | basal cell hyperplasia | | 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) |
| | epidermal cyst | | 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) | (0) | (0) | (0) |
| subcutis | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | hemorrhage | | 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) |
| {Respiratory system} | | | | | | | | | | | | | | | | | | |
| nasal cavit | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | eosinophilic change:olfactory epithelium | | 12 | 28 | 1 | 0 | 7 | 36 | 4 | 0 | 5 | 34 | 5 | 0 | 8 | 35 | 0 | 0 |
| | | | (24) | (56) | (2) | (0) | (14) | (72) | (8) | (0) | (10) | (68) | (10) | (0) | (16) | (70) | (0) | (0) |
| | eosinophilic change:respiratory epithelium | | 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) |

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. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 2

| | | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|----------------------|---|-------------------------|---------|-------|------|------|-------|-------|------|------|--------|-------|------|------|--------|-------|------|------|
| | | 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> | | | |
| | inflammation:foreign body | | 4 | 12 | 0 | 0 | 5 | 6 | 0 | 0 | 5 | 11 | 2 | 0 | 3 | 18 | 1 | 0 |
| | | | (8) | (24) | (0) | (0) | (10) | (12) | (0) | (0) | (10) | (22) | (4) | (0) | (6) | (36) | (2) | (0) |
| | inflammation:respiratory epithelium | | 0 | 0 | 0 | 0 | 6 | 2 | 0 | 0 * | 5 | 2 | 0 | 0 * | 13 | 13 | 0 | 0 ** |
| | | | (0) | (0) | (0) | (0) | (12) | (4) | (0) | (0) | (10) | (4) | (0) | (0) | (26) | (26) | (0) | (0) |
| | respiratory metaplasia:olfactory epithelium | | 2 | 2 | 0 | 0 | 4 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 7 | 9 | 0 | 0 * |
| | | | (4) | (4) | (0) | (0) | (8) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (14) | (18) | (0) | (0) |
| | respiratory metaplasia:gland | | 15 | 15 | 0 | 0 | 14 | 21 | 0 | 0 | 16 | 22 | 0 | 0 | 2 | 37 | 0 | 0 ** |
| | | | (30) | (30) | (0) | (0) | (28) | (42) | (0) | (0) | (32) | (44) | (0) | (0) | (4) | (74) | (0) | (0) |
| | squamous cell metaplasia:respiratory epithelium | | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 16 | 7 | 0 | 0 ** |
| | | | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (32) | (14) | (0) | (0) |
| | hyperplasia with atypia:transitional epithelium | | 0 | 0 | 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) | (2) | (6) | (0) | (0) |
| | atrophy:olfactory epithelium | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 11 | 18 | 1 | 0 ** |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (22) | (36) | (2) | (0) |
| | necrosis:olfactory epithelium | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 5 | 3 | 0 | 0 * |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (10) | (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

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 3

| Organ | Findings | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|----------------------|---------------------------|-------------------------|-------|-------|-------|-------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
| | | No. of Animals on Study | | | | 50 | | | | 50 | | | | 50 | | | |
| | | Grade | | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Respiratory system} | | | | | | | | | | | | | | | | | |
| nasopharynx | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | inflammation:foreign body | 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) |
| larynx | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | inflammation | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| | inflammation:foreign body | 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) |
| trachea | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | proliferation:histiocyte | 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) |
| lung | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | congestion | 1 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | (2) | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) |
| | hemorrhage | 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) | (4) | (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) |

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. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 4

| | | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|------------------------|---------------------------------------|-------------------------|---------|-------|-------|-------|-------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
| | | 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> | | | |
| | inflammatory infiltration | | 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) |
| | | | | | | | | | | | | | | | | | | |
| | accumulation of foamy cells | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | bronchiolar-alveolar cell hyperplasia | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (6) | (0) | (0) | (0) |
| {Hematopoietic system} | | | | | | | | | | | | | | | | | | |
| bone marrow | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | granulation | | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | | | | | | | | | | | | | | | | | | |
| | increased hematopoiesis | | 2 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 3 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | | (4) | (0) | (0) | (0) | (4) | (2) | (0) | (0) | (6) | (0) | (0) | (0) | (4) | (0) | (0) | (0) |
| | myelofibrosis | | 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) |
| | granulopoiesis:increased | | 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) |

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. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 5

| | | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|------------------------|------------------------------|-------------------------|---------|-------|-------|--------|--------|-------|-------|--------|--------|--------|-------|--------|--------|-------|-------|-------|
| | | 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 | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Hematopoietic system} | | | | | | | | | | | | | | | | | | |
| lymph node | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | lymphadenitis | | 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) |
| spleen | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | congestion | | 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) |
| | 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) | (2) | (0) | (0) |
| | deposit of hemosiderin | | 10 | 22 | 0 | 0 | 8 | 25 | 2 | 0 | 5 | 30 | 0 | 0 | 7 | 32 | 3 | 0 * |
| | | (20) | (44) | (0) | (0) | (16) | (50) | (4) | (0) | (10) | (60) | (0) | (0) | (14) | (64) | (6) | (0) | |
| | fibrosis | | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) |
| | extramedullary hematopoiesis | | 0 | 2 | 1 | 0 | 0 | 4 | 0 | 0 | 0 | 8 | 0 | 0 | 0 | 4 | 2 | 0 |
| | | | (0) | (4) | (2) | (0) | (0) | (8) | (0) | (0) | (0) | (16) | (0) | (0) | (0) | (8) | (4) | (0) |
| {Circulatory system} | | | | | | | | | | | | | | | | | | |
| heart | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | thrombus | | 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 : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 6

| | | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|----------------------|------------------------|-------------------------|---------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|
| | | 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 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Circulatory system} | | | | | | | | | | | | | | | | | | |
| heart | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | fibrosis:focal | | 0 | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 1 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (6) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (2) | (0) | (2) | (0) | (0) | (0) |
| | myocardial fibrosis | | 22 | 17 | 0 | 0 | 14 | 13 | 0 | 0 * | 21 | 10 | 0 | 0 | 20 | 12 | 0 | 0 |
| | | | (44) | (34) | (0) | (0) | (28) | (26) | (0) | (0) | (42) | (20) | (0) | (0) | (40) | (24) | (0) | (0) |
| {Digestive system} | | | | | | | | | | | | | | | | | | |
| tooth | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | inflammation | | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 2 | 0 | 0 |
| | | | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (4) | (0) | (0) |
| tongue | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | arteritis | | 0 | 2 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (4) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| salivary gl | | | <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) |
| stomach | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | basal cell hyperplasia | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |

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

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

b : Number of animals with lesion

(c) c : b / a * 100

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

STUDY NO. : 0417
 ANIMAL : RAT 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 Grade | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|--------------------|---------------------------|--|---------|--------|-------|-------|-------|--------|-------|-------|--------|-------|-------|-------|--------|--------|-------|-------|
| | | | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Digestive system} | | | | | | | | | | | | | | | | | | |
| stomach | | | | | | | | | | | | | | | | | | |
| | erosion:forestomach | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | | 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) |
| | ulcer:forestomach | | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 4 | 0 | 0 | 1 | 2 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (2) | (8) | (0) | (0) | (2) | (4) | (0) | (0) |
| | hyperplasia:forestomach | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (6) | (0) | (0) | (0) |
| | inflammation:forestomach | | 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) |
| | erosion:glandular stomach | | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | | (2) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) |
| | ulcer:glandular stomach | | 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) |
| liver | | | | | | | | | | | | | | | | | | |
| | herniation | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | | 0 | 7 | 0 | 0 | 0 | 6 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 5 | 0 | 0 |
| | | | (0) | (14) | (0) | (0) | (0) | (12) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (10) | (0) | (0) |
| | angiectasis | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) |

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

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

b : Number of animals with lesion

(c) c : b / a * 100

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

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 8

| Organ | Findings | Group Name No. of Animals on Study | | | | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|--------------------|------------------------|---------------------------------------|--------|-------|-------|---------|-------|-------|-------|--------|--------|-------|-------|--------|--------|--------|-------|--------|--------|--------|-------|
| | | Grade | | | | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Digestive system} | | | | | | | | | | | | | | | | | | | | | |
| liver | | | | | | | | | | | | | | | | | | | | | |
| | necrosis:central | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (4) | (0) | (0) |
| | necrosis:focal | 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) |
| | spongiosis | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) |
| | mineralization | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | (0) | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) |
| | degeneration:central | 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) |
| | granulation | 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) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | inflammatory cell nest | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (2) | (0) | (0) |
| | clear cell focus | 7 | 9 | 0 | 0 | 9 | 4 | 0 | 0 | 17 | 12 | 0 | 0 * | 0 | 13 | 27 | 0 ** | 0 | 13 | 27 | 0 ** |
| | | (14) | (18) | (0) | (0) | (18) | (8) | (0) | (0) | (34) | (24) | (0) | (0) | (0) | (26) | (54) | (0) | (0) | (26) | (54) | (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. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 9

| Organ | Findings | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|--------------------|------------------------|-------------------------|--------|-------|-------|-------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|
| | | 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 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Digestive system} | | | | | | | | | | | | | | | | | |
| liver | | | | | | | | | | | | | | | | | |
| | acidophilic cell focus | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 7 | 13 | 0 | 0 ** |
| | | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (2) | (0) | (0) | (14) | (26) | (0) | (0) |
| | basophilic cell focus | 2 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 2 | 5 | 0 | 0 | 1 | 8 | 0 | 0 * |
| | | (4) | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (4) | (10) | (0) | (0) | (2) | (16) | (0) | (0) |
| | vacuolated 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) | (2) | (2) | (0) | (0) |
| | spongiosis hepatitis | 0 | 3 | 0 | 0 | 1 | 1 | 0 | 0 | 2 | 3 | 0 | 0 | 0 | 3 | 0 | 0 |
| | | (0) | (6) | (0) | (0) | (2) | (2) | (0) | (0) | (4) | (6) | (0) | (0) | (0) | (6) | (0) | (0) |
| | bile duct hyperplasia | 2 | 47 | 0 | 0 | 0 | 47 | 0 | 0 | 2 | 46 | 1 | 0 | 5 | 41 | 0 | 0 |
| | | (4) | (94) | (0) | (0) | (0) | (94) | (0) | (0) | (4) | (92) | (2) | (0) | (10) | (82) | (0) | (0) |
| pancreas | | | | | | | | | | | | | | | | | |
| | atrophy | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 3 | 6 | 0 | 0 | 1 | 13 | 0 | 0 | 1 | 7 | 1 | 0 | 3 | 5 | 0 | 0 |
| | | (6) | (12) | (0) | (0) | (2) | (26) | (0) | (0) | (2) | (14) | (2) | (0) | (6) | (10) | (0) | (0) |
| | 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) |
| | arteritis | 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 ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 10

| Organ | Findings | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|--------------------|-------------------------------------|-------------------------|---------|--------|--------|-------|--------|--------|-------|-------|--------|--------|--------|--------|--------|--------|--------|-------|
| | | 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} | | | | | | | | | | | | | | | | | | |
| pancreas | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | islet cell hyperplasia | | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (4) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (0) | (0) | (0) |
| {Urinary system} | | | | | | | | | | | | | | | | | | |
| kidney | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | hyperplasia:tubular epithelial cell | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (2) | (0) | (0) |
| | infarct | | 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) |
| | inflammation | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| | inflammatory 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) |
| | chronic nephropathy | | 6 | 28 | 6 | 2 | 5 | 35 | 3 | 1 | 1 | 27 | 13 | 5 | 2 | 28 | 14 | 2 |
| | | | (12) | (56) | (12) | (4) | (10) | (70) | (6) | (2) | (2) | (54) | (26) | (10) | (4) | (56) | (28) | (4) |
| | pyelitis | | 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. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 11

| | | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|--------------------|--|-------------------------|---------|------|------|------|-------|------|------|------|--------|------|------|------|--------|------|------|------|
| | | 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 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Urinary system} | | | | | | | | | | | | | | | | | | |
| kidney | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | mineralization:papilla | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | mineralization:pelvis | | 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) |
| urin bladd | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | simple hyperplasia:transitional 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) |
| {Endocrine system} | | | | | | | | | | | | | | | | | | |
| pituitary | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | angiectasis | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 |
| | | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) |
| | cyst | | 0 | 1 | 0 | 0 | 1 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (2) | (0) | (0) | (2) | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | deposit of hemosiderin | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |

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

(HPT150)

BAIS4

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 12

| Organ_____ | Findings_____ | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|--------------------|---------------------------|-------------------------|---------|--------|-------|-------|-------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
| | | 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 | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | hyperplasia | | 4 | 6 | 0 | 0 | 3 | 4 | 0 | 0 | 4 | 4 | 0 | 0 | 2 | 1 | 0 | 0 |
| | | | (8) | (12) | (0) | (0) | (6) | (8) | (0) | (0) | (8) | (8) | (0) | (0) | (4) | (2) | (0) | (0) |
| | Rathke pouch | | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| thyroid | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | follicular hyperplasia | | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| | | | (0) | (2) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) |
| | C-cell hyperplasia | | 1 | 4 | 3 | 0 | 2 | 4 | 1 | 0 | 8 | 2 | 0 | 0 * | 2 | 3 | 0 | 0 |
| | | | (2) | (8) | (6) | (0) | (4) | (8) | (2) | (0) | (16) | (4) | (0) | (0) | (4) | (6) | (0) | (0) |
| adrenal | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | angiectasis | | 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:cortical cell | | 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) |
| | hyperplasia:medulla | | 0 | 5 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 2 | 0 | 0 | 2 | 3 | 0 | 0 |
| | | | (0) | (10) | (0) | (0) | (2) | (2) | (0) | (0) | (2) | (4) | (0) | (0) | (4) | (6) | (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. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 13

| Organ | Findings | Group Name No. of Animals on Study | | | | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|-----------------------|-------------------------------|---------------------------------------|-------|-------|-------|---------|--------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|--------|-------|-------|
| | | 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 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Reproductive system} | | | | | | | | | | | | | | | | | | | | | |
| testis | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | atrophy | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 |
| | | (0) | (4) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (4) | (0) | (0) |
| | mineralization | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) |
| | arteritis | 1 | 2 | 0 | 0 | 3 | 2 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (2) | (4) | (0) | (0) | (6) | (4) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (0) | (0) | (0) |
| | interstitial cell hyperplasia | 6 | 3 | 0 | 0 | 8 | 5 | 0 | 0 | 9 | 2 | 0 | 0 | 9 | 2 | 0 | 0 | 3 | 4 | 0 | 0 |
| | | (12) | (6) | (0) | (0) | (16) | (10) | (0) | (0) | (18) | (4) | (0) | (0) | (18) | (4) | (0) | (0) | (6) | (8) | (0) | (0) |
| prostate | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | inflammation | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (4) | (0) | (0) |
| | hyperplasia | 1 | 2 | 2 | 0 | 3 | 4 | 2 | 0 | 3 | 2 | 1 | 0 | 3 | 2 | 1 | 0 | 5 | 6 | 1 | 0 |
| | | (2) | (4) | (4) | (0) | (6) | (8) | (4) | (0) | (6) | (4) | (2) | (0) | (6) | (4) | (2) | (0) | (10) | (12) | (2) | (0) |
| prep/cli gl | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | duct ectasia | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) |

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. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 14

| Organ | Findings | Group Name No. of Animals on Study | | | | Control 50 | | | | 25ppm 50 | | | | 100ppm 50 | | | | 400ppm 50 | | | |
|----------------------------------|-----------------|---------------------------------------|-------|-------|-------|---------------|-------|-------|-------|-------------|--------|-------|-------|--------------|-------|-------|-------|--------------|-------|-------|-------|
| | | Grade | | | | | | | | | | | | | | | | | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Nervous system} | | | | | | | | | | | | | | | | | | | | | |
| brain | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | angiectasis | 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) |
| | hemorrhage | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | gliosis | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) |
| {Special sense organs/appendage} | | | | | | | | | | | | | | | | | | | | | |
| eye | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | cataract | 3 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 6 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (6) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (12) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| | retinal atrophy | 2 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 0 | 6 | 0 | 0 * | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 |
| | | (4) | (0) | (0) | (0) | (4) | (2) | (0) | (0) | (0) | (12) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (4) | (0) | (0) |
| | keratitis | 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) |
| | iritis | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (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. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 15

| | | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|----------------------------------|---------------------------------|-------------------------|---------|-------|-------|-------|-------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
| | | 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 |
| | | | | | | | | | | | | | | | | | | |
| {Special sense organs/appendage} | | | | | | | | | | | | | | | | | | |
| eye | squamous cell metaplasia:cornea | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 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) | (0) |
| nasolacr d | inflammation | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) |
| | squamous cell metaplasia | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| 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) | (2) | (0) | (0) |
| {Musculoskeletal system} | | | | | | | | | | | | | | | | | | |
| muscle | hemorrhage | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) |
| bone | osteosclerosis | | <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) | (0) |
| {Body cavities} | | | | | | | | | | | | | | | | | | |
| adipose | granulation | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |

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

APPENDIX L 2

HISTOPATHOLOGICAL FINDINGS :
NON-NEOPLASTIC LESIONS : SUMMARY,
RAT : MALE :
DEAD AND MORIBUND ANIMALS
(2-YEAR STUDY)

STUDY NO. : 0417
ANIMAL : RAT 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 | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|----------------------------------|---|--|---------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|
| | | | 10 | | | | 15 | | | | 12 | | | | 20 | | | |
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Integumentary system/appandage} | | | | | | | | | | | | | | | | | | |
| subcutis | | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | hemorrhage | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) |
| {Respiratory system} | | | | | | | | | | | | | | | | | | |
| nasal cavit | | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | eosinophilic change:olfactory epithelium | | 2 | 4 | 0 | 0 | 4 | 9 | 0 | 0 | 2 | 3 | 1 | 0 | 3 | 12 | 0 | 0 |
| | | | (20) | (40) | (0) | (0) | (27) | (60) | (0) | (0) | (17) | (25) | (8) | (0) | (15) | (60) | (0) | (0) |
| | inflammation:foreign body | | 1 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 4 | 0 | 0 | 1 | 8 | 1 | 0 |
| | | | (10) | (10) | (0) | (0) | (7) | (0) | (0) | (0) | (8) | (33) | (0) | (0) | (5) | (40) | (5) | (0) |
| | inflammation:respiratory epithelium | | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 6 | 3 | 0 | 0 * |
| | | | (0) | (0) | (0) | (0) | (13) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (30) | (15) | (0) | (0) |
| | respiratory metaplasia:olfactory epithelium | | 0 | 1 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 2 | 0 | 0 |
| | | | (0) | (10) | (0) | (0) | (13) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (15) | (10) | (0) | (0) |
| | respiratory metaplasia:gland | | 5 | 1 | 0 | 0 | 3 | 6 | 0 | 0 | 6 | 1 | 0 | 0 | 0 | 15 | 0 | 0 ** |
| | | | (50) | (10) | (0) | (0) | (20) | (40) | (0) | (0) | (50) | (8) | (0) | (0) | (0) | (75) | (0) | (0) |
| | squamous cell metaplasia:respiratory epithelium | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 4 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (7) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (20) | (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 ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 2

| Organ | Findings | Group Name No. of Animals on Study Grade | Control 10 | | | | 25ppm 15 | | | | 100ppm 12 | | | | 400ppm 20 | | | |
|----------------------|---|--|---------------|--------|-------|-------|-------------|-------|-------|-------|--------------|-------|-------|-------|--------------|--------|-------|-------|
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Respiratory system} | | | | | | | | | | | | | | | | | | |
| nasal cavit | | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | hyperplasia with atypia:transitional 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) | (5) | (0) | (0) | (0) |
| | | | | | | | | | | | | | | | | | | |
| | atrophy:olfactory epithelium | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 10 | 1 | 0 * |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (5) | (50) | (5) | (0) |
| | | | | | | | | | | | | | | | | | | |
| | necrosis:olfactory epithelium | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 2 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (5) | (10) | (0) | (0) |
| | | | | | | | | | | | | | | | | | | |
| nasopharynx | | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | inflammation:foreign body | | 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) |
| larynx | | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | 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) | (5) | (0) | (0) | (0) |
| lung | | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | congestion | | 1 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | (10) | (20) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (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) | (10) | (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. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 3

| | | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|------------------------|---------------------------------------|-------------------------|---------|--------|-------|-------|--------|--------|--------|-------|--------|--------|-------|-------|--------|--------|--------|-------|
| | | No. of Animals on Study | 10 | | | | 15 | | | | 12 | | | | 20 | | | |
| Organ | Findings | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Respiratory system} | | | | | | | | | | | | | | | | | | |
| lung | | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | 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) | (5) | (0) | (0) |
| | inflammatory infiltration | | 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) |
| | accumulation of foamy cells | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | bronchiolar-alveolar cell hyperplasia | | 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) | (10) | (0) | (0) | (0) |
| {Hematopoietic system} | | | | | | | | | | | | | | | | | | |
| bone marrow | | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | increased hematopoiesis | | 0 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (13) | (7) | (0) | (0) | (17) | (0) | (0) | (0) | (10) | (0) | (0) | (0) |
| | granulopoiesis:increased | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (7) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| spleen | | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | deposit of hemosiderin | | 1 | 6 | 0 | 0 | 2 | 5 | 2 | 0 | 1 | 8 | 0 | 0 | 1 | 13 | 2 | 0 |
| | | | (10) | (60) | (0) | (0) | (13) | (33) | (13) | (0) | (8) | (67) | (0) | (0) | (5) | (65) | (10) | (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. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 4

| | | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|------------------------|------------------------------|-------------------------|---------|--------|--------|-------|--------|--------|-------|-------|--------|--------|-------|-------|--------|--------|--------|-------|
| | | No. of Animals on Study | 10 | | | | 15 | | | | 12 | | | | 20 | | | |
| Organ | Findings | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Hematopoietic system} | | | | | | | | | | | | | | | | | | |
| spleen | | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | extramedullary hematopoiesis | | 0 | 1 | 1 | 0 | 0 | 4 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 3 | 2 | 0 |
| | | | (0) | (10) | (10) | (0) | (0) | (27) | (0) | (0) | (0) | (25) | (0) | (0) | (0) | (15) | (10) | (0) |
| {Circulatory system} | | | | | | | | | | | | | | | | | | |
| heart | | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | myocardial fibrosis | | 3 | 4 | 0 | 0 | 6 | 4 | 0 | 0 | 2 | 4 | 0 | 0 | 8 | 5 | 0 | 0 |
| | | | (30) | (40) | (0) | (0) | (40) | (27) | (0) | (0) | (17) | (33) | (0) | (0) | (40) | (25) | (0) | (0) |
| {Digestive system} | | | | | | | | | | | | | | | | | | |
| salivary gl | | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | abscess | | 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) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| stomach | | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | basal cell hyperplasia | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) | (0) |
| | erosion:forestomach | | 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) | (5) | (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. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 5

| | | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|--------------------|---------------------------|-------------------------|---------|--------|-------|-------|-------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|
| | | No. of Animals on Study | 10 | | | | 15 | | | | 12 | | | | 20 | | | |
| Organ | Findings | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| (Digestive system) | | | | | | | | | | | | | | | | | | |
| stomach | | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | ulcer:forestomach | | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 2 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (7) | (0) | (0) | (0) | (33) | (0) | (0) | (0) | (10) | (0) | (0) |
| | inflammation:forestomach | | 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) |
| | erosion:glandular stomach | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) | (0) |
| | ulcer:glandular stomach | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (7) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| liver | | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | herniation | | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 0 | 0 |
| | | | (0) | (20) | (0) | (0) | (0) | (13) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (20) | (0) | (0) |
| | angiectasis | | 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) |
| | necrosis:central | | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (7) | (0) | (0) | (0) | (17) | (0) | (0) | (0) | (10) | (0) | (0) |
| | necrosis:focal | | 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) | (10) | (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. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 6

| Organ_____ | Findings_____ | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|------------------------|------------------------|-------------------------|---------|-------|-------|-------|-------|-------|-------|-------|--------|-------|-------|--------|--------|--------|-------|-------|
| | | No. of Animals on Study | 10 | | | | 15 | | | | 12 | | | | 20 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Digestive system} | | | | | | | | | | | | | | | | | | |
| liver | | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | spongiosis | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) |
| | mineralization | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) |
| | degeneration:central | | 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) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | inflammatory cell nest | | 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) |
| clear cell focus | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 7 | 4 | 0 * | |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (35) | (20) | (0) | |
| acidophilic cell focus | | 0 | 0 | 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) | (10) | (20) | (0) | (0) | |
| basophilic cell focus | | 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) | (15) | (0) | (0) | |
| spongiosis hepatitis | | 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) | (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. : 0417
 ANIMAL : RAT 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 No. of Animals on Study Grade | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|--------------------|------------------------|--|---------|--------|-------|-------|--------|--------|-------|-------|--------|--------|--------|--------|--------|--------|--------|-------|
| | | | 10 | | | | 15 | | | | 12 | | | | 20 | | | |
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Digestive system} | | | | | | | | | | | | | | | | | | |
| liver | | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | bile duct hyperplasia | | 2 | 7 | 0 | 0 | 0 | 12 | 0 | 0 | 2 | 8 | 1 | 0 | 5 | 11 | 0 | 0 |
| | | | (20) | (70) | (0) | (0) | (0) | (80) | (0) | (0) | (17) | (67) | (8) | (0) | (25) | (55) | (0) | (0) |
| pancreas | | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | atrophy | | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 1 | 1 | 0 | 0 |
| | | | (0) | (10) | (0) | (0) | (0) | (7) | (0) | (0) | (0) | (17) | (0) | (0) | (5) | (5) | (0) | (0) |
| | arteritis | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) |
| | islet cell hyperplasia | | 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) | (17) | (0) | (0) | (0) | (0) | (0) | (0) |
| {Urinary system} | | | | | | | | | | | | | | | | | | |
| kidney | | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | infarct | | 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) |
| | chronic nephropathy | | 0 | 2 | 0 | 0 | 2 | 6 | 0 | 1 | 1 | 3 | 2 | 2 | 2 | 10 | 4 | 0 * |
| | | | (0) | (20) | (0) | (0) | (13) | (40) | (0) | (7) | (8) | (25) | (17) | (17) | (10) | (50) | (20) | (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. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 8

| | | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|--------------------|--|-------------------------|---------|--------|-------|-------|-------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
| | | No. of Animals on Study | 10 | | | | 15 | | | | 12 | | | | 20 | | | |
| Organ | Findings | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Urinary system} | | | | | | | | | | | | | | | | | | |
| kidney | mineralization:papilla | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | mineralization:pelvis | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| urin bladd | simple hyperplasia:transitional epithelium | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | | | 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) |
| {Endocrine system} | | | | | | | | | | | | | | | | | | |
| pituitary | hyperplasia | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (0) | (0) | (0) |
| thyroid | C-cell hyperplasia | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (5) | (0) | (0) | (0) |
| adrenal | angiectasis | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | | | 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) | (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. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 9

| | | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|-----------------------|-------------------------------|-------------------------|---------|-------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|
| | | No. of Animals on Study | 10 | | | | 15 | | | | 12 | | | | 20 | | | |
| Organ | Findings | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| <hr/> | | | | | | | | | | | | | | | | | | |
| {Reproductive system} | | | | | | | | | | | | | | | | | | |
| testis | | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | atrophy | | 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) | (10) | (0) | (0) |
| | mineralization | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (7) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) |
| | arteritis | | 0 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (13) | (7) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (0) | (0) | (0) |
| | interstitial cell hyperplasia | | 0 | 0 | 0 | 0 | 2 | 2 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 3 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (13) | (13) | (0) | (0) | (8) | (8) | (0) | (0) | (5) | (15) | (0) | (0) |
| prostate | | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | inflammation | | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (13) | (0) | (0) | (0) | (17) | (0) | (0) | (0) | (5) | (0) | (0) |
| | hyperplasia | | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (7) | (0) | (7) | (0) | (0) | (0) | (0) | (0) | (5) | (5) | (0) | (0) |
| <hr/> | | | | | | | | | | | | | | | | | | |
| {Nervous system} | | | | | | | | | | | | | | | | | | |
| brain | | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | hemorrhage | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (7) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |

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

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

b : Number of animals with lesion

(c) c : b / a * 100

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

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 10

| | | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|----------------------------------|---------------------------------|-------------------------|---------|-------|-------|-------|-------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
| | | No. of Animals on Study | 10 | | | | 15 | | | | 12 | | | | 20 | | | |
| Organ | Findings | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| <hr/> | | | | | | | | | | | | | | | | | | |
| {Nervous system} | | | | | | | | | | | | | | | | | | |
| brain | | | | | | | | | | | | | | | | | | |
| | gliosis | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) |
| {Special sense organs/appendage} | | | | | | | | | | | | | | | | | | |
| eye | | | | | | | | | | | | | | | | | | |
| | cataract | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | | | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (10) | (0) | (0) | (0) | (7) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | retinal atrophy | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (0) | (0) | (0) |
| | keratitis | | 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) |
| | iritis | | 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) | (10) | (0) | (0) | (0) |
| | squamous cell metaplasia:cornea | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) | (0) |
| nasolacr d | | | | | | | | | | | | | | | | | | |
| | inflammation | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | | | 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) |

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. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 11

| | | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|--------------------------|----------------|-------------------------|---------|-------|-------|-------|-------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
| | | No. of Animals on Study | 10 | | | | 15 | | | | 12 | | | | 20 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| Organ_____ | Findings_____ | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| <hr/> | | | | | | | | | | | | | | | | | | |
| {Musculoskeletal system} | | | | | | | | | | | | | | | | | | |
| muscle | hemorrhage | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) | |
| bone | osteosclerosis | | <10> | | | | <15> | | | | <12> | | | | <20> | | | |
| | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) | (0) |

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 3

HISTOPATHOLOGICAL FINDINGS :
NON-NEOPLASTIC LESIONS : SUMMARY,
RAT : MALE :
SACRIFICED ANIMALS
(2-YEAR STUDY)

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 1

| | | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|----------------------------------|--|-------------------------|---------|--------|-------|-------|--------|--------|--------|-------|--------|--------|--------|-------|--------|--------|-------|-------|
| | | No. of Animals on Study | 40 | | | | 35 | | | | 38 | | | | 30 | | | |
| Organ | Findings | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Integumentary system/appandage} | | | | | | | | | | | | | | | | | | |
| skin/app | | | <40> | | | | <35> | | | | <38> | | | | <30> | | | |
| | squamous cell hyperplasia | | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (3) | (0) | (0) | (0) | (3) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | basal cell hyperplasia | | 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) |
| | epidermal cyst | | 0 | 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) |
| {Respiratory system} | | | | | | | | | | | | | | | | | | |
| nasal cavit | | | <40> | | | | <35> | | | | <38> | | | | <30> | | | |
| | eosinophilic change:olfactory epithelium | | 10 | 24 | 1 | 0 | 3 | 27 | 4 | 0 * | 3 | 31 | 4 | 0 ** | 5 | 23 | 0 | 0 |
| | | | (25) | (60) | (3) | (0) | (9) | (77) | (11) | (0) | (8) | (82) | (11) | (0) | (17) | (77) | (0) | (0) |
| | eosinophilic change:respiratory epithelium | | 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) |
| | inflammation:foreign body | | 3 | 11 | 0 | 0 | 4 | 6 | 0 | 0 | 4 | 7 | 2 | 0 | 2 | 10 | 0 | 0 |
| | | | (8) | (28) | (0) | (0) | (11) | (17) | (0) | (0) | (11) | (18) | (5) | (0) | (7) | (33) | (0) | (0) |
| | inflammation:respiratory epithelium | | 0 | 0 | 0 | 0 | 4 | 2 | 0 | 0 * | 5 | 2 | 0 | 0 * | 7 | 10 | 0 | 0 ** |
| | | | (0) | (0) | (0) | (0) | (11) | (6) | (0) | (0) | (13) | (5) | (0) | (0) | (23) | (33) | (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. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 2

| | | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|----------------------|---|-------------------------|-------------|-------------|-----------|-----------|-------------|-------------|-----------|-----------|-------------|-------------|-----------|-----------|-------------|-------------|-----------|--------------|
| | | No. of Animals on Study | 40 | | | | 35 | | | | 38 | | | | 30 | | | |
| Organ | Findings | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Respiratory system} | | | | | | | | | | | | | | | | | | |
| nasal cavit | | | <40> | | | | <35> | | | | <38> | | | | <30> | | | |
| | respiratory metaplasia:olfactory epithelium | | 2 (5) | 1 (3) | 0 (0) | 0 (0) | 2 (6) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 4 (13) | 7 (23) | 0 (0) | 0 ** (0) |
| | respiratory metaplasia:gland | | 10 (25) | 14 (35) | 0 (0) | 0 (0) | 11 (31) | 15 (43) | 0 (0) | 0 (0) | 10 (26) | 21 (55) | 0 (0) | 0 (0) | 2 (7) | 22 (73) | 0 (0) | 0 ** (0) |
| | squamous cell metaplasia:respiratory epithelium | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 12 (40) | 3 (10) | 0 (0) | 0 ** (0) |
| | hyperplasia with atypia:transitional epithelium | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 3 (10) | 0 (0) | 0 (0) |
| | atrophy:olfactory epithelium | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 10 (33) | 8 (27) | 0 (0) | 0 ** (0) |
| | necrosis: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) | 4 (13) | 1 (3) | 0 (0) | 0 * (0) |
| larynx | | | <40> | | | | <35> | | | | <38> | | | | <30> | | | |
| | inflammation:foreign body | | 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) | 1 (3) | 0 (0) | 0 (0) |
| trachea | | | <40> | | | | <35> | | | | <38> | | | | <30> | | | |
| | proliferation:histiocyte | | 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) |

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. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 3

| | | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|------------------------|---------------------------------------|-------------------------|---------|-------|-------|-------|-------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
| | | No. of Animals on Study | 40 | | | | 35 | | | | 38 | | | | 30 | | | |
| Organ | Findings | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Respiratory system} | | | | | | | | | | | | | | | | | | |
| lung | | | <40> | | | | <35> | | | | <38> | | | | <30> | | | |
| | bronchiolar-alveolar cell hyperplasia | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (3) | (0) | (0) | (0) |
| {Hematopoietic system} | | | | | | | | | | | | | | | | | | |
| bone marrow | | | <40> | | | | <35> | | | | <38> | | | | <30> | | | |
| | granulation | | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (3) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | increased hematopoiesis | | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (5) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | myelofibrosis | | 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) |
| | granulopoiesis:increased | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| lymph node | | | <40> | | | | <35> | | | | <38> | | | | <30> | | | |
| | lymphadenitis | | 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. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 4

| Organ_____ | Findings_____ | Group Name No. of Animals on Study Grade | Control 40 | | | | 25ppm 35 | | | | 100ppm 38 | | | | 400ppm 30 | | | |
|------------------------|------------------------------|--|---------------|--------------|------------|------------|-------------|--------------|------------|------------|--------------|--------------|------------|------------|--------------|--------------|------------|------------|
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Hematopoietic system} | | | | | | | | | | | | | | | | | | |
| spleen | | | <40> | | | | <35> | | | | <38> | | | | <30> | | | |
| | congestion | | 0 (0) | 0 (0) | 0 (0) | 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) |
| | angiectasis | | 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) |
| | deposit of hemosiderin | | 9 (23) | 16 (40) | 0 (0) | 0 (0) | 6 (17) | 20 (57) | 0 (0) | 0 (0) | 4 (11) | 22 (58) | 0 (0) | 0 (0) | 6 (20) | 19 (63) | 1 (3) | 0 (0) |
| | fibrosis | | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | extramedullary hematopoiesis | | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 5 (13) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) |
| {Circulatory system} | | | | | | | | | | | | | | | | | | |
| heart | | | <40> | | | | <35> | | | | <38> | | | | <30> | | | |
| | thrombus | | 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) |
| | fibrosis:focal | | 0 (0) | 3 (8) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 1 (3) | 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 ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 5

| | | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|----------------------|---------------------------|-------------------------|---------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|
| | | No. of Animals on Study | 40 | | | | 35 | | | | 38 | | | | 30 | | | |
| Organ | Findings | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Circulatory system} | | | | | | | | | | | | | | | | | | |
| heart | | | <40> | | | | <35> | | | | <38> | | | | <30> | | | |
| | myocardial fibrosis | | 19 | 13 | 0 | 0 | 8 | 9 | 0 | 0 * | 19 | 6 | 0 | 0 | 12 | 7 | 0 | 0 |
| | | | (48) | (33) | (0) | (0) | (23) | (26) | (0) | (0) | (50) | (16) | (0) | (0) | (40) | (23) | (0) | (0) |
| {Digestive system} | | | | | | | | | | | | | | | | | | |
| tooth | | | <40> | | | | <35> | | | | <38> | | | | <30> | | | |
| | inflammation | | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 2 | 0 | 0 |
| | | | (0) | (3) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (7) | (0) | (0) |
| tongue | | | <40> | | | | <35> | | | | <38> | | | | <30> | | | |
| | arteritis | | 0 | 2 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (5) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) |
| stomach | | | <40> | | | | <35> | | | | <38> | | | | <30> | | | |
| | ulcer:forestomach | | 0 | 0 | 0 | 0 | 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) |
| | hyperplasia:forestomach | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (10) | (0) | (0) | (0) |
| | erosion:glandular stomach | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (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. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 6

| Organ | Findings | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|------------------------|----------------|-------------------------|---------|--------|-------|--------|--------|--------|-------|--------|--------|--------|-------|--------|--------|--------|-------|-------|
| | | No. of Animals on Study | 40 | | | | 35 | | | | 38 | | | | 30 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Digestive system} | | | | | | | | | | | | | | | | | | |
| liver | | | <40> | | | | <35> | | | | <38> | | | | <30> | | | |
| | herniation | | 0 | 5 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | (0) | (13) | (0) | (0) | (0) | (11) | (0) | (0) | (0) | (11) | (0) | (0) | (0) | (3) | (0) | (0) |
| | spongiosis | | 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) |
| | mineralization | | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (5) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) |
| | granulation | | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (3) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| inflammatory cell nest | | 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) | (3) | (0) | (0) | (0) | (3) | (0) | (0) | |
| clear cell focus | | 7 | 9 | 0 | 0 | 9 | 4 | 0 | 0 | 17 | 12 | 0 | 0 ** | 0 | 6 | 23 | 0 ** | |
| | | (18) | (23) | (0) | (0) | (26) | (11) | (0) | (0) | (45) | (32) | (0) | (0) | (0) | (20) | (77) | (0) | |
| acidophilic cell focus | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 5 | 9 | 0 | 0 ** | |
| | | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (3) | (0) | (0) | (17) | (30) | (0) | (0) | |
| basophilic cell focus | | 2 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 2 | 5 | 0 | 0 | 1 | 5 | 0 | 0 | |
| | | (5) | (3) | (0) | (0) | (0) | (3) | (0) | (0) | (5) | (13) | (0) | (0) | (3) | (17) | (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. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 7

| Organ | Findings | Group Name No. of Animals on Study Grade | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|--------------------|-------------------------------------|--|------------|-------------|------------|------------|------------|--------------|------------|------------|------------|-------------|------------|------------|------------|-------------|------------|------------|
| | | | 40 | | | | 35 | | | | 38 | | | | 30 | | | |
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| {Digestive system} | | | | | | | | | | | | | | | | | | |
| liver | | | | | | | | | | | | | | | | | | |
| | vacuolated cell focus | | <40> | | | | <35> | | | | <38> | | | | <30> | | | |
| | | | 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) | 1 (3) | 0 (0) | 0 (0) |
| | spongiosis hepatitis | | 0 (0) | 3 (8) | 0 (0) | 0 (0) | 1 (3) | 1 (3) | 0 (0) | 0 (0) | 1 (3) | 3 (8) | 0 (0) | 0 (0) | 0 (0) | 2 (7) | 0 (0) | 0 (0) |
| | bile duct hyperplasia | | 0 (0) | 40 (100) | 0 (0) | 0 (0) | 0 (0) | 35 (100) | 0 (0) | 0 (0) | 0 (0) | 38 (100) | 0 (0) | 0 (0) | 0 (0) | 30 (100) | 0 (0) | 0 (0) |
| pancreas | | | | | | | | | | | | | | | | | | |
| | atrophy | | <40> | | | | <35> | | | | <38> | | | | <30> | | | |
| | | | 3 (8) | 5 (13) | 0 (0) | 0 (0) | 1 (3) | 12 (34) | 0 (0) | 0 (0) | 1 (3) | 5 (13) | 1 (3) | 0 (0) | 2 (7) | 4 (13) | 0 (0) | 0 (0) |
| | 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) |
| | arteritis | | 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) | 0 (0) | 0 (0) | 0 (0) |
| | islet cell hyperplasia | | 0 (0) | 2 (5) | 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) | 0 (0) |
| {Urinary system} | | | | | | | | | | | | | | | | | | |
| kidney | | | | | | | | | | | | | | | | | | |
| | hyperplasia:tubular epithelial cell | | <40> | | | | <35> | | | | <38> | | | | <30> | | | |
| | | | 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) | 1 (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. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 8

| | | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|--------------------|---------------------------|-------------------------|---------|--------|-------|-------|--------|-------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|
| | | No. of Animals on Study | 40 | | | | 35 | | | | 38 | | | | 30 | | | |
| Organ | Findings | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Urinary system} | | | | | | | | | | | | | | | | | | |
| kidney | | | <40> | | | | <35> | | | | <38> | | | | <30> | | | |
| | 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) | (3) | (0) | (0) |
| | inflammatory infiltration | | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | chronic nephropathy | | 6 | 26 | 6 | 2 | 3 | 29 | 3 | 0 | 0 | 24 | 11 | 3 | 0 | 18 | 10 | 2 |
| | | (15) | (65) | (15) | (5) | (9) | (83) | (9) | (0) | (0) | (63) | (29) | (8) | (0) | (60) | (33) | (7) | |
| | pyelitis | | 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) |
| | mineralization:pelvis | | 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) |
| {Endocrine system} | | | | | | | | | | | | | | | | | | |
| pituitary | | | <40> | | | | <35> | | | | <38> | | | | <30> | | | |
| | angiectasis | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (3) | (0) | (0) |
| | cyst | | 0 | 1 | 0 | 0 | 1 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (3) | (0) | (0) | (3) | (6) | (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. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 9

| Organ_____ | Findings_____ | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|--------------------|---------------------------|-------------------------|---------|-------|------|------|-------|-------|------|------|--------|------|------|------|--------|-------|------|------|
| | | No. of Animals on Study | 40 | | | | 35 | | | | 38 | | | | 30 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Endocrine system} | | | | | | | | | | | | | | | | | | |
| pituitary | | | <40> | | | | <35> | | | | <38> | | | | <30> | | | |
| | deposit of hemosiderin | | 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) |
| | hyperplasia | | 4 | 5 | 0 | 0 | 3 | 4 | 0 | 0 | 4 | 3 | 0 | 0 | 2 | 1 | 0 | 0 |
| | | | (10) | (13) | (0) | (0) | (9) | (11) | (0) | (0) | (11) | (8) | (0) | (0) | (7) | (3) | (0) | (0) |
| | Rathke pouch | | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| | | | (0) | (0) | (0) | (0) | (9) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | |
| thyroid | | | <40> | | | | <35> | | | | <38> | | | | <30> | | | |
| | follicular hyperplasia | | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| | | | (0) | (3) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) |
| | C-cell hyperplasia | | 1 | 3 | 3 | 0 | 2 | 4 | 1 | 0 | 8 | 1 | 0 | 0 * | 1 | 3 | 0 | 0 |
| | | | (3) | (8) | (8) | (0) | (6) | (11) | (3) | (0) | (21) | (3) | (0) | (0) | (3) | (10) | (0) | (0) |
| adrenal | | | <40> | | | | <35> | | | | <38> | | | | <30> | | | |
| | hyperplasia:cortical cell | | 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) |
| | hyperplasia:medulla | | 0 | 5 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 2 | 0 | 0 | 2 | 3 | 0 | 0 |
| | | | (0) | (13) | (0) | (0) | (3) | (3) | (0) | (0) | (3) | (5) | (0) | (0) | (7) | (10) | (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. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 10

| | | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|-----------------------|-------------------------------|-------------------------|---------|-------|-------|-------|--------|--------|-------|-------|--------|-------|-------|-------|--------|--------|-------|-------|
| | | No. of Animals on Study | 40 | | | | 35 | | | | 38 | | | | 30 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| Organ_____ | Findings_____ | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| <hr/> | | | | | | | | | | | | | | | | | | |
| {Reproductive system} | | | | | | | | | | | | | | | | | | |
| testis | | | <40> | | | | <35> | | | | <38> | | | | <30> | | | |
| | atrophy | | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (5) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) |
| | mineralization | | 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) |
| | arteritis | | 1 | 2 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (3) | (5) | (0) | (0) | (3) | (3) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (0) | (0) | (0) |
| | interstitial cell hyperplasia | | 6 | 3 | 0 | 0 | 6 | 3 | 0 | 0 | 8 | 1 | 0 | 0 | 2 | 1 | 0 | 0 |
| | | | (15) | (8) | (0) | (0) | (17) | (9) | (0) | (0) | (21) | (3) | (0) | (0) | (7) | (3) | (0) | (0) |
| prostate | | | <40> | | | | <35> | | | | <38> | | | | <30> | | | |
| | 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) | (3) | (0) | (0) |
| | hyperplasia | | 1 | 2 | 2 | 0 | 2 | 4 | 1 | 0 | 3 | 2 | 1 | 0 | 4 | 5 | 1 | 0 |
| | | | (3) | (5) | (5) | (0) | (6) | (11) | (3) | (0) | (8) | (5) | (3) | (0) | (13) | (17) | (3) | (0) |
| prep/cli gl | | | <40> | | | | <35> | | | | <38> | | | | <30> | | | |
| | duct ectasia | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (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. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 11

| Organ | Findings | Group Name No. of Animals on Study Grade | Control 40 | | | | 25ppm 35 | | | | 100ppm 38 | | | | 400ppm 30 | | | |
|----------------------------------|---------------------------------|--|---------------|-------|-------|-------|-------------|-------|-------|--------|--------------|-------|-------|-------|--------------|-------|-------|-------|
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Nervous system} | | | | | | | | | | | | | | | | | | |
| brain | | | <40> | | | | <35> | | | | <38> | | | | <30> | | | |
| | angiectasis | | 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) | (0) |
| {Special sense organs/appendage} | | | | | | | | | | | | | | | | | | |
| eye | | | <40> | | | | <35> | | | | <38> | | | | <30> | | | |
| | cataract | | 2 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (5) | (0) | (0) | (0) | (9) | (0) | (0) | (0) | (13) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) |
| | retinal atrophy | | 2 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 0 | 5 | 0 | 0 * | 0 | 2 | 0 | 0 |
| | | (5) | (0) | (0) | (0) | (6) | (3) | (0) | (0) | (0) | (13) | (0) | (0) | (0) | (7) | (0) | (0) | (0) |
| | keratitis | | 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) |
| | squamous cell metaplasia:cornea | | 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) | (0) | (0) | (0) | (0) |
| nasolacr d | | | <40> | | | | <35> | | | | <38> | | | | <30> | | | |
| | squamous cell metaplasia | | 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) | (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. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 12

| Organ | Findings | Group Name No. of Animals on Study Grade | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|-------|----------|--|---------|-----|-----|-----|-------|-----|-----|-----|--------|-----|-----|-----|--------|-----|-----|-----|
| | | | 40 | | | | 35 | | | | 38 | | | | 30 | | | |
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |

{Body cavities}

| | | | | | | | | | | | | | | | | | |
|---------|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| adipose | granulation | <40> | | | | <35> | | | | <38> | | | | <30> | | | |
| | | 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) |

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

(HPT150)

BAIS4

APPENDIX L 4

HISTOPATHOLOGICAL FINDINGS :
NON-NEOPLASTIC LESIONS : SUMMARY,
RAT : FEMALE :
ALL ANIMALS
(2-YEAR STUDY)

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 16

| Organ | Findings | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|----------------------------------|--|-------------------------|---------|--------|--------|-------|-------|--------|--------|-------|--------|--------|--------|-------|--------|--------|-------|-------|
| | | No. of Animals on Study | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Integumentary system/appandage} | | | | | | | | | | | | | | | | | | |
| skin/app | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | inflammation | | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | (0) | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) |
| | epidermal cyst | | 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) | (4) | (0) | (0) |
| {Respiratory system} | | | | | | | | | | | | | | | | | | |
| nasal cavit | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | mineralization | | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (6) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | eosinophilic change:olfactory epithelium | | 3 | 33 | 12 | 0 | 0 | 27 | 23 | 0 * | 1 | 32 | 17 | 0 | 1 | 43 | 3 | 0 * |
| | | | (6) | (66) | (24) | (0) | (0) | (54) | (46) | (0) | (2) | (64) | (34) | (0) | (2) | (86) | (6) | (0) |
| | eosinophilic change:respiratory epithelium | | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 6 | 0 | 0 | 0 * | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (12) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | inflammation:foreign body | | 1 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 1 | 0 | 0 |
| | | | (2) | (2) | (0) | (0) | (2) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (4) | (2) | (0) | (0) |
| | inflammation:respiratory epithelium | | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 12 | 1 | 0 | 0 ** |
| | | | (0) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (24) | (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 ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 17

| Organ | Findings | Group Name No. of Animals on Study Grade | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|-------|----------|--|---------|-----|-----|-----|-------|-----|-----|-----|--------|-----|-----|-----|--------|-----|-----|-----|
| | | | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |

| | | | | | | | | | | | | | | | | | | |
|---|--|--|--------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|
| {Respiratory system} | | | | | | | | | | | | | | | | | | |
| nasal cavit | | | | | | | | | | | | | | | | | | |
| | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| respiratory metaplasia:olfactory 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) |
| respiratory metaplasia:gland | | | 17 | 15 | 0 | 0 | 22 | 16 | 0 | 0 | 25 | 18 | 0 | 0 * | 3 | 30 | 0 | 0 ** |
| | | | (34) | (30) | (0) | (0) | (44) | (32) | (0) | (0) | (50) | (36) | (0) | (0) | (6) | (60) | (0) | (0) |
| squamous cell metaplasia:respiratory epithelium | | | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 2 | 0 | 0 | 0 | 16 | 9 | 0 | 0 ** |
| | | | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (4) | (0) | (0) | (0) | (32) | (18) | (0) | (0) |
| hyperplasia with atypia:transitional epithelium | | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 1 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (2) | (2) | (0) | (0) |
| atrophy:olfactory epithelium | | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 21 | 16 | 2 | 0 ** |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (42) | (32) | (4) | (0) |
| necrosis: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) |
| lung | | | | | | | | | | | | | | | | | | |
| inflammatory infiltration | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 1 | 0 | 0 |
| | | | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (2) | (2) | (0) | (0) |
| bronchiolar-alveolar cell hyperplasia | | | 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) | (0) | (0) | (0) | (0) |

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

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

b b : Number of animals with lesion

(c) c : b / a * 100

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

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 18

| | | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|------------------------|------------------------------|-------------------------|---------|-------|------|------|-------|-------|------|------|--------|-------|------|------|--------|-------|------|------|
| | | 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 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| (Hematopoietic system) | | | | | | | | | | | | | | | | | | |
| bone marrow | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | granulation | | 5 | 0 | 0 | 0 | 5 | 1 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 1 | 0 | 0 |
| | | | (10) | (0) | (0) | (0) | (10) | (2) | (0) | (0) | (4) | (0) | (0) | (0) | (4) | (2) | (0) | (0) |
| | | | | | | | | | | | | | | | | | | |
| | histiocytosis | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| | increased hematopoiesis | | 2 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 11 | 0 | 0 | 0 * |
| | | | (4) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (22) | (0) | (0) | (0) |
| spleen | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | deposit of hemosiderin | | 2 | 38 | 4 | 0 | 1 | 43 | 1 | 0 | 1 | 38 | 2 | 0 | 1 | 28 | 0 | 0 ** |
| | | | (4) | (76) | (8) | (0) | (2) | (86) | (2) | (0) | (2) | (76) | (4) | (0) | (2) | (56) | (0) | (0) |
| | | | | | | | | | | | | | | | | | | |
| | fibrosis: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) |
| | extramedullary hematopoiesis | | 0 | 4 | 1 | 0 | 0 | 3 | 0 | 0 | 0 | 5 | 2 | 0 | 0 | 9 | 3 | 0 |
| | | | (0) | (8) | (2) | (0) | (0) | (6) | (0) | (0) | (0) | (10) | (4) | (0) | (0) | (18) | (6) | (0) |
| (Circulatory system) | | | | | | | | | | | | | | | | | | |
| heart | | | <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) |

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. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 19

| Organ_____ | Findings_____ | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|----------------------|---------------------------|-------------------------|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
| | | 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 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| | | | | | | | | | | | | | | | | | | |
| {Circulatory system} | | | | | | | | | | | | | | | | | | |
| heart | | | | | | | | | | | | | | | | | | |
| | inflammatory infiltration | | <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) |
| | fibrosis:focal | | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (2) | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) |
| | myocardial fibrosis | | 7 | 0 | 0 | 0 | 11 | 0 | 0 | 0 | 13 | 3 | 0 | 0 | 11 | 0 | 0 | 0 |
| | | | (14) | (0) | (0) | (0) | (22) | (0) | (0) | (0) | (26) | (6) | (0) | (0) | (22) | (0) | (0) | (0) |
| | | | | | | | | | | | | | | | | | | |
| {Digestive system} | | | | | | | | | | | | | | | | | | |
| tooth | | | | | | | | | | | | | | | | | | |
| | inflammation | | <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) |
| | | | | | | | | | | | | | | | | | | |
| tongue | | | | | | | | | | | | | | | | | | |
| | inflammation | | <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) |
| | squamous cell hyperplasia | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 1 | 1 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (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. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 20

| | | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|--------------------|-------------------------------|-------------------------|---------|-------|-------|-------|-------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
| | | No. of Animals on Study | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| Organ | Findings | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| <hr/> | | | | | | | | | | | | | | | | | | |
| {Digestive system} | | | | | | | | | | | | | | | | | | |
| tongue | | | | | | | | | | | | | | | | | | |
| | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | arteritis | | 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) |
| stomach | | | | | | | | | | | | | | | | | | |
| | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | basal cell hyperplasia | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | ulcer:forestomach | | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 1 | 0 | 0 |
| | | | (0) | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (2) | (0) | (0) | (2) | (2) | (0) | (0) |
| | hyperplasia:forestomach | | 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) |
| | inflammation:forestomach | | 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) |
| | erosion:glandular stomach | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| | ulcer:glandular stomach | | 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) |
| | hyperplasia:glandular stomach | | 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 ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 21

| Organ | Findings | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|--------------------|--------------------------------|-------------------------|---------|-------|------|------|-------|-------|------|------|--------|-------|------|------|--------|-------|------|------|
| | | 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 | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | inflammation:glandular stomach | | 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) |
| small intes | | | <50> | | | | <50> | | | | <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) |
| liver | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | herniation | | 0 | 9 | 0 | 0 | 0 | 9 | 0 | 0 | 0 | 10 | 0 | 0 | 0 | 6 | 0 | 0 |
| | | | (0) | (18) | (0) | (0) | (0) | (18) | (0) | (0) | (0) | (20) | (0) | (0) | (0) | (12) | (0) | (0) |
| | necrosis:central | | 0 | 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) |
| | fatty change | | 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) | (0) | (0) |
| | fatty change:central | | 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) |
| | granulation | | 7 | 13 | 1 | 0 | 5 | 5 | 0 | 0 | 0 | 3 | 0 | 0 ** | 1 | 2 | 0 | 0 ** |
| | | | (14) | (26) | (2) | (0) | (10) | (10) | (0) | (0) | (0) | (6) | (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 ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square

STUDY NO. : 0417
ANIMAL : RAT 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 | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|--------------------|------------------------|---------------------------------------|--------|-------|-------|---------|--------|-------|-------|--------|--------|-------|-------|--------|--------|--------|-------|--------|--------|--------|-------|
| | | Grade | | | | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Digestive system} | | | | | | | | | | | | | | | | | | | | | |
| liver | | | | | | | | | | | | | | | | | | | | | |
| | inflammatory cell nest | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | (0) | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| | clear cell focus | 3 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 7 | 0 | 0 | 0 | 1 | 12 | 20 | 1 ** | (2) | (24) | (40) | (2) |
| | | (6) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (14) | (0) | (0) | (0) | (2) | (24) | (40) | (2) | (2) | (24) | (40) | (2) |
| | acidophilic cell focus | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 4 | 9 | 0 | 0 ** | (8) | (18) | (0) | (0) |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (8) | (18) | (0) | (0) | (8) | (18) | (0) | (0) |
| | basophilic cell focus | 15 | 8 | 0 | 0 | 9 | 5 | 0 | 0 | 11 | 9 | 0 | 0 | 1 | 5 | 0 | 0 ** | (30) | (16) | (0) | (0) |
| | | (30) | (16) | (0) | (0) | (18) | (10) | (0) | (0) | (22) | (18) | (0) | (0) | (2) | (10) | (0) | (0) | (30) | (16) | (0) | (0) |
| | bile duct hyperplasia | 1 | 3 | 0 | 0 | 4 | 7 | 0 | 0 | 17 | 12 | 0 | 0 ** | 13 | 9 | 0 | 0 ** | (2) | (6) | (0) | (0) |
| | | (2) | (6) | (0) | (0) | (8) | (14) | (0) | (0) | (34) | (24) | (0) | (0) | (26) | (18) | (0) | (0) | (2) | (6) | (0) | (0) |
| | biliary cyst | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | (0) | (2) | (0) | (0) |
| | | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) |
| pancreas | | | | | | | | | | | | | | | | | | | | | |
| | atrophy | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 1 | 3 | 0 | 0 | 1 | 5 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 |
| | | (2) | (6) | (0) | (0) | (2) | (10) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (4) | (0) | (0) |
| | hyperplasia | 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. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 23

| | | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|--------------------|-------------------------------------|-------------------------|---------|-------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|--------|--------|--------|-------|
| | | 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 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Urinary system} | | | | | | | | | | | | | | | | | | |
| kidney | | | | | | | | | | | | | | | | | | |
| | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | hyperplasia:tubular epithelial cell | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (4) | (0) | (0) |
| | deposit of hemosiderin | | 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) | (4) | (0) | (0) |
| | chronic nephropathy | | 20 | 2 | 0 | 0 | 11 | 12 | 1 | 0 * | 19 | 17 | 1 | 1 ** | 9 | 31 | 5 | 0 ** |
| | | | (40) | (4) | (0) | (0) | (22) | (24) | (2) | (0) | (38) | (34) | (2) | (2) | (18) | (62) | (10) | (0) |
| | tubular necrosis | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | mineralization:papilla | | 0 | 2 | 0 | 0 | 0 | 4 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | (0) | (4) | (0) | (0) | (0) | (8) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (2) | (0) | (0) |
| | mineralization:pelvis | | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 4 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (8) | (0) | (0) |
| | glomerulosclerosis | | 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) |
| {Endocrine system} | | | | | | | | | | | | | | | | | | |
| pituitary | | | | | | | | | | | | | | | | | | |
| | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | angiectasis | | 1 | 4 | 0 | 0 | 3 | 4 | 0 | 0 | 3 | 1 | 0 | 0 | 0 | 3 | 0 | 0 |
| | | | (2) | (8) | (0) | (0) | (6) | (8) | (0) | (0) | (6) | (2) | (0) | (0) | (0) | (6) | (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. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 24

| Organ_____ | Findings_____ | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|-----------------------------|----------------------|-------------------------|---------|------|-------|-------|-------|------|-------|-------|--------|------|------|------|--------|------|------|-----|
| | | 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 | 2 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 2 | 0 | 0 | |
| | | (4) | (4) | (0) | (0) | (2) | (2) | (0) | (0) | (2) | (2) | (0) | (0) | (2) | (4) | (0) | (0) | |
| | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | |
| hyperplasia | 2 | 8 | 0 | 0 | 3 | 12 | 0 | 0 | 4 | 5 | 0 | 0 | 4 | 4 | 0 | 0 | | |
| | (4) | (16) | (0) | (0) | (6) | (24) | (0) | (0) | (8) | (10) | (0) | (0) | (8) | (8) | (0) | (0) | | |
| | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | |
| Rathke pouch | 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) | | |
| | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | |
| thyroid | 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) | |
| | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | |
| ultimibranhial body remanet | 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) | | |
| | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | |
| follicular hyperplasia | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | | |
| | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | | |
| | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | |
| C-cell hyperplasia | 4 | 3 | 0 | 0 | 10 | 6 | 0 | 0 | 7 | 4 | 0 | 0 | 2 | 3 | 0 | 0 | | |
| | (8) | (6) | (0) | (0) | (20) | (12) | (0) | (0) | (14) | (8) | (0) | (0) | (4) | (6) | (0) | (0) | | |
| | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | |
| adrenal | peliosis-like lesion | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | |
| | | (4) | (2) | (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 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. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 25

| | | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|-----------------------|--------------------------------|-------------------------|---------|------|------|------|-------|------|------|------|--------|------|------|------|--------|------|------|------|
| | | 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} | | | | | | | | | | | | | | | | | | |
| adrenal | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | hyperplasia:medulla | | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| | focal fatty change:cortex | | 0 | 1 | 0 | 0 | 2 | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 2 | 0 | 0 |
| | | | (0) | (2) | (0) | (0) | (4) | (6) | (0) | (0) | (0) | (2) | (0) | (0) | (2) | (4) | (0) | (0) |
| {Reproductive system} | | | | | | | | | | | | | | | | | | |
| ovary | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | cyst | | 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) |
| uterus | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | blood retention | | 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) |
| | cystic endometrial hyperplasia | | 2 | 3 | 0 | 0 | 3 | 1 | 0 | 0 | 2 | 0 | 0 | 0 | 6 | 1 | 0 | 0 |
| | | | (4) | (6) | (0) | (0) | (6) | (2) | (0) | (0) | (4) | (0) | (0) | (0) | (12) | (2) | (0) | (0) |
| vagina | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | blood retention | | 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

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 26

| | | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|----------------------------------|--------------|-------------------------|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
| | | 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 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Reproductive system} | | | | | | | | | | | | | | | | | | |
| prep/cli gl | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | duct ectasia | | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) |
| {Nervous system} | | | | | | | | | | | | | | | | | | |
| brain | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | gliosis | | 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) |
| spinal cord | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | hemorrhage | | 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 | 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) |
| {Special sense organs/appendage} | | | | | | | | | | | | | | | | | | |
| eye | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | cataract | | 2 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (4) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (4) | (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. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 27

| Organ | Findings | Group Name No. of Animals on Study | | | | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|----------------------------------|---------------------------------|---------------------------------------|--------|-------|-------|---------|--------|-------|-------|-------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
| | | 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> | | | |
| | retinal atrophy | 0 | 2 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 2 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 1 | 0 | 0 |
| | | (0) | (4) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (4) | (0) | (0) | (2) | (2) | (0) | (0) | (2) | (2) | (0) | (0) |
| | iritis | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | squamous cell metaplasia:cornea | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (4) | (0) | (0) | (0) |
| Harder gl | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | inflammation | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| nasolacr d | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | inflammation | 2 | 5 | 0 | 0 | 1 | 3 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | (4) | (10) | (0) | (0) | (2) | (6) | (0) | (0) | (2) | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) |
| {Musculoskeletal system} | | | | | | | | | | | | | | | | | | | | | |
| bone | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | osteosclerosis | 4 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 3 | 3 | 1 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | (8) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (6) | (6) | (2) | (0) | (4) | (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 ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 28

| Organ_____ | Findings_____ | Group Name | | | | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|------------|---------------|-------------------------|-----|-----|-----|---------|-----|-----|-----|-------|-----|-----|-----|--------|-----|-----|-----|--------|--|--|--|
| | | No. of Animals on Study | | | | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | Grade | | | | | | | | | | | | | | | | | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | | | | |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | | | |

{Body cavities}

| | | | | | | | | | | | | | | | | | |
|------------|--------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| peritoneum | inflammation | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (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 : 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 : SUMMARY,
RAT : FEMALE :
DEAD AND MORIBUND ANIMALS
(2-YEAR STUDY)

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 12

| | | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|----------------------------------|---|-------------------------|---------|--------|-------|-------|--------|--------|--------|-------|--------|--------|--------|-------|--------|--------|-------|-------|
| | | No. of Animals on Study | 12 | | | | 5 | | | | 11 | | | | 24 | | | |
| Organ | Findings | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Integumentary system/appandage} | | | | | | | | | | | | | | | | | | |
| skin/app | | | <12> | | | | < 5> | | | | <11> | | | | <24> | | | |
| | epidermal 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) | (4) | (0) | (0) |
| {Respiratory system} | | | | | | | | | | | | | | | | | | |
| nasal cavit | | | <12> | | | | < 5> | | | | <11> | | | | <24> | | | |
| | eosinophilic change:olfactory epithelium | | 2 | 8 | 1 | 0 | 0 | 2 | 3 | 0 | 1 | 7 | 3 | 0 | 1 | 20 | 1 | 0 |
| | | | (17) | (67) | (8) | (0) | (0) | (40) | (60) | (0) | (9) | (64) | (27) | (0) | (4) | (83) | (4) | (0) |
| | inflammation:foreign body | | 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) | (4) | (0) | (0) | (0) |
| | inflammation:respiratory epithelium | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 6 | 1 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (25) | (4) | (0) | (0) |
| | respiratory metaplasia:gland | | 7 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 4 | 5 | 0 | 0 * | 1 | 15 | 0 | 0 ** |
| | | | (58) | (0) | (0) | (0) | (60) | (0) | (0) | (0) | (36) | (45) | (0) | (0) | (4) | (63) | (0) | (0) |
| | squamous cell metaplasia:respiratory epithelium | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 9 | 5 | 0 | 0 ** |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (18) | (0) | (0) | (0) | (38) | (21) | (0) | (0) |
| | atrophy:olfactory epithelium | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 9 | 2 | 0 ** |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (13) | (38) | (8) | (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. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 13

| Organ | Findings | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|------------------------|-------------------------------|-------------------------|---------|--------|--------|--------|-------|--------|--------|-------|--------|--------|-------|--------|--------|--------|-------|-------|
| | | No. of Animals on Study | 12 | | | | 5 | | | | 11 | | | | 24 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Respiratory system} | | | | | | | | | | | | | | | | | | |
| nasal cavit | necrosis:olfactory epithelium | | <12> | | | | < 5> | | | | <11> | | | | <24> | | | |
| | | 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) | (13) | (0) | (0) | (0) | |
| lung | inflammatory infiltration | | <12> | | | | < 5> | | | | <11> | | | | <24> | | | |
| | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | |
| | | | (0) | (8) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (4) | (0) | (0) | |
| {Hematopoietic system} | | | | | | | | | | | | | | | | | | |
| bone marrow | granulation | | <12> | | | | < 5> | | | | <11> | | | | <24> | | | |
| | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | |
| | | (0) | (0) | (0) | (0) | (20) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | |
| | increased hematopoiesis | | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 7 | 0 | 0 | 0 | |
| | | | (17) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (9) | (0) | (0) | (29) | (0) | (0) | (0) | |
| spleen | deposit of hemosiderin | | <12> | | | | < 5> | | | | <11> | | | | <24> | | | |
| | | 1 | 6 | 2 | 0 | 0 | 3 | 1 | 0 | 0 | 6 | 0 | 0 | 1 | 11 | 0 | 0 | |
| | | | (8) | (50) | (17) | (0) | (0) | (60) | (20) | (0) | (0) | (55) | (0) | (4) | (46) | (0) | (0) | |
| | extramedullary hematopoiesis | | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 7 | 2 | 0 | |
| | | | (0) | (0) | (8) | (0) | (0) | (0) | (0) | (0) | (0) | (18) | (9) | (0) | (0) | (29) | (8) | (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. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 14

| Organ | Findings | Group Name No. of Animals on Study | | | | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|----------------------|---------------------------|---------------------------------------|--------|-------|-------|---------|--------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
| | | Grade | | | | 12 | | | | 5 | | | | 11 | | | | 24 | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Circulatory system} | | | | | | | | | | | | | | | | | | | | | |
| heart | | <12> | | | | < 5> | | | | <11> | | | | <24> | | | | | | | |
| | thrombus | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (8) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | myocardial fibrosis | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 4 | 0 | 0 | 0 | 4 | 0 | 0 | 0 |
| | | (8) | (0) | (0) | (0) | (20) | (0) | (0) | (0) | (18) | (9) | (0) | (0) | (17) | (0) | (0) | (0) | (17) | (0) | (0) | (0) |
| {Digestive system} | | | | | | | | | | | | | | | | | | | | | |
| stomach | | <12> | | | | < 5> | | | | <11> | | | | <24> | | | | | | | |
| | ulcer:forestomach | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 1 | 0 | 0 |
| | | (0) | (17) | (0) | (0) | (0) | (0) | (0) | (0) | (9) | (9) | (0) | (0) | (4) | (4) | (0) | (0) | (4) | (4) | (0) | (0) |
| | hyperplasia:forestomach | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (4) | (0) | (0) |
| | inflammation:forestomach | 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) | (20) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | erosion:glandular stomach | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (8) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | ulcer:glandular stomach | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (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. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 15

| Organ | Findings | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|--------------------|------------------------|-------------------------|---------|--------|-------|-------|-------|--------|-------|-------|--------|-------|-------|-------|--------|--------|-------|-------|
| | | No. of Animals on Study | 12 | | | | 5 | | | | 11 | | | | 24 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Digestive system} | | | | | | | | | | | | | | | | | | |
| small intes | | | <12> | | | | < 5> | | | | <11> | | | | <24> | | | |
| | 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) | (4) | (0) | (0) |
| liver | | | <12> | | | | < 5> | | | | <11> | | | | <24> | | | |
| | herniation | | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 3 | 0 | 0 |
| | | | (0) | (17) | (0) | (0) | (0) | (20) | (0) | (0) | (0) | (9) | (0) | (0) | (0) | (13) | (0) | (0) |
| | necrosis:central | | 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) | (4) | (0) | (0) |
| | fatty change | | 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) | (0) | (0) |
| | fatty change:central | | 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) |
| | granulation | | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (17) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (18) | (0) | (0) | (0) | (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) | (4) | (0) | (0) | |
| | clear cell focus | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 6 | 5 | 0 * | |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (25) | (21) | (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. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 16

| Organ | Findings | Group Name No. of Animals on Study Grade | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|--------------------|-------------------------------------|--|---------|-------|-------|-------|--------|-------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|
| | | | 12 | | | | 5 | | | | 11 | | | | 24 | | | |
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Digestive system} | | | | | | | | | | | | | | | | | | |
| liver | | | | | | | | | | | | | | | | | | |
| | acidophilic cell focus | | <12> | | | | < 5> | | | | <11> | | | | <24> | | | |
| | | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 3 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (13) | (13) | (0) | (0) |
| | basophilic cell focus | | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | (8) | (0) | (0) | (0) | (20) | (0) | (0) | (0) | (9) | (0) | (0) | (0) | (0) | (4) | (0) | (0) |
| | bile duct hyperplasia | | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 4 | 0 | 0 | 3 | 6 | 0 | 0 |
| | | | (8) | (8) | (0) | (0) | (0) | (0) | (0) | (0) | (18) | (36) | (0) | (0) | (13) | (25) | (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) | (4) | (0) | (0) |
| {Urinary system} | | | | | | | | | | | | | | | | | | |
| kidney | | | | | | | | | | | | | | | | | | |
| | hyperplasia:tubular epithelial cell | | <12> | | | | < 5> | | | | <11> | | | | <24> | | | |
| | | | 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) | (4) | (0) | (0) |
| | deposit of hemosiderin | | 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) | (4) | (0) | (0) |
| | chronic nephropathy | | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 2 | 1 | 1 | 6 | 13 | 1 | 0 ** |
| | | | (17) | (8) | (0) | (0) | (0) | (0) | (0) | (0) | (18) | (18) | (9) | (9) | (25) | (54) | (4) | (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. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 17

| | | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|--------------------|------------------------|-------------------------|---------|-------|-------|-------|-------|--------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
| | | No. of Animals on Study | 12 | | | | 5 | | | | 11 | | | | 24 | | | |
| Organ | Findings | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Urinary system} | | | | | | | | | | | | | | | | | | |
| kidney | | | <12> | | | | < 5> | | | | <11> | | | | <24> | | | |
| | tubular necrosis | | 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) | (0) | (0) | (0) | (0) |
| | mineralization:papilla | | 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) | (4) | (0) | (0) |
| | mineralization:pelvis | | 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) | (4) | (0) | (0) |
| | glomerulosclerosis | | 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) |
| {Endocrine system} | | | | | | | | | | | | | | | | | | |
| pituitary | | | <12> | | | | < 5> | | | | <11> | | | | <24> | | | |
| | angiectasis | | 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) | (8) | (0) | (0) |
| | 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) | (9) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | hyperplasia | | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (8) | (0) | (0) | (0) | (20) | (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. : 0417
 ANIMAL : RAT 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 | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|-----------------------|--------------------------------|-------------------------|---------|------|------|------|-------|------|------|------|--------|------|------|------|--------|------|------|------|
| | | No. of Animals on Study | 12 | | | | 5 | | | | 11 | | | | 24 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| | | | | | | | | | | | | | | | | | | |
| {Endocrine system} | | | | | | | | | | | | | | | | | | |
| thyroid | | | <12> | | | | < 5> | | | | <11> | | | | <24> | | | |
| | C-cell hyperplasia | | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 |
| | | | (8) | (0) | (0) | (0) | (20) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (0) | (0) |
| adrenal | | | <12> | | | | < 5> | | | | <11> | | | | <24> | | | |
| | hyperplasia:medulla | | 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) | (4) | (0) | (0) | (0) | |
| {Reproductive system} | | | | | | | | | | | | | | | | | | |
| uterus | | | <12> | | | | < 5> | | | | <11> | | | | <24> | | | |
| | blood retention | | 1 | 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) | |
| | cystic endometrial hyperplasia | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | |
| | | | (0) | (8) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (4) | (0) | (0) | |
| vagina | | | <12> | | | | < 5> | | | | <11> | | | | <24> | | | |
| | blood retention | | 0 | 1 | 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) | |
| {Nervous system} | | | | | | | | | | | | | | | | | | |
| spinal cord | | | <12> | | | | < 5> | | | | <11> | | | | <24> | | | |
| | hemorrhage | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (9) | (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. : 0417
ANIMAL : RAT 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 No. of Animals on Study Grade | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|-------|----------|--|---------|-----|-----|-----|-------|-----|-----|-----|--------|-----|-----|-----|--------|-----|-----|-----|
| | | | 12 | | | | 5 | | | | 11 | | | | 24 | | | |
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |

{Special sense organs/appendage}

| | | | | | | | | | | | | | | | | | | |
|-----|---------------------------------|--|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| eye | | | <12> | | | | < 5> | | | | <11> | | | | <24> | | | |
| | cataract | | 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) | (4) | (0) | (0) | (0) |
| | retinal atrophy | | 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) | (4) | (4) | (0) | (0) |
| | iritis | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (8) | (0) | (0) | (0) | (0) | (0) | (0) | (9) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | squamous cell metaplasia:cornea | | 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) | (8) | (0) | (0) | (0) |

{Musculoskeletal system}

| | | | | | | | | | | | | | | | | | | |
|------|----------------|--|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| bone | | | <12> | | | | < 5> | | | | <11> | | | | <24> | | | |
| | osteosclerosis | | 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) | (8) | (0) | (0) | (0) |

{Body cavities}

| | | | | | | | | | | | | | | | | | | |
|------------|--------------|--|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| peritoneum | | | <12> | | | | < 5> | | | | <11> | | | | <24> | | | |
| | inflammation | | 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

APPENDIX L 6

HISTOPATHOLOGICAL FINDINGS :
NON-NEOPLASTIC LESIONS : SUMMARY,
RAT : FEMALE :
SACRIFICED ANIMALS
(2-YEAR STUDY)

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 13

| Organ | Findings | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|----------------------------------|--|-------------------------|--------|--------|-------|-------|--------|--------|-------|--------|--------|--------|-------|--------|--------|-------|-------|
| | | No. of Animals on Study | | | | 38 | | | | 45 | | | | 39 | | | |
| | | Grade | | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Integumentary system/appandage} | | | | | | | | | | | | | | | | | |
| skin/app | | <38> | | | | <45> | | | | <39> | | | | <26> | | | |
| | inflammation | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | (0) | (5) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (4) | (0) | (0) |
| | epidermal 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) | (4) | (0) | (0) |
| {Respiratory system} | | | | | | | | | | | | | | | | | |
| nasal cavit | | <38> | | | | <45> | | | | <39> | | | | <26> | | | |
| | mineralization | 3 | 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) | (0) | (0) | (0) | (0) |
| | eosinophilic change:olfactory epithelium | 1 | 25 | 11 | 0 | 0 | 25 | 20 | 0 | 0 | 25 | 14 | 0 | 0 | 23 | 2 | 0 |
| | | (3) | (66) | (29) | (0) | (0) | (56) | (44) | (0) | (0) | (64) | (36) | (0) | (0) | (88) | (8) | (0) |
| | eosinophilic change:respiratory epithelium | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 6 | 0 | 0 | 0 * | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (7) | (0) | (0) | (0) | (15) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | inflammation:foreign body | 1 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 1 | 0 | 0 |
| | | (3) | (3) | (0) | (0) | (2) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (4) | (4) | (0) | (0) |
| | inflammation:respiratory epithelium | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 6 | 0 | 0 | 0 ** |
| | | (0) | (0) | (0) | (0) | (7) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (23) | (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. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 14

| Organ_____ | Findings_____ | Group Name No. of Animals on Study Grade | Control 38 | | | | 25ppm 45 | | | | 100ppm 39 | | | | 400ppm 26 | | | |
|---------------------------------------|---|--|---------------|-------|------|------|-------------|-------|------|------|--------------|-------|------|-------|--------------|-------|------|------|
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Respiratory system} | | | | | | | | | | | | | | | | | | |
| nasal cavit | respiratory metaplasia:olfactory epithelium | | <38> | | | | <45> | | | | <39> | | | | <26> | | | |
| | | | 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) |
| | respiratory metaplasia:gland | | 10 | 15 | 0 | 0 | 19 | 16 | 0 | 0 | 21 | 13 | 0 | 0 * | 2 | 15 | 0 | 0 |
| | | | (26) | (39) | (0) | (0) | (42) | (36) | (0) | (0) | (54) | (33) | (0) | (0) | (8) | (58) | (0) | (0) |
| | squamous cell metaplasia:respiratory epithelium | | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 7 | 4 | 0 | 0 ** |
| | | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (27) | (15) | (0) | (0) | |
| lung | hyperplasia with atypia:transitional epithelium | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 1 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (4) | (4) | (0) | (0) |
| | atrophy:olfactory epithelium | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 18 | 7 | 0 | 0 ** |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (69) | (27) | (0) | (0) |
| | necrosis:olfactory epithelium | | 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) | (19) | (0) | (0) | (0) |
| inflammatory infiltration | | <38> | | | | <45> | | | | <39> | | | | <26> | | | | |
| | | | 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) | (0) | (0) | (0) |
| bronchiolar-alveolar cell hyperplasia | | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |

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

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 15

| | | Group Name No. of Animals on Study | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | | |
|------------------------|------------------------------|---------------------------------------|--------|--------|-------|-------|-------|--------|-------|--------|-------|--------|-------|--------|--------|--------|-------|-------|
| | | Control | | | | | | | | | | | | | | | | |
| | | 38 | | | | 45 | | | | 39 | | | | 26 | | | | |
| Organ | Findings | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | | | | | | | | | | | | | | | | |
| {Hematopoietic system} | | | | | | | | | | | | | | | | | | |
| bone marrow | | | <38> | | | | <45> | | | | <39> | | | | <26> | | | |
| | granulation | | 5 | 0 | 0 | 0 | 4 | 1 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 1 | 0 | 0 |
| | | | (13) | (0) | (0) | (0) | (9) | (2) | (0) | (0) | (5) | (0) | (0) | (0) | (4) | (4) | (0) | (0) |
| | | | | | | | | | | | | | | | | | | |
| | histiocytosis | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) |
| | increased hematopoiesis | | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 4 | 0 | 0 | 0 * |
| | | | (0) | (0) | (0) | (0) | (7) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (15) | (0) | (0) | (0) |
| spleen | | | <38> | | | | <45> | | | | <39> | | | | <26> | | | |
| | deposit of hemosiderin | | 1 | 32 | 2 | 0 | 1 | 40 | 0 | 0 | 1 | 32 | 2 | 0 | 0 | 17 | 0 | 0 * |
| | | | (3) | (84) | (5) | (0) | (2) | (89) | (0) | (0) | (3) | (82) | (5) | (0) | (0) | (65) | (0) | (0) |
| | | | | | | | | | | | | | | | | | | |
| | fibrosis:focal | | 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) |
| | extramedullary hematopoiesis | | 0 | 4 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 3 | 1 | 0 | 0 | 2 | 1 | 0 |
| | | | (0) | (11) | (0) | (0) | (0) | (7) | (0) | (0) | (0) | (8) | (3) | (0) | (0) | (8) | (4) | (0) |
| {Circulatory system} | | | | | | | | | | | | | | | | | | |
| heart | | | <38> | | | | <45> | | | | <39> | | | | <26> | | | |
| | inflammatory 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) |

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. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 16

| | | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|----------------------|---------------------------|-------------------------|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
| | | No. of Animals on Study | 38 | | | | 45 | | | | 39 | | | | 26 | | | |
| Organ | Findings | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Circulatory system} | | | | | | | | | | | | | | | | | | |
| heart | | | <38> | | | | <45> | | | | <39> | | | | <26> | | | |
| | fibrosis:focal | | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (2) | (2) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) |
| | myocardial fibrosis | | 6 | 0 | 0 | 0 | 10 | 0 | 0 | 0 | 11 | 2 | 0 | 0 | 7 | 0 | 0 | 0 |
| | | | (16) | (0) | (0) | (0) | (22) | (0) | (0) | (0) | (28) | (5) | (0) | (0) | (27) | (0) | (0) | (0) |
| {Digestive system} | | | | | | | | | | | | | | | | | | |
| tooth | | | <38> | | | | <45> | | | | <39> | | | | <26> | | | |
| | 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) | (4) | (0) | (0) |
| tongue | | | <38> | | | | <45> | | | | <39> | | | | <26> | | | |
| | 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) | (4) | (0) | (0) |
| | squamous cell hyperplasia | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 1 | 1 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) | (4) | (4) | (0) | (0) | |
| | arteritis | | 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. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 17

| Organ | Findings | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|--------------------|--------------------------------|-------------------------|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
| | | No. of Animals on Study | 38 | | | | 45 | | | | 39 | | | | 26 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Digestive system} | | | | | | | | | | | | | | | | | | |
| stomach | | | <38> | | | | <45> | | | | <39> | | | | <26> | | | |
| | basal cell hyperplasia | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | hyperplasia:forestomach | | 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) |
| | erosion:glandular stomach | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (4) | (0) | (0) | (0) |
| liver | ulcer:glandular stomach | | 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) | (4) | (0) | (0) | (0) |
| | hyperplasia:glandular stomach | | 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) |
| | inflammation:glandular stomach | | 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) | (4) | (0) | (0) |
| herniation | | <38> | | | | <45> | | | | <39> | | | | <26> | | | | |
| | | 0 | 7 | 0 | 0 | 0 | 8 | 0 | 0 | 0 | 9 | 0 | 0 | 0 | 3 | 0 | 0 | |
| | | (0) | (18) | (0) | (0) | (0) | (18) | (0) | (0) | (0) | (23) | (0) | (0) | (0) | (12) | (0) | (0) | |
| necrosis:central | | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| | | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | |

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

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 18

| Organ | Findings | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | | |
|--------------------|------------------------|-------------------------|---------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|--------|--------|--------|-------|----|
| | | No. of Animals on Study | 38 | | | | 45 | | | | 39 | | | | 26 | | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | |
| {Digestive system} | | | | | | | | | | | | | | | | | | | |
| liver | | | | | | | | | | | | | | | | | | | |
| | granulation | | <38> | | | | <45> | | | | <39> | | | | <26> | | | | |
| | | | 7 | 11 | 1 | 0 | 5 | 5 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 2 | 0 | 0 |
| | | | (18) | (29) | (3) | (0) | (11) | (11) | (0) | (0) | (0) | (3) | (0) | (0) | (4) | (8) | (0) | (0) | |
| | inflammatory cell nest | | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (5) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | |
| | clear cell focus | | 3 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 7 | 0 | 0 | 0 | 1 | 6 | 15 | 1 | ** |
| | | | (8) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (18) | (0) | (0) | (0) | (4) | (23) | (58) | (4) | |
| | acidophilic cell focus | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 6 | 0 | 0 | ** |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (4) | (23) | (0) | (0) | |
| | basophilic cell focus | | 14 | 8 | 0 | 0 | 8 | 5 | 0 | 0 * | 10 | 9 | 0 | 0 | 1 | 4 | 0 | 0 | ** |
| | | | (37) | (21) | (0) | (0) | (18) | (11) | (0) | (0) | (26) | (23) | (0) | (0) | (4) | (15) | (0) | (0) | |
| | bile duct hyperplasia | | 0 | 2 | 0 | 0 | 4 | 7 | 0 | 0 * | 15 | 8 | 0 | 0 ** | 10 | 3 | 0 | 0 | ** |
| | | | (0) | (5) | (0) | (0) | (9) | (16) | (0) | (0) | (38) | (21) | (0) | (0) | (38) | (12) | (0) | (0) | |
| | biliary cyst | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | |
| pancreas | | | | | | | | | | | | | | | | | | | |
| | atrophy | | <38> | | | | <45> | | | | <39> | | | | <26> | | | | |
| | | | 1 | 3 | 0 | 0 | 1 | 5 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | | (3) | (8) | (0) | (0) | (2) | (11) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (8) | (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. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 19

| | | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|--------------------|-------------------------------------|-------------------------|---------|-------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|--------|--------|--------|-------|
| | | No. of Animals on Study | 38 | | | | 45 | | | | 39 | | | | 26 | | | |
| Organ_____ | Findings_____ | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Digestive system} | | | | | | | | | | | | | | | | | | |
| pancreas | | | <38> | | | | <45> | | | | <39> | | | | <26> | | | |
| | 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) | (4) | (0) | (0) |
| {Urinary system} | | | | | | | | | | | | | | | | | | |
| kidney | | | <38> | | | | <45> | | | | <39> | | | | <26> | | | |
| | hyperplasia:tubular epithelial cell | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (4) | (0) | (0) |
| | deposit of hemosiderin | | 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) | (4) | (0) | (0) |
| | chronic nephropathy | | 18 | 1 | 0 | 0 | 11 | 12 | 1 | 0 ** | 17 | 15 | 0 | 0 ** | 3 | 18 | 4 | 0 ** |
| | | | (47) | (3) | (0) | (0) | (24) | (27) | (2) | (0) | (44) | (38) | (0) | (0) | (12) | (69) | (15) | (0) |
| | tubular necrosis | | 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 | 2 | 0 | 0 | 0 | 4 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (5) | (0) | (0) | (0) | (9) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | mineralization:pelvis | | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 3 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (12) | (0) | (0) |

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

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 20

| Organ | Findings | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|--------------------|-----------------------------|-------------------------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|
| | | No. of Animals on Study | | | | Grade | | | | Grade | | | | Grade | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Endocrine system} | | | | | | | | | | | | | | | | | |
| pituitary | | <38> | | | | <45> | | | | <39> | | | | <26> | | | |
| | angiectasis | 1 | 4 | 0 | 0 | 3 | 4 | 0 | 0 | 3 | 1 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | (3) | (11) | (0) | (0) | (7) | (9) | (0) | (0) | (8) | (3) | (0) | (0) | (0) | (4) | (0) | (0) |
| | cyst | 2 | 2 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 2 | 0 | 0 |
| | | (5) | (5) | (0) | (0) | (2) | (2) | (0) | (0) | (3) | (0) | (0) | (0) | (4) | (8) | (0) | (0) |
| | hyperplasia | 2 | 7 | 0 | 0 | 3 | 11 | 0 | 0 | 4 | 5 | 0 | 0 | 3 | 4 | 0 | 0 |
| | | (5) | (18) | (0) | (0) | (7) | (24) | (0) | (0) | (10) | (13) | (0) | (0) | (12) | (15) | (0) | (0) |
| | Rathke pouch | 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) |
| thyroid | | <38> | | | | <45> | | | | <39> | | | | <26> | | | |
| | 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) | (4) | (0) | (0) |
| | ultimibranhial body remanet | 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) |
| | follicular hyperplasia | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (4) | (0) | (0) |
| | C-cell hyperplasia | 3 | 3 | 0 | 0 | 9 | 6 | 0 | 0 | 7 | 4 | 0 | 0 | 2 | 1 | 0 | 0 |
| | | (8) | (8) | (0) | (0) | (20) | (13) | (0) | (0) | (18) | (10) | (0) | (0) | (8) | (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. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 21

| | | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | | |
|-----------------------|--------------------------------|-------------------------|---------|------|------|------|-------|------|------|------|--------|------|------|------|--------|------|------|------|------|
| | | No. of Animals on Study | 38 | | | | 45 | | | | 39 | | | | 26 | | | | |
| Organ | Findings | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | |
| {Endocrine system} | | | | | | | | | | | | | | | | | | | |
| adrenal | | | <38> | | | | <45> | | | | <39> | | | | <26> | | | | |
| | peliosis-like lesion | | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (5) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | hyperplasia:medulla | | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (5) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | |
| | focal fatty change:cortex | | 0 | 1 | 0 | 0 | 2 | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 2 | 0 | 0 | |
| | | | (0) | (3) | (0) | (0) | (4) | (7) | (0) | (0) | (0) | (3) | (0) | (0) | (4) | (8) | (0) | (0) | |
| {Reproductive system} | | | | | | | | | | | | | | | | | | | |
| ovary | | | <38> | | | | <45> | | | | <39> | | | | <26> | | | | |
| | cyst | | 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) | (3) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | |
| uterus | | | <38> | | | | <45> | | | | <39> | | | | <26> | | | | |
| | cystic endometrial hyperplasia | | 2 | 2 | 0 | 0 | 3 | 1 | 0 | 0 | 2 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 0 |
| | | | (5) | (5) | (0) | (0) | (7) | (2) | (0) | (0) | (5) | (0) | (0) | (0) | (15) | (0) | (0) | (0) | |
| prep/cli gl | | | <38> | | | | <45> | | | | <39> | | | | <26> | | | | |
| | duct ectasia | | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (3) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (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 : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 22

| | | Group Name | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|----------------------------------|-----------------|-------------------------|---------|-------|--------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
| | | No. of Animals on Study | 38 | | | | 45 | | | | 39 | | | | 26 | | | |
| Organ | Findings | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| {Nervous system} | | | | | | | | | | | | | | | | | | |
| brain | gliosis | | <38> | | | | <45> | | | | <39> | | | | <26> | | | |
| | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| spinal cord | gliosis | | <38> | | | | <45> | | | | <39> | | | | <26> | | | |
| | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| {Special sense organs/appendage} | | | | | | | | | | | | | | | | | | |
| eye | cataract | | <38> | | | | <45> | | | | <39> | | | | <26> | | | |
| | | 2 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | (5) | (0) | (0) | (0) | (11) | (0) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | |
| | retinal atrophy | | <38> | | | | <45> | | | | <39> | | | | <26> | | | |
| | | 0 | 2 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (5) | (0) | (0) | (0) | (11) | (0) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (0) | (0) | (0) |
| Harder gl | inflammation | | <38> | | | | <45> | | | | <39> | | | | <26> | | | |
| | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| nasolacr d | inflammation | | <38> | | | | <45> | | | | <39> | | | | <26> | | | |
| | | 2 | 5 | 0 | 0 | 1 | 3 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (5) | (13) | (0) | (0) | (2) | (7) | (0) | (0) | (3) | (3) | (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 : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 23

| Organ_____ | Findings_____ | Group Name | | | | Control | | | | 25ppm | | | | 100ppm | | | | 400ppm | | | |
|------------|---------------|-------------------------|-----|-----|-----|---------|-----|-----|-----|-------|-----|-----|-----|--------|-----|-----|-----|--------|--|--|--|
| | | No. of Animals on Study | | | | 38 | | | | 45 | | | | 39 | | | | 26 | | | |
| | | Grade | | | | | | | | | | | | | | | | | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | | | | |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | | | |

{Musculoskeletal system}

| | | | | | | | | | | | | | | | | | |
|------|----------------|-------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| bone | osteosclerosis | <38> | | | | <45> | | | | <39> | | | | <26> | | | |
| | | 4 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 3 | 3 | 1 | 0 | 0 | 0 | 0 | 0 |
| | | (11) | (0) | (0) | (0) | (7) | (0) | (0) | (0) | (8) | (8) | (3) | (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 M 1

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

RAT : MALE

(2-YEAR STUDY)

STUDY NO. : 0417
 ANIMAL : RAT 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 | 25ppm | 100ppm | 400ppm |
|-----------------------|-------------------------------------|------------|---------|-------|--------|--------|
| 0 - 52 | NO. OF EXAMINED ANIMALS | | 0 | 1 | 2 | 2 |
| | NO. OF ANIMALS WITH TUMORS | | 0 | 1 | 1 | 1 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 0 | 1 | 1 | 1 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 0 | 0 | 0 | 0 |
| | NO. OF BENIGN TUMORS | | 0 | 0 | 0 | 0 |
| | NO. OF MALIGNANT TUMORS | | 0 | 1 | 1 | 1 |
| | NO. OF TOTAL TUMORS | | 0 | 1 | 1 | 1 |
| 53 - 78 | NO. OF EXAMINED ANIMALS | | 4 | 4 | 0 | 3 |
| | NO. OF ANIMALS WITH TUMORS | | 3 | 4 | 0 | 1 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 2 | 4 | 0 | 1 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 1 | 0 | 0 | 0 |
| | NO. OF BENIGN TUMORS | | 1 | 2 | 0 | 1 |
| | NO. OF MALIGNANT TUMORS | | 3 | 2 | 0 | 0 |
| | NO. OF TOTAL TUMORS | | 4 | 4 | 0 | 1 |
| 79 - 104 | NO. OF EXAMINED ANIMALS | | 6 | 10 | 10 | 15 |
| | NO. OF ANIMALS WITH TUMORS | | 6 | 10 | 10 | 15 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 1 | 1 | 4 | 1 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 5 | 9 | 6 | 14 |
| | NO. OF BENIGN TUMORS | | 9 | 19 | 9 | 27 |
| | NO. OF MALIGNANT TUMORS | | 4 | 5 | 7 | 11 |
| | NO. OF TOTAL TUMORS | | 13 | 24 | 16 | 38 |
| 105 - 105 | NO. OF EXAMINED ANIMALS | | 40 | 35 | 38 | 30 |
| | NO. OF ANIMALS WITH TUMORS | | 40 | 35 | 37 | 30 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 16 | 15 | 10 | 8 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 24 | 20 | 27 | 22 |
| | NO. OF BENIGN TUMORS | | 73 | 53 | 67 | 64 |
| | NO. OF MALIGNANT TUMORS | | 5 | 7 | 12 | 9 |
| | NO. OF TOTAL TUMORS | | 78 | 60 | 79 | 73 |

STUDY NO. : 0417
ANIMAL : RAT 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 | 25ppm | 100ppm | 400ppm |
|-----------------------|-------------------------------------|------------|---------|-------|--------|--------|
| 0 - 105 | NO. OF EXAMINED ANIMALS | | 50 | 50 | 50 | 50 |
| | NO. OF ANIMALS WITH TUMORS | | 49 | 50 | 48 | 47 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 19 | 21 | 15 | 11 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 30 | 29 | 33 | 36 |
| | NO. OF BENIGN TUMORS | | 83 | 74 | 76 | 92 |
| | NO. OF MALIGNANT TUMORS | | 12 | 15 | 20 | 21 |
| | NO. OF TOTAL TUMORS | | 95 | 89 | 96 | 113 |

(HPT070)

BAIS4

APPENDIX M 2

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

RAT : FEMALE

(2-YEAR STUDY)

STUDY NO. : 0417
ANIMAL : RAT 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 | 25ppm | 100ppm | 400ppm |
|-----------------------|-------------------------------------|------------|---------|-------|--------|--------|
| 0 - 52 | NO. OF EXAMINED ANIMALS | | 0 | 0 | 1 | 0 |
| | NO. OF ANIMALS WITH TUMORS | | 0 | 0 | 1 | 0 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 0 | 0 | 1 | 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 | 1 | 0 |
| | NO. OF TOTAL TUMORS | | 0 | 0 | 1 | 0 |
| 53 - 78 | NO. OF EXAMINED ANIMALS | | 3 | 1 | 1 | 3 |
| | NO. OF ANIMALS WITH TUMORS | | 1 | 0 | 1 | 3 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 1 | 0 | 1 | 2 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 0 | 0 | 0 | 1 |
| | NO. OF BENIGN TUMORS | | 1 | 0 | 0 | 2 |
| | NO. OF MALIGNANT TUMORS | | 0 | 0 | 1 | 3 |
| | NO. OF TOTAL TUMORS | | 1 | 0 | 1 | 5 |
| 79 - 104 | NO. OF EXAMINED ANIMALS | | 9 | 4 | 9 | 21 |
| | NO. OF ANIMALS WITH TUMORS | | 7 | 3 | 8 | 21 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 4 | 3 | 3 | 1 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 3 | 0 | 5 | 20 |
| | NO. OF BENIGN TUMORS | | 7 | 2 | 11 | 27 |
| | NO. OF MALIGNANT TUMORS | | 3 | 1 | 3 | 31 |
| | NO. OF TOTAL TUMORS | | 10 | 3 | 14 | 58 |
| 105 - 105 | NO. OF EXAMINED ANIMALS | | 38 | 45 | 39 | 26 |
| | NO. OF ANIMALS WITH TUMORS | | 25 | 30 | 26 | 25 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 16 | 21 | 16 | 1 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 9 | 9 | 10 | 24 |
| | NO. OF BENIGN TUMORS | | 29 | 37 | 34 | 46 |
| | NO. OF MALIGNANT TUMORS | | 6 | 3 | 3 | 28 |
| | NO. OF TOTAL TUMORS | | 35 | 40 | 37 | 74 |

STUDY NO. : 0417
ANIMAL : RAT 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 | 25ppm | 100ppm | 400ppm |
|-----------------------|-------------------------------------|------------|---------|-------|--------|--------|
| 0 - 105 | NO. OF EXAMINED ANIMALS | | 50 | 50 | 50 | 50 |
| | NO. OF ANIMALS WITH TUMORS | | 33 | 33 | 36 | 49 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 21 | 24 | 21 | 4 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 12 | 9 | 15 | 45 |
| | NO. OF BENIGN TUMORS | | 37 | 39 | 45 | 75 |
| | NO. OF MALIGNANT TUMORS | | 9 | 4 | 8 | 62 |
| | NO. OF TOTAL TUMORS | | 46 | 43 | 53 | 137 |
| (HPT070) | | | BAIS4 | | | |

APPENDIX N 1

HISTOPATHOLOGICAL FINDINGS :
NEOPLASTIC LESIONS : SUMMARY,
RAT : MALE
(2-YEAR STUDY)

STUDY NO. : 0417
ANIMAL : RAT 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 | 25ppm 50 | 100ppm 50 | 400ppm 50 |
|----------------------------------|------------------------------|---------------------------------------|-----------------|------------------|-----------------|------------------|
| {Integumentary system/appandage} | | | | | | |
| skin/app | squamous cell papilloma | | <50> 1 (2%) | <50> 1 (2%) | <50> 1 (2%) | <50> 1 (2%) |
| | trichoepithelioma | | 0 (0%) | 1 (2%) | 0 (0%) | 3 (6%) |
| | keratoacanthoma | | 1 (2%) | 2 (4%) | 0 (0%) | 1 (2%) |
| | sebaceous adenoma | | 1 (2%) | 0 (0%) | 3 (6%) | 0 (0%) |
| | squamous cell carcinoma | | 0 (0%) | 0 (0%) | 2 (4%) | 0 (0%) |
| subcutis | fibroma | | <50> 1 (2%) | <50> 7 (14%) | <50> 3 (6%) | <50> 1 (2%) |
| | leiomyoma | | 1 (2%) | 1 (2%) | 0 (0%) | 0 (0%) |
| | osteoma | | 1 (2%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | hemangioma | | 0 (0%) | 0 (0%) | 0 (0%) | 1 (2%) |
| brown fat | liposarcoma | | <50> 0 (0%) | <50> 1 (2%) | <50> 0 (0%) | <50> 0 (0%) |
| {Respiratory system} | | | | | | |
| nasal cavit | ethesioneuroepithelioma | | <50> 0 (0%) | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) |
| lung | bronchiolar-alveolar adenoma | | <50> 2 (4%) | <50> 1 (2%) | <50> 1 (2%) | <50> 7 (14%) |

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

(HPT085)

BAIS4

STUDY NO. : 0417
 ANIMAL : RAT 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 | 25ppm 50 | 100ppm 50 | 400ppm 50 |
|------------------------|--------------------------------|---------------------------------------|-----------------|-----------------|-----------------|-----------------|
| {Respiratory system} | | | | | | |
| lung | bronchiolar-alveolar carcinoma | | <50> 0 (0%) | <50> 2 (4%) | <50> 0 (0%) | <50> 0 (0%) |
| {Hematopoietic system} | | | | | | |
| lymph node | malignant lymphoma | | <50> 1 (2%) | <50> 0 (0%) | <50> 0 (0%) | <50> 0 (0%) |
| thymus | thymoma:benign | | <50> 1 (2%) | <50> 0 (0%) | <50> 0 (0%) | <50> 0 (0%) |
| spleen | hemangioma | | <50> 0 (0%) | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) |
| | leiomyosarcoma | | <50> 1 (2%) | <50> 0 (0%) | <50> 0 (0%) | <50> 0 (0%) |
| | histiocytic sarcoma | | <50> 0 (0%) | <50> 1 (2%) | <50> 0 (0%) | <50> 0 (0%) |
| | mononuclear cell leukemia | | <50> 3 (6%) | <50> 3 (6%) | <50> 4 (8%) | <50> 4 (8%) |
| {Circulatory system} | | | | | | |
| heart | atriocaval node tumor:benign | | <50> 0 (0%) | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) |
| {Digestive system} | | | | | | |
| oral cavity | squamous cell papilloma | | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) | <50> 1 (2%) |
| | squamous cell carcinoma | | <50> 0 (0%) | <50> 0 (0%) | <50> 0 (0%) | <50> 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. : 0417
 ANIMAL : RAT 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 | 25ppm 50 | 100ppm 50 | 400ppm 50 |
|--------------------|-----------------------------|---------------------------------------|---------------|-------------|--------------|--------------|
| {Digestive system} | | | | | | |
| small intes | | | <50> | <50> | <50> | <50> |
| | leiomyosarcoma | | 0 (0%) | 0 (0%) | 2 (4%) | 1 (2%) |
| large intes | | | <50> | <50> | <50> | <50> |
| | adenoma | | 0 (0%) | 0 (0%) | 0 (0%) | 3 (6%) |
| | adenocarcinoma | | 0 (0%) | 0 (0%) | 0 (0%) | 1 (2%) |
| liver | | | <50> | <50> | <50> | <50> |
| | hepatocellular adenoma | | 1 (2%) | 1 (2%) | 2 (4%) | 10 (20%) |
| | hemangiosarcoma | | 1 (2%) | 0 (0%) | 0 (0%) | 2 (4%) |
| | hepatocellular carcinoma | | 0 (0%) | 0 (0%) | 1 (2%) | 6 (12%) |
| pancreas | | | <50> | <50> | <50> | <50> |
| | islet cell adenoma | | 3 (6%) | 3 (6%) | 2 (4%) | 0 (0%) |
| | acinar cell adenoma | | 0 (0%) | 0 (0%) | 0 (0%) | 1 (2%) |
| | ductal adenocarcinoma | | 0 (0%) | 0 (0%) | 0 (0%) | 1 (2%) |
| {Urinary system} | | | | | | |
| kidney | | | <50> | <50> | <50> | <50> |
| | renal cell adenoma | | 0 (0%) | 0 (0%) | 0 (0%) | 1 (2%) |
| urin bladd | | | <50> | <50> | <50> | <50> |
| | transitional cell papilloma | | 0 (0%) | 0 (0%) | 2 (4%) | 1 (2%) |
| {Endocrine system} | | | | | | |
| pituitary | | | <50> | <50> | <50> | <50> |
| | adenoma | | 8 (16%) | 6 (12%) | 7 (14%) | 4 (8%) |

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

STUDY NO. : 0417
 ANIMAL : RAT 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 | 25ppm 50 | 100ppm 50 | 400ppm 50 |
|-----------------------|----------------------------|---------------------------------------|---------------|-------------|--------------|--------------|
| {Endocrine system} | | | | | | |
| pituitary | | | <50> | <50> | <50> | <50> |
| | adenocarcinoma | | 1 (2%) | 0 (0%) | 0 (0%) | 0 (0%) |
| thyroid | | | <50> | <50> | <50> | <50> |
| | C-cell adenoma | | 8 (16%) | 4 (8%) | 4 (8%) | 3 (6%) |
| | follicular adenoma | | 1 (2%) | 1 (2%) | 2 (4%) | 2 (4%) |
| | C-cell carcinoma | | 0 (0%) | 3 (6%) | 0 (0%) | 1 (2%) |
| | follicular adenocarcinoma | | 1 (2%) | 0 (0%) | 1 (2%) | 0 (0%) |
| parathyroid | | | <50> | <50> | <50> | <50> |
| | adenoma | | 0 (0%) | 0 (0%) | 0 (0%) | 1 (2%) |
| adrenal | | | <50> | <50> | <50> | <50> |
| | pheochromocytoma | | 3 (6%) | 3 (6%) | 3 (6%) | 2 (4%) |
| | cortical adenoma | | 0 (0%) | 0 (0%) | 1 (2%) | 0 (0%) |
| | pheochromocytoma:malignant | | 3 (6%) | 1 (2%) | 0 (0%) | 0 (0%) |
| {Reproductive system} | | | | | | |
| testis | | | <50> | <50> | <50> | <50> |
| | interstitial cell tumor | | 45 (90%) | 39 (78%) | 39 (78%) | 42 (84%) |
| epididymis | | | <50> | <50> | <50> | <50> |
| | histiocytic sarcoma | | 0 (0%) | 0 (0%) | 0 (0%) | 1 (2%) |
| prostate | | | <50> | <50> | <50> | <50> |
| | adenoma | | 1 (2%) | 0 (0%) | 0 (0%) | 1 (2%) |

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

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 5

| Organ | Findings | Group Name No. of animals on Study | Control 50 | 25ppm 50 | 100ppm 50 | 400ppm 50 |
|----------------------------------|------------------------------|---------------------------------------|-----------------|-----------------|-----------------|-----------------|
| {Reproductive system} | | | | | | |
| mammary gl | adenoma | | <50> 2 (4%) | <50> 0 (0%) | <50> 0 (0%) | <50> 0 (0%) |
| | fibroma | | 0 (0%) | 1 (2%) | 0 (0%) | 0 (0%) |
| | fibroadenoma | | 0 (0%) | 1 (2%) | 0 (0%) | 0 (0%) |
| prep/cli gl | adenoma | | <50> 2 (4%) | <50> 1 (2%) | <50> 2 (4%) | <50> 4 (8%) |
| {Nervous system} | | | | | | |
| brain | meningioma:benign | | <50> 0 (0%) | <50> 1 (2%) | <50> 0 (0%) | <50> 0 (0%) |
| | glioma | | 0 (0%) | 0 (0%) | 1 (2%) | 0 (0%) |
| {Special sense organs/appendage} | | | | | | |
| Zymbal gl | Zmbal gland tumor:benign | | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) | <50> 0 (0%) |
| | squamous cell carcinoma | | 0 (0%) | 0 (0%) | 0 (0%) | 1 (2%) |
| | Zymbal gland tumor:malignant | | 0 (0%) | 1 (2%) | 1 (2%) | 0 (0%) |
| {Musculoskeletal system} | | | | | | |
| bone | osteoma | | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) | <50> 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

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 6

| Organ | Findings | Group Name No. of animals on Study | Control 50 | 25ppm 50 | 100ppm 50 | 400ppm 50 |
|--------------------------|----------------------------------|---------------------------------------|---------------|-------------|--------------|--------------|
| {Musculoskeletal system} | | | | | | |
| bone | | | <50> | <50> | <50> | <50> |
| | osteosarcoma | | 1 (2%) | 1 (2%) | 1 (2%) | 0 (0%) |
| {Body cavities} | | | | | | |
| peritoneum | | | <50> | <50> | <50> | <50> |
| | mesothelioma | | 0 (0%) | 2 (4%) | 7 (14%) | 1 (2%) |
| retroperit | | | <50> | <50> | <50> | <50> |
| | neuroendocrine cell tumor: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

(HPT085)

BAIS4

APPENDIX N 2

HISTOPATHOLOGICAL FINDINGS :
NEOPLASTIC LESIONS : SUMMARY,
RAT : FEMALE
(2-YEAR STUDY)

STUDY NO. : 0417
 ANIMAL : RAT 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 | 25ppm 50 | 100ppm 50 | 400ppm 50 |
|----------------------------------|------------------------------|---------------------------------------|-----------------|-----------------|-----------------|------------------|
| {Integumentary system/appandage} | | | | | | |
| skin/app | squamous cell papilloma | | <50> 1 (2%) | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) |
| | trichoepithelioma | | 0 (0%) | 0 (0%) | 1 (2%) | 2 (4%) |
| | basal cell epithelioma | | 0 (0%) | 0 (0%) | 1 (2%) | 0 (0%) |
| subcutis | fibroma | | <50> 0 (0%) | <50> 1 (2%) | <50> 0 (0%) | <50> 0 (0%) |
| | osteosarcoma | | 0 (0%) | 0 (0%) | 1 (2%) | 0 (0%) |
| {Respiratory system} | | | | | | |
| nasal cavit | adenoma | | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) | <50> 0 (0%) |
| | chondroma | | 0 (0%) | 0 (0%) | 1 (2%) | 0 (0%) |
| lung | bronchiolar-alveolar adenoma | | <50> 1 (2%) | <50> 0 (0%) | <50> 1 (2%) | <50> 5 (10%) |
| {Hematopoietic system} | | | | | | |
| lymph node | malignant lymphoma | | <50> 1 (2%) | <50> 0 (0%) | <50> 0 (0%) | <50> 0 (0%) |
| spleen | hemangioma | | <50> 0 (0%) | <50> 0 (0%) | <50> 0 (0%) | <50> 2 (4%) |
| | mononuclear cell leukemia | | 5 (10%) | 3 (6%) | 5 (10%) | 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. : 0417
 ANIMAL : RAT 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 | 25ppm 50 | 100ppm 50 | 400ppm 50 |
|--------------------|-----------------------------|---------------------------------------|---------------|-------------|--------------|--------------|
| {Digestive system} | | | | | | |
| oral cavity | | | <50> | <50> | <50> | <50> |
| | squamous cell papilloma | | 0 (0%) | 0 (0%) | 0 (0%) | 1 (2%) |
| tongue | | | <50> | <50> | <50> | <50> |
| | squamous cell papilloma | | 0 (0%) | 0 (0%) | 0 (0%) | 1 (2%) |
| stomach | | | <50> | <50> | <50> | <50> |
| | leiomyosarcoma | | 0 (0%) | 0 (0%) | 0 (0%) | 1 (2%) |
| large intes | | | <50> | <50> | <50> | <50> |
| | adenoma | | 0 (0%) | 0 (0%) | 0 (0%) | 2 (4%) |
| liver | | | <50> | <50> | <50> | <50> |
| | hemangioma | | 0 (0%) | 0 (0%) | 0 (0%) | 1 (2%) |
| | hepatocellular adenoma | | 1 (2%) | 0 (0%) | 2 (4%) | 32 (64%) |
| | hemangiosarcoma | | 0 (0%) | 0 (0%) | 0 (0%) | 6 (12%) |
| | hepatocellular carcinoma | | 0 (0%) | 0 (0%) | 0 (0%) | 38 (76%) |
| pancreas | | | <50> | <50> | <50> | <50> |
| | islet cell adenoma | | 0 (0%) | 1 (2%) | 0 (0%) | 0 (0%) |
| {Urinary system} | | | | | | |
| urin bladd | | | <50> | <50> | <50> | <50> |
| | transitional cell papilloma | | 0 (0%) | 1 (2%) | 1 (2%) | 0 (0%) |
| {Endocrine system} | | | | | | |
| pituitary | | | <50> | <50> | <50> | <50> |
| | adenoma | | 9 (18%) | 9 (18%) | 9 (18%) | 6 (12%) |

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

STUDY NO. : 0417
ANIMAL : RAT 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 | 25ppm 50 | 100ppm 50 | 400ppm 50 |
|-----------------------|----------------------------|---------------------------------------|---------------|-------------|--------------|--------------|
| {Endocrine system} | | | | | | |
| pituitary | | | <50> | <50> | <50> | <50> |
| | adenocarcinoma | | 1 (2%) | 0 (0%) | 0 (0%) | 0 (0%) |
| thyroid | | | <50> | <50> | <50> | <50> |
| | C-cell adenoma | | 6 (12%) | 7 (14%) | 7 (14%) | 5 (10%) |
| | follicular adenoma | | 2 (4%) | 0 (0%) | 0 (0%) | 1 (2%) |
| | C-cell carcinoma | | 1 (2%) | 1 (2%) | 1 (2%) | 0 (0%) |
| | follicular adenocarcinoma | | 0 (0%) | 0 (0%) | 0 (0%) | 1 (2%) |
| adrenal | | | <50> | <50> | <50> | <50> |
| | pheochromocytoma | | 2 (4%) | 0 (0%) | 0 (0%) | 1 (2%) |
| {Reproductive system} | | | | | | |
| ovary | | | <50> | <50> | <50> | <50> |
| | granulosa-theca cell tumor | | 0 (0%) | 1 (2%) | 0 (0%) | 1 (2%) |
| uterus | | | <50> | <50> | <50> | <50> |
| | hemangioma | | 0 (0%) | 1 (2%) | 0 (0%) | 1 (2%) |
| | endometrial stromal polyp | | 7 (14%) | 6 (12%) | 7 (14%) | 7 (14%) |
| | yolk sack tumor:malignant | | 1 (2%) | 0 (0%) | 0 (0%) | 0 (0%) |
| mammary gl | | | <50> | <50> | <50> | <50> |
| | fibroadenoma | | 6 (12%) | 9 (18%) | 10 (20%) | 3 (6%) |
| prep/cli gl | | | <50> | <50> | <50> | <50> |
| | adenoma | | 1 (2%) | 3 (6%) | 4 (8%) | 3 (6%) |

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

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 10

| Organ | Findings | Group Name No. of animals on Study | Control 50 | 25ppm 50 | 100ppm 50 | 400ppm 50 |
|----------------------------------|-------------------------|---------------------------------------|-----------------|-----------------|-----------------|-----------------|
| {Nervous system} | | | | | | |
| brain | glioma | | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) | <50> 1 (2%) |
| {Special sense organs/appendage} | | | | | | |
| Zymbal gl | squamous cell carcinoma | | <50> 0 (0%) | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) |
| {Musculoskeletal system} | | | | | | |
| bone | osteosarcoma | | <50> 0 (0%) | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) |
| {Body cavities} | | | | | | |
| adipose | lipoma | | <50> 1 (2%) | <50> 0 (0%) | <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

(HPT085)

BAIS4

APPENDIX O 1

NEOPLASTIC LESIONS-INCIDENCE AND

STATISTICAL ANALYSIS,

RAT : MALE

(2-YEAR STUDY)

STUDY No. : 0417
ANIMAL : RAT F344/DuCrj
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 1

| Group Name | Control | 25ppm | 100ppm | 400ppm |
|--|-------------|------------|------------|------------|
| SITE : skin/appendage TUMOR : trichoepithelioma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 0/50(0.0) | 1/50(2.0) | 0/50(0.0) | 3/50(6.0) |
| Adjusted rates(b) | 0.0 | 2.86 | 0.0 | 6.67 |
| Terminal rates(c) | 0/40(0.0) | 1/35(2.9) | 0/38(0.0) | 2/30(6.7) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.1436 | | | |
| Prevalence method(d) | P = 0.0567 | | | |
| Combined analysis(d) | P = 0.0145* | | | |
| Cochran-Armitage test(e) | P = 0.0266* | | | |
| Fisher Exact test(e) | | P = 0.5000 | P = N. C. | P = 0.1212 |
| SITE : skin/appendage TUMOR : sebaceous adenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 1/50(2.0) | 0/50(0.0) | 3/50(6.0) | 0/50(0.0) |
| Adjusted rates(b) | 2.50 | 0.0 | 7.89 | 0.0 |
| Terminal rates(c) | 1/40(2.5) | 0/35(0.0) | 3/38(7.9) | 0/30(0.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.6672 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.4761 | | | |
| Fisher Exact test(e) | | P = 0.5000 | P = 0.3087 | P = 0.5000 |
| SITE : skin/appendage TUMOR : squamous cell papilloma, keratoacanthoma, squamous cell carcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 2/50(4.0) | 3/50(6.0) | 3/50(6.0) | 2/50(4.0) |
| Adjusted rates(b) | 5.00 | 8.57 | 5.26 | 5.41 |
| Terminal rates(c) | 2/40(5.0) | 3/35(8.6) | 2/38(5.3) | 1/30(3.3) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.3420 | | | |
| Prevalence method(d) | P = 0.5403 | | | |
| Combined analysis(d) | P = 0.5630 | | | |
| Cochran-Armitage test(e) | P = 0.7797 | | | |
| Fisher Exact test(e) | | P = 0.5000 | P = 0.5000 | P = 0.6913 |

STUDY No. : 0417
 ANIMAL : RAT F344/DuCrj
 SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 2

| Group Name | Control | 25ppm | 100ppm | 400ppm |
|---|--------------|-------------|------------|-------------|
| SITE : subcutis TUMOR : fibroma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 1/50(2.0) | 7/50(14.0) | 3/50(6.0) | 1/50(2.0) |
| Adjusted rates(b) | 2.50 | 12.50 | 7.89 | 3.33 |
| Terminal rates(c) | 1/40(2.5) | 3/35(8.6) | 3/38(7.9) | 1/30(3.3) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.8065 | | | |
| Prevalence method(d) | P = 0.8260 | | | |
| Combined analysis(d) | P = 0.9024 | | | |
| Cochran-Armitage test(e) | P = 0.1912 | | | |
| Fisher Exact test(e) | | P = 0.0297* | P = 0.3087 | P = 0.7525 |
| SITE : lung TUMOR : bronchiolar-alveolar adenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 2/50(4.0) | 1/50(2.0) | 1/50(2.0) | 7/50(14.0) |
| Adjusted rates(b) | 5.00 | 2.56 | 2.63 | 20.00 |
| Terminal rates(c) | 2/40(5.0) | 0/35(0.0) | 1/38(2.6) | 6/30(20.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.0023** | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.0040** | | | |
| Fisher Exact test(e) | | P = 0.5000 | P = 0.5000 | P = 0.0798 |
| SITE : lung TUMOR : bronchiolar-alveolar adenoma, bronchiolar-alveolar carcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 2/50(4.0) | 3/50(6.0) | 1/50(2.0) | 7/50(14.0) |
| Adjusted rates(b) | 5.00 | 7.69 | 2.63 | 20.00 |
| Terminal rates(c) | 2/40(5.0) | 2/35(5.7) | 1/38(2.6) | 6/30(20.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.0108* | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.0225* | | | |
| Fisher Exact test(e) | | P = 0.5000 | P = 0.5000 | P = 0.0798 |

STUDY No. : 0417
 ANIMAL : RAT F344/DuCrj
 SEX : MALE

NEOPLASTIC LESIONS—INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 3

| Group Name | Control | 25ppm | 100ppm | 400ppm |
|---|---------------|------------|------------|-------------|
| SITE : spleen TUMOR : mononuclear cell leukemia | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 3/50(6.0) | 3/50(6.0) | 4/50(8.0) | 4/50(8.0) |
| Adjusted rates(b) | 5.00 | 2.86 | 5.26 | 10.00 |
| Terminal rates(c) | 2/40(5.0) | 1/35(2.9) | 2/38(5.3) | 3/30(10.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.5829 | | | |
| Prevalence method(d) | P = 0.1273 | | | |
| Combined analysis(d) | P = 0.2474 | | | |
| Cochran-Armitage test(e) | P = 0.6798 | | | |
| Fisher Exact test(e) | | P = 0.6611 | P = 0.5000 | P = 0.5000 |
| SITE : large intestine TUMOR : adenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 0/50(0.0) | 0/50(0.0) | 0/50(0.0) | 3/50(6.0) |
| Adjusted rates(b) | 0.0 | 0.0 | 0.0 | 10.00 |
| Terminal rates(c) | 0/40(0.0) | 0/35(0.0) | 0/38(0.0) | 3/30(10.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.0008**? | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.0033** | | | |
| Fisher Exact test(e) | | P = N. C. | P = N. C. | P = 0.1212 |
| SITE : large intestine TUMOR : adenoma, adenocarcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 0/50(0.0) | 0/50(0.0) | 0/50(0.0) | 4/50(8.0) |
| Adjusted rates(b) | 0.0 | 0.0 | 0.0 | 10.00 |
| Terminal rates(c) | 0/40(0.0) | 0/35(0.0) | 0/38(0.0) | 3/30(10.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.1512 | | | |
| Prevalence method(d) | P = 0.0008**? | | | |
| Combined analysis(d) | P = 0.0001**? | | | |
| Cochran-Armitage test(e) | P = 0.0007** | | | |
| Fisher Exact test(e) | | P = N. C. | P = N. C. | P = 0.0587 |

STUDY No. : 0417
 ANIMAL : RAT F344/DuCrj
 SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 4

| Group Name | Control | 25ppm | 100ppm | 400ppm |
|--|---------------|------------|------------|--------------|
| SITE : liver TUMOR : hepatocellular adenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 1/50(2.0) | 1/50(2.0) | 2/50(4.0) | 10/50(20.0) |
| Adjusted rates(b) | 2.50 | 2.86 | 5.26 | 25.81 |
| Terminal rates(c) | 1/40(2.5) | 1/35(2.9) | 2/38(5.3) | 7/30(23.3) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P < 0.0001** | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P < 0.0001** | | | |
| Fisher Exact test(e) | | P = 0.7525 | P = 0.5000 | P = 0.0039** |
| SITE : liver TUMOR : hepatocellular carcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 0/50(0.0) | 0/50(0.0) | 1/50(2.0) | 6/50(12.0) |
| Adjusted rates(b) | 0.0 | 0.0 | 2.63 | 10.81 |
| Terminal rates(c) | 0/40(0.0) | 0/35(0.0) | 1/38(2.6) | 3/30(10.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.0145* ? | | | |
| Prevalence method(d) | P = 0.0023** | | | |
| Combined analysis(d) | P = 0.0001** | | | |
| Cochran-Armitage test(e) | P = 0.0001** | | | |
| Fisher Exact test(e) | | P = N. C. | P = 0.5000 | P = 0.0133* |
| SITE : liver TUMOR : hepatocellular adenoma, hepatocellular carcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 1/50(2.0) | 1/50(2.0) | 3/50(6.0) | 15/50(30.0) |
| Adjusted rates(b) | 2.50 | 2.86 | 7.89 | 35.48 |
| Terminal rates(c) | 1/40(2.5) | 1/35(2.9) | 3/38(7.9) | 10/30(33.3) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.0145* ? | | | |
| Prevalence method(d) | P < 0.0001** | | | |
| Combined analysis(d) | P < 0.0001** | | | |
| Cochran-Armitage test(e) | P < 0.0001** | | | |
| Fisher Exact test(e) | | P = 0.7525 | P = 0.3087 | P = 0.0001** |

STUDY No. : 0417
 ANIMAL : RAT F344/DuCrj
 SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 5

| Group Name | Control | 25ppm | 100ppm | 400ppm |
|---|-------------|-------------|-------------|------------|
| SITE : pancreas TUMOR : islet cell adenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 3/50(6.0) | 3/50(6.0) | 2/50(4.0) | 0/50(0.0) |
| Adjusted rates(b) | 6.98 | 6.67 | 5.26 | 0.0 |
| Terminal rates(c) | 2/40(5.0) | 2/35(5.7) | 2/38(5.3) | 0/30(0.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.9739 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.0795 | | | |
| Fisher Exact test(e) | | P = 0.6611 | P = 0.5000 | P = 0.1212 |
| SITE : pituitary gland TUMOR : adenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 8/50(16.0) | 6/50(12.0) | 7/50(14.0) | 4/50(8.0) |
| Adjusted rates(b) | 13.64 | 5.71 | 11.63 | 8.57 |
| Terminal rates(c) | 5/40(12.5) | 2/35(5.7) | 3/38(7.9) | 1/30(3.3) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.8284 | | | |
| Prevalence method(d) | P = 0.7038 | | | |
| Combined analysis(d) | P = 0.8512 | | | |
| Cochran-Armitage test(e) | P = 0.2651 | | | |
| Fisher Exact test(e) | | P = 0.3871 | P = 0.5000 | P = 0.1783 |
| SITE : pituitary gland TUMOR : adenoma, adenocarcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 9/50(18.0) | 6/50(12.0) | 7/50(14.0) | 4/50(8.0) |
| Adjusted rates(b) | 13.64 | 5.71 | 11.63 | 8.57 |
| Terminal rates(c) | 5/40(12.5) | 2/35(5.7) | 3/38(7.9) | 1/30(3.3) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.8835 | | | |
| Prevalence method(d) | P = 0.7038 | | | |
| Combined analysis(d) | P = 0.8843 | | | |
| Cochran-Armitage test(e) | P = 0.2044 | | | |
| Fisher Exact test(e) | | P = 0.2883 | P = 0.3929 | P = 0.1168 |

STUDY No. : 0417
 ANIMAL : RAT F344/DuCrj
 SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 6

| Group Name | Control | 25ppm | 100ppm | 400ppm |
|--|-------------|-------------|------------|-------------|
| SITE : thyroid TUMOR : C-cell adenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 8/50(16.0) | 4/50(8.0) | 4/50(8.0) | 3/50(6.0) |
| Adjusted rates(b) | 20.00 | 10.81 | 10.00 | 10.00 |
| Terminal rates(c) | 8/40(20.0) | 3/35(8.6) | 3/38(7.9) | 3/30(10.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.8725 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.2300 | | | |
| Fisher Exact test(e) | | P = 0.1783 | P = 0.1783 | P = 0.0999 |
| SITE : thyroid TUMOR : C-cell carcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 0/50(0.0) | 3/50(6.0) | 0/50(0.0) | 1/50(2.0) |
| Adjusted rates(b) | 0.0 | 7.32 | 0.0 | 3.23 |
| Terminal rates(c) | 0/40(0.0) | 2/35(5.7) | 0/38(0.0) | 0/30(0.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.5232 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.8742 | | | |
| Fisher Exact test(e) | | P = 0.1212 | P = N. C. | P = 0.5000 |
| SITE : thyroid TUMOR : C-cell adenoma, C-cell carcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 8/50(16.0) | 7/50(14.0) | 4/50(8.0) | 4/50(8.0) |
| Adjusted rates(b) | 20.00 | 17.07 | 10.00 | 12.90 |
| Terminal rates(c) | 8/40(20.0) | 5/35(14.3) | 3/38(7.9) | 3/30(10.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.8757 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.2409 | | | |
| Fisher Exact test(e) | | P = 0.5000 | P = 0.1783 | P = 0.1783 |

STUDY No. : 0417
 ANIMAL : RAT F344/DuCrj
 SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 7

| Group Name | Control | 25ppm | 100ppm | 400ppm |
|---|--------------|------------|------------|------------|
| SITE : thyroid TUMOR : follicular adenoma, follicular adenocarcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 2/50(4.0) | 1/50(2.0) | 3/50(6.0) | 2/50(4.0) |
| Adjusted rates(b) | 5.00 | 2.86 | 7.89 | 6.67 |
| Terminal rates(c) | 2/40(5.0) | 1/35(2.9) | 3/38(7.9) | 2/30(6.7) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.3073 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.8652 | | | |
| Fisher Exact test(e) | | P = 0.5000 | P = 0.5000 | P = 0.6913 |
| SITE : adrenal gland TUMOR : pheochromocytoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 3/50(6.0) | 3/50(6.0) | 3/50(6.0) | 2/50(4.0) |
| Adjusted rates(b) | 7.50 | 8.33 | 7.89 | 4.76 |
| Terminal rates(c) | 3/40(7.5) | 2/35(5.7) | 3/38(7.9) | 1/30(3.3) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.6816 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.6012 | | | |
| Fisher Exact test(e) | | P = 0.6611 | P = 0.6611 | P = 0.5000 |
| SITE : adrenal gland TUMOR : pheochromocytoma:malignant | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 3/50(6.0) | 1/50(2.0) | 0/50(0.0) | 0/50(0.0) |
| Adjusted rates(b) | 2.50 | 0.0 | 0.0 | 0.0 |
| Terminal rates(c) | 1/40(2.5) | 0/35(0.0) | 0/38(0.0) | 0/30(0.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.9389 | | | |
| Prevalence method(d) | P = 1.0000 ? | | | |
| Combined analysis(d) | P = 0.9690 | | | |
| Cochran-Armitage test(e) | P = 0.1133 | | | |
| Fisher Exact test(e) | | P = 0.3087 | P = 0.1212 | P = 0.1212 |

STUDY No. : 0417
ANIMAL : RAT F344/DuCrj
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 8

| Group Name | Control | 25ppm | 100ppm | 400ppm |
|--|--------------|--------------|--------------|--------------|
| SITE : adrenal gland TUMOR : pheochromocytoma, pheochromocytoma:malignant | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 6/50(12.0) | 4/50(8.0) | 3/50(6.0) | 2/50(4.0) |
| Adjusted rates(b) | 10.00 | 8.33 | 7.89 | 4.76 |
| Terminal rates(c) | 4/40(10.0) | 2/35(5.7) | 3/38(7.9) | 1/30(3.3) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.9389 | | | |
| Prevalence method(d) | P = 0.7658 | | | |
| Combined analysis(d) | P = 0.9054 | | | |
| Cochran-Armitage test(e) | P = 0.1956 | | | |
| Fisher Exact test(e) | | P = 0.3703 | P = 0.2435 | P = 0.1343 |
| SITE : testis TUMOR : interstitial cell tumor | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 45/50(90.0) | 39/50(78.0) | 39/50(78.0) | 42/50(84.0) |
| Adjusted rates(b) | 97.67 | 91.89 | 92.11 | 96.67 |
| Terminal rates(c) | 39/40(97.5) | 32/35(91.4) | 35/38(92.1) | 29/30(96.7) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.2120 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.9825 | | | |
| Fisher Exact test(e) | | P = 0.0857 | P = 0.0857 | P = 0.2768 |
| SITE : preputial/clitoral gland TUMOR : adenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 2/50(4.0) | 1/50(2.0) | 2/50(4.0) | 4/50(8.0) |
| Adjusted rates(b) | 5.00 | 2.86 | 5.26 | 10.00 |
| Terminal rates(c) | 2/40(5.0) | 1/35(2.9) | 2/38(5.3) | 3/30(10.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.1369 | | | |
| Prevalence method(d) | P = 0.1273 | | | |
| Combined analysis(d) | P = 0.0527 | | | |
| Cochran-Armitage test(e) | P = 0.1685 | | | |
| Fisher Exact test(e) | | P = 0.5000 | P = 0.6913 | P = 0.3389 |

STUDY No. : 0417
ANIMAL : RAT F344/DuCrj
SEX : MALE

NEOPLASTIC LESIONS--INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 9

| Group Name | Control | 25ppm | 100ppm | 400ppm |
|---|------------|------------|--------------|------------|
| SITE : peritoneum TUMOR : mesothelioma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 0/50(0.0) | 2/50(4.0) | 7/50(14.0) | 1/50(2.0) |
| Adjusted rates(b) | 0.0 | 5.71 | 15.79 | 0.0 |
| Terminal rates(c) | 0/40(0.0) | 2/35(5.7) | 6/38(15.8) | 0/30(0.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.1647 | | | |
| Prevalence method(d) | P = 0.7322 | | | |
| Combined analysis(d) | P = 0.5067 | | | |
| Cochran-Armitage test(e) | P = 0.7409 | | | |
| Fisher Exact test(e) | | P = 0.2475 | P = 0.0062** | 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,

RAT : FEMALE

(2-YEAR STUDY)

STUDY No. : 0417
 ANIMAL : RAT F344/DuCrj
 SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 10

| Group Name | Control | 25ppm | 100ppm | 400ppm |
|---|---------------|------------|-------------|--------------|
| SITE : lung TUMOR : bronchiolar-alveolar adenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 1/50(2.0) | 0/50(0.0) | 1/50(2.0) | 5/50(10.0) |
| Adjusted rates(b) | 2.63 | 0.0 | 2.56 | 19.23 |
| Terminal rates(c) | 1/38(2.6) | 0/45(0.0) | 1/39(2.6) | 5/26(19.2) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.0004** | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.0044** | | | |
| Fisher Exact test(e) | | P = 0.5000 | P = 0.7525 | P = 0.1022 |
| SITE : spleen TUMOR : mononuclear cell leukemia | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 5/50(10.0) | 3/50(6.0) | 5/50(10.0) | 13/50(26.0) |
| Adjusted rates(b) | 7.89 | 4.44 | 5.13 | 19.23 |
| Terminal rates(c) | 3/38(7.9) | 2/45(4.4) | 2/39(5.1) | 5/26(19.2) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.0055** | | | |
| Prevalence method(d) | P = 0.0147* | | | |
| Combined analysis(d) | P = 0.0004** | | | |
| Cochran-Armitage test(e) | P = 0.0018** | | | |
| Fisher Exact test(e) | | P = 0.3575 | P = 0.6297 | P = 0.0332* |
| SITE : liver TUMOR : hepatocellular adenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 1/50(2.0) | 0/50(0.0) | 2/50(4.0) | 32/50(64.0) |
| Adjusted rates(b) | 2.63 | 0.0 | 5.13 | 80.77 |
| Terminal rates(c) | 1/38(2.6) | 0/45(0.0) | 2/39(5.1) | 21/26(80.8) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P < 0.0001**? | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P < 0.0001** | | | |
| Fisher Exact test(e) | | P = 0.5000 | P = 0.5000 | P < 0.0001** |

STUDY No. : 0417
ANIMAL : RAT F344/DuCrj
SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 11

| Group Name | Control | 25ppm | 100ppm | 400ppm |
|---|---------------|------------|------------|--------------|
| SITE : liver TUMOR : hemangiosarcoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 0/50(0.0) | 0/50(0.0) | 0/50(0.0) | 6/50(12.0) |
| Adjusted rates(b) | 0.0 | 0.0 | 0.0 | 0.0 |
| Terminal rates(c) | 0/38(0.0) | 0/45(0.0) | 0/39(0.0) | 0/26(0.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P < 0.0001**? | | | |
| Prevalence method(d) | P = ----- | | | |
| Combined analysis(d) | P < 0.0001**? | | | |
| Cochran-Armitage test(e) | P < 0.0001** | | | |
| Fisher Exact test(e) | | P = N. C. | P = N. C. | P = 0.0133* |
| SITE : liver TUMOR : hepatocellular carcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 0/50(0.0) | 0/50(0.0) | 0/50(0.0) | 38/50(76.0) |
| Adjusted rates(b) | 0.0 | 0.0 | 0.0 | 90.91 |
| Terminal rates(c) | 0/38(0.0) | 0/45(0.0) | 0/39(0.0) | 23/26(88.5) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.0008**? | | | |
| 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 : liver TUMOR : hemangioma, hemangiosarcoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 0/50(0.0) | 0/50(0.0) | 0/50(0.0) | 7/50(14.0) |
| Adjusted rates(b) | 0.0 | 0.0 | 0.0 | 3.85 |
| Terminal rates(c) | 0/38(0.0) | 0/45(0.0) | 0/39(0.0) | 1/26(3.8) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P < 0.0001**? | | | |
| Prevalence method(d) | P = 0.0989 | | | |
| Combined analysis(d) | P < 0.0001**? | | | |
| Cochran-Armitage test(e) | P < 0.0001** | | | |
| Fisher Exact test(e) | | P = N. C. | P = N. C. | P = 0.0062** |

STUDY No. : 0417
ANIMAL : RAT F344/DuCrj
SEX : FEMALE

NEOPLASTIC LESIONS—INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 12

| Group Name | Control | 25ppm | 100ppm | 400ppm |
|--|---------------|-------------|-------------|--------------|
| SITE : liver TUMOR : hepatocellular adenoma, hepatocellular carcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 1/50(2.0) | 0/50(0.0) | 2/50(4.0) | 43/50(86.0) |
| Adjusted rates(b) | 2.63 | 0.0 | 5.13 | 95.12 |
| Terminal rates(c) | 1/38(2.6) | 0/45(0.0) | 2/39(5.1) | 24/26(92.3) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.0008**? | | | |
| Prevalence method(d) | P < 0.0001**? | | | |
| Combined analysis(d) | P < 0.0001**? | | | |
| Cochran-Armitage test(e) | P < 0.0001** | | | |
| Fisher Exact test(e) | | P = 0.5000 | P = 0.5000 | P < 0.0001** |
| SITE : pituitary gland TUMOR : adenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 9/50(18.0) | 9/50(18.0) | 9/50(18.0) | 6/50(12.0) |
| Adjusted rates(b) | 10.53 | 18.37 | 13.64 | 17.86 |
| Terminal rates(c) | 4/38(10.5) | 8/45(17.8) | 5/39(12.8) | 4/26(15.4) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.8015 | | | |
| Prevalence method(d) | P = 0.4972 | | | |
| Combined analysis(d) | P = 0.6897 | | | |
| Cochran-Armitage test(e) | P = 0.3355 | | | |
| Fisher Exact test(e) | | P = 0.6024 | P = 0.6024 | P = 0.2883 |
| SITE : pituitary gland TUMOR : adenoma, adenocarcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 10/50(20.0) | 9/50(18.0) | 9/50(18.0) | 6/50(12.0) |
| Adjusted rates(b) | 13.16 | 18.37 | 13.64 | 17.86 |
| Terminal rates(c) | 5/38(13.2) | 8/45(17.8) | 5/39(12.8) | 4/26(15.4) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.8015 | | | |
| Prevalence method(d) | P = 0.5621 | | | |
| Combined analysis(d) | P = 0.7353 | | | |
| Cochran-Armitage test(e) | P = 0.2684 | | | |
| Fisher Exact test(e) | | P = 0.5000 | P = 0.5000 | P = 0.2070 |

STUDY No. : 0417
 ANIMAL : RAT F344/DuCrj
 SEX : FEMALE

NEOPLASTIC LESIONS--INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 13

| Group Name | Control | 25ppm | 100ppm | 400ppm |
|--|-------------|-------------|-------------|-------------|
| SITE : thyroid TUMOR : C-cell adenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 6/50(12.0) | 7/50(14.0) | 7/50(14.0) | 5/50(10.0) |
| Adjusted rates(b) | 15.79 | 15.56 | 15.91 | 15.38 |
| Terminal rates(c) | 6/38(15.8) | 7/45(15.6) | 4/39(10.3) | 4/26(15.4) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.5223 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.5860 | | | |
| Fisher Exact test(e) | | P = 0.5000 | P = 0.5000 | P = 0.5000 |
| SITE : thyroid TUMOR : C-cell adenoma, C-cell carcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 7/50(14.0) | 8/50(16.0) | 8/50(16.0) | 5/50(10.0) |
| Adjusted rates(b) | 18.42 | 17.78 | 18.18 | 15.38 |
| Terminal rates(c) | 7/38(18.4) | 8/45(17.8) | 5/39(12.8) | 4/26(15.4) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.6363 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.3884 | | | |
| Fisher Exact test(e) | | P = 0.5000 | P = 0.5000 | P = 0.3798 |
| SITE : uterus TUMOR : endometrial stromal polyp | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 7/50(14.0) | 6/50(12.0) | 7/50(14.0) | 7/50(14.0) |
| Adjusted rates(b) | 15.79 | 13.33 | 17.95 | 17.14 |
| Terminal rates(c) | 6/38(15.8) | 6/45(13.3) | 7/39(17.9) | 4/26(15.4) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.2978 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.8903 | | | |
| Fisher Exact test(e) | | P = 0.5000 | P = 0.6129 | P = 0.6129 |

STUDY No. : 0417
ANIMAL : RAT F344/DuCrj
SEX : FEMALE

NEOPLASTIC LESIONS--INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 14

| Group Name | Control | 25ppm | 100ppm | 400ppm |
|--|-------------|-------------|--------------|-------------|
| SITE : mammary gland TUMOR : fibroadenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 6/50(12.0) | 9/50(18.0) | 10/50(20.0) | 3/50(6.0) |
| Adjusted rates(b) | 15.79 | 20.00 | 21.74 | 11.54 |
| Terminal rates(c) | 6/38(15.8) | 9/45(20.0) | 8/39(20.5) | 3/26(11.5) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.8586 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.1102 | | | |
| Fisher Exact test(e) | | P = 0.2883 | P = 0.2070 | P = 0.2435 |
| SITE : preputial/clitoral gland TUMOR : adenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 1/50(2.0) | 3/50(6.0) | 4/50(8.0) | 3/50(6.0) |
| Adjusted rates(b) | 2.50 | 6.67 | 10.26 | 5.13 |
| Terminal rates(c) | 0/38(0.0) | 3/45(6.7) | 4/39(10.3) | 1/26(3.8) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.1613 | | | |
| Prevalence method(d) | P = 0.4496 | | | |
| Combined analysis(d) | P = 0.2671 | | | |
| Cochran-Armitage test(e) | P = 0.6529 | | | |
| Fisher Exact test(e) | | P = 0.3087 | P = 0.1811 | P = 0.3087 |

(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 cannot 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 : SYMMARY,
RAT : MALE :
ALL ANIMALS
(2-YEAR STUDY)

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 1

| Organ | Findings | Group Name No. of Animals on Study | Control 50 | 25ppm 50 | 100ppm 50 | 400ppm 50 |
|------------------------|--|---------------------------------------|---------------|-------------|--------------|--------------|
| {Respiratory system} | | | | | | |
| nasal cavit | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 0 | 1 | 1 | 0 |
| lung | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 3 | 2 | 3 | 0 |
| | metastasis:liver tumor | | 0 | 0 | 0 | 2 |
| | metastasis:bone tumor | | 0 | 0 | 1 | 0 |
| | metastasis:spleen tumor | | 0 | 1 | 0 | 0 |
| | metastasis:zybal gland tumor | | 0 | 0 | 1 | 0 |
| | metastasis:epididymis tumor | | 0 | 0 | 0 | 1 |
| {Hematopoietic system} | | | | | | |
| bone marrow | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 2 | 0 | 1 | 0 |
| lymph node | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 0 | 3 | 1 | 0 |
| | metastasis:spleen tumor | | 0 | 1 | 0 | 0 |
| | metastasis:epididymis tumor | | 0 | 0 | 0 | 1 |
| | metastasis:skin/appendage tumor | | 0 | 0 | 1 | 0 |
| thymus | | | <50> | <50> | <50> | <50> |
| | metastasis:epididymis tumor | | 0 | 0 | 0 | 1 |
| spleen | | | <50> | <50> | <50> | <50> |
| | metastasis:pancreas tumor | | 0 | 0 | 0 | 1 |
| < a > | a : Number of animals examined at the site | | | | | |
| b | b : Number of animals with lesion | | | | | |

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 2

| Group Name No. of Animals on Study | | Control 50 | 25ppm 50 | 100ppm 50 | 400ppm 50 |
|---------------------------------------|----------------------------------|---------------|-------------|--------------|--------------|
| Organ | Findings | | | | |
| {Hematopoietic system} | | | | | |
| spleen | metastasis:epididymis tumor | <50> 0 | <50> 0 | <50> 0 | <50> 1 |
| {Circulatory system} | | | | | |
| heart | metastasis:epididymis tumor | <50> 0 | <50> 0 | <50> 0 | <50> 1 |
| {Digestive system} | | | | | |
| stomach | metastasis:pancreas tumor | <50> 0 | <50> 0 | <50> 0 | <50> 1 |
| liver | leukemic cell infiltration | <50> 3 | <50> 2 | <50> 3 | <50> 0 |
| | metastasis:pancreas tumor | 0 | 0 | 0 | 1 |
| | metastasis:spleen tumor | 1 | 1 | 0 | 0 |
| | metastasis:small intestine tumor | 0 | 0 | 1 | 0 |
| pancreas | leukemic cell infiltration | <50> 0 | <50> 2 | <50> 0 | <50> 0 |
| | metastasis:spleen tumor | 1 | 0 | 0 | 0 |
| | metastasis:epididymis tumor | 0 | 0 | 0 | 1 |
| {Urinary system} | | | | | |
| kidney | leukemic cell infiltration | <50> 2 | <50> 2 | <50> 1 | <50> 0 |

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

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 3

| Organ | Findings | Group Name No. of Animals on Study | Control 50 | 25ppm 50 | 100ppm 50 | 400ppm 50 |
|---|----------------------------------|---------------------------------------|---------------|-------------|--------------|--------------|
| {Endocrine system} | | | | | | |
| pituitary | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 0 | 1 | 0 | 0 |
| adrenal | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 0 | 0 | 1 | 0 |
| {Reproductive system} | | | | | | |
| semin ves | | | <50> | <50> | <50> | <50> |
| | metastasis:epididymis tumor | | 0 | 0 | 0 | 1 |
| prostate | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 0 | 1 | 0 | 0 |
| {Nervous system} | | | | | | |
| brain | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 1 | 1 | 1 | 0 |
| | metastasis:pituitary tumor | | 1 | 0 | 0 | 0 |
| spinal cord | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 1 | 1 | 0 | 0 |
| {Body cavities} | | | | | | |
| peritoneum | | | <50> | <50> | <50> | <50> |
| | metastasis:pancreas tumor | | 0 | 0 | 0 | 1 |
| | metastasis:spleen tumor | | 1 | 0 | 0 | 0 |
| | metastasis:small intestine tumor | | 0 | 0 | 1 | 0 |
| < a > a : Number of animals examined at the site b b : Number of animals with lesion | | | | | | |

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 4

| | | Group Name | Control | 25ppm | 100ppm | 400ppm |
|-----------------|--|-------------------------|---------|-------|--------|--------|
| Organ_____ | Findings_____ | No. of Animals on Study | 50 | 50 | 50 | 50 |
| <hr/> | | | | | | |
| {Body cavities} | | | | | | |
| retroperit | | | <50> | <50> | <50> | <50> |
| | metastasis:epididymis tumor | | 0 | 0 | 0 | 1 |
| mesenterium | | | <50> | <50> | <50> | <50> |
| | metastasis:epididymis tumor | | 0 | 0 | 0 | 1 |
| adipose | | | <50> | <50> | <50> | <50> |
| | metastasis:pancreas tumor | | 0 | 0 | 0 | 1 |
| <hr/> | | | | | | |
| < 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 : SYMMARY,
RAT : MALE :
DEAD AND MORIBUND ANIMALS
(2-YEAR STUDY)

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 1

| Organ | Findings | Group Name No. of Animals on Study | Control 10 | 25ppm 15 | 100ppm 12 | 400ppm 20 |
|------------------------|-----------------------------|---------------------------------------|---------------|-------------|--------------|--------------|
| {Respiratory system} | | | | | | |
| nasal cavit | | | <10> | <15> | <12> | <20> |
| | leukemic cell infiltration | | 0 | 1 | 1 | 0 |
| lung | | | <10> | <15> | <12> | <20> |
| | leukemic cell infiltration | | 2 | 2 | 2 | 0 |
| | metastasis:liver tumor | | 0 | 0 | 0 | 1 |
| | metastasis:bone tumor | | 0 | 0 | 1 | 0 |
| | metastasis:spleen tumor | | 0 | 1 | 0 | 0 |
| | metastasis:epididymis tumor | | 0 | 0 | 0 | 1 |
| {Hematopoietic system} | | | | | | |
| bone marrow | | | <10> | <15> | <12> | <20> |
| | leukemic cell infiltration | | 1 | 0 | 1 | 0 |
| lymph node | | | <10> | <15> | <12> | <20> |
| | leukemic cell infiltration | | 0 | 2 | 1 | 0 |
| | metastasis:spleen tumor | | 0 | 1 | 0 | 0 |
| | metastasis:epididymis tumor | | 0 | 0 | 0 | 1 |
| thymus | | | <10> | <15> | <12> | <20> |
| | metastasis:epididymis tumor | | 0 | 0 | 0 | 1 |
| | | | <10> | <15> | <12> | <20> |
| spleen | | | <10> | <15> | <12> | <20> |
| | metastasis:epididymis tumor | | 0 | 0 | 0 | 1 |
| {Circulatory system} | | | | | | |
| heart | | | <10> | <15> | <12> | <20> |
| | metastasis:epididymis tumor | | 0 | 0 | 0 | 1 |

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

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 2

| Organ | Findings | Group Name No. of Animals on Study | Control 10 | 25ppm 15 | 100ppm 12 | 400ppm 20 |
|-----------------------|--|---------------------------------------|---------------|-------------|--------------|--------------|
| {Digestive system} | | | | | | |
| liver | leukemic cell infiltration | | <10> 2 | <15> 2 | <12> 2 | <20> 0 |
| | metastasis:spleen tumor | | 1 | 1 | 0 | 0 |
| | metastasis:small intestine tumor | | 0 | 0 | 1 | 0 |
| pancreas | leukemic cell infiltration | | <10> 0 | <15> 2 | <12> 0 | <20> 0 |
| | metastasis:spleen tumor | | 1 | 0 | 0 | 0 |
| | metastasis:epididymis tumor | | 0 | 0 | 0 | 1 |
| {Urinary system} | | | | | | |
| kidney | leukemic cell infiltration | | <10> 2 | <15> 2 | <12> 1 | <20> 0 |
| | | | | | | |
| {Endocrine system} | | | | | | |
| pituitary | leukemic cell infiltration | | <10> 0 | <15> 1 | <12> 0 | <20> 0 |
| | | | | | | |
| adrenal | leukemic cell infiltration | | <10> 0 | <15> 0 | <12> 1 | <20> 0 |
| | | | | | | |
| {Reproductive system} | | | | | | |
| semin ves | metastasis:epididymis tumor | | <10> 0 | <15> 0 | <12> 0 | <20> 1 |
| | | | | | | |
| prostate | leukemic cell infiltration | | <10> 0 | <15> 1 | <12> 0 | <20> 0 |
| | | | | | | |
| < a > | a : Number of animals examined at the site | | | | | |
| b | b : Number of animals with lesion | | | | | |

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 3

| | | Group Name | Control | 25ppm | 100ppm | 400ppm |
|------------------|--|-------------------------|-----------|-----------|-----------|-----------|
| | | No. of Animals on Study | 10 | 15 | 12 | 20 |
| Organ | Findings | | | | | |
| {Nervous system} | | | | | | |
| brain | leukemic cell infiltration | | <10> 1 | <15> 1 | <12> 1 | <20> 0 |
| | metastasis:pituitary tumor | | 1 | 0 | 0 | 0 |
| spinal cord | leukemic cell infiltration | | <10> 1 | <15> 1 | <12> 0 | <20> 0 |
| {Body cavities} | | | | | | |
| peritoneum | metastasis:spleen tumor | | <10> 1 | <15> 0 | <12> 0 | <20> 0 |
| | metastasis:small intestine tumor | | 0 | 0 | 1 | 0 |
| retroperit | metastasis:epididymis tumor | | <10> 0 | <15> 0 | <12> 0 | <20> 1 |
| mesenterium | metastasis:epididymis tumor | | <10> 0 | <15> 0 | <12> 0 | <20> 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 : SYMMARY,
RAT : MALE :
SACRIFICED ANIMALS
(2-YEAR STUDY)

STUDY NO. : 0417
 ANIMAL : RAT 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 40 | 25ppm 35 | 100ppm 38 | 400ppm 30 |
|---------------------------------------|--|---------------|-------------|--------------|--------------|
| Organ | Findings | | | | |
| {Respiratory system} | | | | | |
| lung | | <40> | <35> | <38> | <30> |
| | leukemic cell infiltration | 1 | 0 | 1 | 0 |
| | metastasis:liver tumor | 0 | 0 | 0 | 1 |
| | metastasis:zymlal gland tumor | 0 | 0 | 1 | 0 |
| {Hematopoietic system} | | | | | |
| bone marrow | | <40> | <35> | <38> | <30> |
| | leukemic cell infiltration | 1 | 0 | 0 | 0 |
| lymph node | | <40> | <35> | <38> | <30> |
| | leukemic cell infiltration | 0 | 1 | 0 | 0 |
| spleen | | <40> | <35> | <38> | <30> |
| | metastasis:pancreas tumor | 0 | 0 | 0 | 1 |
| {Digestive system} | | | | | |
| stomach | | <40> | <35> | <38> | <30> |
| | metastasis:pancreas tumor | 0 | 0 | 0 | 1 |
| liver | | <40> | <35> | <38> | <30> |
| | leukemic cell infiltration | 1 | 0 | 1 | 0 |
| | metastasis:pancreas tumor | 0 | 0 | 0 | 1 |
| {Body cavities} | | | | | |
| peritoneum | | <40> | <35> | <38> | <30> |
| | metastasis:pancreas tumor | 0 | 0 | 0 | 1 |
| < a > | a : Number of animals examined at the site | | | | |
| b | b : Number of animals with lesion | | | | |

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 2

| Organ | Findings | Group Name No. of Animals on Study | Control 40 | 25ppm 35 | 100ppm 38 | 400ppm 30 |
|-------|----------|---------------------------------------|---------------|-------------|--------------|--------------|
|-------|----------|---------------------------------------|---------------|-------------|--------------|--------------|

{Body cavities}

| | | | | | |
|---------|---------------------------|------|------|------|------|
| adipose | | <40> | <35> | <38> | <30> |
| | metastasis:pancreas tumor | 0 | 0 | 0 | 1 |

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

(JPT150)

BAIS4

APPENDIX P 4

HISTOPATHOLOGICAL FINDINGS:
METASTASIS OF TUMOR : SYMMARY,
RAT : FEMALE :
ALL ANIMALS
(2-YEAR STUDY)

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 5

| | | Group Name | Control | 25ppm | 100ppm | 400ppm |
|------------------------|--|-------------------------|---------|-------|--------|--------|
| | | No. of Animals on Study | 50 | 50 | 50 | 50 |
| Organ | Findings | | | | | |
| {Respiratory system} | | | | | | |
| lung | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 6 | 1 | 3 | 9 |
| | metastasis:liver tumor | | 0 | 0 | 0 | 14 |
| | metastasis:bone tumor | | 0 | 0 | 0 | 1 |
| {Hematopoietic system} | | | | | | |
| bone marrow | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 1 | 0 | 2 | 4 |
| lymph node | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 1 | 0 | 2 | 2 |
| spleen | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 1 | 0 | 0 | 0 |
| {Circulatory system} | | | | | | |
| heart | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 0 | 0 | 2 | 1 |
| {Digestive system} | | | | | | |
| stomach | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 0 | 0 | 1 | 0 |
| liver | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 6 | 2 | 3 | 10 |
| pancreas | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 1 | 0 | 2 | 1 |
| < a > | a : Number of animals examined at the site | | | | | |
| b | b : Number of animals with lesion | | | | | |

STUDY NO. : 0417
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 6

| Organ | Findings | Group Name No. of Animals on Study | Control 50 | 25ppm 50 | 100ppm 50 | 400ppm 50 |
|----------------------------------|----------------------------|---------------------------------------|---------------|-------------|--------------|--------------|
| {Urinary system} | | | | | | |
| kidney | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 2 | 0 | 1 | 1 |
| {Endocrine system} | | | | | | |
| pituitary | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 0 | 1 | 2 | 0 |
| adrenal | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 1 | 1 | 2 | 1 |
| | metastasis:liver tumor | | 0 | 0 | 0 | 1 |
| {Nervous system} | | | | | | |
| brain | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 1 | 0 | 0 | 1 |
| | metastasis:pituitary tumor | | 1 | 0 | 0 | 0 |
| spinal cord | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 1 | 0 | 0 | 0 |
| {Special sense organs/appendage} | | | | | | |
| eye | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 0 | 0 | 1 | 0 |
| Harder gl | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 1 | 0 | 0 | 0 |
| {Musculoskeletal system} | | | | | | |
| muscle | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 1 | 0 | 0 | 0 |

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

APPENDIX P 5

HISTOPATHOLOGICAL FINDINGS :
METASTASIS OF TUMOR : SYMMARY,
RAT : FEMALE :
DEAD AND MORIBUND ANIMALS
(2-YEAR STUDY)

STUDY NO. : 0417
 ANIMAL : RAT 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 12 | 25ppm 5 | 100ppm 11 | 400ppm 24 |
|---------------------------------------|----------------------------|---------------|------------|--------------|--------------|
| Organ | Findings | | | | |
| {Respiratory system} | | | | | |
| lung | | <12> | < 5> | <11> | <24> |
| | leukemic cell infiltration | 3 | 1 | 2 | 7 |
| | metastasis:liver tumor | 0 | 0 | 0 | 5 |
| | metastasis:bone tumor | 0 | 0 | 0 | 1 |
| {Hematopoietic system} | | | | | |
| bone marrow | | <12> | < 5> | <11> | <24> |
| | leukemic cell infiltration | 0 | 0 | 2 | 3 |
| lymph node | | <12> | < 5> | <11> | <24> |
| | leukemic cell infiltration | 1 | 0 | 2 | 1 |
| spleen | | <12> | < 5> | <11> | <24> |
| | leukemic cell infiltration | 1 | 0 | 0 | 0 |
| {Circulatory system} | | | | | |
| heart | | <12> | < 5> | <11> | <24> |
| | leukemic cell infiltration | 0 | 0 | 2 | 1 |
| {Digestive system} | | | | | |
| stomach | | <12> | < 5> | <11> | <24> |
| | leukemic cell infiltration | 0 | 0 | 1 | 0 |
| liver | | <12> | < 5> | <11> | <24> |
| | leukemic cell infiltration | 3 | 1 | 2 | 7 |
| pancreas | | <12> | < 5> | <11> | <24> |
| | leukemic cell infiltration | 1 | 0 | 2 | 1 |

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

STUDY NO. : 0417
 ANIMAL : RAT 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 12 | 25ppm 5 | 100ppm 11 | 400ppm 24 |
|----------------------------------|----------------------------|---------------------------------------|---------------|------------|--------------|--------------|
| Organ | Findings | | | | | |
| {Urinary system} | | | | | | |
| kidney | | | <12> | < 5> | <11> | <24> |
| | leukemic cell infiltration | | 2 | 0 | 1 | 1 |
| {Endocrine system} | | | | | | |
| pituitary | | | <12> | < 5> | <11> | <24> |
| | leukemic cell infiltration | | 0 | 1 | 2 | 0 |
| adrenal | | | <12> | < 5> | <11> | <24> |
| | leukemic cell infiltration | | 1 | 1 | 2 | 1 |
| {Nervous system} | | | | | | |
| brain | | | <12> | < 5> | <11> | <24> |
| | leukemic cell infiltration | | 1 | 0 | 0 | 1 |
| spinal cord | | | <12> | < 5> | <11> | <24> |
| | leukemic cell infiltration | | 1 | 0 | 0 | 0 |
| {Special sense organs/appendage} | | | | | | |
| eye | | | <12> | < 5> | <11> | <24> |
| | leukemic cell infiltration | | 0 | 0 | 1 | 0 |
| Harder gl | | | <12> | < 5> | <11> | <24> |
| | leukemic cell infiltration | | 1 | 0 | 0 | 0 |
| {Musculoskeletal system} | | | | | | |
| muscle | | | <12> | < 5> | <11> | <24> |
| | leukemic cell infiltration | | 1 | 0 | 0 | 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 : SYMMARY,
RAT : FEMALE :
SACRIFICED ANIMALS
(2-YEAR STUDY)

STUDY NO. : 0417
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 3

| | | Group Name No. of Animals on Study | Control 38 | 25ppm 45 | 100ppm 39 | 400ppm 26 |
|------------------------|----------------------------|---------------------------------------|---------------|-------------|--------------|--------------|
| Organ | Findings | | | | | |
| {Respiratory system} | | | | | | |
| lung | | | <38> | <45> | <39> | <26> |
| | leukemic cell infiltration | | 3 | 0 | 1 | 2 |
| | metastasis:liver tumor | | 0 | 0 | 0 | 9 |
| {Hematopoietic system} | | | | | | |
| bone marrow | | | <38> | <45> | <39> | <26> |
| | leukemic cell infiltration | | 1 | 0 | 0 | 1 |
| lymph node | | | <38> | <45> | <39> | <26> |
| | leukemic cell infiltration | | 0 | 0 | 0 | 1 |
| {Digestive system} | | | | | | |
| liver | | | <38> | <45> | <39> | <26> |
| | leukemic cell infiltration | | 3 | 1 | 1 | 3 |
| {Endocrine system} | | | | | | |
| adrenal | | | <38> | <45> | <39> | <26> |
| | metastasis:liver tumor | | 0 | 0 | 0 | 1 |
| {Nervous system} | | | | | | |
| brain | | | <38> | <45> | <39> | <26> |
| | metastasis:pituitary tumor | | 1 | 0 | 0 | 0 |

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

APPENDIX Q

METHODS, UNITS AND DECIMAL PLACE FOR
HEMATOLOGY AND BIOCHEMISTRY
IN THE 2-YEAR INHALATION STUDY OF
1-BROMO-3-CHLOROPROPANE

METHODS, UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY
IN THE 2-YEAR INHALATION STUDY OF 1-BROMO-3-CHLOROPROPANE

| 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 |
| Glutamic oxaloacetic transaminase (GOT) | JSCC method ³⁾ | IU/L | 0 |
| Glutamic pyruvic transaminase (GPT) | 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) | L· γ -Glutamyl-p-nitroanilide method ³⁾ | IU/L | 0 |
| Creatine phosphokinase (CPK) | 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.)