

ジクロロメタ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：0278

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APPENDIX A 1

CLINICAL OBSERVATION: SUMMARY, RAT: MALE

(2-YEAR STUDY)

STUDY NO. : 0278
 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 | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|
| | | 1-1 | 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 |
| | | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| MORIBUND SACRIFICE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| LOCOMOTOR MOVEMENT DECR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| LATERAL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PARALYTIC GAIT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PILOERECTION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
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REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 14-7 | 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 |
| | | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| MORIBUND SACRIFICE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| LOCOMOTOR MOVEMENT DECR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| LATERAL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PARALYTIC GAIT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PILOERECTOR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 28-7 | 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 |
| | | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| MORIBUND SACRIFICE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| LOCOMOTOR MOVEMENT DECR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| LATERAL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PARALYTIC GAIT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PILOERECTOR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 42-7 | 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 |
| | | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| MORIBUND SACRIFICE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| LOCOMOTOR MOVEMENT DECR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| LATERAL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PARALYTIC GAIT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
ANIMAL : RAT F344/DuGrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 56-7 | 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 |
| | | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| MORIBUND SACRIFICE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| LOCOMOTOR MOVEMENT DECR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| LATERAL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PARALYTIC GAIT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PILOERECTION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
ANIMAL : RAT F344/DuGrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 70-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| DEATH | Control | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 |
| | 1000 ppm | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 1 | 1 | 1 | 2 | 2 | 2 | 3 | 4 | 4 | 4 | 4 | 4 | 5 | 5 |
| MORIBUND SACRIFICE | Control | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| LOCOMOTOR MOVEMENT DECR | Control | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| LATERAL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PARALYTIC GAIT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PILOERECTON | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
ANIMAL : RAT F344/DuGrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 84-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| DEATH | Control | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 5 | 6 | 6 | 6 |
| | 1000 ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 3 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 3 |
| | 4000 ppm | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 8 | 8 | 9 | 11 | 11 | 11 |
| MORIBUND SACRIFICE | Control | 2 | 2 | 2 | 4 | 5 | 5 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 7 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 2000 ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 2 |
| LOCOMOTOR MOVEMENT DECR | Control | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| LATERAL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| PARALYTIC GAIT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 2 | 2 | 1 | 1 | 1 | 2 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| WASTING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| SOILED | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PILOERECTON | Control | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |

STUDY NO. : 0278
ANIMAL : RAT F344/DuGrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | |
|-------------------------|------------|-------------------------|------|-------|-------|-------|-------|-------|
| | | 98-7 | 99-7 | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| DEATH | Control | 6 | 6 | 6 | 6 | 6 | 6 | 7 |
| | 1000 ppm | 3 | 3 | 3 | 3 | 4 | 4 | 4 |
| | 2000 ppm | 4 | 4 | 4 | 4 | 4 | 4 | 4 |
| | 4000 ppm | 11 | 11 | 13 | 15 | 17 | 17 | 18 |
| MORIBUND SACRIFICE | Control | 7 | 7 | 7 | 8 | 8 | 11 | 11 |
| | 1000 ppm | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| | 2000 ppm | 2 | 2 | 3 | 4 | 5 | 7 | 8 |
| | 4000 ppm | 3 | 3 | 3 | 3 | 3 | 3 | 4 |
| LOCOMOTOR MOVEMENT DECR | Control | 0 | 0 | 0 | 1 | 0 | 1 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 1 | 1 | 1 | 2 | 1 |
| | 4000 ppm | 1 | 0 | 0 | 0 | 0 | 0 | 1 |
| LATERAL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PARALYTIC GAIT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | Control | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| | 4000 ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PILOERECTION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
ANIMAL : RAT F344/DuGrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|--------------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|
| | | 1-1 | 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 |
| | | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED PERI GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXOPHTHALMOS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EYE OPACITY | Control | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CATARACT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CORNEAL OPACITY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANTERIOR CHAMBER OPACITY | Control | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
ANIMAL : RAT F344/DuGrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|--------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 14-7 | 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 |
| | | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED PERI GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXOPHTHALMOS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EYE OPACITY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CATARACT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CORNEAL OPACITY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANTERIOR CHAMBER OPACITY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|--------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 28-7 | 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 |
| | | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED PERI GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXOPHTHALMOS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EYE OPACITY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 2 |
| | 2000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CATARACT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 2000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CORNEAL OPACITY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANTERIOR CHAMBER OPACITY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|--------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 42-7 | 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 |
| | | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED PERI GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXOPHTHALMOS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EYE OPACITY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 |
| | 1000 ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 2000 ppm | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CATARACT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 |
| | 1000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 2000 ppm | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CORNEAL OPACITY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANTERIOR CHAMBER OPACITY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXTERNAL MASS | Control | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 2000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 4 | 4 | 4 | 2 | 3 | 3 | 3 | 3 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 0 |

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|--------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 56-7 | 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 |
| | | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED PERI GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXOPHTHALMOS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EYE OPACITY | Control | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 |
| | 1000 ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 2000 ppm | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CATARACT | Control | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 |
| | 1000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 2000 ppm | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CORNEAL OPACITY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANTERIOS CHAMBER OPACITY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXTERNAL MASS | Control | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 |
| | 1000 ppm | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 3 | 2 | 3 | 3 | 3 | 2 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 |
| | 4000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 3 | 3 |

STUDY NO. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|--------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 70-7 | 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 |
| | | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 |
| SOILED PERI GENITALIA | Control | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXOPHTHALMOS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EYE OPACITY | Control | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 1000 ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 2000 ppm | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CATARACT | Control | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 1000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 2000 ppm | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CORNEAL OPACITY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANTERIOR CHAMBER OPACITY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXTERNAL MASS | Control | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 2 | 2 | 2 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 |
| | 2000 ppm | 4 | 4 | 6 | 6 | 6 | 5 | 5 | 5 | 5 | 6 | 5 | 5 | 5 | 6 |
| | 4000 ppm | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | 4 | 5 | 5 | 6 | 7 |

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ANIMAL : RAT F344/DuGrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|--------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 84-7 | 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 |
| | | 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 |
| | 1000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED PERI GENITALIA | Control | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 1 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXOPHTHALMOS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EYE OPACITY | Control | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 1000 ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 2000 ppm | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | 4 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CATARACT | Control | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 1000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 2000 ppm | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | 4 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CORNEAL OPACITY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANTERIOR CHAMBER OPACITY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXTERNAL MASS | Control | 2 | 2 | 2 | 1 | 2 | 2 | 3 | 4 | 4 | 4 | 4 | 4 | 5 | 5 |
| | 1000 ppm | 1 | 1 | 1 | 3 | 3 | 5 | 5 | 5 | 6 | 6 | 7 | 8 | 11 | 11 |
| | 2000 ppm | 6 | 7 | 7 | 8 | 8 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 10 |
| | 4000 ppm | 6 | 8 | 10 | 12 | 13 | 15 | 16 | 16 | 16 | 16 | 16 | 15 | 15 | 17 |

STUDY NO. : 0278
ANIMAL : RAT F344/DuGrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
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SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | |
|--------------------------|------------|-------------------------|------|-------|-------|-------|-------|-------|
| | | 98-7 | 99-7 | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| FROG BELLY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 1 | 1 | 1 | 1 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED PERI GENITALIA | Control | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 1 | 2 | 1 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 1 | 1 | 0 | 0 | 0 |
| EXOPHTHALMOS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EYE OPACITY | Control | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 1000 ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 2000 ppm | 4 | 4 | 4 | 4 | 3 | 3 | 3 |
| | 4000 ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| CATARACT | Control | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 1000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 2000 ppm | 4 | 4 | 4 | 4 | 3 | 3 | 3 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CORNEAL OPACITY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANTERIOR CHAMBER OPACITY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXTERNAL MASS | Control | 5 | 5 | 6 | 7 | 6 | 6 | 5 |
| | 1000 ppm | 11 | 11 | 11 | 11 | 12 | 13 | 14 |
| | 2000 ppm | 11 | 11 | 10 | 9 | 11 | 11 | 10 |
| | 4000 ppm | 15 | 17 | 16 | 18 | 17 | 17 | 16 |

STUDY NO. : 0278
ANIMAL : RAT F344/DuGrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
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SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|---------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|
| | | 1-1 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| INTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.NOSE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.PERI MOUTH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.PERI EAR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.NECK | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.BREAST | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.ABDOMEN | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|---------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 14-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| INTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.NOSE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.PERI MOUTH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.PERI EAR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.NECK | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.BREAST | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.ABDOMEN | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
 ANIMAL : RAT F344/DuGrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|---------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 28-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| INTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.NOSE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.PERI MOUTH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.PERI EAR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.NECK | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.BREAST | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.ABDOMEN | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|---------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 42-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| INTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.NOSE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.PERI MOUTH | Control | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.PERI EAR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.NECK | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.BREAST | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.ABDOMEN | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 3 | 3 | 1 | 2 | 2 | 2 | 2 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 0 |

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|---------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 56-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| INTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.NOSE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.PERI MOUTH | Control | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M.EAR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.PERI EAR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.NECK | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.BREAST | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 |
| M.ABDOMEN | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 |
| | 1000 ppm | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 2 | 1 | 3 | 2 | 2 | 1 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|---------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 70-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| INTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 2 | 2 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| M.NOSE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.PERI MOUTH | Control | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M.EAR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.PERI EAR | Control | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.NECK | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 2 |
| M.BREAST | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| M.ABDOMEN | Control | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 2000 ppm | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 |
| | 4000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 |

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|---------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 84-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| INTERNAL MASS | Control | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.NOSE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.PERI MOUTH | Control | 2 | 2 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 1 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 1 | 1 | 1 |
| M.EAR | Control | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.PERI EAR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.NECK | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 2 | 2 | 2 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 4000 ppm | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 1 |
| M.BREAST | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 |
| | 2000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 |
| | 4000 ppm | 2 | 3 | 3 | 3 | 4 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 7 |
| M.ABDOMEN | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| | 1000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 |
| | 2000 ppm | 4 | 5 | 5 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| | 4000 ppm | 2 | 2 | 3 | 3 | 4 | 5 | 6 | 6 | 6 | 6 | 6 | 5 | 5 | 5 |

STUDY NO. : 0278
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 | | | | | | |
|---------------|------------|-------------------------|------|-------|-------|-------|-------|-------|
| | | 98-7 | 99-7 | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| INTERNAL MASS | Control | 0 | 0 | 0 | 1 | 1 | 1 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 1 | 1 | 1 | 2 | 2 | 2 | 2 |
| | 4000 ppm | 1 | 1 | 1 | 0 | 1 | 1 | 1 |
| M.NOSE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 1 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.PERI MOUTH | Control | 1 | 1 | 1 | 1 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 1 | 1 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M.EAR | Control | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.PERI EAR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.NECK | Control | 0 | 0 | 0 | 1 | 1 | 1 | 1 |
| | 1000 ppm | 2 | 2 | 2 | 3 | 3 | 3 | 3 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M.BREAST | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 2 | 2 | 2 | 2 | 2 | 3 | 3 |
| | 2000 ppm | 2 | 3 | 3 | 3 | 4 | 4 | 3 |
| | 4000 ppm | 5 | 6 | 6 | 6 | 6 | 6 | 6 |
| M.ABDOMEN | Control | 1 | 1 | 1 | 1 | 1 | 1 | 0 |
| | 1000 ppm | 3 | 3 | 3 | 3 | 4 | 4 | 5 |
| | 2000 ppm | 5 | 5 | 5 | 5 | 5 | 5 | 4 |
| | 4000 ppm | 5 | 5 | 5 | 6 | 6 | 6 | 6 |

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|--------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|
| | | 1-1 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.POSTERIOR DORSUM | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.HINDLIMB | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.TAIL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANEMIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| JAUNDISE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ASCITES | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
ANIMAL : RAT F344/DuGrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|--------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 14-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.POSTERIOR DORSUM | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.HINDLIMB | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.TAIL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANEMIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| JAUNDISE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ASCITES | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|--------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 28-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.POSTERIOR DORSUM | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.HINDLIMB | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.TAIL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANEMIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| JAUNDISE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ASCITES | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|--------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 42-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.POSTERIOR DORSUM | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.HINDLIMB | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.TAIL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANEMIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| JAUNDISE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ASCITES | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|--------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 56-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.POSTERIOR DORSUM | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.HINDLIMB | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.TAIL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANEMIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| JAUNDISE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ASCITES | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|--------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 70-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| N.ANTERIOR.DORSUM | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.POSTERIOR DORSUM | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.HINDLIMB | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.TAIL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANEMIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| JAUNDISE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ASCITES | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|--------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 84-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M.ANTERIOR.DORSUM | Control | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 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 |
| | 1000 ppm | 0 | 0 | 0 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| M.HINDLIMB | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| M.GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.TAIL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANEMIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| JAUNDISE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ASCITES | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
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 | | | | | | |
|--------------------|------------|-------------------------|------|-------|-------|-------|-------|-------|
| | | 98-7 | 99-7 | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M.ANTERIOR.DORSUM | Control | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 4000 ppm | 1 | 2 | 2 | 3 | 2 | 2 | 2 |
| M.POSTERIOR DORSUM | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 2 | 3 | 3 | 2 | 2 | 2 | 2 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 2 | 2 | 2 | 2 | 2 | 2 | 1 |
| M.HINDLIMB | Control | 0 | 0 | 1 | 1 | 1 | 1 | 1 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 1 | 1 | 1 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 1 | 1 | 0 | 0 | 0 | 0 | 0 |
| M.GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.TAIL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANEMIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 1 | 1 | 2 | 1 | 2 | 1 | 0 |
| | 4000 ppm | 1 | 1 | 1 | 0 | 0 | 1 | 1 |
| JAUNDISE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ASCITES | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
 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 | | | | | | | | | | | | | |
|----------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|
| | | 1-1 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| IRREGULAR BREATHING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| BRADYPNEA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SUBNORMAL TEMP | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
 ANIMAL : RAT F344/DuGrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|----------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 14-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| IRREGULAR BREATHING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| BRADYPNEA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SUBNORMAL TEMP | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

(HAN190)

BAIS3

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|----------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 28-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| IRREGULAR BREATHING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| BRADYPNEA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SUBNORMAL TEMP | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

(HAN190)

BA153

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|----------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 42-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| IRREGULAR BREATHING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| BRADYPNEA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SUBNORMAL TEMP | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|----------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 56-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| IRREGULAR BREATHING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| BRADYPNEA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SUBNORMAL TEMP | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
 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 | | | | | | | | | | | | | |
|----------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 70-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| IRREGULAR BREATHING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | | | | | | | | | | | | | |
| BRADYPNEA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | | | | | | | | | | | | | |
| SUBNORMAL TEMP | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | | | | | | | | | | | | | |

(HAN190)

BAIS3

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|----------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 84-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| IRREGULAR BREATHING | Control | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRATION | Control | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| BRADYPNEA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SUBNORMAL TEMP | Control | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

(HAN190)

BAIS3

STUDY NO. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

PAGE : 40

| Clinical sign | Group Name | Administration Week-day | | | | | | |
|----------------------|------------|-------------------------|------|-------|-------|-------|-------|-------|
| | | 98-7 | 99-7 | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| IRREGULAR BREATHING | Control | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 2 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRATION | Control | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 1 | 0 | 2 | 1 |
| | 4000 ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| BRADYPNEA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 1 | 0 | 2 | 1 |
| | 4000 ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| SUBNORMAL TEMP | Control | 0 | 0 | 0 | 0 | 0 | 2 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 2 | 0 |
| | 4000 ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 |

(HAN190)

BAIS3

APPENDIX A 2

CLINICAL OBSERVATION: SUMMARY, RAT: FEMALE

(2-YEAR STUDY)

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|
| | | 1-1 | 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 |
| | | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| MORIBUND SACRIFICE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| LOCOMOTOR MOVEMENT DECR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PARALYTIC GAIT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| FROG BELLY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED PERI GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXOPHTHALMOS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
ANIMAL : RAT F344/DuGrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 14-7 | 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 |
| | | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| MORIBUND SACRIFICE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| LOCOMOTOR MOVEMENT DECR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PARALYTIC GAIT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| FROG BELLY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED PERI GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXOPHTHALMOS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 28-7 | 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 |
| | | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| MORIBUND SACRIFICE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| LOCOMOTOR MOVEMENT DECR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PARALYTIC GAIT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| FROG BELLY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED PERI GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXOPHTHALMOS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
ANIMAL : RAT F344/DuGrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 42-7 | 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 |
| | | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| MORIBUND SACRIFICE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| LOCOMOTOR MOVEMENT DECR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PARALYTIC GAIT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| FROG BELLY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED PERI GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXOPHTHALMOS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
ANIMAL : RAT F344/DuGrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 56-7 | 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 |
| | | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 2 | 2 | 2 | 2 |
| MORIBUND SACRIFICE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 1 | 1 | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 1 | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| FROG BELLY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED PERI GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXOPHTHALMOS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 70-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| DEATH | Control | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 1000 ppm | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 4 | 4 | 4 | 4 | 4 | 4 |
| MORIBUND SACRIFICE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| LOCOMOTOR MOVEMENT DECR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| PARALYTIC GAIT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| FROG BELLY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 1 | 1 | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXOPHTHALMOS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 84-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| DEATH | Control | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 1000 ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 4 | 4 | 4 | 4 | 4 | 4 | 4 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 3 | 3 | 3 |
| | 4000 ppm | 4 | 4 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 8 | 9 |
| MORIBUND SACRIFICE | Control | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 2 | 3 |
| | 2000 ppm | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 4000 ppm | 2 | 2 | 2 | 2 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 5 |
| LOCOMOTOR MOVEMENT DECR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 1 | 0 | 0 | 0 | 1 | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| FROG BELLY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 1 | 1 | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXOPHTHALMOS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
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 | | | | | | |
|-------------------------|------------|-------------------------|------|-------|-------|-------|-------|-------|
| | | 98-7 | 99-7 | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| DEATH | Control | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 1000 ppm | 4 | 4 | 4 | 4 | 5 | 6 | 6 |
| | 2000 ppm | 3 | 4 | 4 | 5 | 5 | 5 | 5 |
| | 4000 ppm | 9 | 9 | 10 | 11 | 13 | 13 | 13 |
| MORIBUND SACRIFICE | Control | 2 | 3 | 3 | 3 | 3 | 3 | 3 |
| | 1000 ppm | 4 | 4 | 4 | 4 | 4 | 4 | 4 |
| | 2000 ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 4000 ppm | 5 | 5 | 5 | 5 | 6 | 6 | 7 |
| LOCOMOTOR MOVEMENT DECR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 1 | 0 | 1 |
| PARALYTIC GAIT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 1 | 1 | 1 | 1 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| WASTING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| FROG BELLY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SOILED PERI GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXOPHTHALMOS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|-----------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|
| | | 1-1 | 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 |
| | | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CATARACT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CORNEAL OPACITY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| INTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.EYE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.PERI MOUTH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.NECK | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|-----------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 14-7 | 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 |
| | | 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 |
| | 1000 ppm | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CATARACT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 2 | 2 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CORNEAL OPACITY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| INTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.EYE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.PERI MOUTH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.NECK | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
ANIMAL : RAT F344/DuGrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-----------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 28-7 | 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 |
| | | 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 |
| | 1000 ppm | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| | 2000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CATARACT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| | 2000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CORNEAL OPACITY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| INTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.EYE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.PERI MOUTH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.NECK | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|-----------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 42-7 | 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 |
| | | 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 | 1 |
| | 1000 ppm | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 |
| | 2000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CATARACT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 1000 ppm | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 |
| | 2000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CORNEAL OPACITY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| INTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M.EYE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.PERI MOUTH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.NECK | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|-----------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 56-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| EYE OPACITY | Control | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 1000 ppm | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 |
| | 2000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CATARACT | Control | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 1000 ppm | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 |
| | 2000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CORNEAL OPACITY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 1 | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 |
| M.EYE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.PERI MOUTH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M.NECK | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|-----------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 70-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| EYE OPACITY | Control | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 1000 ppm | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 |
| | 2000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CATARACT | Control | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 1000 ppm | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 |
| | 2000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CORNEAL OPACITY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 2 | 2 |
| | 1000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 1 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 2 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 2 | 2 |
| M.EYE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.PERI MOUTH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M.NECK | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|-----------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 84-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| EYE OPACITY | Control | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 1000 ppm | 4 | 4 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 4 | 3 |
| | 2000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CATARACT | Control | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 1000 ppm | 4 | 4 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 4 | 3 |
| | 2000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CORNEAL OPACITY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXTERNAL MASS | Control | 3 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 5 | 6 |
| | 1000 ppm | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 |
| | 2000 ppm | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2 | 3 |
| | 4000 ppm | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 3 | 3 | 3 | 3 | 3 | 5 |
| INTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 |
| | 2000 ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 2 | 3 | 3 | 3 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 |
| M.EYE | Control | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| M.PERI MOUTH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M.NECK | Control | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
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 | | | | | | |
|-----------------|------------|-------------------------|------|-------|-------|-------|-------|-------|
| | | 98-7 | 99-7 | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| EYE OPACITY | Control | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 1000 ppm | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| | 2000 ppm | 1 | 1 | 1 | 1 | 1 | 2 | 2 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CATARACT | Control | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 1000 ppm | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| | 2000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| CORNEAL OPACITY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| EXTERNAL MASS | Control | 5 | 6 | 6 | 6 | 6 | 8 | 9 |
| | 1000 ppm | 2 | 2 | 3 | 4 | 5 | 6 | 6 |
| | 2000 ppm | 3 | 8 | 8 | 8 | 8 | 8 | 8 |
| | 4000 ppm | 5 | 8 | 7 | 9 | 10 | 10 | 10 |
| INTERNAL MASS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 1 | 1 | 1 | 1 | 1 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 1 | 1 | 0 | 1 | 1 | 0 | 0 |
| M.EYE | Control | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M.PERI MOUTH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 1 | 1 | 0 | 0 | 0 | 0 | 0 |
| M.NECK | Control | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|-------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|
| | | 1-1 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M.FORLIMB | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.BREAST | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.ABDOMEN | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.ANTERIOR.DORSUM | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.HINDLIMB | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.ANUS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANEMIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|-------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 14-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M.FORLIMB | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.BREAST | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.ABDOMEN | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.ANTERIOR.DORSUM | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.HINDLIMB | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.ANUS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANEMIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|-------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 28-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M.FORLIMB | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.BREAST | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.ABDOMEN | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.ANTERIOR.DORSUM | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.HINDLIMB | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.ANUS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANEMIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|-------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 42-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M.FORLIMB | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.BREAST | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.ABDOMEN | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.ANTERIOR.DORSUM | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.HINDLIMB | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.ANUS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANEMIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
 ANIMAL : RAT F344/DuGrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 56-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M.FORLIMB | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.BREAST | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M.ABDOMEN | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.ANTERIOR.DORSUM | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.HINDLIMB | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.ANUS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANEMIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
ANIMAL : RAT F344/DuGrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 70-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M.FORLIMB | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.BREAST | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 1000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M.ABDOMEN | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.ANTERIOR.DORSUM | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.HINDLIMB | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.ANUS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANEMIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|-------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 84-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M.FORLIMB | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.BREAST | Control | 1 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 1000 ppm | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 4000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 |
| M.ABDOMEN | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 2000 ppm | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 |
| M.ANTERIOR.DORSUM | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.HINDLIMB | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.GENITALIA | Control | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.ANUS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANEMIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | 2000 ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |

STUDY NO. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

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| Clinical sign | Group Name | Administration Week-day | | | | | | |
|-------------------|------------|-------------------------|------|-------|-------|-------|-------|-------|
| | | 98-7 | 99-7 | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| M.FORLIMB | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.BREAST | Control | 2 | 2 | 2 | 2 | 2 | 3 | 4 |
| | 1000 ppm | 1 | 1 | 2 | 3 | 3 | 4 | 4 |
| | 2000 ppm | 1 | 3 | 3 | 4 | 4 | 4 | 4 |
| | 4000 ppm | 2 | 4 | 4 | 6 | 5 | 5 | 5 |
| M.ABDOMEN | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 1 | 1 | 1 | 1 | 2 | 2 | 2 |
| | 2000 ppm | 1 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 4000 ppm | 1 | 2 | 2 | 2 | 4 | 4 | 4 |
| M.ANTERIOR.DORSUM | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.HINDLIMB | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 1 | 1 | 1 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.GENITALIA | Control | 2 | 3 | 3 | 3 | 3 | 3 | 3 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 2 | 1 | 1 | 1 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| M.ANUS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ANEMIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 1 | 0 | 0 | 0 | 0 | 0 | 1 |

STUDY NO. : 0278
ANIMAL : RAT F344/DuGrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|------------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|
| | | 1-1 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| JAUNDISE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| IRREGULAR BREATHING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| BRADYPNEA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRA.SOUND | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SUBNORMAL TEMP | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
ANIMAL : RAT F344/DuGrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 14-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| JAUNDISE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| IRREGULAR BREATHING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| BRADYPNEA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRA.SOUND | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SUBNORMAL TEMP | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

(HAN190)

BAIS3

STUDY NO. : 0278
ANIMAL : RAT F344/DuGrj
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 28-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| JAUNDISE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| IRREGULAR BREATHING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| BRADYPNEA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRA.SOUND | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SUBNORMAL TEMP | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 42-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| JAUNDISE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| IRREGULAR BREATHING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| BRADYPNEA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRA.SOUND | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SUBNORMAL TEMP | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

(HAN190)

BAIS3

STUDY NO. : 0278
 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 | | | | | | | | | | | | | |
|------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 56-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| JAUNDISE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| IRREGULAR BREATHING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 1 | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| BRADYPNEA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRA.SOUND | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 1 | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

(HAN190)

BAIS3

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 70-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| JAUNDISE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| IRREGULAR BREATHING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| BRADYPNEA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRA.SOUND | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SUBNORMAL TEMP | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

(HAN190)

BAIS3

STUDY NO. : 0278
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 | | | | | | | | | | | | | |
|------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | | 84-7 | 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 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| JAUNDISE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| IRREGULAR BREATHING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 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 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| BRADYPNEA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRA.SOUND | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SUBNORMAL TEMP | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : FEMALE

PAGE : 72

| Clinical sign | Group Name | Administration Week-day | | | | | | |
|----------------------------|------------|-------------------------|------|-------|-------|-------|-------|-------|
| | | 98-7 | 99-7 | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| JAUNDISE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| IRREGULAR BREATHING | Control | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRATION | Control | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| BRADYPNEA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRATORY SOUND | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| SUBNORMAL TEMP | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1000 ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4000 ppm | 0 | 0 | 0 | 0 | 1 | 0 | 1 |

(HAN190)

BAIS 3

APPENDIX B 1

BODY WEIGHT CHANGES: SUMMARY, RAT: MALE

(2-YEAR STUDY)

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 1

| Group Name | Administration | | week | | | | | | | | | | | |
|------------|----------------|---|------|---|------|---|------|-----|------|------|------|------|------|------|
| | 0 | | 1 | | 1 | | 2 | | 3 | | 4 | | 5 | |
| Control | 117± | 4 | 120± | 4 | 145± | 7 | 175± | 11 | 202± | 13 | 226± | 14 | 246± | 15 |
| 1000 ppm | 117± | 4 | 120± | 4 | 144± | 7 | 173± | 11 | 201± | 15 | 224± | 16 | 244± | 18 |
| 2000 ppm | 117± | 4 | 120± | 5 | 146± | 7 | 175± | 11 | 200± | 14 | 222± | 16 | 241± | 17 |
| 4000 ppm | 117± | 4 | 120± | 4 | 142± | 6 | 168± | 9** | 192± | 12** | 214± | 15** | 232± | 17** |

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

Test of Dunnett

(HAN260)

BAIS 3

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 2

| Group Name | Administration week | | 7 | | 8 | | 9 | | 10 | | 11 | | 12 | |
|------------|---------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | 6 | | | | | | | | | | | | | |
| Control | 263± | 15 | 279± | 15 | 293± | 17 | 306± | 17 | 316± | 17 | 326± | 18 | 334± | 17 |
| 1000 ppm | 260± | 18 | 276± | 19 | 290± | 19 | 303± | 21 | 312± | 21 | 321± | 21 | 328± | 21 |
| 2000 ppm | 257± | 19 | 272± | 19 | 286± | 20 | 298± | 20 | 308± | 20 | 317± | 21 | 324± | 20* |
| 4000 ppm | 248± | 19** | 262± | 20** | 275± | 21** | 287± | 21** | 297± | 21** | 306± | 21** | 312± | 21** |

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

Test of Dunnett

(HAN260)

BAIS3

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 3

| Group Name | Administration week | | 14 | | 18 | | 22 | | 26 | | 30 | | 34 | |
|------------|---------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | 13 | | | | | | | | | | | | | |
| Control | 343± | 18 | 350± | 18 | 373± | 20 | 389± | 21 | 402± | 22 | 417± | 23 | 429± | 23 |
| 1000 ppm | 337± | 22 | 344± | 21 | 367± | 22 | 386± | 22 | 398± | 22 | 412± | 23 | 426± | 24 |
| 2000 ppm | 332± | 20* | 340± | 20* | 362± | 22* | 381± | 22 | 394± | 22 | 410± | 23 | 423± | 24 |
| 4000 ppm | 322± | 21** | 328± | 22** | 351± | 21** | 369± | 23** | 381± | 24** | 397± | 23** | 408± | 25** |

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

Test of Dunnett

(HAN260)

BAIS 3

STUDY NO. : 0278
 ANIMAL : RAT F344/DuGrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 4

| Group Name | Administration week | | | | | | | | | | | |
|------------|---------------------|--|-----------|--|-----------|--|-----------|--|-----------|--|-----------|--|
| | 38 | | 42 | | 46 | | 50 | | 54 | | 58 | |
| Control | 438± 23 | | 446± 24 | | 452± 23 | | 459± 23 | | 461± 23 | | 465± 23 | |
| 1000 ppm | 434± 25 | | 443± 25 | | 448± 25 | | 455± 25 | | 460± 26 | | 463± 25 | |
| 2000 ppm | 431± 24 | | 441± 25 | | 447± 25 | | 455± 24 | | 452± 23 | | 456± 23 | |
| 4000 ppm | 417± 25** | | 424± 26** | | 431± 26** | | 436± 26** | | 440± 27** | | 440± 26** | |

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

Test of Dunnett

(HAN260)

BAIS 3

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 5

| Group Name | Administration week | | | | | | | | | | | | | |
|------------|---------------------|------|------|------|------|------|------|------|------|----|------|-----|------|----|
| | 66 | | 70 | | 74 | | 78 | | 82 | | 86 | | 90 | |
| Control | 471± | 22 | 467± | 24 | 466± | 23 | 463± | 29 | 463± | 26 | 448± | 48 | 455± | 30 |
| 1000 ppm | 471± | 27 | 470± | 28 | 472± | 27 | 466± | 33 | 473± | 30 | 475± | 32* | 468± | 34 |
| 2000 ppm | 462± | 23 | 461± | 23 | 459± | 38 | 464± | 25 | 460± | 35 | 462± | 28 | 462± | 30 |
| 4000 ppm | 444± | 28** | 440± | 28** | 440± | 34** | 444± | 27** | 448± | 37 | 445± | 29 | 443± | 31 |

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

Test of Dunnett

(HAN260)

BATS 3

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 6

| Group Name | Administration | | week | | | | | |
|------------|----------------|----|------|-----|------|-----|------|-----|
| | 94 | | 98 | | 102 | | 104 | |
| Control | 446± | 38 | 436± | 32 | 419± | 47 | 412± | 39 |
| 1000 ppm | 463± | 40 | 459± | 34* | 448± | 35* | 437± | 35* |
| 2000 ppm | 454± | 35 | 437± | 42 | 423± | 47 | 416± | 46 |
| 4000 ppm | 438± | 41 | 430± | 60 | 424± | 46 | 417± | 59 |

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

Test of Dunnett

(HAN260)

BAIS 3

APPENDIX B 2

BODY WEIGHT CHANGES: SUMMARY, RAT: FEMALE

(2-YEAR STUDY)

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 7

| Group Name | Administration week | | | | | | | | | | | |
|------------|---------------------|--|-------|--|----------|--|----------|--|----------|--|----------|----------|
| | 0 | | 1 | | 1 | | 2 | | 3 | | 4 | 5 |
| Control | 96± 3 | | 97± 4 | | 110± 4 | | 124± 5 | | 135± 6 | | 144± 7 | 154± 8 |
| 1000 ppm | 96± 3 | | 97± 3 | | 109± 4 | | 122± 5 | | 133± 6 | | 142± 7 | 152± 8 |
| 2000 ppm | 96± 3 | | 97± 3 | | 110± 4 | | 123± 5 | | 134± 6 | | 143± 7 | 151± 8 |
| 4000 ppm | 96± 3 | | 97± 3 | | 107± 4** | | 118± 4** | | 128± 5** | | 135± 6** | 144± 8** |

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

Test of Dunnett

(HAN260)

BAIS3

STUDY NO. : 0278
 ANIMAL : RAT F344/DuGrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 8

| Group Name | Administration week | | | | | | | | | | | |
|---|---------------------|-----|------|------|------|------|------|------|------|------|------|------|
| | 6 | | 7 | | 8 | | 9 | | 10 | | 11 | |
| Control | 161± | 8 | 168± | 9 | 174± | 10 | 179± | 9 | 184± | 10 | 189± | 10 |
| 1000 ppm | 160± | 9 | 166± | 9 | 171± | 9 | 177± | 10 | 181± | 10 | 187± | 10 |
| 2000 ppm | 158± | 9 | 164± | 10 | 168± | 10* | 174± | 11* | 178± | 11* | 185± | 12 |
| 4000 ppm | 150± | 9** | 155± | 10** | 160± | 11** | 166± | 11** | 170± | 12** | 177± | 13** |
| Significant difference : * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett | | | | | | | | | | | | |

(HAN260)

BAIS3

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 9

| Group Name | Administration week | | | | | | | | | | | | | |
|------------|---------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| | 13 | | 14 | | 18 | | 22 | | 26 | | 30 | | 34 | |
| Control | 197± | 10 | 199± | 11 | 209± | 12 | 215± | 12 | 222± | 13 | 233± | 14 | 240± | 14 |
| 1000 ppm | 194± | 11 | 196± | 11 | 206± | 12 | 214± | 11 | 219± | 12 | 231± | 13 | 237± | 13 |
| 2000 ppm | 191± | 12* | 194± | 12 | 204± | 12 | 210± | 13 | 217± | 14 | 228± | 15 | 234± | 16 |
| 4000 ppm | 184± | 13** | 186± | 13** | 196± | 13** | 205± | 14** | 210± | 15** | 222± | 16** | 227± | 18** |

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

Test of Dunnett

(HAN260)

BAIS3

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 10

| Group Name | Administration week | | | | | | | | | | | |
|------------|---------------------|--|-----------|--|----------|--|-----------|--|----------|--|-----------|--|
| | 38 | | 42 | | 46 | | 50 | | 54 | | 58 | |
| Control | 242± 15 | | 248± 15 | | 253± 16 | | 263± 17 | | 268± 17 | | 271± 18 | |
| 1000 ppm | 241± 13 | | 248± 14 | | 251± 15 | | 261± 16 | | 266± 18 | | 273± 19 | |
| 2000 ppm | 236± 15 | | 243± 16 | | 248± 17 | | 259± 19 | | 260± 19 | | 264± 22 | |
| 4000 ppm | 230± 16** | | 239± 18** | | 244± 19* | | 251± 21** | | 257± 24* | | 259± 25** | |

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

Test of Dunnett

(HAN260)

BATS3

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 11

| Group Name | Administration | | week | | | | | | | | | | | |
|------------|----------------|-----|-------|----|-------|-----|-------|-----|-------|-----|-------|-----|-------|-----|
| | 66 | | 70 | | 74 | | 78 | | 82 | | 86 | | 90 | |
| Control | 282 ± | 20 | 288 ± | 21 | 295 ± | 22 | 301 ± | 23 | 308 ± | 24 | 314 ± | 32 | 323 ± | 26 |
| 1000 ppm | 284 ± | 21 | 291 ± | 21 | 300 ± | 23 | 305 ± | 24 | 312 ± | 24 | 321 ± | 24 | 320 ± | 28 |
| 2000 ppm | 277 ± | 24 | 284 ± | 25 | 291 ± | 26 | 298 ± | 26 | 303 ± | 31 | 316 ± | 28 | 322 ± | 28 |
| 4000 ppm | 270 ± | 26* | 278 ± | 27 | 281 ± | 27* | 286 ± | 28* | 293 ± | 28* | 298 ± | 34* | 306 ± | 32* |

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

Test of Dunnett

(HAN260)

BAIS3

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 12

| Group Name | Administration week | | | | | | | |
|------------|---------------------|-----|------|-----|------|------|------|-----|
| | 94 | | 98 | | 102 | | 104 | |
| Control | 326± | 27 | 324± | 28 | 324± | 29 | 315± | 31 |
| 1000 ppm | 323± | 28 | 319± | 32 | 320± | 30 | 312± | 32 |
| 2000 ppm | 329± | 30 | 324± | 31 | 322± | 30 | 315± | 26 |
| 4000 ppm | 307± | 36* | 309± | 43* | 301± | 37** | 293± | 38* |

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

Test of Dunnett

(HAN260)

BAIS3

APPENDIX C 1

FOOD CONSUMPTION CHANGES: SUMMARY, RAT: MALE

(2-YEAR STUDY)

STUDY NO. : 0278
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

PAGE : 1

| Group Name | Administration week | | | | | | |
|------------|---------------------|-------------|-------------|-------------|-------------|-------------|-------------|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| Control | 15.0± 0.8 | 16.5± 1.4 | 17.8± 1.6 | 18.7± 1.7 | 19.0± 1.6 | 18.9± 1.6 | 18.5± 1.4 |
| 1000 ppm | 15.0± 0.9 | 16.3± 1.5 | 17.5± 1.6 | 18.3± 1.7 | 18.9± 1.9 | 18.6± 1.7 | 18.2± 1.6 |
| 2000 ppm | 15.0± 0.9 | 16.2± 1.2 | 17.0± 1.5* | 17.8± 1.5* | 18.1± 1.7* | 18.3± 1.7 | 17.8± 1.5 |
| 4000 ppm | 14.3± 1.1** | 15.0± 1.2** | 16.1± 1.3** | 17.0± 1.5** | 17.6± 1.8** | 17.5± 1.6** | 17.2± 1.4** |

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

Test of Dunnett

(HAN260)

BAIS3

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 2

| Group Name | Administration week | | | | | | |
|------------|---------------------|-------------|-------------|-------------|-------------|-------------|-------------|
| | 8 | 9 | 10 | 11 | 12 | 13 | 14 |
| Control | 18.7± 1.4 | 19.2± 1.3 | 19.0± 1.4 | 19.1± 1.3 | 18.8± 1.1 | 18.9± 1.3 | 18.6± 1.3 |
| 1000 ppm | 18.5± 1.5 | 19.0± 1.5 | 18.8± 1.4 | 18.6± 1.5 | 18.2± 1.3* | 18.2± 1.4* | 18.1± 1.4 |
| 2000 ppm | 18.0± 1.6 | 18.4± 1.5* | 18.3± 1.4 | 18.2± 1.2** | 17.6± 1.2** | 18.0± 1.3** | 17.8± 1.3* |
| 4000 ppm | 17.4± 1.7** | 17.8± 1.6** | 17.9± 1.5** | 18.2± 1.7* | 17.4± 1.4** | 17.9± 1.3** | 17.5± 1.3** |

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

Test of Dunnett

(HAN260)

BAIS3

STUDY NO. : 0278
 ANIMAL : RAT F344/DuGrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 3

| Group Name | Administration week | | | | | | |
|------------|---------------------|-------------|------------|-----------|-----------|------------|-------------|
| | 18 | 22 | 26 | 30 | 34 | 38 | 42 |
| Control | 18.6± 1.6 | 18.7± 1.6 | 18.7± 1.2 | 18.8± 1.4 | 18.7± 1.3 | 18.9± 1.3 | 18.8± 1.2 |
| 1000 ppm | 18.2± 1.3 | 18.4± 1.1 | 18.3± 1.2* | 18.3± 1.2 | 18.5± 1.2 | 18.3± 1.2* | 18.4± 1.1 |
| 2000 ppm | 17.8± 1.4* | 18.4± 1.4 | 18.3± 1.1 | 18.2± 1.1 | 18.4± 1.1 | 18.2± 1.2* | 18.4± 1.1 |
| 4000 ppm | 17.6± 1.4** | 17.9± 1.3** | 18.1± 1.6* | 18.4± 1.0 | 18.5± 1.2 | 18.3± 1.2* | 18.0± 1.2** |

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

Test of Dunnett

(HAN260)

BAIS3

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 4

| Group Name | Administration week | | | | | | |
|------------|---------------------|-----------|-------------|------------|-----------|-----------|-----------|
| | 46 | 50 | 54 | 58 | 62 | 66 | 70 |
| Control | 18.5± 1.1 | 18.6± 1.1 | 18.1± 1.1 | 18.9± 1.0 | 18.6± 1.3 | 18.7± 1.7 | 18.5± 1.7 |
| 1000 ppm | 18.1± 0.9 | 18.1± 1.0 | 18.5± 1.0 | 19.0± 1.0 | 18.8± 1.2 | 18.8± 1.1 | 18.5± 1.1 |
| 2000 ppm | 18.3± 1.0 | 18.5± 1.0 | 17.3± 0.9** | 18.6± 0.9 | 18.5± 1.1 | 18.5± 1.0 | 18.2± 1.0 |
| 4000 ppm | 18.2± 1.1 | 18.1± 1.4 | 18.2± 1.1 | 18.4± 1.0* | 18.7± 1.2 | 18.1± 1.7 | 18.1± 1.5 |

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

Test of Dunnett

(HAN260)

BAIS3

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 5

| Group Name | Administration week | | | | | | |
|---|---------------------|-----------|-----------|-------------|-------------|-----------|-------------|
| | 74 | 78 | 82 | 86 | 90 | 94 | 98 |
| Control | 19.0± 1.6 | 19.0± 2.5 | 19.3± 2.5 | 17.8± 3.2 | 18.5± 2.3 | 18.3± 2.0 | 17.9± 2.3 |
| 1000 ppm | 18.9± 1.1 | 18.4± 2.8 | 18.7± 1.6 | 19.5± 1.6* | 18.8± 2.3 | 18.3± 1.8 | 18.0± 1.3 |
| 2000 ppm | 18.6± 2.7 | 19.0± 1.3 | 18.2± 2.9 | 18.6± 1.3 | 19.4± 2.0 | 18.0± 2.1 | 17.9± 2.5 |
| 4000 ppm | 19.0± 2.6 | 18.9± 1.4 | 18.8± 1.7 | 20.1± 2.2** | 20.0± 2.0** | 18.6± 3.7 | 19.5± 4.6** |
| Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett | | | | | | | |

(HAN260)

BAIS3

STUDY NO. : 0278
ANIMAL : RAT F344/DuGrj
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

PAGE : 6

| Group Name | Administration week | |
|---|---------------------|-------------|
| | 102 | 104 |
| Control | 17.2± 4.3 | 17.3± 2.9 |
| 1000 ppm | 18.3± 2.1 | 17.4± 1.3 |
| 2000 ppm | 17.5± 2.5 | 16.6± 3.4 |
| 4000 ppm | 19.0± 2.8* | 18.6± 4.6** |
| Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett | | |

(HAN260)

BAIS3

APPENDIX C 2

FOOD CONSUMPTION CHANGES: SUMMARY, RAT: FEMALE

(2-YEAR STUDY)

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 7

| Group Name | Administration week | | | | | | |
|------------|---------------------|-------------|-------------|-------------|-------------|-------------|-------------|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| Control | 12.0± 0.7 | 12.2± 0.8 | 12.0± 0.9 | 12.4± 0.9 | 13.1± 1.3 | 12.9± 1.0 | 12.6± 1.1 |
| 1000 ppm | 12.0± 0.8 | 12.1± 1.0 | 12.1± 1.0 | 12.5± 1.0 | 13.0± 1.0 | 12.6± 1.1 | 12.5± 1.1 |
| 2000 ppm | 12.0± 0.8 | 11.9± 0.9 | 12.0± 1.0 | 12.3± 1.1 | 12.6± 1.4 | 12.4± 1.6* | 11.8± 1.5** |
| 4000 ppm | 11.2± 0.9** | 11.0± 0.8** | 11.4± 0.8** | 11.4± 0.9** | 12.1± 1.1** | 11.8± 1.3** | 11.3± 1.5** |

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

Test of Dunnett

(HAN260)

BAIS3

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 8

| Group Name | Administration week | | | | | | |
|------------|---------------------|-------------|-------------|-----------|-------------|-----------|------------|
| | 8 | 9 | 10 | 11 | 12 | 13 | 14 |
| Control | 12.6± 1.3 | 13.1± 1.3 | 12.9± 1.2 | 12.8± 1.4 | 13.2± 1.5 | 13.2± 1.6 | 12.8± 1.2 |
| 1000 ppm | 12.4± 1.0 | 12.7± 1.1 | 12.8± 1.4 | 13.0± 1.2 | 12.7± 1.4 | 12.8± 1.4 | 12.9± 1.5 |
| 2000 ppm | 11.8± 1.3** | 12.3± 1.8** | 12.5± 1.7 | 12.8± 1.7 | 12.3± 1.5** | 12.5± 1.4 | 12.3± 1.2 |
| 4000 ppm | 11.4± 1.6** | 11.9± 1.3** | 11.9± 1.5** | 12.3± 1.4 | 11.9± 1.5** | 12.5± 1.4 | 12.1± 1.2* |

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

Test of Dunnett

(HAN260)

BAIS3

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 9

| Group Name | Administration week | | | | | | |
|------------|---------------------|------------|-----------|-----------|-----------|-----------|-----------|
| | 18 | 22 | 26 | 30 | 34 | 38 | 42 |
| Control | 12.4± 1.5 | 12.9± 1.7 | 12.5± 1.1 | 13.5± 2.0 | 12.9± 1.2 | 12.6± 1.0 | 13.3± 1.1 |
| 1000 ppm | 12.7± 1.3 | 12.8± 1.1 | 12.9± 1.2 | 13.7± 1.6 | 13.3± 1.5 | 12.8± 0.9 | 13.2± 1.2 |
| 2000 ppm | 12.3± 1.2 | 12.3± 1.3* | 12.4± 1.3 | 13.2± 1.5 | 12.7± 1.3 | 12.2± 1.0 | 12.8± 0.9 |
| 4000 ppm | 12.1± 1.3 | 12.7± 1.2 | 12.6± 1.4 | 13.3± 1.4 | 13.1± 1.3 | 13.0± 1.0 | 13.2± 1.1 |

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

Test of Dunnett

(HAN260)

BAIS3

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 10

| Group Name | Administration week | | | | | | |
|------------|---------------------|-----------|-------------|-------------|-----------|-----------|-----------|
| | 46 | 50 | 54 | 58 | 62 | 66 | 70 |
| Control | 13.2± 1.0 | 13.7± 1.3 | 12.9± 0.9 | 13.2± 1.0 | 13.2± 1.1 | 13.7± 1.0 | 13.7± 1.8 |
| 1000 ppm | 13.0± 1.1 | 13.5± 1.2 | 13.1± 1.2 | 13.9± 1.1** | 13.1± 1.2 | 13.9± 1.1 | 14.0± 1.3 |
| 2000 ppm | 12.8± 0.9 | 13.3± 1.4 | 12.2± 1.3** | 12.7± 1.0 | 13.0± 1.1 | 13.6± 1.0 | 13.7± 1.0 |
| 4000 ppm | 13.1± 1.2 | 13.5± 1.3 | 13.3± 1.3 | 12.9± 1.0 | 13.6± 1.4 | 14.0± 1.2 | 14.3± 1.2 |

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

Test of Dunnett

(HAN260)

BA1S3

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 104
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 11

| Group Name | Administration week | | | | | | |
|------------|---------------------|-----------|-----------|-------------|-----------|-----------|-----------|
| | 74 | 78 | 82 | 86 | 90 | 94 | 98 |
| Control | 14.2± 1.2 | 14.3± 1.3 | 14.3± 1.3 | 14.8± 1.5 | 15.1± 1.5 | 14.5± 1.3 | 14.4± 2.5 |
| 1000 ppm | 14.9± 1.2* | 14.7± 1.4 | 14.6± 1.2 | 15.1± 1.7 | 14.3± 2.6 | 14.6± 2.0 | 13.6± 2.7 |
| 2000 ppm | 14.3± 1.4 | 14.8± 1.3 | 13.8± 2.0 | 15.1± 1.7 | 15.4± 1.7 | 15.0± 1.9 | 13.7± 2.8 |
| 4000 ppm | 14.4± 2.0 | 14.8± 1.1 | 14.7± 1.6 | 15.6± 2.8** | 15.6± 1.4 | 14.6± 2.6 | 15.2± 2.5 |

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

Test of Dunnett

(HAN260)

BAIS3

STUDY NO. : 0278
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

PAGE : 12

| Group Name | Administration week | |
|------------|---------------------|-----------|
| | 102 | 104 |
| Control | 15.2± 1.7 | 13.6± 2.0 |
| 1000 ppm | 14.0± 2.7 | 13.3± 2.2 |
| 2000 ppm | 14.5± 2.4 | 13.7± 1.7 |
| 4000 ppm | 14.5± 3.4 | 13.9± 3.0 |

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

Test of Dunnett

(HAN260)

BAIS3

APPENDIX D 1

HEMATOLOGY: SUMMARY, RAT: MALE

(2-YEAR STUDY)

STUDY NO. : 0278
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 | 32 | 7.80± | 1.70 | 13.3± | 3.4 | 40.0± | 8.4 | 51.4± | 2.4 | 16.9± | 1.6 | 32.9± | 2.6 | 1129± | 376 |
| 1000 ppm | 43 | 8.17± | 1.85 | 14.3± | 3.2 | 42.8± | 8.8 | 52.8± | 4.0 | 17.7± | 2.1 | 33.3± | 2.0 | 982± | 288 |
| 2000 ppm | 36 | 7.93± | 1.63 | 14.2± | 2.7 | 42.4± | 7.1 | 54.1± | 5.3** | 17.9± | 1.1** | 33.3± | 2.0 | 901± | 189* |
| 4000 ppm | 27 | 7.65± | 2.09 | 13.5± | 3.2 | 40.8± | 8.5 | 54.7± | 6.5** | 18.0± | 1.9** | 32.9± | 2.1 | 980± | 225 |

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS3

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : MALE

REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
 ALL ANIMALS (105W)

PAGE : 2

| Group Name | NO. of Animals | WBC 10 ³ /μl | | Differential N-BAND | | WBC (%) N-SEG | | EOSINO | | BASO | | MONO | | LYMPHO | | OTHERS | |
|------------|-------------------|----------------------------|-------|------------------------|---|------------------|----|--------|---|------|---|------|---|--------|----|--------|----|
| Control | 32 | 6.09± | 1.56 | 1± | 1 | 60± | 9 | 1± | 1 | 0± | 0 | 4± | 2 | 30± | 9 | 4± | 3 |
| 1000 ppm | 43 | 8.63± | 17.50 | 1± | 1 | 54± | 13 | 1± | 1 | 0± | 0 | 5± | 2 | 33± | 11 | 6± | 13 |
| 2000 ppm | 36 | 11.04± | 29.70 | 1± | 1 | 53± | 12 | 1± | 1 | 0± | 0 | 5± | 2 | 34± | 10 | 6± | 14 |
| 4000 ppm | 27 | 8.93± | 9.95 | 1± | 1 | 54± | 13 | 1± | 1 | 0± | 0 | 5± | 2 | 31± | 10 | 8± | 15 |

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS3

APPENDIX D 2

HEMATOLOGY: SUMMARY, RAT: FEMALE

(2-YEAR STUDY)

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : FEMALE

REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
 ALL ANIMALS (105W)

PAGE : 3

| Group Name | NO. of Animals | RED BLOOD CELL 10 ⁶ /μl | | HEMOGLOBIN g/dl | | HEMATOCRIT % | | MCV fl | | MCH pg | | MCHC g/dl | | PLATELET 10 ³ /μl | |
|------------|-------------------|---------------------------------------|--------|--------------------|-----|-----------------|-------|-----------|-----|-----------|-----|--------------|-----|---------------------------------|-----|
| Control | 44 | 8.00± | 0.85 | 14.7± | 1.4 | 43.0± | 3.2 | 54.1± | 3.3 | 18.4± | 1.0 | 34.1± | 1.5 | 728± | 149 |
| 1000 ppm | 38 | 8.31± | 0.90 | 15.1± | 2.0 | 44.0± | 5.1 | 52.9± | 1.8 | 18.1± | 1.1 | 34.1± | 1.6 | 709± | 242 |
| 2000 ppm | 42 | 8.29± | 1.12* | 15.2± | 1.8 | 44.3± | 4.6* | 53.9± | 3.6 | 18.4± | 1.1 | 34.2± | 1.8 | 719± | 174 |
| 4000 ppm | 29 | 8.28± | 1.52** | 15.2± | 2.1 | 45.0± | 5.6** | 55.9± | 9.3 | 18.8± | 2.4 | 33.7± | 1.4 | 708± | 135 |

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

Test of Dunnett

(HCL070)

BAIS3

STUDY NO. : 0278
 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 | | OTHERS | |
|------------|-------------------|----------------------------|--------|------------------------|---|------------------|----|--------|---|------|---|------|---|--------|----|--------|----|
| Control | 44 | 3.37± | 2.03 | 1± | 1 | 51± | 13 | 1± | 1 | 0± | 0 | 5± | 2 | 37± | 11 | 5± | 11 |
| 1000 ppm | 38 | 3.80± | 2.85 | 1± | 2 | 50± | 11 | 1± | 1 | 0± | 0 | 5± | 2 | 35± | 9 | 8± | 13 |
| 2000 ppm | 42 | 24.87± | 141.29 | 2± | 2 | 49± | 13 | 1± | 1 | 0± | 0 | 5± | 2 | 35± | 10 | 8± | 15 |
| 4000 ppm | 29 | 6.92± | 19.05 | 2± | 4 | 47± | 14 | 1± | 1 | 0± | 0 | 4± | 2 | 36± | 13 | 10± | 18 |

Significant difference : * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS3

APPENDIX E 1

BIOCHEMISTRY: SUMMARY, RAT: MALE

(2-YEAR STUDY)

STUDY NO. : 0278
 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 | 32 | 6.4± | 0.4 | 3.1± | 0.2 | 0.9± | 0.1 | 0.18± | 0.04 | 144± | 29 | 222± | 61 | 216± | 119 |
| 1000 ppm | 43 | 6.3± | 0.2 | 3.2± | 0.2 | 1.0± | 0.1 | 0.19± | 0.04 | 137± | 25 | 169± | 42** | 142± | 86** |
| 2000 ppm | 37 | 6.2± | 0.4 | 3.2± | 0.2 | 1.1± | 0.1** | 0.20± | 0.08 | 139± | 18 | 169± | 57** | 138± | 109** |
| 4000 ppm | 27 | 6.0± | 0.6 | 2.9± | 0.4 | 1.0± | 0.1 | 0.21± | 0.08 | 132± | 26 | 171± | 59** | 103± | 92** |

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS3

STUDY NO. : 0278
 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 | 32 | 320± | 83 | 64± | 23 | 37± | 17 | 201± | 40 | 158± | 46 | 8± | 4 | 98± | 20 |
| 1000 ppm | 43 | 249± | 60** | 100± | 50** | 47± | 26* | 334± | 464** | 157± | 69 | 6± | 3 | 103± | 54 |
| 2000 ppm | 37 | 252± | 85** | 98± | 56** | 45± | 19* | 250± | 156 | 161± | 86 | 7± | 6 | 154± | 383 |
| 4000 ppm | 27 | 259± | 89** | 106± | 62** | 44± | 18 | 222± | 56 | 190± | 119 | 9± | 6 | 114± | 105 |

Significant difference : * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS3

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : MALE

REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
 ALL ANIMALS (105W)

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 | 32 | 26.2± | 6.3 | 0.8± | 0.2 | 141± | 1 | 3.7± | 0.3 | 104± | 2 | 10.6± | 0.6 | 4.3± | 0.7 |
| 1000 ppm | 43 | 26.4± | 20.8 | 0.7± | 0.2 | 141± | 1 | 3.8± | 0.5 | 105± | 2 | 10.6± | 0.4 | 4.2± | 1.1 |
| 2000 ppm | 37 | 23.6± | 6.7 | 0.7± | 0.2 | 141± | 1 | 3.9± | 0.5* | 105± | 2* | 10.6± | 0.9 | 4.3± | 1.3 |
| 4000 ppm | 27 | 26.5± | 19.5 | 0.7± | 0.3 | 142± | 3 | 4.0± | 0.3** | 106± | 2** | 10.5± | 0.8 | 4.6± | 1.4 |

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

Test of Dunnett

(HCL074)

BAIS3

APPENDIX E 2

BIOCHEMISTRY: SUMMARY, RAT: FEMALE

(2-YEAR STUDY)

STUDY NO. : 0278
 ANIMAL : RAT F344/DuGrj
 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 | 44 | 6.7± | 0.4 | 3.7± | 0.2 | 1.2± | 0.1 | 0.19± | 0.12 | 142± | 16 | 179± | 56 | 164± | 198 |
| 1000 ppm | 38 | 6.7± | 0.4 | 3.8± | 0.3 | 1.3± | 0.1 | 0.17± | 0.04 | 133± | 16* | 173± | 38 | 66± | 26** |
| 2000 ppm | 42 | 6.8± | 0.4 | 3.8± | 0.3 | 1.3± | 0.1 | 0.18± | 0.03 | 130± | 18** | 209± | 65* | 68± | 34** |
| 4000 ppm | 29 | 6.6± | 0.4 | 3.7± | 0.2 | 1.3± | 0.1 | 0.20± | 0.12 | 131± | 12* | 201± | 59 | 66± | 39** |

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

Test of Dunnett

(HCL074)

BAIS3

STUDY NO. : 0278
 ANIMAL : RAT F344/DuGrj
 MEASURE. TIME : 1
 SEX : FEMALE

REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
 ALL ANIMALS (105W)

PAGE : 5

| Group Name | NO. of Animals | PHOSPHOLIPID mg/dl | | GOT I U/l | | GPT I U/l | | LDH I U/l | | ALP I U/l | | G-GTP I U/l | | CPK I U/l | |
|------------|-------------------|-----------------------|----|--------------|-------|--------------|------|--------------|-------|--------------|----|----------------|---|--------------|-------|
| Control | 44 | 306± | 90 | 104± | 79 | 54± | 25 | 246± | 74 | 118± | 48 | 5± | 2 | 91± | 16 |
| 1000 ppm | 38 | 281± | 57 | 167± | 60** | 86± | 32** | 325± | 123** | 133± | 53 | 5± | 3 | 214± | 634** |
| 2000 ppm | 42 | 324± | 97 | 170± | 111** | 88± | 43** | 393± | 304** | 145± | 76 | 5± | 6 | 115± | 28** |
| 4000 ppm | 29 | 311± | 83 | 113± | 57 | 63± | 23 | 303± | 188 | 137± | 66 | 6± | 4 | 103± | 15** |

Significant difference : * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS3

STUDY NO. : 0278
 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 | 44 | 16.2± | 2.5 | 0.5± | 0.1 | 140± | 2 | 3.6± | 0.4 | 103± | 2 | 10.5± | 0.4 | 3.5± | 0.7 |
| 1000 ppm | 38 | 16.5± | 3.0 | 0.5± | 0.1 | 140± | 2 | 3.8± | 0.4 | 103± | 2 | 10.4± | 0.3 | 3.8± | 1.0 |
| 2000 ppm | 42 | 21.3± | 32.3 | 0.6± | 0.8 | 140± | 2 | 3.8± | 0.8 | 103± | 3 | 10.5± | 0.4 | 4.4± | 3.8 |
| 4000 ppm | 29 | 15.9± | 1.8 | 0.5± | 0.1 | 139± | 2 | 3.9± | 0.5** | 104± | 2 | 10.5± | 0.4 | 4.0± | 0.7* |

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS3

APPENDIX F 1

URINALYSIS: SUMMARY, RAT: MALE

(2-YEAR STUDY)

STUDY NO. : 0278
 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 | 32 | 0 | 1 | 5 | 8 | 12 | 6 | 0 | | 0 | 0 | 0 | 0 | 4 | 28 | | 32 | 0 | 0 | 0 | 0 | 0 | | 32 | 0 | 0 | 0 | 0 | 0 | | 32 | 0 | 0 | 0 | |
| 1000 ppm | 43 | 0 | 0 | 3 | 13 | 17 | 10 | 0 | | 0 | 0 | 0 | 0 | 13 | 30 | | 43 | 0 | 0 | 0 | 0 | 0 | | 43 | 0 | 0 | 0 | 0 | 0 | | 43 | 0 | 0 | 0 | |
| 2000 ppm | 39 | 0 | 1 | 8 | 15 | 10 | 5 | 0 | | 0 | 0 | 1 | 3 | 8 | 27 | | 39 | 0 | 0 | 0 | 0 | 0 | | 39 | 0 | 0 | 0 | 0 | 0 | | 38 | 1 | 0 | 0 | |
| 4000 ppm | 29 | 0 | 3 | 12 | 5 | 7 | 2 | 0 | | 0 | 1 | 0 | 1 | 6 | 21 | | 29 | 0 | 0 | 0 | 0 | 0 | | 29 | 0 | 0 | 0 | 0 | 0 | | 27 | 1 | 0 | 1 | |

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

Test of CHI SQUARE

(HCL101)

BAIS3

STUDY NO. : 0278
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE

URINALYSIS

REPORT TYPE : A1

PAGE : 2

| Group Name | NO. of Animals | Occult blood | | | | | CHI | Urobilinogen | | | | | CHI |
|------------|-------------------|--------------|---|---|----|----|-----|--------------|---|----|----|----|-----|
| | | - | ± | + | 2+ | 3+ | | ± | + | 2+ | 3+ | 4+ | |
| Control | 32 | 31 | 1 | 0 | 0 | 0 | | 32 | 0 | 0 | 0 | 0 | |
| 1000 ppm | 43 | 43 | 0 | 0 | 0 | 0 | | 43 | 0 | 0 | 0 | 0 | |
| 2000 ppm | 39 | 39 | 0 | 0 | 0 | 0 | | 38 | 1 | 0 | 0 | 0 | |
| 4000 ppm | 29 | 28 | 1 | 0 | 0 | 0 | | 29 | 0 | 0 | 0 | 0 | |

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

Test of CHI SQUARE

(HCL101)

BAIS3

APPENDIX F 2

URINALYSIS: SUMMARY, RAT: FEMALE

(2-YEAR STUDY)

STUDY NO. : 0278
 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 | 45 | 0 | 2 | 1 | 19 | 14 | 9 | 0 | | 0 | 0 | 1 | 2 | 11 | 31 | | 45 | 0 | 0 | 0 | 0 | 0 | | 44 | 1 | 0 | 0 | 0 | 0 | | 45 | 0 | 0 | 0 | |
| 1000 ppm | 40 | 0 | 3 | 6 | 13 | 11 | 6 | 1 | | 0 | 0 | 3 | 7 | 10 | 20 | | 40 | 0 | 0 | 0 | 0 | 0 | | 40 | 0 | 0 | 0 | 0 | 0 | | 40 | 0 | 0 | 0 | |
| 2000 ppm | 43 | 0 | 1 | 3 | 18 | 12 | 9 | 0 | | 0 | 0 | 0 | 7 | 12 | 24 | | 43 | 0 | 0 | 0 | 0 | 0 | | 43 | 0 | 0 | 0 | 0 | 0 | | 43 | 0 | 0 | 0 | |
| 4000 ppm | 31 | 0 | 1 | 4 | 9 | 10 | 7 | 0 | | 0 | 1 | 2 | 5 | 11 | 12 | | 31 | 0 | 0 | 0 | 0 | 0 | | 31 | 0 | 0 | 0 | 0 | 0 | | 30 | 0 | 1 | 0 | |

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

Test of CHI SQUARE

(HCL101)

BAIS3

STUDY NO. : 0278
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 | 45 | 44 | 0 | 0 | 0 | 0 | 1 | 45 | 0 | 0 | 0 | 0 | 0 |
| 1000 ppm | 40 | 40 | 0 | 0 | 0 | 0 | 0 | 40 | 0 | 0 | 0 | 0 | 0 |
| 2000 ppm | 43 | 43 | 0 | 0 | 0 | 0 | 0 | 43 | 0 | 0 | 0 | 0 | 0 |
| 4000 ppm | 31 | 30 | 1 | 0 | 0 | 0 | 0 | 30 | 1 | 0 | 0 | 0 | 0 |

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

Test of CHI SQUARE

(HCL101)

BATS3

APPENDIX G 1

GROSS FINDINGS: SUMMARY, RAT: MALE: ALL ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 1

| Organ | Findings | Group Name NO. of Animals | Control 50 (%) | 1000 ppm 50 (%) | 2000 ppm 50 (%) | 4000 ppm 50 (%) |
|-------------|------------|------------------------------|-------------------|--------------------|--------------------|--------------------|
| skin/app | nodule | | 3 (6) | 3 (6) | 2 (4) | 5 (10) |
| subcutis | jaundice | | 0 (0) | 1 (2) | 0 (0) | 0 (0) |
| | nodule | | 1 (2) | 1 (2) | 0 (0) | 0 (0) |
| | mass | | 5 (10) | 12 (24) | 17 (34) | 20 (40) |
| lung | red | | 0 (0) | 0 (0) | 0 (0) | 1 (2) |
| | white zone | | 2 (4) | 0 (0) | 0 (0) | 1 (2) |
| | red zone | | 0 (0) | 0 (0) | 1 (2) | 0 (0) |
| | red patch | | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| | nodule | | 7 (14) | 2 (4) | 2 (4) | 3 (6) |
| lymph node | enlarged | | 2 (4) | 2 (4) | 2 (4) | 2 (4) |
| thymus | nodule | | 0 (0) | 0 (0) | 1 (2) | 0 (0) |
| spleen | enlarged | | 3 (6) | 4 (8) | 9 (18) | 6 (12) |
| | white zone | | 0 (0) | 0 (0) | 1 (2) | 0 (0) |
| | nodule | | 0 (0) | 1 (2) | 1 (2) | 2 (4) |
| | deformed | | 1 (2) | 0 (0) | 1 (2) | 5 (10) |
| heart | white zone | | 0 (0) | 1 (2) | 2 (4) | 1 (2) |
| artery/aort | hard | | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| tongue | nodule | | 0 (0) | 1 (2) | 0 (0) | 0 (0) |
| forestomach | nodule | | 3 (6) | 0 (0) | 0 (0) | 1 (2) |
| | ulcer | | 3 (6) | 0 (0) | 0 (0) | 1 (2) |
| gl stomach | ulcer | | 2 (4) | 0 (0) | 1 (2) | 0 (0) |
| small intes | thick | | 2 (4) | 0 (0) | 0 (0) | 0 (0) |

STUDY NO. : 0278
 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 50 (%) | 1000 ppm 50 (%) | 2000 ppm 50 (%) | 4000 ppm 50 (%) |
|-------------|------------------------|------------------------------|-------------------|--------------------|--------------------|--------------------|
| large intes | nodule | | 0 (0) | 0 (0) | 0 (0) | 1 (2) |
| | fluid:black | | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| liver | enlarged | | 0 (0) | 1 (2) | 0 (0) | 0 (0) |
| | pale | | 2 (4) | 0 (0) | 0 (0) | 2 (4) |
| | white zone | | 0 (0) | 0 (0) | 1 (2) | 1 (2) |
| | brown zone | | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| | nodule | | 2 (4) | 0 (0) | 2 (4) | 2 (4) |
| | rough | | 0 (0) | 0 (0) | 1 (2) | 2 (4) |
| | herniation | | 1 (2) | 1 (2) | 2 (4) | 4 (8) |
| pancreas | nodule | | 1 (2) | 2 (4) | 0 (0) | 2 (4) |
| kidney | enlarged | | 0 (0) | 0 (0) | 0 (0) | 1 (2) |
| | pale | | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| | white zone | | 0 (0) | 0 (0) | 2 (4) | 0 (0) |
| | nodule | | 1 (2) | 2 (4) | 0 (0) | 0 (0) |
| | cyst | | 1 (2) | 0 (0) | 1 (2) | 0 (0) |
| | deformed | | 0 (0) | 1 (2) | 0 (0) | 0 (0) |
| | granular | | 41 (82) | 38 (76) | 32 (64) | 31 (62) |
| | nodular | | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| | urine:marked retention | | 0 (0) | 1 (2) | 1 (2) | 0 (0) |
| urin bladd | urine:red | | 1 (2) | 0 (0) | 0 (0) | 2 (4) |
| | enlarged | | 7 (14) | 0 (0) | 4 (8) | 4 (8) |
| pituitary | red zone | | 3 (6) | 1 (2) | 1 (2) | 2 (4) |

STUDY NO. : 0278
 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 50 (%) | 1000 ppm 50 (%) | 2000 ppm 50 (%) | 4000 ppm 50 (%) |
|-------------|--------------|------------------------------|-------------------|--------------------|--------------------|--------------------|
| pituitary | nodule | | 6 (12) | 5 (10) | 5 (10) | 5 (10) |
| | cyst | | 0 (0) | 1 (2) | 0 (0) | 0 (0) |
| thyroid | enlarged | | 2 (4) | 2 (4) | 2 (4) | 2 (4) |
| | nodule | | 4 (8) | 0 (0) | 1 (2) | 4 (8) |
| adrenal | enlarged | | 0 (0) | 0 (0) | 1 (2) | 1 (2) |
| testis | enlarged | | 0 (0) | 0 (0) | 0 (0) | 1 (2) |
| | atrophic | | 1 (2) | 0 (0) | 1 (2) | 2 (4) |
| | nodule | | 40 (80) | 47 (94) | 46 (92) | 41 (82) |
| brain | red zone | | 0 (0) | 0 (0) | 1 (2) | 0 (0) |
| spinal cord | hemorrhage | | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| eye | white | | 2 (4) | 1 (2) | 4 (8) | 0 (0) |
| | exophthalmos | | 0 (0) | 0 (0) | 1 (2) | 0 (0) |
| Zymbal gl | nodule | | 0 (0) | 1 (2) | 0 (0) | 0 (0) |
| pleura | nodule | | 1 (2) | 1 (2) | 1 (2) | 0 (0) |
| mediastinum | mass | | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| peritoneum | nodule | | 2 (4) | 1 (2) | 0 (0) | 7 (14) |
| | mass | | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| | hemorrhage | | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| retroperit | mass | | 0 (0) | 0 (0) | 0 (0) | 1 (2) |
| | cyst | | 0 (0) | 0 (0) | 1 (2) | 0 (0) |
| | red | | 0 (0) | 0 (0) | 0 (0) | 1 (2) |
| abdominal c | hemorrhage | | 1 (2) | 0 (0) | 0 (0) | 1 (2) |

STUDY NO. : 0278
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 50 (%) | 1000 ppm 50 (%) | 2000 ppm 50 (%) | 4000 ppm 50 (%) |
|-------------|---------------|------------------------------|-------------------|--------------------|--------------------|--------------------|
| abdominal c | ascites | | 3 (6) | 1 (2) | 1 (2) | 6 (12) |
| mesenterium | nodule | | 0 (0) | 0 (0) | 0 (0) | 1 (2) |
| | nodular | | 0 (0) | 1 (2) | 0 (0) | 0 (0) |
| thoracic ca | pleural fluid | | 1 (2) | 2 (4) | 2 (4) | 5 (10) |
| other | swollen | | 0 (0) | 0 (0) | 0 (0) | 1 (2) |
| | nodule | | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| | tail:nodule | | 0 (0) | 1 (2) | 1 (2) | 0 (0) |
| | ear:nodule | | 1 (2) | 0 (0) | 3 (6) | 0 (0) |
| whole body | anemic | | 1 (2) | 1 (2) | 0 (0) | 0 (0) |

(HPT080)

BAIS3

APPENDIX G 2

GROSS FINDINGS: SUMMARY, RAT: MALE: DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0278
 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 18 (%) | 1000 ppm 7 (%) | 2000 ppm 12 (%) | 4000 ppm 22 (%) |
|-------------|-------------|------------------------------|-------------------|-------------------|--------------------|--------------------|
| skin/app | nodule | | 1 (6) | 0 (0) | 1 (8) | 1 (5) |
| subcutis | jaundice | | 0 (0) | 1 (14) | 0 (0) | 0 (0) |
| | mass | | 3 (17) | 0 (0) | 5 (42) | 5 (23) |
| lung | red | | 0 (0) | 0 (0) | 0 (0) | 1 (5) |
| | red patch | | 1 (6) | 0 (0) | 0 (0) | 0 (0) |
| | nodule | | 2 (11) | 0 (0) | 1 (8) | 2 (9) |
| lymph node | enlarged | | 2 (11) | 1 (14) | 1 (8) | 1 (5) |
| thymus | nodule | | 0 (0) | 0 (0) | 1 (8) | 0 (0) |
| spleen | enlarged | | 1 (6) | 2 (29) | 5 (42) | 4 (18) |
| | nodule | | 0 (0) | 0 (0) | 0 (0) | 1 (5) |
| | deformed | | 0 (0) | 0 (0) | 0 (0) | 1 (5) |
| heart | white zone | | 0 (0) | 1 (14) | 0 (0) | 1 (5) |
| artery/aort | hard | | 1 (6) | 0 (0) | 0 (0) | 0 (0) |
| forestomach | nodule | | 2 (11) | 0 (0) | 0 (0) | 1 (5) |
| | ulcer | | 3 (17) | 0 (0) | 0 (0) | 1 (5) |
| gl stomach | ulcer | | 2 (11) | 0 (0) | 1 (8) | 0 (0) |
| small intes | thick | | 2 (11) | 0 (0) | 0 (0) | 0 (0) |
| large intes | fluid:black | | 1 (6) | 0 (0) | 0 (0) | 0 (0) |
| liver | enlarged | | 0 (0) | 1 (14) | 0 (0) | 0 (0) |
| | pale | | 2 (11) | 0 (0) | 0 (0) | 2 (9) |
| | nodule | | 1 (6) | 0 (0) | 0 (0) | 0 (0) |
| | rough | | 0 (0) | 0 (0) | 1 (8) | 1 (5) |

STUDY NO. : 0278
 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 18 (%) | 1000 ppm 7 (%) | 2000 ppm 12 (%) | 4000 ppm 22 (%) |
|------------|------------------------|------------------------------|-------------------|-------------------|--------------------|--------------------|
| liver | herniation | | 1 (6) | 0 (0) | 1 (8) | 1 (5) |
| pancreas | nodule | | 0 (0) | 1 (14) | 0 (0) | 1 (5) |
| kidney | enlarged | | 0 (0) | 0 (0) | 0 (0) | 1 (5) |
| | pale | | 1 (6) | 0 (0) | 0 (0) | 0 (0) |
| | white zone | | 0 (0) | 0 (0) | 1 (8) | 0 (0) |
| | nodule | | 1 (6) | 2 (29) | 0 (0) | 0 (0) |
| | cyst | | 1 (6) | 0 (0) | 0 (0) | 0 (0) |
| | deformed | | 0 (0) | 1 (14) | 0 (0) | 0 (0) |
| | granular | | 10 (56) | 0 (0) | 5 (42) | 5 (23) |
| | | | | | | |
| urin bladd | urine:marked retention | | 0 (0) | 0 (0) | 1 (8) | 0 (0) |
| | urine:red | | 1 (6) | 0 (0) | 0 (0) | 2 (9) |
| pituitary | enlarged | | 6 (33) | 0 (0) | 2 (17) | 1 (5) |
| | red zone | | 2 (11) | 0 (0) | 1 (8) | 2 (9) |
| | nodule | | 0 (0) | 0 (0) | 1 (8) | 1 (5) |
| | cyst | | 0 (0) | 1 (14) | 0 (0) | 0 (0) |
| thyroid | enlarged | | 0 (0) | 1 (14) | 0 (0) | 1 (5) |
| | nodule | | 1 (6) | 0 (0) | 0 (0) | 1 (5) |
| adrenal | enlarged | | 0 (0) | 0 (0) | 0 (0) | 1 (5) |
| testis | enlarged | | 0 (0) | 0 (0) | 0 (0) | 1 (5) |
| | atrophic | | 1 (6) | 0 (0) | 1 (8) | 1 (5) |
| | nodule | | 10 (56) | 4 (57) | 8 (57) | 15 (68) |
| brain | red zone | | 0 (0) | 0 (0) | 1 (8) | 0 (0) |

STUDY NO. : 0278
 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 18 (%) | 1000 ppm 7 (%) | 2000 ppm 12 (%) | 4000 ppm 22 (%) |
|-------------|---------------|------------------------------|-------------------|-------------------|--------------------|--------------------|
| spinal cord | hemorrhage | | 1 (6) | 0 (0) | 0 (0) | 0 (0) |
| eye | white | | 0 (0) | 0 (0) | 1 (8) | 0 (0) |
| Zymbal gl | nodule | | 0 (0) | 1 (14) | 0 (0) | 0 (0) |
| pleura | nodule | | 1 (6) | 1 (14) | 1 (8) | 0 (0) |
| mediastinum | mass | | 1 (6) | 0 (0) | 0 (0) | 0 (0) |
| peritoneum | nodule | | 1 (6) | 1 (14) | 0 (0) | 3 (14) |
| | mass | | 1 (6) | 0 (0) | 0 (0) | 0 (0) |
| retroperit | hemorrhage | | 1 (6) | 0 (0) | 0 (0) | 0 (0) |
| | mass | | 0 (0) | 0 (0) | 0 (0) | 1 (5) |
| abdominal c | hemorrhage | | 1 (6) | 0 (0) | 0 (0) | 1 (5) |
| | ascites | | 2 (11) | 1 (14) | 1 (8) | 3 (14) |
| mesenterium | nodule | | 0 (0) | 0 (0) | 0 (0) | 1 (5) |
| | nodular | | 0 (0) | 1 (14) | 0 (0) | 0 (0) |
| thoracic ca | pleural fluid | | 1 (6) | 1 (14) | 0 (0) | 5 (23) |
| other | swollen | | 0 (0) | 0 (0) | 0 (0) | 1 (5) |
| | nodule | | 1 (6) | 0 (0) | 0 (0) | 0 (0) |
| | tail:nodule | | 0 (0) | 0 (0) | 1 (8) | 0 (0) |
| | ear:nodule | | 0 (0) | 0 (0) | 1 (8) | 0 (0) |
| whole body | anemic | | 1 (6) | 1 (14) | 0 (0) | 0 (0) |

APPENDIX G 3

GROSS FINDINGS: SUMMARY, RAT : MALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0278
 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 32 (%) | 1000 ppm 43 (%) | 2000 ppm 38 (%) | 4000 ppm 28 (%) |
|-------------|------------|------------------------------|-------------------|--------------------|--------------------|--------------------|
| skin/app | nodule | | 2 (6) | 3 (7) | 1 (3) | 4 (14) |
| subcutis | nodule | | 1 (3) | 1 (2) | 0 (0) | 0 (0) |
| | mass | | 2 (6) | 12 (28) | 12 (32) | 15 (54) |
| lung | white zone | | 2 (6) | 0 (0) | 0 (0) | 1 (4) |
| | red zone | | 0 (0) | 0 (0) | 1 (3) | 0 (0) |
| | nodule | | 5 (16) | 2 (5) | 1 (3) | 1 (4) |
| lymph node | enlarged | | 0 (0) | 1 (2) | 1 (3) | 1 (4) |
| spleen | enlarged | | 2 (6) | 2 (5) | 4 (11) | 2 (7) |
| | white zone | | 0 (0) | 0 (0) | 1 (3) | 0 (0) |
| | nodule | | 0 (0) | 1 (2) | 1 (3) | 1 (4) |
| | deformed | | 1 (3) | 0 (0) | 1 (3) | 4 (14) |
| heart | white zone | | 0 (0) | 0 (0) | 2 (5) | 0 (0) |
| tongue | nodule | | 0 (0) | 1 (2) | 0 (0) | 0 (0) |
| forestomach | nodule | | 1 (3) | 0 (0) | 0 (0) | 0 (0) |
| large intes | nodule | | 0 (0) | 0 (0) | 0 (0) | 1 (4) |
| liver | white zone | | 0 (0) | 0 (0) | 1 (3) | 1 (4) |
| | brown zone | | 1 (3) | 0 (0) | 0 (0) | 0 (0) |
| | nodule | | 1 (3) | 0 (0) | 2 (5) | 2 (7) |
| | roush | | 0 (0) | 0 (0) | 0 (0) | 1 (4) |
| | herniation | | 0 (0) | 1 (2) | 1 (3) | 3 (11) |
| pancreas | nodule | | 1 (3) | 1 (2) | 0 (0) | 1 (4) |
| kidney | white zone | | 0 (0) | 0 (0) | 1 (3) | 0 (0) |

STUDY NO. : 0278
 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 32 (%) | 1000 ppm 43 (%) | 2000 ppm 38 (%) | 4000 ppm 28 (%) |
|-------------|------------------------|------------------------------|-------------------|--------------------|--------------------|--------------------|
| kidney | cyst | | 0 (0) | 0 (0) | 1 (3) | 0 (0) |
| | granular | | 31 (97) | 38 (88) | 27 (71) | 26 (93) |
| | nodular | | 1 (3) | 0 (0) | 0 (0) | 0 (0) |
| urin bladd | urine:marked retention | | 0 (0) | 1 (2) | 0 (0) | 0 (0) |
| pituitary | enlarged | | 1 (3) | 0 (0) | 2 (5) | 3 (11) |
| | red zone | | 1 (3) | 1 (2) | 0 (0) | 0 (0) |
| | nodule | | 6 (19) | 5 (12) | 4 (11) | 4 (14) |
| thyroid | enlarged | | 2 (6) | 1 (2) | 2 (5) | 1 (4) |
| | nodule | | 3 (9) | 0 (0) | 1 (3) | 3 (11) |
| adrenal | enlarged | | 0 (0) | 0 (0) | 1 (3) | 0 (0) |
| testis | atrophic | | 0 (0) | 0 (0) | 0 (0) | 1 (4) |
| | nodule | | 30 (94) | 43 (100) | 38 (100) | 26 (93) |
| eye | white | | 2 (6) | 1 (2) | 3 (8) | 0 (0) |
| | exophthalmos | | 0 (0) | 0 (0) | 1 (3) | 0 (0) |
| peritoneum | nodule | | 1 (3) | 0 (0) | 0 (0) | 4 (14) |
| retroperit | cyst | | 0 (0) | 0 (0) | 1 (3) | 0 (0) |
| abdominal c | red | | 0 (0) | 0 (0) | 0 (0) | 1 (4) |
| | ascites | | 1 (3) | 0 (0) | 0 (0) | 3 (11) |
| thoracic ca | pleural fluid | | 0 (0) | 1 (2) | 2 (5) | 0 (0) |
| other | tail:nodule | | 0 (0) | 1 (2) | 0 (0) | 0 (0) |
| | ear:nodule | | 1 (3) | 0 (0) | 2 (5) | 0 (0) |

APPENDIX G 4

GROSS FINDINGS: SUMMARY, RAT: FEMALE: ALL ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0278
 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 50 (%) | 1000 ppm 50 (%) | 2000 ppm 50 (%) | 4000 ppm 50 (%) |
|-------------|------------|------------------------------|-------------------|--------------------|--------------------|--------------------|
| skin/app | nodule | | 1 (2) | 0 (0) | 1 (2) | 0 (0) |
| | mass | | 0 (0) | 0 (0) | 0 (0) | 1 (2) |
| subcutis | jaundice | | 0 (0) | 1 (2) | 1 (2) | 1 (2) |
| | mass | | 10 (20) | 12 (24) | 10 (20) | 15 (30) |
| lung | white zone | | 0 (0) | 0 (0) | 1 (2) | 0 (0) |
| | nodule | | 3 (6) | 1 (2) | 1 (2) | 2 (4) |
| lymph node | enlarged | | 0 (0) | 2 (4) | 2 (4) | 1 (2) |
| thymus | enlarged | | 0 (0) | 0 (0) | 1 (2) | 0 (0) |
| spleen | enlarged | | 0 (0) | 6 (12) | 6 (12) | 6 (12) |
| | nodule | | 0 (0) | 0 (0) | 1 (2) | 0 (0) |
| heart | red zone | | 0 (0) | 1 (2) | 0 (0) | 1 (2) |
| | dilated | | 0 (0) | 0 (0) | 0 (0) | 1 (2) |
| forestomach | ulcer | | 2 (4) | 0 (0) | 0 (0) | 1 (2) |
| gl stomach | ulcer | | 1 (2) | 0 (0) | 0 (0) | 1 (2) |
| small intes | nodule | | 0 (0) | 0 (0) | 1 (2) | 1 (2) |
| large intes | nodule | | 0 (0) | 1 (2) | 0 (0) | 0 (0) |
| liver | enlarged | | 0 (0) | 0 (0) | 1 (2) | 1 (2) |
| | pale | | 0 (0) | 1 (2) | 0 (0) | 1 (2) |
| | red | | 0 (0) | 0 (0) | 0 (0) | 1 (2) |
| | white zone | | 0 (0) | 2 (4) | 0 (0) | 1 (2) |
| | red zone | | 0 (0) | 0 (0) | 0 (0) | 4 (8) |
| | brown zone | | 0 (0) | 0 (0) | 0 (0) | 1 (2) |

STUDY NO. : 0278
 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 50 (%) | 1000 ppm 50 (%) | 2000 ppm 50 (%) | 4000 ppm 50 (%) |
|-------------|------------------------|------------------------------|-------------------|--------------------|--------------------|--------------------|
| Liver | nodule | | 1 (2) | 3 (6) | 2 (4) | 4 (8) |
| | rough | | 0 (0) | 2 (4) | 1 (2) | 6 (12) |
| | granular | | 0 (0) | 0 (0) | 1 (2) | 0 (0) |
| | nodular | | 0 (0) | 0 (0) | 0 (0) | 1 (2) |
| | herniation | | 2 (4) | 4 (8) | 2 (4) | 0 (0) |
| pancreas | nodule | | 1 (2) | 0 (0) | 0 (0) | 1 (2) |
| kidney | pale | | 0 (0) | 1 (2) | 0 (0) | 0 (0) |
| | white zone | | 0 (0) | 0 (0) | 0 (0) | 1 (2) |
| | cyst | | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| | granular | | 11 (22) | 1 (2) | 7 (14) | 6 (12) |
| | nodular | | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| | hydronephrosis | | 0 (0) | 0 (0) | 1 (2) | 0 (0) |
| urin bladd | enlarged | | 0 (0) | 0 (0) | 0 (0) | 1 (2) |
| | urine:marked retention | | 0 (0) | 0 (0) | 0 (0) | 1 (2) |
| pituitary | enlarged | | 9 (18) | 11 (22) | 8 (16) | 5 (10) |
| | red | | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| | red zone | | 5 (10) | 7 (14) | 4 (8) | 6 (12) |
| | nodule | | 4 (8) | 8 (16) | 11 (22) | 6 (12) |
| | cyst | | 0 (0) | 1 (2) | 0 (0) | 0 (0) |
| thyroid | enlarged | | 2 (4) | 1 (2) | 0 (0) | 3 (6) |
| | nodule | | 2 (4) | 0 (0) | 0 (0) | 0 (0) |
| parathyroid | nodule | | 0 (0) | 0 (0) | 1 (2) | 0 (0) |

STUDY NO. : 0278
 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 50 (%) | 1000 ppm 50 (%) | 2000 ppm 50 (%) | 4000 ppm 50 (%) |
|-------------|----------------|------------------------------|-------------------|--------------------|--------------------|--------------------|
| ovary | enlarged | | 0 (0) | 0 (0) | 0 (0) | 2 (4) |
| | cyst | | 1 (2) | 3 (6) | 0 (0) | 0 (0) |
| uterus | black zone | | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| | nodule | | 3 (6) | 2 (4) | 4 (8) | 9 (18) |
| | mass | | 0 (0) | 2 (4) | 0 (0) | 0 (0) |
| | cyst | | 0 (0) | 2 (4) | 0 (0) | 3 (6) |
| brain | red zone | | 0 (0) | 0 (0) | 1 (2) | 0 (0) |
| | hemorrhage | | 0 (0) | 1 (2) | 0 (0) | 0 (0) |
| spinal cord | nodule | | 0 (0) | 0 (0) | 1 (2) | 0 (0) |
| eye | turbid | | 0 (0) | 1 (2) | 0 (0) | 0 (0) |
| | white | | 1 (2) | 4 (8) | 1 (2) | 0 (0) |
| | deformed | | 0 (0) | 0 (0) | 1 (2) | 0 (0) |
| Zymbal gl | nodule | | 0 (0) | 1 (2) | 0 (0) | 0 (0) |
| muscle | nodule | | 0 (0) | 1 (2) | 0 (0) | 0 (0) |
| peritoneum | hemorrhage | | 0 (0) | 0 (0) | 0 (0) | 1 (2) |
| | nodule | | 0 (0) | 0 (0) | 0 (0) | 1 (2) |
| abdominal c | hemorrhage | | 0 (0) | 0 (0) | 1 (2) | 1 (2) |
| | ascites | | 0 (0) | 0 (0) | 0 (0) | 4 (8) |
| adipose | nodule | | 0 (0) | 0 (0) | 0 (0) | 1 (2) |
| thoracic ca | pleural fluid | | 1 (2) | 0 (0) | 1 (2) | 4 (8) |
| other | eye lid:nodule | | 1 (2) | 0 (0) | 0 (0) | 1 (2) |
| | ear:nodule | | 0 (0) | 0 (0) | 1 (2) | 0 (0) |

STUDY NO. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 8

| Organ | Findings | Group Name NO. of Animals | Control | 1000 ppm | 2000 ppm | 4000 ppm |
|------------|------------------|------------------------------|---------|----------|----------|----------|
| | | | 50 (%) | 50 (%) | 50 (%) | 50 (%) |
| other | lower jaw:nodule | | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| whole body | anemic | | 0 (0) | 0 (0) | 0 (0) | 2 (4) |

(IPT080)

BAIS 3

APPENDIX G 5

GROSS FINDINGS: SUMMARY, RAT: FEMALE: DEAD AND MORIBUND ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0278
 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 5 (%) | 1000 ppm 10 (%) | 2000 ppm 7 (%) | 4000 ppm 20 (%) |
|-------------|------------|------------------------------|------------------|--------------------|-------------------|--------------------|
| subcutis | jaundice | | 0 (0) | 1 (10) | 1 (14) | 1 (5) |
| | mass | | 0 (0) | 2 (20) | 0 (0) | 1 (5) |
| lung | white zone | | 0 (0) | 0 (0) | 1 (14) | 0 (0) |
| | nodule | | 0 (0) | 0 (0) | 0 (0) | 2 (10) |
| lymph node | enlarged | | 0 (0) | 2 (20) | 1 (14) | 1 (5) |
| thymus | enlarged | | 0 (0) | 0 (0) | 1 (14) | 0 (0) |
| spleen | enlarged | | 0 (0) | 4 (40) | 4 (57) | 4 (20) |
| heart | red zone | | 0 (0) | 1 (10) | 0 (0) | 1 (5) |
| | dilated | | 0 (0) | 0 (0) | 0 (0) | 1 (5) |
| forestomach | ulcer | | 2 (40) | 0 (0) | 0 (0) | 1 (5) |
| stomach | ulcer | | 1 (20) | 0 (0) | 0 (0) | 1 (5) |
| small intes | nodule | | 0 (0) | 0 (0) | 0 (0) | 1 (5) |
| large intes | nodule | | 0 (0) | 1 (10) | 0 (0) | 0 (0) |
| liver | enlarged | | 0 (0) | 0 (0) | 1 (14) | 1 (5) |
| | pale | | 0 (0) | 1 (10) | 0 (0) | 1 (5) |
| | red | | 0 (0) | 0 (0) | 0 (0) | 1 (5) |
| | red zone | | 0 (0) | 0 (0) | 0 (0) | 1 (5) |
| | nodule | | 1 (20) | 1 (10) | 0 (0) | 3 (15) |
| | rough | | 0 (0) | 1 (10) | 0 (0) | 3 (15) |
| | granular | | 0 (0) | 0 (0) | 1 (14) | 0 (0) |
| | nodular | | 0 (0) | 0 (0) | 0 (0) | 1 (5) |
| | herniation | | 0 (0) | 1 (10) | 0 (0) | 0 (0) |

STUDY NO. : 0278
 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 5 (%) | 1000 ppm 10 (%) | 2000 ppm 7 (%) | 4000 ppm 20 (%) |
|-------------|------------------------|------------------------------|------------------|--------------------|-------------------|--------------------|
| pancreas | nodule | | 0 (0) | 0 (0) | 0 (0) | 1 (5) |
| kidney | white zone | | 0 (0) | 0 (0) | 0 (0) | 1 (5) |
| | granular | | 0 (0) | 0 (0) | 0 (0) | 1 (5) |
| urin bladd | enlarged | | 0 (0) | 0 (0) | 0 (0) | 1 (5) |
| | urine:marked retention | | 0 (0) | 0 (0) | 0 (0) | 1 (5) |
| pituitary | enlarged | | 2 (40) | 6 (60) | 1 (14) | 4 (20) |
| | red zone | | 0 (0) | 0 (0) | 0 (0) | 3 (15) |
| | nodule | | 0 (0) | 1 (10) | 1 (14) | 2 (10) |
| thyroid | enlarged | | 0 (0) | 0 (0) | 0 (0) | 2 (10) |
| ovary | enlarged | | 0 (0) | 0 (0) | 0 (0) | 2 (10) |
| | cyst | | 0 (0) | 1 (10) | 0 (0) | 0 (0) |
| uterus | nodule | | 1 (20) | 0 (0) | 0 (0) | 6 (30) |
| | mass | | 0 (0) | 1 (10) | 0 (0) | 0 (0) |
| brain | red zone | | 0 (0) | 0 (0) | 1 (14) | 0 (0) |
| | hemorrhage | | 0 (0) | 1 (10) | 0 (0) | 0 (0) |
| spinal cord | nodule | | 0 (0) | 0 (0) | 1 (14) | 0 (0) |
| eye | turbid | | 0 (0) | 1 (10) | 0 (0) | 0 (0) |
| | white | | 0 (0) | 1 (10) | 0 (0) | 0 (0) |
| Zymbal gl | nodule | | 0 (0) | 1 (10) | 0 (0) | 0 (0) |
| peritoneum | hemorrhage | | 0 (0) | 0 (0) | 0 (0) | 1 (5) |
| | nodule | | 0 (0) | 0 (0) | 0 (0) | 1 (5) |
| abdominal c | hemorrhage | | 0 (0) | 0 (0) | 1 (14) | 1 (5) |

STUDY NO. : 0278
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 5 (%) | 1000 ppm 10 (%) | 2000 ppm 7 (%) | 4000 ppm 20 (%) |
|-------------|------------------|------------------------------|------------------|--------------------|-------------------|--------------------|
| abdominal c | ascites | | 0 (0) | 0 (0) | 0 (0) | 4 (20) |
| thoracic ca | pleural fluid | | 1 (20) | 0 (0) | 1 (14) | 4 (20) |
| other | lower jaw:nodule | | 1 (20) | 0 (0) | 0 (0) | 0 (0) |
| whole body | anemic | | 0 (0) | 0 (0) | 0 (0) | 2 (10) |

(HPT080)

BAIS3

APPENDIX G 6

GROSS FINDINGS: SUMMARY, RAT : FEMALE : SACRIFICED ANIMALS

(2-YEAR STUDY)

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

GROSS FINDINGS (SUMMARY)
 SACRIFICED ANIMALS (105W)

PAGE : 3

| Organ | Findings | Group Name NO. of Animals | Control 45 (%) | 1000 ppm 40 (%) | 2000 ppm 43 (%) | 4000 ppm 30 (%) |
|-------------|----------------|------------------------------|-------------------|--------------------|--------------------|--------------------|
| skin/app | nodule | | 1 (2) | 0 (0) | 1 (2) | 0 (0) |
| | mass | | 0 (0) | 0 (0) | 0 (0) | 1 (3) |
| subcutis | mass | | 10 (22) | 10 (25) | 10 (23) | 14 (47) |
| lung | nodule | | 3 (7) | 1 (3) | 1 (2) | 0 (0) |
| lymph node | enlarged | | 0 (0) | 0 (0) | 1 (2) | 0 (0) |
| spleen | enlarged | | 0 (0) | 2 (5) | 2 (5) | 2 (7) |
| | nodule | | 0 (0) | 0 (0) | 1 (2) | 0 (0) |
| small intes | nodule | | 0 (0) | 0 (0) | 1 (2) | 0 (0) |
| liver | white zone | | 0 (0) | 2 (5) | 0 (0) | 1 (3) |
| | red zone | | 0 (0) | 0 (0) | 0 (0) | 3 (10) |
| | brown zone | | 0 (0) | 0 (0) | 0 (0) | 1 (3) |
| | nodule | | 0 (0) | 2 (5) | 2 (5) | 1 (3) |
| | rough | | 0 (0) | 1 (3) | 1 (2) | 3 (10) |
| | herniation | | 2 (4) | 3 (8) | 2 (5) | 0 (0) |
| pancreas | nodule | | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| kidney | pale | | 0 (0) | 1 (3) | 0 (0) | 0 (0) |
| | cyst | | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| | granular | | 11 (24) | 1 (3) | 7 (16) | 5 (17) |
| | nodular | | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| | hydronephrosis | | 0 (0) | 0 (0) | 1 (2) | 0 (0) |
| pituitary | enlarged | | 7 (16) | 5 (13) | 7 (16) | 1 (3) |
| | red | | 1 (2) | 0 (0) | 0 (0) | 0 (0) |

STUDY NO. : 0278
 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 45 (%) | 1000 ppm 40 (%) | 2000 ppm 43 (%) | 4000 ppm 30 (%) |
|-------------|----------------|------------------------------|-------------------|--------------------|--------------------|--------------------|
| pituitary | red zone | | 5 (11) | 7 (18) | 4 (9) | 3 (10) |
| | nodule | | 4 (9) | 7 (18) | 10 (23) | 4 (13) |
| | cyst | | 0 (0) | 1 (3) | 0 (0) | 0 (0) |
| thyroid | enlarged | | 2 (4) | 1 (3) | 0 (0) | 1 (3) |
| | nodule | | 2 (4) | 0 (0) | 0 (0) | 0 (0) |
| parathyroid | nodule | | 0 (0) | 0 (0) | 1 (2) | 0 (0) |
| ovary | cyst | | 1 (2) | 2 (5) | 0 (0) | 0 (0) |
| uterus | black zone | | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| | nodule | | 2 (4) | 2 (5) | 4 (9) | 3 (10) |
| | mass | | 0 (0) | 1 (3) | 0 (0) | 0 (0) |
| | cyst | | 0 (0) | 2 (5) | 0 (0) | 3 (10) |
| eye | white | | 1 (2) | 3 (8) | 1 (2) | 0 (0) |
| | deformed | | 0 (0) | 0 (0) | 1 (2) | 0 (0) |
| muscle | nodule | | 0 (0) | 1 (3) | 0 (0) | 0 (0) |
| adipose | nodule | | 0 (0) | 0 (0) | 0 (0) | 1 (3) |
| other | eye lid:nodule | | 1 (2) | 0 (0) | 0 (0) | 1 (3) |
| | ear:nodule | | 0 (0) | 0 (0) | 1 (2) | 0 (0) |

(HPT080)

BAIS 3

APPENDIX H 1

ORGAN WEIGHT , ABSOLUTE: SUMMARY, RAT: MALE

(2-YEAR STUDY)

STUDY NO. : 0278
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 | 32 | 383± | 38 | 0.081± | 0.009 | 5.771± | 1.757 | 1.240± | 0.098 | 1.515± | 0.171 | 3.023± | 0.334 |
| 1000 ppm | 43 | 408± | 36 | 0.081± | 0.015 | 5.961± | 1.526 | 1.288± | 0.106 | 1.503± | 0.194 | 2.906± | 0.257 |
| 2000 ppm | 38 | 392± | 40 | 0.114± | 0.201 | 6.742± | 2.186 | 1.271± | 0.114 | 1.597± | 0.452 | 2.960± | 0.388 |
| 4000 ppm | 28 | 399± | 60 | 0.086± | 0.024 | 6.553± | 2.391 | 1.276± | 0.107 | 1.528± | 0.314 | 2.891± | 0.231 |

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

Test of Dunnett

(HCL040)

BAIS3

STUDY NO. : 0278
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 | 32 | 1.253± | 0.503 | 12.992± | 1.665 | 2.038± | 0.033 |
| 1000 ppm | 43 | 1.351± | 0.870 | 12.112± | 1.557 | 2.030± | 0.044 |
| 2000 ppm | 38 | 1.669± | 1.422 | 12.514± | 1.630 | 2.013± | 0.045 |
| 4000 ppm | 28 | 1.321± | 0.855 | 13.515± | 1.719 | 2.022± | 0.045 |

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

(HCL040)

BAIS3

APPENDIX H 2

ORGAN WEIGHT , ABSOLUTE: SUMMARY, RAT: FEMALE

(2-YEAR STUDY)

STUDY NO. : 0278
 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 | 45 | 295± 30 | 0.080± | 0.012 | 0.140± | 0.128 | 0.949± | 0.065 | 1.064± | 0.075 | 2.063± | 0.173 |
| 1000 ppm | 40 | 293± 32 | 0.081± | 0.012 | 0.151± | 0.202 | 0.992± | 0.087* | 1.110± | 0.188 | 2.014± | 0.172 |
| 2000 ppm | 43 | 295± 25 | 0.081± | 0.013 | 0.113± | 0.022 | 0.996± | 0.078* | 1.134± | 0.250 | 2.098± | 0.287 |
| 4000 ppm | 30 | 281± 31 | 0.080± | 0.010 | 0.123± | 0.024 | 0.995± | 0.084* | 1.104± | 0.150 | 2.040± | 0.194 |

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

(HCL040)

BAIS3

STUDY NO. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

PAGE : 4

| Group Name | NO. of Animals | SPLEEN | | LIVER | | BRAIN | |
|------------|-------------------|--------|--------|--------|---------|--------|-------|
| Control | 45 | 0.582± | 0.201 | 7.864± | 1.393 | 1.836± | 0.043 |
| 1000 ppm | 40 | 0.804± | 0.929 | 8.773± | 1.069** | 1.853± | 0.039 |
| 2000 ppm | 43 | 1.196± | 2.588 | 9.852± | 1.371** | 1.840± | 0.055 |
| 4000 ppm | 30 | 1.074± | 1.596* | 9.941± | 2.078** | 1.834± | 0.051 |

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

Test of Dunnett

(HCL040)

BAIS3

APPENDIX I 1

ORGAN WEIGHT, RELATIVE: SUMMARY, RAT: MALE

(2-YEAR STUDY)

STUDY NO. : 0278
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 | 32 | 383± 38 | 0.021± 0.004 | 1.508± 0.456 | 0.327± 0.045 | 0.398± 0.051 | 0.797± 0.132 |
| 1000 ppm | 43 | 408± 36 | 0.020± 0.005 | 1.461± 0.365 | 0.317± 0.032 | 0.370± 0.050** | 0.719± 0.108 |
| 2000 ppm | 38 | 392± 40 | 0.029± 0.049 | 1.714± 0.547 | 0.327± 0.041 | 0.415± 0.147 | 0.766± 0.150 |
| 4000 ppm | 28 | 399± 60 | 0.021± 0.004 | 1.673± 0.652 | 0.324± 0.037 | 0.392± 0.131 | 0.739± 0.127 |

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

Test of Dunnett

(HCL042)

BAIS3

STUDY NO. : 0278
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 | 32 | 0.325± 0.120 | 3.407± 0.449 | 0.537± 0.061 |
| 1000 ppm | 43 | 0.334± 0.224 | 2.981± 0.383** | 0.501± 0.044* |
| 2000 ppm | 38 | 0.440± 0.440 | 3.222± 0.545 | 0.519± 0.060 |
| 4000 ppm | 28 | 0.324± 0.164 | 3.443± 0.657 | 0.517± 0.074 |

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

Test of Dunnett

(HCL042)

BAIS3

APPENDIX 12

ORGAN WEIGHT, RELATIVE: SUMMARY, RAT: FEMALE

(2-YEAR STUDY)

STUDY NO. : 0278
 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 | 45 | 295± 30 | 0.027± 0.004 | 0.046± 0.033 | 0.324± 0.028 | 0.364± 0.038 | 0.707± 0.091 |
| 1000 ppm | 40 | 293± 32 | 0.028± 0.006 | 0.055± 0.092 | 0.343± 0.057 | 0.384± 0.088 | 0.697± 0.121 |
| 2000 ppm | 43 | 285± 25 | 0.028± 0.005 | 0.038± 0.007 | 0.339± 0.035 | 0.386± 0.089 | 0.718± 0.150 |
| 4000 ppm | 30 | 281± 31 | 0.029± 0.004 | 0.044± 0.008 | 0.357± 0.031** | 0.398± 0.069 | 0.731± 0.062 |

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

(HCL042)

BAIS 3

STUDY NO. : 0278
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 | 45 | 0.198± 0.066 | 2.674± 0.390 | 0.629± 0.061 |
| 1000 ppm | 40 | 0.277± 0.314 | 3.017± 0.464** | 0.640± 0.075 |
| 2000 ppm | 43 | 0.411± 0.917 | 3.341± 0.438** | 0.627± 0.053 |
| 4000 ppm | 30 | 0.388± 0.597** | 3.523± 0.453** | 0.661± 0.075 |

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

Test of Dunnett

(HCL042)

BAIS3

APPENDIX J 1

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

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 1

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 50 | | | | 2000 ppm 50 | | | | 4000 ppm 50 | | | |
|----------------------------------|-----------------------|---|-------|-------|-------|----------------|-------|-------|-------|----------------|-------|-------|-------|----------------|-------|-------|-------|
| | | 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> | | | |
| | hyperplasia:epidermis | 0 | 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) |
| | scab | 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) |
| | epidermal cyst | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| subcutis | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | cyst | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) |
| | abscess | 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 system] | | | | | | | | | | | | | | | | | |
| nasal cavit | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | thrombus | 5 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 4 | 0 | 0 | 0 |
| | | (10) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (8) | (0) | (0) | (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b 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. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 2

| Organ | Findings | Group Name No. of Animals on Study Grade | | | | Control 50 | | | | 1000 ppm 50 | | | | 2000 ppm 50 | | | | 4000 ppm 50 | | | |
|----------------------|---|--|------------|-----------|-----------|---------------|-------------|-----------|-------------|----------------|-------------|-----------|--------------|----------------|-------------|------------|-------------|----------------|-------------|------------|-------------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | | | | |
| nasal cavit | | <50> | | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | mineralization | 30 (60) | 0 (0) | 0 (0) | 0 (0) | 40 (80) | 0 (0) | 0 (0) | 0 * (0) | 40 (80) | 0 (0) | 0 (0) | 0 * (0) | 40 (80) | 0 (0) | 0 (0) | 0 (0) | 23 (46) | 2 (4) | 0 (0) | 0 (0) |
| | inflammatory infiltration | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| | eosinophilic change:olfactory epithelium | 35 (70) | 5 (10) | 3 (6) | 0 (0) | 27 (54) | 17 (34) | 3 (6) | 0 * (0) | 28 (56) | 18 (36) | 3 (6) | 0 ** (0) | 33 (66) | 10 (20) | 5 (10) | 0 (0) | 33 (66) | 10 (20) | 5 (10) | 0 (0) |
| | eosinophilic change:respiratory epithelium | 6 (12) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 3 (6) | 0 (0) | 0 (0) | 0 (0) | 12 (24) | 0 (0) | 0 (0) | 0 (0) | 12 (24) | 0 (0) | 0 (0) | 0 (0) |
| | inflammation:foreign body | 21 (42) | 2 (4) | 0 (0) | 0 (0) | 13 (26) | 3 (6) | 0 (0) | 0 (0) | 12 (24) | 0 (0) | 0 (0) | 0 * (0) | 15 (30) | 0 (0) | 0 (0) | 0 (0) | 15 (30) | 0 (0) | 0 (0) | 0 (0) |
| | inflammation:respiratory epithelium | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 3 (6) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | inflammation:olfactory epithelium | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | respiratory metaplasia:olfactory epithelium | 15 (30) | 6 (12) | 1 (2) | 0 (0) | 11 (22) | 1 (2) | 0 (0) | 0 (0) | 17 (34) | 0 (0) | 0 (0) | 0 (0) | 7 (14) | 1 (2) | 0 (0) | 0 * (0) | 7 (14) | 1 (2) | 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. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 3

| Organ | Findings | Group Name No. of Animals on Study Grade | Control 50 | | | | 1000 ppm 50 | | | | 2000 ppm 50 | | | | 4000 ppm 50 | | | |
|----------------------|------------------------------|--|---------------|------|------|------|----------------|------|------|------|----------------|------|------|------|----------------|------|------|------|
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| nasal cavit | respiratory metaplasia:gland | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | | 46 | 0 | 0 | 0 | 47 | 0 | 0 | 0 | 44 | 0 | 0 | 0 | 40 | 0 | 0 | 0 |
| | | | (92) | (0) | (0) | (0) | (94) | (0) | (0) | (0) | (88) | (0) | (0) | (0) | (80) | (0) | (0) | (0) |
| | | | | | | | | | | | | | | | | | | |
| | atrophy:olfactory epithelium | | 11 | 0 | 0 | 0 | 1 | 0 | 0 | 0 ** | 0 | 0 | 0 | 0 ** | 4 | 0 | 0 | 0 |
| | | | (22) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) |
| | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | |
| | erosion: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) |
| | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | |
| | thickening of bone:turbinate | | 6 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 4 | 0 | 0 | 0 |
| | | | (12) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (8) | (0) | (0) | (0) |
| | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | |
| nasopharynx | eosinophilic change | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| | | | | | | | | | | | | | | | | | | |
| | inflammation | | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (6) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | |
| larynx | mineralization | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| | | | | | | | | | | | | | | | | | | |

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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 4

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 50 | | | | 2000 ppm 50 | | | | 4000 ppm 50 | | | |
|----------------------|---------------------------------------|---|--------|-------|-------|----------------|-------|-------|-------|----------------|--------|-------|-------|----------------|-------|-------|-------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | |
| 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) |
| Lung | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | congestion | 0 | 1 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (0) | (2) | (0) | (0) | (4) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| | foreign body granuloma | 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) |
| | osseous metaplasia | 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) |
| | interstitial pneumonia | 23 | 6 | 0 | 0 | 36 | 2 | 0 | 0 * | 32 | 7 | 3 | 0 * | 20 | 3 | 0 | 0 |
| | | (46) | (12) | (0) | (0) | (72) | (4) | (0) | (0) | (64) | (14) | (6) | (0) | (40) | (6) | (0) | (0) |
| | bronchiolar-alveolar cell hyperplasia | 3 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (6) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| | mineralization:artery | 0 | 1 | 0 | 0 | 2 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (0) | (2) | (0) | (0) | (4) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| | endothelial cell hyperplasia | 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) |

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. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 5

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 50 | | | | 2000 ppm 50 | | | | 4000 ppm 50 | | | |
|------------------------|--------------------------|---|-----------|-----------|-----------|----------------|-----------|-----------|--------------|----------------|-----------|-----------|--------------|----------------|-----------|-----------|-----------|
| | | 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 | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | increased hematopoiesis | 18 (36) | 0 (0) | 0 (0) | 0 (0) | 20 (40) | 0 (0) | 0 (0) | 0 (0) | 15 (30) | 0 (0) | 0 (0) | 0 (0) | 27 (54) | 0 (0) | 0 (0) | 0 (0) |
| | erythropoiesis:increased | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| Lymph node | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | Lymphadenitis | 2 (4) | 0 (0) | 0 (0) | 0 (0) | 2 (4) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| | follicular hyperplasia | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| spleen | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | ectopic tissue | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | congestion | 13 (26) | 4 (8) | 0 (0) | 0 (0) | 3 (6) | 1 (2) | 0 (0) | 0 (0) ** | 2 (4) | 0 (0) | 0 (0) | 0 (0) ** | 11 (22) | 1 (2) | 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. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 6

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 50 | | | | 2000 ppm 50 | | | | 4000 ppm 50 | | | |
|------------------------|------------------------------|---|-------|-------|-------|----------------|-------|-------|-------|----------------|-------|-------|-------|----------------|--------|--------|-------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | |
| spleen | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | karyorrhexis | 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) |
| | deposit of hemosiderin | 6 | 2 | 0 | 0 | 7 | 1 | 0 | 0 | 9 | 2 | 0 | 0 | 8 | 3 | 2 | 0 |
| | | (12) | (4) | (0) | (0) | (14) | (2) | (0) | (0) | (18) | (4) | (0) | (0) | (16) | (6) | (4) | (0) |
| | fibrosis | 1 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 3 | 2 | 0 | 0 | 6 | 5 | 0 | 0 ** |
| | | (2) | (0) | (0) | (0) | (2) | (2) | (0) | (0) | (6) | (4) | (0) | (0) | (12) | (10) | (0) | (0) |
| | extramedullary hematopoiesis | 2 | 2 | 1 | 0 | 2 | 1 | 1 | 0 | 6 | 2 | 0 | 0 | 4 | 2 | 6 | 0 |
| | | (4) | (4) | (2) | (0) | (4) | (2) | (2) | (0) | (12) | (4) | (0) | (0) | (8) | (4) | (12) | (0) |
| | splenitis | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| | stromal 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) |

[Circulatory system]

| | | | | | | | | | | | | | | | | | |
|-------|----------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| heart | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | thrombus | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (2) | (0) |

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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 7

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 50 | | | | 2000 ppm 50 | | | | 4000 ppm 50 | | | |
|----------------------|----------------------|---|-------|------|------|----------------|------|------|------|----------------|-------|------|------|----------------|------|------|------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Circulatory system] | | | | | | | | | | | | | | | | | |
| heart | necrosis:focal | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | mineralization | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) |
| | | | | | | | | | | | | | | | | | |
| | myocardial fibrosis | 4 | 2 | 0 | 0 | 16 | 0 | 0 | 0 ** | 20 | 0 | 0 | 0 ** | 7 | 1 | 0 | 0 |
| | | (8) | (4) | (0) | (0) | (32) | (0) | (0) | (0) | (40) | (0) | (0) | (0) | (14) | (2) | (0) | (0) |
| | | | | | | | | | | | | | | | | | |
| artery/aort | mineralization | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 | 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) |
| | arteritis | 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) |
| | | | | | | | | | | | | | | | | | |
| | periarteritis nodosa | 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) | (0) |
| | | | | | | | | | | | | | | | | | |
| [Digestive system] | | | | | | | | | | | | | | | | | |
| tooth | dysplasia | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 9 | 5 | 0 | 1 | 14 | 2 | 0 | 0 | 7 | 6 | 0 | 0 | 17 | 3 | 0 | 0 |
| | | (18) | (10) | (0) | (2) | (28) | (4) | (0) | (0) | (14) | (12) | (0) | (0) | (34) | (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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 8

| Organ | Findings | Group Name No. of Animals on Study Grade | Control 50 | | | | 1000 ppm 50 | | | | 2000 ppm 50 | | | | 4000 ppm 50 | | | |
|--------------------|-----------------------------------|--|---------------|-------|-------|-------|----------------|-------|-------|-------|----------------|-------|-------|-------|----------------|-------|-------|-------|
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| tongue | mineralization | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 1 | 0 |
| | | | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (4) | (0) | (2) | (0) |
| | 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) |
| | | | | | | | | | | | | | | | | | | |
| | arteritis | | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | | (4) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (4) | (0) | (0) | (0) |
| | | | | | | | | | | | | | | | | | | |
| esophagus | C-cell hyperplasia | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | | 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) |
| | focal follicular 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) |
| | | | | | | | | | | | | | | | | | | |
| stomach | mineralization | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | | 0 | 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) |
| | inflammatory infiltration | | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | | | | | | | | | | | | | | | | | | |

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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 9

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 50 | | | | 2000 ppm 50 | | | | 4000 ppm 50 | | | |
|--------------------|---------------------------|---|-------|-------|-------|----------------|-------|-------|-------|----------------|-------|-------|-------|----------------|-------|-------|-------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | |
| stomach | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | periarthritis nodosa | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | ulcer:forestomach | 0 | 2 | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 2 | 0 | 3 | 1 | 0 |
| | | (0) | (4) | (6) | (0) | (0) | (0) | (2) | (0) | (0) | (2) | (0) | (4) | (0) | (6) | (2) | (0) |
| | hyperplasia:forestomach | 1 | 0 | 4 | 0 | 1 | 0 | 1 | 0 | 1 | 2 | 1 | 0 | 3 | 0 | 0 | 0 |
| | | (2) | (0) | (8) | (0) | (2) | (0) | (2) | (0) | (2) | (4) | (2) | (0) | (6) | (0) | (0) | (0) |
| | erosion:glandular stomach | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 1 | 0 | 0 |
| | | (6) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (2) | (0) | (0) |
| | ulcer:glandular stomach | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | (0) | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) |
| small intes | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | periarthritis nodosa | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| large intes | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | mineralization | 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

STUDY NO. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 10

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 50 | | | | 2000 ppm 50 | | | | 4000 ppm 50 | | | |
|--------------------|-------------------------|---|-------|-------|-------|----------------|--------|-------|-------|----------------|-------|-------|-------|----------------|-------|-------|-------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | |
| large intes | inflammation | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (2) | (0) | (0) |
| liver | herniation | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (6) | (0) | (0) | (0) |
| | peliosis-like lesion | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | necrosis:central | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (6) | (0) | (0) | (0) |
| | necrosis:focal | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 2 | 0 | 0 |
| | | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (4) | (0) | (0) |
| | fatty change | 0 | 0 | 2 | 0 | 1 | 0 | 0 | 0 | 10 | 0 | 0 | 0 ** | 5 | 0 | 0 | 0 * |
| | | (0) | (0) | (4) | (0) | (2) | (0) | (0) | (0) | (20) | (0) | (0) | (0) | (10) | (0) | (0) | (0) |
| | fatty change:central | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 2 | 0 | 0 | 1 | 1 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (2) | (0) | (4) | (0) | (0) | (2) | (2) | (0) |
| | fatty change:peripheral | 2 | 1 | 1 | 0 | 4 | 9 | 0 | 0 * | 6 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | (4) | (2) | (2) | (0) | (8) | (18) | (0) | (0) | (12) | (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 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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 11

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 50 | | | | 2000 ppm 50 | | | | 4000 ppm 50 | | | |
|--------------------|---------------------------|---|-------------|-----------|-----------|----------------|------------|-----------|--------------|----------------|-------------|-----------|-------------|----------------|-------------|-----------|-----------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | |
| Liver | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | granulation | 6 (12) | 0 (0) | 0 (0) | 0 (0) | 5 (10) | 0 (0) | 0 (0) | 0 (0) | 8 (16) | 0 (0) | 0 (0) | 0 (0) | 3 (6) | 0 (0) | 0 (0) | 0 (0) |
| | perivascular inflammation | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | clear cell focus | 2 (4) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 1 (2) | 0 (0) | 0 (0) |
| | acidophilic cell focus | 17 (34) | 5 (10) | 0 (0) | 0 (0) | 23 (46) | 6 (12) | 2 (4) | 0 (0) | 17 (34) | 16 (32) | 0 (0) | 0 * (0) | 13 (26) | 10 (20) | 1 (2) | 0 (0) |
| | basophilic cell focus | 12 (24) | 1 (2) | 0 (0) | 0 (0) | 31 (62) | 5 (10) | 0 (0) | 0 ** (0) | 20 (40) | 1 (2) | 0 (0) | 0 (0) | 11 (22) | 6 (12) | 1 (2) | 0 (0) |
| | vacuolated cell focus | 9 (18) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 * (0) | 12 (24) | 1 (2) | 0 (0) | 0 (0) | 8 (16) | 0 (0) | 0 (0) | 0 (0) |
| | spongiosis hepatitis | 6 (12) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 * (0) | 3 (6) | 0 (0) | 0 (0) | 0 (0) | 6 (12) | 0 (0) | 0 (0) | 0 (0) |
| | bile duct hyperplasia | 24 (48) | 24 (48) | 1 (2) | 0 (0) | 35 (70) | 4 (8) | 0 (0) | 0 ** (0) | 30 (60) | 12 (24) | 0 (0) | 0 * (0) | 27 (54) | 19 (38) | 1 (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. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 12

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 50 | | | | 2000 ppm 50 | | | | 4000 ppm 50 | | | |
|--------------------|-----------------------------|---|-------|-------|-------|----------------|-------|-------|-------|----------------|-------|-------|-------|----------------|-------|-------|-------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | |
| Liver | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | bile ductular proliferation | 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) |
| | biliary cyst | 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) | (0) |
| pancreas | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | atrophy | 7 | 1 | 0 | 0 | 2 | 2 | 0 | 0 | 9 | 1 | 0 | 0 | 9 | 0 | 0 | 0 |
| | | (14) | (2) | (0) | (0) | (4) | (4) | (0) | (0) | (18) | (2) | (0) | (0) | (18) | (0) | (0) | (0) |
| | inflammatory infiltration | 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) |
| | islet cell hyperplasia | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (4) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | hyperplasia:acinar cell | 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) |
| [Urinary system] | | | | | | | | | | | | | | | | | |
| kidney | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | thrombus | 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) |

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. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 13

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 50 | | | | 2000 ppm 50 | | | | 4000 ppm 50 | | | |
|------------------|------------------------|---|--------|--------|--------|----------------|--------|--------|--------|----------------|--------|--------|--------|----------------|--------|--------|--------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Urinary system] | | | | | | | | | | | | | | | | | |
| kidney | cyst | <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) |
| | hyaline droplet | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | basophilic change | 16 | 25 | 0 | 0 | 28 | 7 | 0 | 0 ** | 24 | 10 | 0 | 0 ** | 21 | 8 | 0 | 0 ** |
| | | (32) | (50) | (0) | (0) | (56) | (14) | (0) | (0) | (48) | (20) | (0) | (0) | (42) | (16) | (0) | (0) |
| | deposit of hemosiderin | 15 | 0 | 0 | 0 | 29 | 0 | 0 | 0 ** | 32 | 1 | 0 | 0 ** | 22 | 4 | 0 | 0 * |
| | | (30) | (0) | (0) | (0) | (58) | (0) | (0) | (0) | (64) | (2) | (0) | (0) | (44) | (8) | (0) | (0) |
| | eosinophilic body | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) |
| | chronic nephropathy | 2 | 4 | 16 | 26 | 4 | 10 | 28 | 7 ** | 5 | 12 | 22 | 11 ** | 6 | 12 | 17 | 11 * |
| | | (4) | (8) | (32) | (52) | (8) | (20) | (56) | (14) | (10) | (24) | (44) | (22) | (12) | (24) | (34) | (22) |
| | hydronephrosis | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) |
| | mineralization:papilla | 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. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 14

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 50 | | | | 2000 ppm 50 | | | | 4000 ppm 50 | | | |
|--------------------|-------------------------------|---|------|------|------|----------------|-------|------|------|----------------|-------|------|------|----------------|-------|------|------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Urinary system] | | | | | | | | | | | | | | | | | |
| kidney | mineralization:cortex | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) |
| | urothelial hyperplasia:pelvis | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (4) | (0) | (0) | (0) |
| urin bladd | hemorrhagic inflammation | <50> | | | | <50> | | | | <50> | | | | <49> | | | |
| | | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) |
| [Endocrine system] | | | | | | | | | | | | | | | | | |
| pituitary | angiectasis | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | cyst | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 | 0 | 0 | 0 | 4 | 1 | 0 | 0 | 5 | 0 | 0 | 0 | 5 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (8) | (2) | (0) | (0) | (10) | (0) | (0) | (0) | (10) | (0) | (0) | (0) |
| | hyperplasia | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 13 | 2 | 0 | 0 | 20 | 6 | 2 | 0 * | 11 | 7 | 0 | 0 | 17 | 7 | 0 | 0 |
| | | (26) | (4) | (0) | (0) | (40) | (12) | (4) | (0) | (22) | (14) | (0) | (0) | (34) | (14) | (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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 15

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 50 | | | | 2000 ppm 50 | | | | 4000 ppm 50 | | | |
|--------------------|-----------------------------------|---|-------|-------|-------|----------------|-------|-------|-------|----------------|-------|-------|-------|----------------|-------|-------|-------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Endocrine system] | | | | | | | | | | | | | | | | | |
| pituitary | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | Rathke pouch | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| thyroid | | <50> | | | | <48> | | | | <48> | | | | <50> | | | |
| | ultimibranhial body remanet | 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) |
| | adenomatous goiter | 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) |
| | C-cell hyperplasia | 9 | 0 | 0 | 0 | 7 | 0 | 0 | 0 | 6 | 2 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | (18) | (0) | (0) | (0) | (15) | (0) | (0) | (0) | (12) | (4) | (0) | (0) | (6) | (0) | (0) | (0) |
| | focal follicular cell hyperplasia | 2 | 1 | 0 | 0 | 4 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 1 | 0 | 0 |
| | | (4) | (2) | (0) | (0) | (8) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (2) | (2) | (0) | (0) |
| adrenal | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | peliosis-like lesion | 4 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 10 | 0 | 0 | 0 | 9 | 0 | 0 | 0 |
| | | (8) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (20) | (0) | (0) | (0) | (18) | (0) | (0) | (0) |
| | necrosis:focal | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 16

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 50 | | | | 2000 ppm 50 | | | | 4000 ppm 50 | | | |
|-------|----------|---|-----|-----|-----|----------------|-----|-----|-----|----------------|-----|-----|-----|----------------|-----|-----|-----|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |

[Endocrine system]

| | | | | | | | | | | | | | | | | | |
|---------|---------------------------|--------|--------|-------|-------|--------|-------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|
| adrenal | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | hyperplasia:cortical cell | 2 | 0 | 0 | 0 | 5 | 1 | 0 | 0 | 6 | 1 | 0 | 0 | 6 | 0 | 0 | 0 |
| | | (4) | (0) | (0) | (0) | (10) | (2) | (0) | (0) | (12) | (2) | (0) | (0) | (12) | (0) | (0) | (0) |
| | hyperplasia:medulla | 8 | 5 | 0 | 0 | 17 | 3 | 0 | 0 | 20 | 3 | 0 | 0 * | 16 | 6 | 0 | 0 |
| | | (16) | (10) | (0) | (0) | (34) | (6) | (0) | (0) | (40) | (6) | (0) | (0) | (32) | (12) | (0) | (0) |
| | focal fatty change:cortex | 9 | 1 | 0 | 0 | 7 | 2 | 0 | 0 | 8 | 5 | 0 | 0 | 6 | 4 | 0 | 0 |
| | | (18) | (2) | (0) | (0) | (14) | (4) | (0) | (0) | (16) | (10) | (0) | (0) | (12) | (8) | (0) | (0) |
| | focal hypertrophy:cortex | 2 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 3 | 1 | 0 | 0 | 4 | 1 | 0 | 0 |
| | | (4) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (6) | (2) | (0) | (0) | (8) | (2) | (0) | (0) |

[Reproductive system]

| | | | | | | | | | | | | | | | | | |
|--------|----------------|-------|-------|--------|--------|--------|-------|-------|--------|--------|-------|-------|--------|-------|-------|-------|--------|
| testis | | <49> | | | | <50> | | | | <50> | | | | <50> | | | |
| | atrophy | 0 | 1 | 9 | 39 | 0 | 1 | 1 | 48 * | 0 | 2 | 3 | 44 | 0 | 2 | 3 | 42 |
| | | (0) | (2) | (18) | (80) | (0) | (2) | (2) | (96) | (0) | (4) | (6) | (88) | (0) | (4) | (6) | (84) |
| | mineralization | 2 | 0 | 0 | 0 | 6 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (4) | (0) | (0) | (0) | (12) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| | arteritis | 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) |

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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 17

| Organ_____ | Findings_____ | Group Name | Control | | | | 1000 ppm | | | | 2000 ppm | | | | 4000 ppm | | | |
|------------|---------------|-------------------------|---------|-----|-----|-----|----------|-----|-----|-----|----------|-----|-----|-----|----------|-----|-----|-----|
| | | No. of Animals on Study | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| Grade | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |

| | | | | | | | | | | | | | | | | | | |
|-----------------------|-------------------------------|--|-------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| [Reproductive system] | | | | | | | | | | | | | | | | | | |
| testis | | | <49> | | | | <50> | | | | <50> | | | | <50> | | | |
| | interstitial cell hyperplasia | | 3 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | | (6) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (4) | (0) | (0) | (0) |
| epididymis | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | spermatogenic granuloma | | 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) |
| prostate | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | inflammation | | 5 | 1 | 0 | 0 | 2 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | | (10) | (2) | (0) | (0) | (4) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (6) | (0) | (0) | (0) |
| mammary gl | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | duct ectasia | | 3 | 1 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (6) | (2) | (0) | (0) | (4) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | galactocoele | | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) |
| prep/cli gl | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | duct ectasia | | 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) |
| [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) |

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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 18

| Organ | Findings | Group Name | Control | | | | 1000 ppm | | | | 2000 ppm | | | | 4000 ppm | | | |
|---|--|-------------------------|---------|-------|-------|-------|----------|-------|-------|-------|----------|-------|-------|-------|----------|-------|-------|-------|
| | | No. of Animals on Study | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Nervous system] | | | | | | | | | | | | | | | | | | |
| spinal cord | gliosis | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 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) |
| [Special sense organs/appandage] | | | | | | | | | | | | | | | | | | |
| eye | cataract | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | retinal atrophy | | 2 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 2 | 2 | 0 | 0 | 0 | 1 |
| | | | (4) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (2) | (2) | (4) | (4) | (0) | (0) | (0) | (2) |
| | keratitis | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (6) | (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) | (4) | (0) | (0) | (0) |
| | phthisis bulbi | | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | degeneration:cornea | | 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) |
| 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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 19

| | | Group Name | Control | | | | 1000 ppm | | | | 2000 ppm | | | | 4000 ppm | | | |
|----------------------------------|---------------------------|-------------------------|-----------|-----------|-----------|-------------|-----------|-----------|-----------|-------------|-----------|-----------|-----------|-------------|-----------|-----------|-----------|-----|
| | | No. of Animals on Study | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| Organ_____ | Findings_____ | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Special sense organs/appandage] | | | | | | | | | | | | | | | | | | |
| eye | mineralization:cornea | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 33 (66) | 0 (0) | 0 (0) | 0 (0) | 25 (50) | 0 (0) | 0 (0) | 0 (0) | 26 (52) | 0 (0) | 0 (0) | 0 (0) | 17 (34) | 0 (0) | 0 (0) | 0 (0) | ** |
| Harder gl | atrophy | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 (0) | 2 (4) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | |
| | degeneration | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 22 (44) | 1 (2) | 0 (0) | 0 (0) | 26 (52) | 1 (2) | 0 (0) | 0 (0) | 25 (50) | 3 (6) | 0 (0) | 0 (0) | 16 (32) | 0 (0) | 0 (0) | 0 (0) | |
| | inflammatory infiltration | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | |
| nasolacr d | inflammation | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 2 (4) | 0 (0) | 0 (0) | 0 (0) | 2 (4) | 0 (0) | 0 (0) | 0 (0) | |
| [Musculoskeletal system] | | | | | | | | | | | | | | | | | | |
| muscle | mineralization | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 1 (2) | 0 (0) | 0 (0) | 1 (2) | 1 (2) | 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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 20

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 50 | | | | 2000 ppm 50 | | | | 4000 ppm 50 | | | |
|--------------------------|----------------|---|-------|-------|-------|----------------|-------|-------|-------|----------------|-------|-------|-------|----------------|-------|-------|-------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Musculoskeletal system] | | | | | | | | | | | | | | | | | |
| muscle | inflammation | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| | arteritis | 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) |
| bone | osteosclerosis | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |

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)

BA1S3

APPENDIX J 2

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

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 1

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 7 | | | | 2000 ppm 12 | | | | 4000 ppm 22 | | | |
|----------------------------------|--|---|------|------|------|---------------|------|------|------|----------------|-------|------|------|----------------|------|------|------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Integumentary system/appandage] | | | | | | | | | | | | | | | | | |
| skin/app | scab | <18> | | | | <7> | | | | <12> | | | | <22> | | | |
| | | 0 | 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) |
| subcutis | cyst | <18> | | | | <7> | | | | <12> | | | | <22> | | | |
| | | 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 | thrombus | <18> | | | | <7> | | | | <12> | | | | <22> | | | |
| | | 5 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 4 | 0 | 0 | 0 |
| | | (28) | (0) | (0) | (0) | (14) | (0) | (0) | (0) | (17) | (0) | (0) | (0) | (18) | (0) | (0) | (0) |
| | mineralization | 9 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 10 | 0 | 0 | 0 | 9 | 1 | 0 | 0 |
| | | (50) | (0) | (0) | (0) | (57) | (0) | (0) | (0) | (83) | (0) | (0) | (0) | (41) | (5) | (0) | (0) |
| | inflammatory infiltration | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) | (0) |
| | eosinophilic change:olfactory epithelium | 13 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 9 | 2 | 0 | 0 | 18 | 2 | 0 | 0 |
| | | (72) | (0) | (0) | (0) | (57) | (0) | (0) | (0) | (75) | (17) | (0) | (0) | (82) | (9) | (0) | (0) |

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

STUDY NO. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 2

| Organ | Findings | Group Name | Control | | | | 1000 ppm | | | | 2000 ppm | | | | 4000 ppm | | | |
|---|--|-------------------------|-------------|-----------|-----------|-----------|------------|-----------|-----------|-----------|------------|-----------|-----------|-------------|-----------|-----------|-----------|-----------|
| | | No. of Animals on Study | 18 | | | | 7 | | | | 12 | | | | 22 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| nasal cavity | | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | eosinophilic change:respiratory epithelium | | 1 (6) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (9) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | inflammation:foreign body | | 6 (33) | 1 (6) | 0 (0) | 0 (0) | 4 (57) | 0 (0) | 0 (0) | 0 (0) | 3 (25) | 0 (0) | 0 (0) | 5 (23) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | inflammation:respiratory epithelium | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 3 (25) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | respiratory metaplasia:olfactory epithelium | | 4 (22) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 3 (25) | 0 (0) | 0 (0) | 3 (14) | 1 (5) | 0 (0) | 0 (0) | 0 (0) |
| | respiratory metaplasia:gland | | 16 (89) | 0 (0) | 0 (0) | 0 (0) | 5 (71) | 0 (0) | 0 (0) | 0 (0) | 9 (75) | 0 (0) | 0 (0) | 15 (68) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | atrophy:olfactory epithelium | | 6 (33) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 3 (14) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | erosion:olfactory epithelium | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (14) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | thickening of bone:turbinate | | 1 (6) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (8) | 0 (0) | 0 (0) | 3 (14) | 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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 3

| Organ_____ | Findings_____ | Group Name | Control | | | | 1000 ppm | | | | 2000 ppm | | | | 4000 ppm | | | |
|------------------------|-------------------------|-------------------------|---------|------|------|-------|----------|------|------|-------|----------|-------|------|-------|----------|------|------|-----|
| | | No. of Animals on Study | 18 | | | | 7 | | | | 12 | | | | 22 | | | |
| Grade | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| nasopharynx | eosinophilic change | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | | | 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) | |
| larynx | mineralization | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | | | 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 | congestion | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | | | 0 | 1 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (0) | (6) | (0) | (0) | (29) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | |
| | interstitial pneumonia | | 6 | 2 | 0 | 0 | 1 | 2 | 0 | 0 | 5 | 2 | 2 | 0 | 8 | 1 | 0 | 0 |
| | | (33) | (11) | (0) | (0) | (14) | (29) | (0) | (0) | (42) | (17) | (17) | (0) | (36) | (5) | (0) | (0) | |
| | mineralization:artery | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (6) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| bone marrow | increased hematopoiesis | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | | | 5 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 11 | 0 | 0 | 0 |
| | | (28) | (0) | (0) | (0) | (57) | (0) | (0) | (0) | (17) | (0) | (0) | (0) | (50) | (0) | (0) | (0) | |

[Hematopoietic system]

| | | | | | | | | | | | | | | | | | | |
|-------------|-------------------------|--|------------|-----------|-----------|-----------|------------|-----------|-----------|-----------|------------|-----------|-----------|-----------|-------------|-----------|-----------|-----------|
| bone marrow | increased hematopoiesis | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | | | 5 (28) | 0 (0) | 0 (0) | 0 (0) | 4 (57) | 0 (0) | 0 (0) | 0 (0) | 2 (17) | 0 (0) | 0 (0) | 0 (0) | 11 (50) | 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. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 4

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 7 | | | | 2000 ppm 12 | | | | 4000 ppm 22 | | | |
|------------------------|--------------------------|---|-----------|-----------|-----------|---------------|-----------|-----------|-----------|----------------|-----------|-----------|-----------|----------------|-----------|-----------|-----------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | |
| bone marrow | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | erythropoiesis:increased | 1 (6) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (8) | 0 (0) | 0 (0) | 0 (0) | 1 (5) | 0 (0) | 0 (0) | 0 (0) |
| Lymph node | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | Lymphadenitis | 1 (6) | 0 (0) | 0 (0) | 0 (0) | 1 (14) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | follicular 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) | 1 (5) | 0 (0) | 0 (0) | 0 (0) |
| spleen | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | congestion | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (9) | 0 (0) | 0 (0) | 0 (0) |
| | karyorrhexis | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (14) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | deposit of hemosiderin | 4 (22) | 2 (11) | 0 (0) | 0 (0) | 0 (0) | 1 (14) | 0 (0) | 0 (0) | 0 (0) | 2 (17) | 0 (0) | 0 (0) | 2 (9) | 3 (14) | 2 (9) | 0 (0) |
| | fibrosis | 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 (5) | 2 (9) | 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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 5

| Organ | Findings | Group Name | Control | | | | 1000 ppm | | | | 2000 ppm | | | | 4000 ppm | | | |
|------------------------|------------------------------|-------------------------|---------|--------|-------|-------|----------|--------|--------|--------|----------|-------|-------|-------|----------|-------|--------|-------|
| | | No. of Animals on Study | 18 | | | | 7 | | | | 12 | | | | 22 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| spleen | | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | extramedullary hematopoiesis | | 0 | 2 | 1 | 0 | 1 | 1 | 1 | 0 | 3 | 1 | 0 | 0 | 1 | 2 | 5 | 0 |
| | | | (0) | (11) | (6) | (0) | (14) | (14) | (14) | (0) | (25) | (8) | (0) | (0) | (5) | (9) | (23) | (0) |
| [Circulatory system] | | | | | | | | | | | | | | | | | | |
| heart | | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | thrombus | | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (14) | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (5) | (0) |
| | mineralization | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | (6) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) |
| | myocardial fibrosis | | 1 | 2 | 0 | 0 | 3 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 2 | 1 | 0 | 0 |
| | | | (6) | (11) | (0) | (0) | (43) | (0) | (0) | (0) | (25) | (0) | (0) | (0) | (9) | (5) | (0) | (0) |
| artery/aort | | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | mineralization | | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| | | | (0) | (0) | (6) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) |
| | periarteritis nodosa | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (14) | (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. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 6

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 7 | | | | 2000 ppm 12 | | | | 4000 ppm 22 | | | |
|--------------------|---------------------------|---|-------|-------|------|---------------|------|-------|------|----------------|-------|------|-------|----------------|-------|------|------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | |
| tooth | dysplasia | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | | 2 | 4 | 0 | 0 | 3 | 0 | 0 | 0 | 1 | 2 | 0 | 0 | 6 | 1 | 0 | 0 |
| | | (11) | (22) | (0) | (0) | (43) | (0) | (0) | (0) | (8) | (17) | (0) | (0) | (27) | (5) | (0) | (0) |
| tongue | mineralization | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| | | (0) | (0) | (6) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) |
| | arteritis | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (14) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| stomach | mineralization | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| | | (0) | (0) | (6) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) |
| | inflammatory infiltration | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (6) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | periarteritis nodosa | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (14) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | ulcer:forestomach | 0 | 1 | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 2 | 0 | 3 | 1 | 0 |
| | | (0) | (6) | (17) | (0) | (0) | (0) | (14) | (0) | (0) | (8) | (0) | (17) | (0) | (14) | (5) | (0) |

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

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

b : Number of animals with lesion

(c) c : b / a * 100

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

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 7

| Organ_____ | Findings_____ | Group Name | Control | | | | 1000 ppm | | | | 2000 ppm | | | | 4000 ppm | | | |
|--------------------|---------------------------|-------------------------|------------|------------|-----------|-----------|-----------|------------|-----------|-----------|-----------|-----------|-----------|------------|-----------|-----------|-----------|--|
| | | No. of Animals on Study | 18 | | | | 7 | | | | 12 | | | | 22 | | | |
| Grade | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| stomach | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | | |
| | hyperplasia:forestomach | 1 (6) | 0 (0) | 3 (17) | 0 (0) | 0 (0) | 0 (0) | 1 (14) | 0 (0) | 1 (8) | 1 (8) | 1 (8) | 0 (0) | 1 (5) | 0 (0) | 0 (0) | 0 (0) | |
| | erosion:glandular stomach | 2 (11) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (5) | 1 (5) | 0 (0) | 0 (0) | |
| | ulcer:glandular stomach | 0 (0) | 2 (11) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (5) | 0 (0) | 0 (0) | |
| small intes | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | | |
| | periarteritis nodosa | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (14) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | |
| liver | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | | |
| | herniation | 1 (6) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (8) | 0 (0) | 0 (0) | 0 (0) | 1 (5) | 0 (0) | 0 (0) | 0 (0) | |
| | necrosis:central | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 3 (14) | 0 (0) | 0 (0) | 0 (0) | |
| | necrosis:focal | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (8) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (9) | 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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 8

| | | Group Name No. of Animals on Study Grade | | | | Control 18 | | | | 1000 ppm 7 | | | | 2000 ppm 12 | | | | 4000 ppm 22 | | | |
|--|--|--|------------|-------------|------------|---------------|-------------|------------|------------|---------------|------------|-------------|------------|----------------|------------|------------|------------|----------------|--|--|--|
| Organ | Findings | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | | | | |
| [Digestive system] | | | | | | | | | | | | | | | | | | | | | |
| liver | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | | | | | |
| | fatty change | 0 (0) | 0 (0) | 2 (11) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (5) | 0 (0) | 0 (0) | 0 (0) | | | | |
| | fatty change:central | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (14) | 0 (0) | 0 (0) | 1 (8) | 0 (0) | 2 (17) | 0 (0) | 0 (0) | 1 (5) | 1 (5) | 0 (0) | | | | |
| | fatty change:peripheral | 1 (6) | 1 (6) | 1 (6) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (17) | 0 (0) | 0 (0) | 0 (0) | 1 (5) | 0 (0) | 0 (0) | 0 (0) | | | | |
| | perivascular inflammation | 0 (0) | 1 (6) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | | | | |
| | acidophilic cell focus | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (14) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (5) | 0 (0) | 0 (0) | 0 (0) | | | | |
| | basophilic cell focus | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (29) | 0 (0) | 0 (0) | 0 (0) | 1 (8) | 0 (0) | 0 (0) | 0 (0) | 2 (9) | 2 (9) | 0 (0) | 0 (0) | | | | |
| | vacuolated cell focus | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (8) | 0 (0) | 0 (0) | 0 (0) | 1 (5) | 0 (0) | 0 (0) | 0 (0) | | | | |
| | spongiosis hepatis | 2 (11) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (5) | 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. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 9

| Organ | Findings | Group Name No. of Animals on Study Control Grade | | | | 1000 ppm 7 | | | | 2000 ppm 12 | | | | 4000 ppm 22 | | | |
|--------------------|-----------------------------|---|------------|-----------|-----------|---------------|------------|-----------|-------------|----------------|------------|-----------|-----------|----------------|------------|-----------|-----------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | |
| liver | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | bile duct hyperplasia | 13 (72) | 3 (17) | 1 (6) | 0 (0) | 3 (43) | 0 (0) | 0 (0) | 0 * (0) | 7 (58) | 3 (25) | 0 (0) | 0 (0) | 15 (68) | 5 (23) | 0 (0) | 0 (0) |
| | bile ductular proliferation | 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 (5) | 0 (0) | 0 (0) |
| | biliary cyst | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (8) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| pancreas | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | atrophy | 3 (17) | 1 (6) | 0 (0) | 0 (0) | 0 (0) | 1 (14) | 0 (0) | 0 (0) | 1 (8) | 0 (0) | 0 (0) | 0 (0) | 1 (5) | 0 (0) | 0 (0) | 0 (0) |
| [Urinary system] | | | | | | | | | | | | | | | | | |
| kidney | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | thrombus | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (14) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | cyst | 0 (0) | 1 (6) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |

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. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 10

| Organ_____ | Findings_____ | Group Name | Control | | | | 1000 ppm | | | | 2000 ppm | | | | 4000 ppm | | | |
|------------------|-------------------------------|-------------------------|------------|------------|------------|------------|------------|------------|-----------|-------------|------------|------------|-----------|------------|------------|------------|------------|--------------|
| | | No. of Animals on Study | 18 | | | | 7 | | | | 12 | | | | 22 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | hyaline droplet | | 0 (0) | 0 (0) | 1 (6) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | basophilic change | | 1 (6) | 8 (44) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (17) | 2 (17) | 0 (0) | 0 (0) | 7 (32) | 1 (5) | 0 (0) | 0 (0) ** |
| | deposit of hemosiderin | | 2 (11) | 0 (0) | 0 (0) | 0 (0) | 3 (43) | 0 (0) | 0 (0) | 0 (0) | 5 (42) | 1 (8) | 0 (0) | 0 (0) | 3 (14) | 2 (9) | 0 (0) | 0 (0) |
| | chronic nephropathy | | 2 (11) | 4 (22) | 2 (11) | 8 (44) | 4 (57) | 3 (43) | 0 (0) | 0 (0) * | 3 (25) | 5 (42) | 1 (8) | 3 (25) | 5 (23) | 7 (32) | 3 (14) | 4 (18) |
| | mineralization:papilla | | 1 (6) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | mineralization:cortex | | 2 (11) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (9) | 0 (0) | 0 (0) | 0 (0) |
| urin bladd | urothelial hyperplasia:pelvis | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (8) | 0 (0) | 0 (0) | 0 (0) | 2 (9) | 0 (0) | 0 (0) | 0 (0) |
| | hemorrhagic inflammation | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (5) |

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. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 11

| Organ | Findings | Group Name No. of Animals on Study Grade | Control 18 | | | | 1000 ppm 7 | | | | 2000 ppm 12 | | | | 4000 ppm 22 | | | |
|--------------------|-----------------------------------|--|---------------|-------|-------|-------|---------------|--------|-------|-------|----------------|-------|-------|-------|----------------|--------|-------|-------|
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Endocrine system] | | | | | | | | | | | | | | | | | | |
| pituitary | | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | cyst | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (14) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (9) | (0) | (0) | (0) |
| | hyperplasia | | 3 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 6 | 3 | 0 | 0 |
| | | | (17) | (0) | (0) | (0) | (14) | (14) | (0) | (0) | (0) | (0) | (0) | (0) | (27) | (14) | (0) | (0) |
| | Rathke pouch | | 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) |
| thyroid | | | <18> | | | | < 5> | | | | <12> | | | | <22> | | | |
| | C-cell hyperplasia | | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (11) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (5) | (0) | (0) | (0) |
| | focal follicular cell hyperplasia | | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | (0) | (6) | (0) | (0) | (20) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) |
| | | | | | | | | | | | | | | | | | | |
| adrenal | | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | melanosis-like lesion | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (25) | (0) | (0) | (0) | (5) | (0) | (0) | (0) |
| | hyperplasia:cortical cell | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (6) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) | (0) |
| | | | | | | | | | | | | | | | | | | |

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

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 12

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 7 | | | | 2000 ppm 12 | | | | 4000 ppm 22 | | | |
|-----------------------|-------------------------------|---|-------|-------|-------|---------------|-------|------|-------|----------------|-------|------|-------|----------------|-------|------|-------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Endocrine system] | | | | | | | | | | | | | | | | | |
| adrenal | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | hyperplasia:medulla | 2 | 2 | 0 | 0 | 1 | 0 | 0 | 0 | 3 | 1 | 0 | 0 | 2 | 4 | 0 | 0 |
| | | (11) | (11) | (0) | (0) | (14) | (0) | (0) | (0) | (25) | (8) | (0) | (0) | (9) | (18) | (0) | (0) |
| | | | | | | | | | | | | | | | | | |
| | focal fatty change:cortex | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 2 | 0 | 0 |
| | | (17) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (8) | (0) | (0) | (5) | (9) | (0) | (0) |
| | | | | | | | | | | | | | | | | | |
| | focal hypertrophy:cortex | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (14) | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (5) | (0) | (0) | (0) |
| [Reproductive system] | | | | | | | | | | | | | | | | | |
| testis | | <17> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | atrophy | 0 | 1 | 5 | 11 | 0 | 1 | 0 | 6 | 0 | 2 | 1 | 8 | 0 | 2 | 1 | 17 |
| | | (0) | (6) | (29) | (65) | (0) | (14) | (0) | (86) | (0) | (17) | (8) | (67) | (0) | (9) | (5) | (77) |
| | | | | | | | | | | | | | | | | | |
| | mineralization | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (6) | (0) | (0) | (0) | (14) | (0) | (0) | (0) | (17) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | | | | | | | | | | | | | | | | | |
| | arteritis | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (14) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | interstitial cell hyperplasia | 3 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (18) | (0) | (0) | (0) | (29) | (0) | (0) | (0) | (25) | (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 ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 13

| Organ | Findings | Group Name No. of Animals on Study Grade | Control 18 | | | | 1000 ppm 7 | | | | 2000 ppm 12 | | | | 4000 ppm 22 | | | |
|-----------------------|-------------------------|--|---------------|------|------|------|---------------|-------|------|------|----------------|------|------|------|----------------|------|------|------|
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Reproductive system] | | | | | | | | | | | | | | | | | | |
| epididymis | spermatogenic granuloma | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | | | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (14) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| prostate | inflammation | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | | | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (6) | (6) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (5) | (0) | (0) | (0) |
| mammary gl | duct ectasia | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | | | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (17) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | galactocoele | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | | | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (11) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| prep/cli gl | duct ectasia | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (6) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| [Nervous system] | | | | | | | | | | | | | | | | | | |
| spinal cord | gliosis | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (14) | (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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 14

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm | | | | 2000 ppm | | | | 4000 ppm | | | |
|----------------------------------|-----------------------|---|------|------|------|----------|-------|------|------|----------|-------|------|------|----------|------|------|------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Special sense organs/appandage] | | | | | | | | | | | | | | | | | |
| eye | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | cataract | 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) |
| | retinal atrophy | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 |
| | | (6) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (5) |
| | keratitis | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | (6) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (14) | (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) | (9) | (0) | (0) | (0) |
| | degeneration: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) | (8) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | mineralization:cornea | 8 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 4 | 0 | 0 | 0 |
| | | (44) | (0) | (0) | (0) | (43) | (0) | (0) | (0) | (33) | (0) | (0) | (0) | (18) | (0) | (0) | (0) |
| Harder gl | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | atrophy | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (6) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | degeneration | 6 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 5 | 2 | 0 | 0 | 8 | 0 | 0 | 0 |
| | | (33) | (0) | (0) | (0) | (14) | (14) | (0) | (0) | (42) | (17) | (0) | (0) | (36) | (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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 15

| Organ | Findings | Group Name No. of Animals on Study Grade | Control 18 | | | | 1000 ppm 7 | | | | 2000 ppm 12 | | | | 4000 ppm 22 | | | |
|----------------------------------|----------------|--|---------------|-------|-------|-------|---------------|-------|-------|-------|----------------|-------|-------|-------|----------------|-------|-------|-------|
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Special sense organs/appandage] | | | | | | | | | | | | | | | | | | |
| nasolacr d | inflammation | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (14) | (0) | (0) | (0) | (17) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| [Musculoskeletal system] | | | | | | | | | | | | | | | | | | |
| muscle | mineralization | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 1 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (8) | (0) | (0) | (5) | (5) | (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) | (5) | (0) | (0) | (0) |
| | arteritis | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (14) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| bone | osteosclerosis | | <18> | | | | < 7> | | | | <12> | | | | <22> | | | |
| | | | 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) |

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 J 3

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

STUDY NO. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 1

| Organ | Findings | Group Name No. of Animals on Study Control Grade | | | | 1000 ppm 43 | | | | 2000 ppm 38 | | | | 4000 ppm 28 | | | |
|----------------------------------|-----------------------|---|-------|-------|-------|----------------|-------|-------|-------|----------------|-------|-------|-------|----------------|-------|-------|-------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Integumentary system/appandage] | | | | | | | | | | | | | | | | | |
| skin/app | | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | hyperplasia:epidermis | 0 | 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) |
| | scab | 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) |
| | epidermal cyst | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| subcutis | | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | abscess | 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 system] | | | | | | | | | | | | | | | | | |
| nasal cavit | | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | thrombus | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | mineralization | 21 | 0 | 0 | 0 | 36 | 0 | 0 | 0 | 30 | 0 | 0 | 0 | 14 | 1 | 0 | 0 |
| | | (66) | (0) | (0) | (0) | (84) | (0) | (0) | (0) | (79) | (0) | (0) | (0) | (50) | (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. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 2

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 43 | | | | 2000 ppm 38 | | | | 4000 ppm 28 | | | |
|----------------------|---|---|------------|-----------|-----------|----------------|-------------|-----------|-------------|----------------|-------------|-----------|-------------|----------------|------------|------------|--------------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | |
| nasal cavit | | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | eosinophilic change:olfactory epithelium | 22 (69) | 5 (16) | 3 (9) | 0 (0) | 23 (53) | 17 (40) | 3 (7) | 0 (0) | 19 (50) | 16 (42) | 3 (8) | 0 (0) | 15 (54) | 8 (29) | 5 (18) | 0 (0) |
| | eosinophilic change:respiratory epithelium | 5 (16) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 3 (8) | 0 (0) | 0 (0) | 0 (0) | 10 (36) | 0 (0) | 0 (0) | 0 (0) |
| | inflammation:foreign body | 15 (47) | 1 (3) | 0 (0) | 0 (0) | 9 (21) | 3 (7) | 0 (0) | 0 (0) | 9 (24) | 0 (0) | 0 (0) | 0 (0) | 10 (36) | 0 (0) | 0 (0) | 0 (0) |
| | inflammation:respiratory epithelium | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | inflammation:olfactory epithelium | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | respiratory metaplasia:olfactory epithelium | 11 (34) | 6 (19) | 1 (3) | 0 (0) | 11 (26) | 1 (2) | 0 (0) | 0 * (0) | 14 (37) | 0 (0) | 0 (0) | 0 * (0) | 4 (14) | 0 (0) | 0 (0) | 0 ** (0) |
| | respiratory metaplasia:gland | 30 (94) | 0 (0) | 0 (0) | 0 (0) | 42 (98) | 0 (0) | 0 (0) | 0 (0) | 35 (92) | 0 (0) | 0 (0) | 0 (0) | 25 (89) | 0 (0) | 0 (0) | 0 (0) |
| | atrophy:olfactory epithelium | 5 (16) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 * (0) | 1 (4) | 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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 3

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 43 | | | | 2000 ppm 38 | | | | 4000 ppm 28 | | | |
|----------------------|---------------------------------------|---|--------|-------|-------|----------------|-------|-------|-------|----------------|--------|-------|-------|----------------|-------|-------|-------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | |
| nasal cavity | thickening of bone: turbinate | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | | 5 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (16) | (0) | (0) | (0) | (7) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (4) | (0) | (0) | (0) |
| nasopharynx | inflammation | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | | 3 | 0 | 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) | (0) | (0) | (0) | (0) | (0) |
| larynx | inflammation | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | | 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) |
| lung | foreign body granuloma | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | | 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) |
| | osseous metaplasia | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (4) | (0) | (0) | (0) |
| | interstitial pneumonia | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | | 17 | 4 | 0 | 0 | 35 | 0 | 0 | 0 ** | 27 | 5 | 1 | 0 | 12 | 2 | 0 | 0 |
| | | (53) | (13) | (0) | (0) | (81) | (0) | (0) | (0) | (71) | (13) | (3) | (0) | (43) | (7) | (0) | (0) |
| | bronchiolar-alveolar cell hyperplasia | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | | 3 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (9) | (0) | (0) | (0) | (7) | (0) | (0) | (0) | (3) | (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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 4

| | | Group Name | | | | Control | | | | 1000 ppm | | | | 2000 ppm | | | | 4000 ppm | | | |
|------------|---------------|-------------------------|--|--|--|---------|-----|-----|-----|----------|-----|-----|-----|----------|-----|-----|-----|----------|-----|-----|-----|
| | | No. of Animals on Study | | | | 32 | | | | 43 | | | | 38 | | | | 28 | | | |
| | | Grade | | | | 1 | | | | 2 | | | | 3 | | | | 4 | | | |
| Organ_____ | Findings_____ | | | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |

[Respiratory system]

| | | | | | | | | | | | | | | | | | |
|------|------------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| lung | | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | mineralization:artery | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (4) | (0) | (0) | (0) |
| | | | | | | | | | | | | | | | | | |
| | endothelial cell hyperplasia | 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) |

[Hematopoietic system]

| | | | | | | | | | | | | | | | | | |
|-------------|-------------------------|-------|------|------|------|-------|------|------|------|-------|------|------|------|-------|------|------|------|
| bone marrow | granulation | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | | 1 | 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) | |
| | increased hematopoiesis | | | | | | | | | | | | | | | | |
| | | 13 | 0 | 0 | 0 | 16 | 0 | 0 | 0 | 13 | 0 | 0 | 0 | 16 | 0 | 0 | 0 |
| | | (41) | (0) | (0) | (0) | (37) | (0) | (0) | (0) | (34) | (0) | (0) | (0) | (57) | (0) | (0) | (0) |
| Lymph node | Lymphadenitis | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (3) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) |
| | follicular hyperplasia | | | | | | | | | | | | | | | | |
| | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |

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

STUDY NO. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 5

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 43 | | | | 2000 ppm 38 | | | | 4000 ppm 28 | | | |
|------------------------|------------------------------|---|--------|-------|-------|----------------|-------|-------|-------|----------------|-------|-------|-------|----------------|--------|-------|-------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | |
| spleen | | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | ectopic tissue | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | congestion | 13 | 4 | 0 | 0 | 3 | 1 | 0 | 0 ** | 2 | 0 | 0 | 0 ** | 9 | 1 | 0 | 0 |
| | | (41) | (13) | (0) | (0) | (7) | (2) | (0) | (0) | (5) | (0) | (0) | (0) | (32) | (4) | (0) | (0) |
| | deposit of hemosiderin | 2 | 0 | 0 | 0 | 7 | 0 | 0 | 0 | 9 | 0 | 0 | 0 | 6 | 0 | 0 | 0 |
| | | (6) | (0) | (0) | (0) | (16) | (0) | (0) | (0) | (24) | (0) | (0) | (0) | (21) | (0) | (0) | (0) |
| | fibrosis | 1 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 3 | 2 | 0 | 0 | 5 | 3 | 0 | 0 * |
| | | (3) | (0) | (0) | (0) | (2) | (2) | (0) | (0) | (8) | (5) | (0) | (0) | (18) | (11) | (0) | (0) |
| | extramedullary hematopoiesis | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 3 | 1 | 0 | 0 | 3 | 0 | 1 | 0 |
| | | (6) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (8) | (3) | (0) | (0) | (11) | (0) | (4) | (0) |
| | splenitis | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) |
| | stromal 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) |

[Circulatory system]

| | | | | | | | | | | | | | | | | | |
|-------|----------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| heart | | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | necrosis:focal | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |

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

STUDY NO. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 6

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 43 | | | | 2000 ppm 38 | | | | 4000 ppm 28 | | | |
|----------------------|---------------------|---|------|------|------|----------------|------|------|------|----------------|-------|------|------|----------------|------|------|------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Circulatory system] | | | | | | | | | | | | | | | | | |
| heart | myocardial fibrosis | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | | 3 | 0 | 0 | 0 | 13 | 0 | 0 | 0 | 17 | 0 | 0 | 0 ** | 5 | 0 | 0 | 0 |
| | | (9) | (0) | (0) | (0) | (30) | (0) | (0) | (0) | (45) | (0) | (0) | (0) | (18) | (0) | (0) | (0) |
| artery/aort | arteritis | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | | 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) | (7) | (0) | (0) |
| [Digestive system] | | | | | | | | | | | | | | | | | |
| tooth | dysplasia | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | | 7 | 1 | 0 | 1 | 11 | 2 | 0 | 0 | 6 | 4 | 0 | 0 | 11 | 2 | 0 | 0 |
| | | (22) | (3) | (0) | (3) | (26) | (5) | (0) | (0) | (16) | (11) | (0) | (0) | (39) | (7) | (0) | (0) |
| tongue | mineralization | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (7) | (0) | (0) | (0) |
| | 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) |
| | arteritis | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | (6) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (7) | (0) | (0) | (0) |

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

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 7

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 43 | | | | 2000 ppm 38 | | | | 4000 ppm 28 | | | |
|--------------------|-----------------------------------|---|-------|-------|-------|----------------|-------|-------|-------|----------------|-------|-------|-------|----------------|-------|-------|-------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | |
| esophagus | | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | C-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) |
| | focal follicular 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) |
| stomach | | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | inflammatory infiltration | 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) |
| | ulcer: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) |
| | hyperplasia:forestomach | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | (0) | (0) | (3) | (0) | (2) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (7) | (0) | (0) | (0) |
| | erosion:glandular stomach | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (3) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) |
| Large intes | | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | mineralization | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |

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. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 8

| Organ | Findings | Group Name No. of Animals on Study Grade | Control 32 | | | | 1000 ppm 43 | | | | 2000 ppm 38 | | | | 4000 ppm 28 | | | |
|--------------------|-------------------------|--|---------------|-------|-------|-------|----------------|--------|-------|-------|----------------|-------|-------|-------|----------------|-------|-------|-------|
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| large intes | inflammation | | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (4) | (0) | (0) |
| liver | herniation | | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (7) | (0) | (0) | (0) |
| | peliosis-like lesion | | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (6) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | necrosis:focal | | 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) |
| | fatty change | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 10 | 0 | 0 | 0 | 4 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (26) | (0) | (0) | (0) | (14) | (0) | (0) | (0) |
| | fatty change:peripheral | | 1 | 0 | 0 | 0 | 4 | 9 | 0 | 0 | 4 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (3) | (0) | (0) | (0) | (9) | (21) | (0) | (0) | (11) | (0) | (0) | (0) | (4) | (0) | (0) | (0) |
| | granulation | | 6 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 8 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | | (19) | (0) | (0) | (0) | (12) | (0) | (0) | (0) | (21) | (0) | (0) | (0) | (11) | (0) | (0) | (0) |
| | clear cell focus | | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 |
| | | | (6) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (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. : 0278
 ANIMAL : RAT F344/DuGrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 9

| Organ_____ | Findings_____ | Group Name | Control | | | | 1000 ppm | | | | 2000 ppm | | | | 4000 ppm | | | |
|--------------------|-----------------------------|-------------------------|-------------|-------------|-----------|-----------|-------------|------------|-----------|--------------|-------------|-------------|-----------|--------------|-------------|-------------|-----------|-----------|
| | | No. of Animals on Study | 32 | | | | 43 | | | | 38 | | | | 28 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| liver | | | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | acidophilic cell focus | | 17 (53) | 5 (16) | 0 (0) | 0 (0) | 23 (53) | 5 (12) | 2 (5) | 0 (0) | 17 (45) | 16 (42) | 0 (0) | 0 * (0) | 12 (43) | 10 (36) | 1 (4) | 0 (0) |
| | basophilic cell focus | | 12 (38) | 1 (3) | 0 (0) | 0 (0) | 29 (67) | 5 (12) | 0 (0) | 0 ** (0) | 19 (50) | 1 (3) | 0 (0) | 0 (0) | 9 (32) | 4 (14) | 1 (4) | 0 (0) |
| | vacuolated cell focus | | 9 (28) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 ** (0) | 11 (29) | 1 (3) | 0 (0) | 0 (0) | 7 (25) | 0 (0) | 0 (0) | 0 (0) |
| | spongiosis hepatitis | | 4 (13) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 3 (8) | 0 (0) | 0 (0) | 0 (0) | 5 (18) | 0 (0) | 0 (0) | 0 (0) |
| | bile duct hyperplasia | | 11 (34) | 21 (66) | 0 (0) | 0 (0) | 32 (74) | 4 (9) | 0 (0) | 0 ** (0) | 23 (61) | 9 (24) | 0 (0) | 0 ** (0) | 12 (43) | 14 (50) | 1 (4) | 0 (0) |
| | bile ductular proliferation | | 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 (4) | 0 (0) | 0 (0) | 0 (0) |
| pancreas | biliary cyst | | 2 (6) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | atrophy | | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | | | 4 (13) | 0 (0) | 0 (0) | 0 (0) | 2 (5) | 1 (2) | 0 (0) | 0 (0) | 8 (21) | 1 (3) | 0 (0) | 0 (0) | 8 (29) | 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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 10

| Organ | Findings | Group Name No. of Animals on Study Control Grade | | | | 1000 ppm 43 | | | | 2000 ppm 38 | | | | 4000 ppm 28 | | | |
|--------------------|---------------------------|---|--------|--------|--------|----------------|--------|--------|--------|----------------|--------|--------|--------|----------------|--------|--------|--------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | |
| pancreas | | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | inflammatory infiltration | 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) |
| | islet cell hyperplasia | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (6) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | hyperplasia:acinar cell | 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) |
| [Urinary system] | | | | | | | | | | | | | | | | | |
| kidney | | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | basophilic change | 15 | 17 | 0 | 0 | 28 | 7 | 0 | 0 ** | 22 | 8 | 0 | 0 ** | 14 | 7 | 0 | 0 ** |
| | | (47) | (53) | (0) | (0) | (65) | (16) | (0) | (0) | (58) | (21) | (0) | (0) | (50) | (25) | (0) | (0) |
| | deposit of hemosiderin | 13 | 0 | 0 | 0 | 26 | 0 | 0 | 0 | 27 | 0 | 0 | 0 * | 19 | 2 | 0 | 0 * |
| | | (41) | (0) | (0) | (0) | (60) | (0) | (0) | (0) | (71) | (0) | (0) | (0) | (68) | (7) | (0) | (0) |
| | eosinophilic body | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) |
| | chronic nephropathy | 0 | 0 | 14 | 18 | 0 | 7 | 28 | 7 ** | 2 | 7 | 21 | 8 ** | 1 | 5 | 14 | 7 * |
| | | (0) | (0) | (44) | (56) | (0) | (16) | (65) | (16) | (5) | (18) | (55) | (21) | (4) | (18) | (50) | (25) |

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. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 11

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 43 | | | | 2000 ppm 38 | | | | 4000 ppm 28 | | | |
|--------------------|-------------------------------|---|-------|-------|-------|----------------|--------|-------|-------|----------------|--------|-------|-------|----------------|--------|-------|-------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Urinary system] | | | | | | | | | | | | | | | | | |
| kidney | | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | hydronephrosis | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) |
| | urothelial hyperplasia:pelvis | 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) |
| urin bladd | | <32> | | | | <43> | | | | <38> | | | | <27> | | | |
| | hemorrhagic inflammation | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| [Endocrine system] | | | | | | | | | | | | | | | | | |
| pituitary | | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | angiectasis | 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) |
| | cyst | 0 | 0 | 0 | 0 | 3 | 1 | 0 | 0 | 4 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (7) | (2) | (0) | (0) | (11) | (0) | (0) | (0) | (11) | (0) | (0) | (0) |
| | hyperplasia | 10 | 2 | 0 | 0 | 19 | 5 | 2 | 0 | 11 | 7 | 0 | 0 | 11 | 4 | 0 | 0 |
| | | (31) | (6) | (0) | (0) | (44) | (12) | (5) | (0) | (29) | (18) | (0) | (0) | (39) | (14) | (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. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 12

| Organ_____ | Findings_____ | Group Name | Control | | | | 1000 ppm | | | | 2000 ppm | | | | 4000 ppm | | | | |
|--------------------|-----------------------------------|-------------------------|-------------|------------|------------|------------|-------------|------------|------------|------------|-------------|------------|------------|------------|-------------|------------|------------|------------|------------|
| | | No. of Animals on Study | 32 | | | | 43 | | | | 38 | | | | 28 | | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | |
| [Endocrine system] | | | | | | | | | | | | | | | | | | | |
| pituitary | | | <32> | | | | <43> | | | | <38> | | | | <28> | | | | |
| | Rathke pouch | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 3 (7) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| thyroid | | | <32> | | | | <43> | | | | <37> | | | | <28> | | | | |
| | ultimibranhial body remanet | | 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 (4) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | adenomatous goiter | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | C-cell hyperplasia | | 7 (22) | 0 (0) | 0 (0) | 0 (0) | 7 (16) | 0 (0) | 0 (0) | 0 (0) | 5 (14) | 2 (5) | 0 (0) | 0 (0) | 2 (7) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | focal follicular cell hyperplasia | | 2 (6) | 0 (0) | 0 (0) | 0 (0) | 3 (7) | 0 (0) | 0 (0) | 0 (0) | 2 (5) | 0 (0) | 0 (0) | 0 (0) | 1 (4) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| adrenal | | | <32> | | | | <43> | | | | <38> | | | | <28> | | | | |
| | peliosis-like lesion | | 4 (13) | 0 (0) | 0 (0) | 0 (0) | 5 (12) | 0 (0) | 0 (0) | 0 (0) | 7 (18) | 0 (0) | 0 (0) | 0 (0) | 8 (29) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | necrosis:focal | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | |

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. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 13

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 43 | | | | 2000 ppm 38 | | | | 4000 ppm 28 | | | |
|-------|----------|---|-----|-----|-----|----------------|-----|-----|-----|----------------|-----|-----|-----|----------------|-----|-----|-----|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |

[Endocrine system]

| | | | | | | | | | | | | | | | | | |
|---------|---------------------------|------------|-----------|-----------|-----------|-------------|-----------|-----------|-----------|-------------|------------|-----------|-----------|-------------|-----------|-----------|-------------|
| adrenal | | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | hyperplasia:cortical cell | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 5 (12) | 1 (2) | 0 (0) | 0 (0) | 6 (16) | 1 (3) | 0 (0) | 0 (0) | 5 (18) | 0 (0) | 0 (0) | 0 (0) |
| | hyperplasia:medulla | 6 (19) | 3 (9) | 0 (0) | 0 (0) | 16 (37) | 3 (7) | 0 (0) | 0 (0) | 17 (45) | 2 (5) | 0 (0) | 0 (0) | 14 (50) | 2 (7) | 0 (0) | 0 * (0) |
| | focal fatty change:cortex | 6 (19) | 1 (3) | 0 (0) | 0 (0) | 7 (16) | 2 (5) | 0 (0) | 0 (0) | 7 (18) | 4 (11) | 0 (0) | 0 (0) | 5 (18) | 2 (7) | 0 (0) | 0 (0) |
| | focal hypertrophy:cortex | 2 (6) | 0 (0) | 0 (0) | 0 (0) | 2 (5) | 0 (0) | 0 (0) | 0 (0) | 3 (8) | 0 (0) | 0 (0) | 0 (0) | 3 (11) | 1 (4) | 0 (0) | 0 (0) |

[Reproductive system]

| | | | | | | | | | | | | | | | | | |
|--------|----------------|-----------|-----------|------------|-------------|------------|-----------|-----------|-------------|-----------|-----------|-----------|-------------|-----------|-----------|-----------|-------------|
| testis | | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | atrophy | 0 (0) | 0 (0) | 4 (13) | 28 (88) | 0 (0) | 0 (0) | 1 (2) | 42 (98) | 0 (0) | 0 (0) | 2 (5) | 36 (95) | 0 (0) | 0 (0) | 2 (7) | 25 (89) |
| | mineralization | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 5 (12) | 0 (0) | 0 (0) | 0 (0) | 3 (8) | 0 (0) | 0 (0) | 0 (0) | 1 (4) | 0 (0) | 0 (0) | 0 (0) |
| | arteritis | 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) | 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. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 14

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 43 | | | | 2000 ppm 38 | | | | 4000 ppm 28 | | | |
|----------------------------------|-------------------------------|---|-------|-------|-------|----------------|-------|-------|-------|----------------|-------|-------|-------|----------------|-------|-------|-------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Reproductive system] | | | | | | | | | | | | | | | | | |
| testis | | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | interstitial cell hyperplasia | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (4) | (0) | (0) | (0) |
| prostate | | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | inflammation | 4 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | (13) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (8) | (0) | (0) | (0) | (7) | (0) | (0) | (0) |
| mammary gl | | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | duct ectasia | 0 | 1 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (3) | (0) | (0) | (5) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | galactocoele | 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) |
| [Nervous system] | | | | | | | | | | | | | | | | | |
| brain | | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | 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) |
| [Special sense organs/appandage] | | | | | | | | | | | | | | | | | |
| eye | | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | cataract | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (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. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 15

| | | Group Name No. of Animals on Study | Control 32 | | | | 1000 ppm 43 | | | | 2000 ppm 38 | | | | 4000 ppm 28 | | | |
|----------------------------------|---------------------------|---------------------------------------|---------------|-----------|-----------|-----------|----------------|-----------|-----------|-----------|----------------|-----------|-----------|-----------|----------------|-----------|-----------|-----------|
| Organ | Findings | Grade | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Special sense organs/appandage] | | | | | | | | | | | | | | | | | | |
| eye | | | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | retinal atrophy | | 1 (3) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 1 (3) | 2 (5) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | phthisis bulbi | | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 2 (5) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | degeneration:cornea | | 2 (6) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (4) | 0 (0) | 0 (0) | 0 (0) |
| | mineralization:cornea | | 25 (78) | 0 (0) | 0 (0) | 0 (0) | 22 (51) | 0 (0) | 0 (0) | 0 (0) | 22 (58) | 0 (0) | 0 (0) | 0 (0) | 13 (46) | 0 (0) | 0 (0) | 0 (0) |
| Harder gl | | | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | atrophy | | 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) |
| | degeneration | | 16 (50) | 1 (3) | 0 (0) | 0 (0) | 25 (58) | 0 (0) | 0 (0) | 0 (0) | 20 (53) | 1 (3) | 0 (0) | 0 (0) | 8 (29) | 0 (0) | 0 (0) | 0 (0) |
| | inflammatory infiltration | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (4) | 0 (0) | 0 (0) | 0 (0) |
| nasolacr d | | | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | inflammation | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (7) | 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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 16

| Organ | Findings | Group Name No. of Animals on Study Grade | Control 32 | | | | 1000 ppm 43 | | | | 2000 ppm 38 | | | | 4000 ppm 28 | | | |
|-------|----------|--|---------------|-----|-----|-----|----------------|-----|-----|-----|----------------|-----|-----|-----|----------------|-----|-----|-----|
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |

[Musculoskeletal system]

| | | | | | | | | | | | | | | | | | |
|------|----------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| bone | osteosclerosis | <32> | | | | <43> | | | | <38> | | | | <28> | | | |
| | | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (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)

BAIS3

APPENDIX J 4

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

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 21

| Organ | Findings | Group Name No. of Animals on Study Grade | Control 50 | | | | 1000 ppm 50 | | | | 2000 ppm 50 | | | | 4000 ppm 50 | | | |
|----------------------------------|--|--|---------------|--------|--------|-------|----------------|--------|--------|-------|----------------|--------|--------|-------|----------------|--------|--------|-------|
| | | | 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> | | | |
| | sebaceous 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) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| nasal cavit | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | thrombus | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 4 | 0 | 0 | 0 |
| | | | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (8) | (0) | (0) | (0) |
| | mineralization | | 26 | 0 | 0 | 0 | 23 | 0 | 0 | 0 | 25 | 0 | 0 | 0 | 34 | 1 | 0 | 0 |
| | | | (52) | (0) | (0) | (0) | (46) | (0) | (0) | (0) | (50) | (0) | (0) | (0) | (68) | (2) | (0) | (0) |
| | eosinophilic change:olfactory epithelium | | 20 | 24 | 5 | 0 | 7 | 23 | 19 | 0 ** | 11 | 25 | 13 | 0 | 12 | 19 | 16 | 1 * |
| | | | (40) | (48) | (10) | (0) | (14) | (46) | (38) | (0) | (22) | (50) | (26) | (0) | (24) | (38) | (32) | (2) |
| | eosinophilic change:respiratory epithelium | | 11 | 0 | 0 | 0 | 27 | 2 | 0 | 0 ** | 25 | 10 | 0 | 0 ** | 26 | 1 | 0 | 0 ** |
| | | | (22) | (0) | (0) | (0) | (54) | (4) | (0) | (0) | (50) | (20) | (0) | (0) | (52) | (2) | (0) | (0) |
| | inflammation:foreign body | | 2 | 0 | 0 | 0 | 3 | 1 | 0 | 0 | 5 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (4) | (0) | (0) | (0) | (6) | (2) | (0) | (0) | (10) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| | inflammation:respiratory epithelium | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |

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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 22

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 50 | | | | 2000 ppm 50 | | | | 4000 ppm 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 | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| | respiratory metaplasia:gland | 45 (90) | 0 (0) | 0 (0) | 0 (0) | 45 (90) | 0 (0) | 0 (0) | 0 (0) | 47 (94) | 0 (0) | 0 (0) | 0 (0) | 37 (74) | 0 (0) | 0 (0) | 0 (0) |
| | thickening of bone:turbinate | 7 (14) | 2 (4) | 0 (0) | 0 (0) | 19 (38) | 3 (6) | 0 (0) | 0 * (0) | 6 (12) | 2 (4) | 0 (0) | 0 (0) | 12 (24) | 0 (0) | 0 (0) | 0 (0) |
| larynx | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | inflammation | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 3 (6) | 0 (0) | 0 (0) | 0 (0) | 3 (6) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 1 (2) | 0 (0) | 0 (0) |
| lung | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | congestion | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 5 (10) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 3 (6) | 0 (0) | 0 (0) | 0 (0) |
| | osseous metaplasia | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| | accumulation of foamy cells | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |

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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 23

| Organ_____ | Findings_____ | Group Name | Control | | | | 1000 ppm | | | | 2000 ppm | | | | 4000 ppm | | | |
|------------------------|---------------------------------------|-------------------------|---------|------|------|------|----------|------|------|------|----------|------|------|------|----------|------|------|------|
| | | No. of Animals on Study | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| lung | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | interstitial pneumonia | | 7 | 0 | 0 | 0 | 21 | 1 | 0 | 0 ** | 13 | 3 | 0 | 0 | 20 | 3 | 0 | 0 ** |
| | | | (14) | (0) | (0) | (0) | (42) | (2) | (0) | (0) | (26) | (6) | (0) | (0) | (40) | (6) | (0) | (0) |
| | bronchiolar-alveolar cell hyperplasia | | 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) | (0) | (0) | (0) | (0) | (0) |
| | mineralization:artery | | 3 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (6) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| bone marrow | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | granulation | | 4 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (8) | (2) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | increased hematopoiesis | | 5 | 0 | 0 | 0 | 6 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 10 | 0 | 0 | 0 |
| | | | (10) | (0) | (0) | (0) | (12) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (20) | (0) | (0) | (0) |
| | myelofibrosis | | 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) |
| | erythropoiesis:increased | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 0 | 0 | 0 |
| | | | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (8) | (0) | (0) | (0) |

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

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 24

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 50 | | | | 2000 ppm 50 | | | | 4000 ppm 50 | | | |
|------------------------|------------------------------|---|-------|-------|-------|----------------|-------|-------|-------|----------------|-------|-------|-------|----------------|-------|-------|-------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | |
| Lymph node | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | Lymphadenitis | 0 | 0 | 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) |
| spleen | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | congestion | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (4) | (0) | (0) |
| | deposit of hemosiderin | 13 | 0 | 0 | 0 | 15 | 1 | 0 | 0 | 12 | 0 | 0 | 0 | 14 | 1 | 0 | 0 |
| | | (26) | (0) | (0) | (0) | (30) | (2) | (0) | (0) | (24) | (0) | (0) | (0) | (28) | (2) | (0) | (0) |
| | granulation | 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) |
| | fibrosis | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 4 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (8) | (0) | (0) | (0) |
| | extramedullary hematopoiesis | 0 | 1 | 0 | 0 | 5 | 1 | 0 | 0 | 4 | 1 | 1 | 0 | 2 | 3 | 2 | 0 |
| | | (0) | (2) | (0) | (0) | (10) | (2) | (0) | (0) | (8) | (2) | (2) | (0) | (4) | (6) | (4) | (0) |
| | stromal hyperplasia | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) |
| | increased:Leydig 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) |

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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 25

| Organ_____ | Findings_____ | Group Name | Control | | | | 1000 ppm | | | | 2000 ppm | | | | 4000 ppm | | | |
|----------------------|---------------------|-------------------------|------------|------------|------------|------------|-------------|------------|------------|------------|-------------|------------|------------|------------|------------|------------|------------|------------|
| | | No. of Animals on Study | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Circulatory system] | | | | | | | | | | | | | | | | | | |
| heart | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | thrombus | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 1 (2) | 0 (0) |
| | inflammation | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) |
| | myocardial fibrosis | | 3 (6) | 0 (0) | 0 (0) | 0 (0) | 5 (10) | 0 (0) | 0 (0) | 0 (0) | 4 (8) | 0 (0) | 0 (0) | 0 (0) | 2 (4) | 0 (0) | 0 (0) | 0 (0) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| tooth | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | dysplasia | | 1 (2) | 2 (4) | 0 (0) | 0 (0) | 1 (2) | 2 (4) | 0 (0) | 0 (0) | 2 (4) | 1 (2) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| tongue | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | arteritis | | 4 (8) | 0 (0) | 0 (0) | 0 (0) | 2 (4) | 0 (0) | 0 (0) | 0 (0) | 5 (10) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| salivary gl | | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | atrophy | | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 b 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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 26

| Organ | Findings | Group Name No. of Animals on Study Grade | Control 50 | | | | 1000 ppm 50 | | | | 2000 ppm 50 | | | | 4000 ppm 50 | | | |
|--------------------|---------------------------|--|---------------|-------|-------|-------|----------------|-------|-------|-------|----------------|-------|-------|-------|----------------|-------|-------|-------|
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| stomach | | | | | | | | | | | | | | | | | | |
| | hemorrhage | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) |
| | mineralization | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | concretion | | 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) |
| | 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) |
| | ulcer:forestomach | | 0 | 0 | 2 | 0 | 0 | 1 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 4 | 0 |
| | | | (0) | (0) | (4) | (0) | (0) | (2) | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (8) | (0) |
| | hyperplasia:forestomach | | 3 | 0 | 2 | 0 | 0 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 8 | 4 | 1 | 0 |
| | | | (6) | (0) | (4) | (0) | (0) | (4) | (2) | (0) | (0) | (0) | (0) | (0) | (16) | (8) | (2) | (0) |
| | erosion:glandular stomach | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 2 | 1 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (4) | (2) | (0) | (0) |
| | ulcer:glandular stomach | | 0 | 0 | 0 | 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) |

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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 27

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 50 | | | | 2000 ppm 50 | | | | 4000 ppm 50 | | | |
|--------------------|-------------------------|---|--------|-------|-------|----------------|--------|-------|-------|----------------|--------|-------|-------|----------------|--------|-------|-------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | |
| Liver | | | | | | | | | | | | | | | | | |
| | herniation | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 2 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (4) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | peliosis-like lesion | 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) |
| | necrosis:central | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (2) | (0) | (0) | (0) |
| | necrosis:focal | 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) |
| | fatty change | 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) |
| | fatty change:central | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 1 | 1 | 4 | 0 |
| | | (0) | (0) | (2) | (0) | (0) | (0) | (2) | (0) | (2) | (0) | (0) | (0) | (2) | (2) | (8) | (0) |
| | fatty change:peripheral | 3 | 0 | 0 | 0 | 15 | 25 | 1 | 0 ** | 8 | 29 | 1 | 0 ** | 7 | 23 | 2 | 0 ** |
| | | (6) | (0) | (0) | (0) | (30) | (50) | (2) | (0) | (16) | (58) | (2) | (0) | (14) | (46) | (4) | (0) |
| | granulation | 31 | 7 | 0 | 0 | 29 | 13 | 0 | 0 | 27 | 12 | 1 | 0 | 15 | 10 | 1 | 0 * |
| | | (62) | (14) | (0) | (0) | (58) | (26) | (0) | (0) | (54) | (24) | (2) | (0) | (30) | (20) | (2) | (0) |

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

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 28

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 50 | | | | 2000 ppm 50 | | | | 4000 ppm 50 | | | |
|--------------------|-----------------------------|---|------------|------------|------------|----------------|-------------|------------|---------------|----------------|--------------|------------|---------------|----------------|--------------|------------|---------------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | |
| liver | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | perivascular inflammation | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | fibrosis:focal | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| | acidophilic cell focus | 2 (4) | 1 (2) | 0 (0) | 0 (0) | 8 (16) | 0 (0) | 0 (0) | 0 (0) | 9 (18) | 5 (10) | 0 (0) | 0 (0) | 13 (26) | 10 (20) | 0 (0) | 0 (0) ** |
| | basophilic cell focus | 18 (36) | 0 (0) | 0 (0) | 0 (0) | 28 (56) | 8 (16) | 1 (2) | 0 (0) ** | 15 (30) | 25 (50) | 0 (0) | 0 (0) ** | 11 (22) | 23 (46) | 2 (4) | 0 (0) ** |
| | vacuolated cell focus | 2 (4) | 0 (0) | 0 (0) | 0 (0) | 7 (14) | 0 (0) | 0 (0) | 0 (0) | 12 (24) | 1 (2) | 0 (0) | 0 (0) ** | 8 (16) | 3 (6) | 0 (0) | 0 (0) * |
| | mixed cell focus | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 2 (4) | 0 (0) | 0 (0) |
| | bile duct hyperplasia | 1 (2) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) |
| | bile ductular proliferation | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 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. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 29

| Organ | Findings | Group Name | Control | | | | 1000 ppm | | | | 2000 ppm | | | | 4000 ppm | | | |
|---|--|-------------------------|-------------|-----------|-----------|-----------|-------------|-----------|-----------|-----------|-------------|-----------|-----------|-----------|-------------|------------|-----------|-----------|
| | | No. of Animals on Study | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| pancreas | atrophy | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | | 3 (6) | 1 (2) | 0 (0) | 0 (0) | 2 (4) | 0 (0) | 0 (0) | 0 (0) | 2 (4) | 0 (0) | 0 (0) | 0 (0) | 3 (6) | 0 (0) | 0 (0) | 0 (0) |
| | hyperplasia:acinar cell | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | hyaline droplet | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | basophilic change | | 18 (36) | 3 (6) | 0 (0) | 0 (0) | 3 (6) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 3 (6) | 0 (0) | 0 (0) | 0 (0) | 5 (10) | 0 (0) | 0 (0) |
| | deposit of hemosiderin | | 45 (90) | 0 (0) | 0 (0) | 0 (0) | 44 (88) | 0 (0) | 0 (0) | 0 (0) | 43 (86) | 2 (4) | 0 (0) | 0 (0) | 44 (88) | 1 (2) | 0 (0) | 0 (0) |
| | eosinophilic body | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | inflammation | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) |
| Grade | 1 : Slight 2 : Moderate 3 : Marked 4 : Severe | | | | | | | | | | | | | | | | | |
| < a > | a : Number of animals examined at the site | | | | | | | | | | | | | | | | | |
| b | b : Number of animals with lesion | | | | | | | | | | | | | | | | | |
| (c) | c : b / a * 100 | | | | | | | | | | | | | | | | | |
| Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square | | | | | | | | | | | | | | | | | | |

STUDY NO. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 30

| Organ | Findings | Group Name | Control | | | | 1000 ppm | | | | 2000 ppm | | | | 4000 ppm | | | |
|---|--|-------------------------|---------|-------|-------|------|----------|-------|------|-------|----------|-------|-------|------|----------|-------|-------|------|
| | | No. of Animals on Study | 50 | | | | 50 | | | | 50 | | | | 50 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | chronic nephropathy | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | | 8 | 23 | 14 | 3 | 22 | 21 | 2 | 0 ** | 19 | 17 | 5 | 0 ** | 27 | 6 | 5 | 0 ** |
| | | | (16) | (46) | (28) | (6) | (44) | (42) | (4) | (0) | (38) | (34) | (10) | (0) | (54) | (12) | (10) | (0) |
| | hydronephrosis | | 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) |
| | mineralization:cortico-medullary junction | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| | mineralization:papilla | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| | mineralization:pelvis | | 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) |
| [Endocrine system] | | | | | | | | | | | | | | | | | | |
| pituitary | angiectasis | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 6 | 1 | 0 | 0 * | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (12) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | |
| | hemorrhage | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| 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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 31

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 50 | | | | 2000 ppm 50 | | | | 4000 ppm 50 | | | |
|--------------------|-----------------------------------|---|-------------|-----------|-----------|----------------|-------------|-----------|-----------|----------------|-------------|-----------|-----------|----------------|-------------|-----------|-----------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Endocrine system] | | | | | | | | | | | | | | | | | |
| pituitary | cyst | 17 (34) | 2 (4) | 0 (0) | 0 (0) | 13 (26) | 4 (8) | 0 (0) | 0 (0) | 13 (26) | 3 (6) | 1 (2) | 0 (0) | 10 (20) | 3 (6) | 0 (0) | 0 (0) |
| | hyperplasia | 14 (28) | 3 (6) | 1 (2) | 0 (0) | 6 (12) | 7 (14) | 0 (0) | 0 (0) | 13 (26) | 2 (4) | 0 (0) | 0 (0) | 7 (14) | 1 (2) | 1 (2) | 0 (0) |
| thyroid | ultimibranhial body remanet | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | G-cell hyperplasia | 7 (14) | 0 (0) | 0 (0) | 0 (0) | 2 (4) | 0 (0) | 0 (0) | 0 (0) | 3 (6) | 1 (2) | 0 (0) | 0 (0) | 11 (22) | 0 (0) | 0 (0) | 0 (0) |
| | focal follicular cell hyperplasia | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (4) | 0 (0) | 0 (0) | 0 (0) | 3 (6) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| adrenal | peliosis-like lesion | 27 (54) | 17 (34) | 0 (0) | 0 (0) | 31 (62) | 12 (24) | 0 (0) | 0 (0) | 23 (46) | 19 (38) | 0 (0) | 0 (0) | 26 (52) | 15 (30) | 1 (2) | 0 (0) |
| | extramedullary hematopoiesis | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 2 (4) | 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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 32

| Organ | Findings | Group Name No. of Animals on Study Control Grade | | | | 1000 ppm 50 | | | | 2000 ppm 50 | | | | 4000 ppm 50 | | | |
|-----------------------|--------------------------------|---|-------|-------|-------|----------------|-------|-------|-------|----------------|-------|-------|-------|----------------|--------|-------|-------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Endocrine system] | | | | | | | | | | | | | | | | | |
| adrenal | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | hyperplasia:cortical cell | 3 | 0 | 0 | 0 | 6 | 0 | 0 | 0 | 5 | 1 | 0 | 0 | 4 | 0 | 0 | 0 |
| | | (6) | (0) | (0) | (0) | (12) | (0) | (0) | (0) | (10) | (2) | (0) | (0) | (8) | (0) | (0) | (0) |
| | | | | | | | | | | | | | | | | | |
| | hyperplasia:medulla | 3 | 1 | 0 | 0 | 8 | 0 | 0 | 0 | 4 | 1 | 0 | 0 | 9 | 1 | 0 | 0 |
| | | (6) | (2) | (0) | (0) | (16) | (0) | (0) | (0) | (8) | (2) | (0) | (0) | (18) | (2) | (0) | (0) |
| | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | |
| | focal fatty change:cortex | 10 | 3 | 0 | 0 | 7 | 3 | 0 | 0 | 5 | 3 | 0 | 0 | 15 | 5 | 0 | 0 |
| | | (20) | (6) | (0) | (0) | (14) | (6) | (0) | (0) | (10) | (6) | (0) | (0) | (30) | (10) | (0) | (0) |
| | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | |
| | focal hypertrophy:cortex | 1 | 0 | 0 | 0 | 4 | 1 | 0 | 0 | 4 | 1 | 0 | 0 | 4 | 2 | 0 | 0 |
| | | (2) | (0) | (0) | (0) | (8) | (2) | (0) | (0) | (8) | (2) | (0) | (0) | (8) | (4) | (0) | (0) |
| | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | |
| [Reproductive system] | | | | | | | | | | | | | | | | | |
| ovary | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | cyst | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) |
| uterus | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | cystic endometrial hyperplasia | 13 | 0 | 0 | 0 | 5 | 2 | 4 | 1 * | 15 | 2 | 3 | 0 | 5 | 0 | 4 | 0 * |
| | | (26) | (0) | (0) | (0) | (10) | (4) | (8) | (2) | (30) | (4) | (6) | (0) | (10) | (0) | (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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 33

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 50 | | | | 2000 ppm 50 | | | | 4000 ppm 50 | | | |
|----------------------------------|--------------|---|------------|------------|------------|----------------|------------|------------|------------|----------------|------------|------------|------------|----------------|------------|------------|------------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Reproductive system] | | | | | | | | | | | | | | | | | |
| mammary gl | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | duct ectasia | 1 (2) | 0 (0) | 1 (2) | 0 (0) | 2 (4) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 2 (4) | 0 (0) | 0 (0) | 0 (0) |
| | hyperplasia | 2 (4) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (4) | 0 (0) | 0 (0) | 0 (0) |
| | galactocoele | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 1 (2) | 0 (0) | 0 (0) |
| [Nervous system] | | | | | | | | | | | | | | | | | |
| brain | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | hemorrhage | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| [Special sense organs/appandage] | | | | | | | | | | | | | | | | | |
| eye | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | cataract | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 2 (4) | 0 (0) | 0 (0) | 0 (0) | 1 (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. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 34

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 50 | | | | 2000 ppm 50 | | | | 4000 ppm 50 | | | |
|----------------------------------|--------------------------|---|-------|-------|-------|----------------|-------|-------|-------|----------------|-------|-------|-------|----------------|-------|-------|-------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Special sense organs/appandage] | | | | | | | | | | | | | | | | | |
| eye | retinal atrophy | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 2 | 0 | 0 | 0 | 1 | 1 | 0 | 3 | 5 | 0 | 1 | 1 | 2 | 0 | 2 | 0 |
| | | (4) | (0) | (0) | (0) | (2) | (2) | (0) | (6) | (10) | (0) | (2) | (2) | (4) | (0) | (4) | (0) |
| | keratitis | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (4) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) |
| | phthisis bulbi | 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) |
| | degeneration:cornea | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | mineralization:cornea | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | (2) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) |
| Harder gl | degeneration | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 17 | 0 | 0 | 0 | 27 | 0 | 0 | 0 | 31 | 0 | 0 | 0 ** | 21 | 0 | 0 | 0 |
| | | (34) | (0) | (0) | (0) | (54) | (0) | (0) | (0) | (62) | (0) | (0) | (0) | (42) | (0) | (0) | (0) |
| | lymphocytic infiltration | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| nasolacr d | inflammation | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | 11 | 0 | 0 | 0 | 3 | 0 | 0 | 0 * | 2 | 0 | 0 | 0 * | 7 | 0 | 0 | 0 |
| | | (22) | (0) | (0) | (0) | (6) | (0) | (0) | (0) | (4) | (0) | (0) | (0) | (14) | (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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 35

| Organ | Findings | Group Name No. of Animals on Study Grade | Control 50 | | | | 1000 ppm 50 | | | | 2000 ppm 50 | | | | 4000 ppm 50 | | | |
|--------------------------|----------------|--|---------------|--------|-------|-------|----------------|--------|-------|-------|----------------|--------|-------|-------|----------------|--------|-------|-------|
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Musculoskeletal system] | | | | | | | | | | | | | | | | | | |
| muscle | mineralization | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) |
| bone | osteosclerosis | | <50> | | | | <50> | | | | <50> | | | | <50> | | | |
| | | | 14 | 7 | 0 | 0 | 16 | 7 | 3 | 0 | 16 | 6 | 3 | 0 | 13 | 6 | 0 | 0 |
| | | | (28) | (14) | (0) | (0) | (32) | (14) | (6) | (0) | (32) | (12) | (6) | (0) | (26) | (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

(HPT150)

BA1S3

APPENDIX J 5

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

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 16

| Organ | Findings | Group Name No. of Animals on Study Grade | Control 5 | | | | 1000 ppm 10 | | | | 2000 ppm 7 | | | | 4000 ppm 20 | | | |
|----------------------|--|--|--------------|--------|-------|-------|----------------|--------|--------|-------|---------------|--------|--------|-------|----------------|--------|--------|-------|
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| nasal cavit | thrombus | | < 5> | | | | <10> | | | | < 7> | | | | <20> | | | |
| | | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 4 | 0 | 0 | 0 |
| | | | (20) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (14) | (0) | (0) | (0) | (20) | (0) | (0) | (0) |
| | mineralization | | 3 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 12 | 1 | 0 | 0 |
| | | | (60) | (0) | (0) | (0) | (40) | (0) | (0) | (0) | (71) | (0) | (0) | (0) | (60) | (5) | (0) | (0) |
| | eosinophilic change:olfactory epithelium | | 2 | 3 | 0 | 0 | 3 | 5 | 1 | 0 | 3 | 2 | 1 | 0 | 6 | 7 | 4 | 1 |
| | | | (40) | (60) | (0) | (0) | (30) | (50) | (10) | (0) | (43) | (29) | (14) | (0) | (30) | (35) | (20) | (5) |
| | eosinophilic change:respiratory epithelium | | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 5 | 1 | 0 | 0 |
| | | | (20) | (0) | (0) | (0) | (20) | (0) | (0) | (0) | (14) | (14) | (0) | (0) | (25) | (5) | (0) | (0) |
| lung | inflammation:respiratory epithelium | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (14) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | respiratory metaplasia:gland | | 4 | 0 | 0 | 0 | 8 | 0 | 0 | 0 | 6 | 0 | 0 | 0 | 10 | 0 | 0 | 0 |
| | | | (80) | (0) | (0) | (0) | (80) | (0) | (0) | (0) | (86) | (0) | (0) | (0) | (50) | (0) | (0) | (0) |
| | thickening of bone:turbinate | | 2 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | | (40) | (0) | (0) | (0) | (20) | (10) | (0) | (0) | (14) | (0) | (0) | (0) | (15) | (0) | (0) | (0) |
| | congestion | | < 5> | | | | <10> | | | | < 7> | | | | <20> | | | |
| | | | 0 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (40) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (15) | (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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 17

| Organ | Findings | Group Name No. of Animals on Study Grade | Control 5 | | | | 1000 ppm 10 | | | | 2000 ppm 7 | | | | 4000 ppm 20 | | | |
|------------------------|--------------------------|--|--------------|-------|-------|-------|----------------|--------|-------|-------|---------------|--------|-------|-------|----------------|--------|-------|-------|
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| Lung | interstitial pneumonia | | < 5> | | | | <10> | | | | < 7> | | | | <20> | | | |
| | | | 0 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 2 | 2 | 0 | 0 | 9 | 3 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (20) | (10) | (0) | (0) | (29) | (29) | (0) | (0) | (45) | (15) | (0) | (0) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| bone marrow | increased hematopoiesis | | < 5> | | | | <10> | | | | < 7> | | | | <20> | | | |
| | | | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 4 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (20) | (0) | (0) | (0) | (14) | (0) | (0) | (0) | (20) | (0) | (0) | (0) |
| | myelofibrosis | | < 5> | | | | <10> | | | | < 7> | | | | <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) |
| | erythropoiesis:increased | | < 5> | | | | <10> | | | | < 7> | | | | <20> | | | |
| | | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | | (20) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (15) | (0) | (0) | (0) |
| Lymph node | | | | | | | | | | | | | | | | | | |
| | Lymphadenitis | | < 5> | | | | <10> | | | | < 7> | | | | <20> | | | |
| | | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| spleen | | | | | | | | | | | | | | | | | | |
| | congestion | | < 5> | | | | <10> | | | | < 7> | | | | <20> | | | |
| | | | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (20) | (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 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. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 18

| Organ | Findings | Group Name No. of Animals on Study Grade | Control 5 | | | | 1000 ppm 10 | | | | 2000 ppm 7 | | | | 4000 ppm 20 | | | |
|------------------------|------------------------------|--|--------------|------|------|------|----------------|-------|------|-------|---------------|------|-------|------|----------------|-------|-------|------|
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| spleen | | | < 5> | | | | <10> | | | | < 7> | | | | <20> | | | |
| | deposit of hemosiderin | | 3 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 1 | 0 | 0 * |
| | | | (60) | (0) | (0) | (0) | (20) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (10) | (5) | (0) | (0) |
| | fibrosis | | 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) |
| | extramedullary hematopoiesis | | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 3 | 2 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (0) | (14) | (0) | (0) | (15) | (10) | (0) |
| [Circulatory system] | | | | | | | | | | | | | | | | | | |
| heart | | | < 5> | | | | <10> | | | | < 7> | | | | <20> | | | |
| | thrombus | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (5) | (5) | (0) |
| | inflammation | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) |
| | myocardial fibrosis | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (14) | (0) | (0) | (0) | (10) | (0) | (0) | (0) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| tooth | | | < 5> | | | | <10> | | | | < 7> | | | | <20> | | | |
| | dysplasia | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (29) | (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 ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 19

| Organ | Findings | Group Name No. of Animals on Study Grade | Control 5 | | | | 1000 ppm 10 | | | | 2000 ppm 7 | | | | 4000 ppm 20 | | | |
|--------------------|---------------------------|--|--------------|-------|--------|-------|----------------|--------|--------|-------|---------------|--------|-------|-------|----------------|--------|--------|-------|
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| salivary gl | atrophy | | < 5> | | | | <10> | | | | < 7> | | | | <20> | | | |
| | | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| stomach | hemorrhage | | < 5> | | | | <10> | | | | < 7> | | | | <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) | (14) | (0) | (0) | (0) | (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) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | ulcer:forestomach | | 0 | 0 | 2 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 4 | 0 |
| | | | (0) | (0) | (40) | (0) | (0) | (10) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (20) | (0) |
| | hyperplasia:forestomach | | 0 | 0 | 2 | 0 | 0 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 5 | 4 | 1 | 0 |
| | | | (0) | (0) | (40) | (0) | (0) | (20) | (10) | (0) | (0) | (0) | (0) | (0) | (25) | (20) | (5) | (0) |
| | erosion:glandular stomach | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 2 | 1 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (0) | (14) | (0) | (0) | (10) | (5) | (0) | (0) |
| | ulcer:glandular stomach | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (14) | (0) | (0) | (0) | (10) | (0) | (0) | (0) |
| liver | herniation | | < 5> | | | | <10> | | | | < 7> | | | | <20> | | | |
| | | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 20

| Organ_____ | Findings_____ | Group Name | Control | | | | 1000 ppm | | | | 2000 ppm | | | | 4000 ppm | | | |
|--|--|-------------------------|------------|------------|--------|-------|----------|--------|--------|-------|----------|--------|--------|-------|----------|--------|--------|-------|
| | | No. of Animals on Study | 5 | | | | 10 | | | | 7 | | | | 20 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| Liver | | | < 5> | | | | <10> | | | | < 7> | | | | <20> | | | |
| | necrosis:central | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (14) | (0) | (5) | (0) | (0) | (0) |
| | necrosis:focal | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) | (0) |
| | fatty change:central | | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 4 | 0 |
| | | | (0) | (0) | (20) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (5) | (5) | (20) | (0) |
| | fatty change:peripheral | | 0 | 0 | 0 | 0 | 1 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 3 | 3 | 1 | 0 |
| | | | (0) | (0) | (0) | (0) | (10) | (20) | (0) | (0) | (0) | (14) | (0) | (0) | (15) | (15) | (5) | (0) |
| | granulation | | 2 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 2 | 0 | 0 |
| | | | (40) | (0) | (0) | (0) | (40) | (0) | (0) | (0) | (14) | (0) | (0) | (0) | (5) | (10) | (0) | (0) |
| | acidophilic cell focus | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (20) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) | (0) |
| | basophilic cell focus | | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 4 | 3 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (20) | (0) | (0) | (0) | (14) | (0) | (0) | (0) | (20) | (15) | (0) | (0) |
| | bile ductular proliferation | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) |
| Grade | 1 : Slight | 2 : Moderate | 3 : Marked | 4 : Severe | | | | | | | | | | | | | | |
| < a > | a : Number of animals examined at the site | | | | | | | | | | | | | | | | | |
| b | 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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 21

| Organ | Findings | Group Name No. of Animals on Study Grade | Control 5 | | | | 1000 ppm 10 | | | | 2000 ppm 7 | | | | 4000 ppm 20 | | | |
|--------------------------|------------------------|---|--|------------|-------------|-------------|----------------|------------|-------------|-------------|---------------|-------------|-------------|------------|----------------|------------|-------------|------------|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| pancreas | atrophy | | < 5> | | | | <10> | | | | < 7> | | | | <20> | | | |
| | | 1 (20) | 0 (0) | 0 (0) | 0 (0) | 2 (20) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (5) | 0 (0) | 0 (0) | 0 (0) | |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | hyaline droplet | | < 5> | | | | <10> | | | | < 7> | | | | <20> | | | |
| | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (14) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | |
| | deposit of hemosiderin | | 3 (60) | 0 (0) | 0 (0) | 0 (0) | 7 (70) | 0 (0) | 0 (0) | 0 (0) | 2 (28) | 1 (14) | 0 (0) | 0 (0) | 14 (70) | 1 (5) | 0 (0) | 0 (0) |
| | | | inflammation | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (5) |
| | chronic nephropathy | | | | 3 (60) | 1 (20) | 0 (0) | 0 (0) | 3 (30) | 2 (20) | 0 (0) | 0 (0) | 1 (14) | 0 (0) | 0 (0) | 0 (0) | 9 (45) | 0 (0) |
| | | | mineralization:cortico-medullary junction | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (5) | 0 (0) | 0 (0) |
| | mineralization:papilla | | | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (5) | 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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 22

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 10 | | | | 2000 ppm 7 | | | | 4000 ppm 20 | | | |
|--------------------|---------------------------|---|--------|-------|-------|----------------|--------|-------|-------|---------------|--------|-------|-------|----------------|--------|-------|-------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Endocrine system] | | | | | | | | | | | | | | | | | |
| pituitary | | < 5> | | | | <10> | | | | < 7> | | | | <20> | | | |
| | hemorrhage | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) | (0) |
| | cyst | 3 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 * |
| | | (60) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (5) | (0) | (0) |
| | hyperplasia | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | (20) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) |
| thyroid | | < 5> | | | | <10> | | | | < 7> | | | | <20> | | | |
| | C-cell hyperplasia | 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) | (0) |
| adrenal | | < 5> | | | | <10> | | | | < 7> | | | | <20> | | | |
| | peliosis-like lesion | 1 | 2 | 0 | 0 | 4 | 3 | 0 | 0 | 1 | 3 | 0 | 0 | 10 | 4 | 0 | 0 |
| | | (20) | (40) | (0) | (0) | (40) | (30) | (0) | (0) | (14) | (43) | (0) | (0) | (50) | (20) | (0) | (0) |
| | hyperplasia:cortical cell | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | hyperplasia:medulla | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 5 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (30) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (25) | (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. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 23

| Organ | Findings | Group Name No. of Animals on Study Grade | Control 5 | | | | 1000 ppm 10 | | | | 2000 ppm 7 | | | | 4000 ppm 20 | | | |
|-----------------------|--------------------------------|--|--------------|------|------|------|----------------|-------|-------|------|---------------|------|-------|------|----------------|-------|------|------|
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Endocrine system] | | | | | | | | | | | | | | | | | | |
| adrenal | focal fatty change:cortex | | < 5> | | | | <10> | | | | < 7> | | | | <20> | | | |
| | | | 1 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 2 | 0 | 0 |
| | | | (20) | (0) | (0) | (0) | (10) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (15) | (10) | (0) | (0) |
| | focal hypertrophy:cortex | | < 5> | | | | <10> | | | | < 7> | | | | <20> | | | |
| | | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 2 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (14) | (0) | (0) | (0) | (5) | (10) | (0) | (0) |
| [Reproductive system] | | | | | | | | | | | | | | | | | | |
| uterus | cystic endometrial hyperplasia | | < 5> | | | | <10> | | | | < 7> | | | | <20> | | | |
| | | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 2 | 0 | 2 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (14) | (0) | (29) | (0) | (10) | (0) | (0) | (0) |
| mammary gl | duct ectasia | | < 5> | | | | <10> | | | | < 7> | | | | <20> | | | |
| | | | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (20) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) | (0) |
| | hyperplasia | | < 5> | | | | <10> | | | | < 7> | | | | <20> | | | |
| | | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) |
| [Nervous system] | | | | | | | | | | | | | | | | | | |
| brain | hemorrhage | | < 5> | | | | <10> | | | | < 7> | | | | <20> | | | |
| | | | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 24

| Organ | Findings | Group Name No. of Animals on Study Grade | Control 5 | | | | 1000 ppm 10 | | | | 2000 ppm 7 | | | | 4000 ppm 20 | | | |
|----------------------------------|--------------------------|--|--------------|-------|-------|-------|----------------|--------|-------|-------|---------------|-------|-------|-------|----------------|-------|-------|-------|
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Special sense organs/appandage] | | | | | | | | | | | | | | | | | | |
| eye | | | < 5> | | | | <10> | | | | < 7> | | | | <20> | | | |
| | retinal atrophy | | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (14) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | keratitis | | 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) |
| | phthisis bulbi | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | mineralization: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) |
| | | | < 5> | | | | <10> | | | | < 7> | | | | <20> | | | |
| Harder gl | degeneration | | 1 | 0 | 0 | 0 | 7 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 6 | 0 | 0 | 0 |
| | | | (20) | (0) | (0) | (0) | (70) | (0) | (0) | (0) | (71) | (0) | (0) | (0) | (30) | (0) | (0) | (0) |
| | lymphocytic infiltration | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| nasolacr d | | | < 5> | | | | <10> | | | | < 7> | | | | <20> | | | |
| | inflammation | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | (20) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (5) | (0) | (0) | (0) |

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

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 25

| Organ | Findings | Group Name No. of Animals on Study Grade | Control 5 | | | | 1000 ppm 10 | | | | 2000 ppm 7 | | | | 4000 ppm 20 | | | |
|--------------------------|----------------|--|--------------|--------|-------|-------|----------------|-------|--------|-------|---------------|--------|--------|-------|----------------|--------|-------|-------|
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Musculoskeletal system] | | | | | | | | | | | | | | | | | | |
| muscle | mineralization | | < 5> | | | | <10> | | | | < 7> | | | | <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) | (14) | (0) | (0) | (0) | (0) | (0) | (0) |
| bone | osteosclerosis | | < 5> | | | | <10> | | | | < 7> | | | | <20> | | | |
| | | | 1 | 1 | 0 | 0 | 4 | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 6 | 2 | 0 | 0 |
| | | | (20) | (20) | (0) | (0) | (40) | (0) | (10) | (0) | (14) | (0) | (14) | (0) | (30) | (10) | (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)

BAIS3

APPENDIX J 6

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

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 17

| Organ | Findings | Group Name No. of Animals on Study Grade | | | | Control 45 | | | | 1000 ppm 40 | | | | 2000 ppm 43 | | | | 4000 ppm 30 | | | |
|----------------------------------|---|--|--------|--------|-------|---------------|--------|--------|-------|----------------|--------|--------|-------|----------------|--------|--------|-------|----------------|-------|-------|-------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Integumentary system/appandage] | | | | | | | | | | | | | | | | | | | | | |
| skin/app | | <45> | | | | <40> | | | | <43> | | | | <30> | | | | | | | |
| | sebaceous hyperplasia | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | | | | |
| nasal cavit | | <45> | | | | <40> | | | | <43> | | | | <30> | | | | | | | |
| | mineralization | 23 | 0 | 0 | 0 | 19 | 0 | 0 | 0 | 20 | 0 | 0 | 0 | 22 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (51) | (0) | (0) | (0) | (48) | (0) | (0) | (0) | (47) | (0) | (0) | (0) | (73) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | eosinophilic change:olfactory epithelium | 18 | 21 | 5 | 0 | 4 | 18 | 18 | 0 ** | 8 | 23 | 12 | 0 | 6 | 12 | 12 | 0 * | 0 | 0 | 0 | 0 |
| | | (40) | (47) | (11) | (0) | (10) | (45) | (45) | (0) | (19) | (53) | (28) | (0) | (20) | (40) | (40) | (0) | (0) | (0) | (0) | (0) |
| | eosinophilic change:respiratory epithelium | 10 | 0 | 0 | 0 | 25 | 2 | 0 | 0 ** | 24 | 9 | 0 | 0 ** | 21 | 0 | 0 | 0 ** | 0 | 0 | 0 | 0 |
| | | (22) | (0) | (0) | (0) | (63) | (5) | (0) | (0) | (56) | (21) | (0) | (0) | (70) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | inflammation:foreign body | 2 | 0 | 0 | 0 | 3 | 1 | 0 | 0 | 5 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (4) | (0) | (0) | (0) | (8) | (3) | (0) | (0) | (12) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | inflammation:respiratory epithelium | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | respiratory metaplasia:olfactory epithelium | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (2) | (0) | (0) | (0) | (3) | (0) | (0) | (0) | (2) | (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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 18

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 40 | | | | 2000 ppm 43 | | | | 4000 ppm 30 | | | |
|----------------------|------------------------------|---|-----------|-----------|-----------|----------------|-----------|-----------|-----------|----------------|-----------|-----------|-----------|----------------|-----------|-----------|-----------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | |
| nasal cavit | | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | respiratory metaplasia:gland | 41 (91) | 0 (0) | 0 (0) | 0 (0) | 37 (93) | 0 (0) | 0 (0) | 0 (0) | 41 (95) | 0 (0) | 0 (0) | 0 (0) | 27 (90) | 0 (0) | 0 (0) | 0 (0) |
| | thickening of bone:turbinate | 5 (11) | 2 (4) | 0 (0) | 0 (0) | 17 (43) | 2 (5) | 0 (0) | 0 (0) | 5 (12) | 2 (5) | 0 (0) | 0 (0) | 9 (30) | 0 (0) | 0 (0) | 0 (0) |
| larynx | | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | inflammation | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 3 (8) | 0 (0) | 0 (0) | 0 (0) | 3 (7) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 1 (3) | 0 (0) | 0 (0) |
| lung | | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | congestion | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | osseous metaplasia | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) |
| | accumulation of foamy cells | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | interstitial pneumonia | 7 (16) | 0 (0) | 0 (0) | 0 (0) | 19 (48) | 0 (0) | 0 (0) | 0 (0) | 11 (26) | 1 (2) | 0 (0) | 0 (0) | 11 (37) | 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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 19

| | | Group Name No. of Animals on Study Grade | Control 45 | | | | 1000 ppm 40 | | | | 2000 ppm 43 | | | | 4000 ppm 30 | | | |
|------------------------|---------------------------------------|--|---------------|------------|------------|------------|----------------|------------|------------|------------|----------------|------------|------------|------------|----------------|------------|------------|------------|
| Organ_____ | Findings_____ | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| Lung | | | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | bronchiolar-alveolar cell hyperplasia | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 2 (5) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | mineralization:artery | | 3 (7) | 0 (0) | 0 (0) | 0 (0) | 2 (5) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| bone marrow | | | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | granulation | | 4 (9) | 1 (2) | 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) | 0 (0) |
| | increased hematopoiesis | | 5 (11) | 0 (0) | 0 (0) | 0 (0) | 4 (10) | 0 (0) | 0 (0) | 0 (0) | 4 (9) | 0 (0) | 0 (0) | 0 (0) | 6 (20) | 0 (0) | 0 (0) | 0 (0) |
| | myelofibrosis | | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | erythropoiesis:increased | | 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) |
| Lymph node | | | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | Lymphadenitis | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (5) | 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. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 20

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 40 | | | | 2000 ppm 43 | | | | 4000 ppm 30 | | | |
|------------------------|------------------------------|---|------------|------------|------------|----------------|------------|------------|--------------|----------------|------------|------------|------------|----------------|------------|------------|------------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | |
| spleen | | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | congestion | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | deposit of hemosiderin | 10 (22) | 0 (0) | 0 (0) | 0 (0) | 13 (33) | 0 (0) | 0 (0) | 0 (0) | 12 (28) | 0 (0) | 0 (0) | 0 (0) | 12 (40) | 0 (0) | 0 (0) | 0 (0) |
| | granulation | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | fibrosis | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 3 (8) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 2 (7) | 0 (0) | 0 (0) | 0 (0) |
| | extramedullary hematopoiesis | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 5 (13) | 0 (0) | 0 (0) | 0 * (0) | 4 (9) | 1 (2) | 0 (0) | 0 (0) | 2 (7) | 0 (0) | 0 (0) | 0 (0) |
| | stromal hyperplasia | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | increased:Leydig cell | 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) |

[Circulatory system]

| | | | | | | | | | | | | | | | | | |
|-------|---------------------|------------|------------|------------|------------|-------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| heart | | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | myocardial fibrosis | 3 (7) | 0 (0) | 0 (0) | 0 (0) | 5 (13) | 0 (0) | 0 (0) | 0 (0) | 3 (7) | 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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 21

| Organ_____ | Findings_____ | Group Name | Control | | | | 1000 ppm | | | | 2000 ppm | | | | 4000 ppm | | | |
|-------------------------|-------------------|-------------------------|---------|-------|-------|-------|----------|-------|-------|-------|----------|-------|-------|--------|----------|-------|-------|-------|
| | | No. of Animals on Study | 45 | | | | 40 | | | | 43 | | | | 30 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| tooth | dysplasia | | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | | 1 | 2 | 0 | 0 | 1 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | (2) | (4) | (0) | (0) | (3) | (5) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) |
| tongue | arteritis | | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | | 4 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | |
| | | | (9) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (12) | (0) | (0) | (0) | (3) | (0) | (0) | (0) |
| salivary gl | atrophy | | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | | 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) |
| stomach | mineralization | | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | |
| | concretion | | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | |
| | ulcer:forestomach | | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | | 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) | (0) | | |
| hyperplasia:forestomach | | <45> | | | | <40> | | | | <43> | | | | <30> | | | | |
| | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | |
| | (7) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (10) | (0) | (0) | (0) | |

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
 < a > a : Number of animals examined at the site
 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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 22

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 40 | | | | 2000 ppm 43 | | | | 4000 ppm 30 | | | |
|--------------------|-------------------------|---|--------|-------|-------|----------------|--------|-------|-------|----------------|--------|-------|-------|----------------|--------|-------|-------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | |
| stomach | ulcer:glandular stomach | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| liver | herniation | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (4) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | peliosis-like lesion | 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) |
| | necrosis: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) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | fatty change | 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) |
| | fatty change:central | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | fatty change:peripheral | 3 | 0 | 0 | 0 | 14 | 23 | 1 | 0 ** | 8 | 28 | 1 | 0 ** | 4 | 20 | 1 | 0 ** |
| | | (7) | (0) | (0) | (0) | (35) | (58) | (3) | (0) | (19) | (65) | (2) | (0) | (13) | (67) | (3) | (0) |
| | granulation | 29 | 7 | 0 | 0 | 25 | 13 | 0 | 0 * | 26 | 12 | 1 | 0 | 14 | 8 | 1 | 0 |
| | | (64) | (16) | (0) | (0) | (63) | (33) | (0) | (0) | (60) | (28) | (2) | (0) | (47) | (27) | (3) | (0) |

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

STUDY NO. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 23

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 40 | | | | 2000 ppm 43 | | | | 4000 ppm 30 | | | |
|--------------------|-----------------------------|---|------------|------------|------------|----------------|-------------|------------|------------|----------------|--------------|------------|------------|----------------|--------------|------------|------------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | |
| liver | | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | perivascular inflammation | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | fibrosis:focal | 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) |
| | acidophilic cell focus | 2 (4) | 0 (0) | 0 (0) | 0 (0) | 8 (20) | 0 (0) | 0 (0) | 0 (0) | 9 (21) | 5 (12) | 0 (0) | 0 (0) | 12 (40) | 10 (33) | 0 (0) | 0 (0) |
| | basophilic cell focus | 18 (40) | 0 (0) | 0 (0) | 0 (0) | 26 (65) | 8 (20) | 1 (3) | 0 (0) | 14 (33) | 25 (58) | 0 (0) | 0 (0) | 7 (23) | 20 (67) | 2 (7) | 0 (0) |
| | vacuolated cell focus | 2 (4) | 0 (0) | 0 (0) | 0 (0) | 7 (18) | 0 (0) | 0 (0) | 0 (0) | 12 (28) | 1 (2) | 0 (0) | 0 (0) | 8 (27) | 3 (10) | 0 (0) | 0 (0) |
| | mixed cell focus | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 2 (7) | 0 (0) | 0 (0) |
| | bile duct hyperplasia | 1 (2) | 0 (0) | 1 (2) | 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) |
| | bile ductular proliferation | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |

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. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 24

| Organ | Findings | Group Name | Control | | | | 1000 ppm | | | | 2000 ppm | | | | 4000 ppm | | | |
|---|--|-------------------------|-------------|-------------|-------------|-----------|-------------|-------------|-----------|--------------|--------------|-------------|------------|-----------|--------------|--------------|------------|------------|
| | | No. of Animals on Study | 45 | | | | 40 | | | | 43 | | | | 30 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| pancreas | | | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | atrophy | | 2 (4) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (5) | 0 (0) | 0 (0) | 0 (0) | 2 (7) | 0 (0) | 0 (0) | 0 (0) |
| | hyperplasia:acinar cell | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | | | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | basophilic change | | 18 (40) | 3 (7) | 0 (0) | 0 (0) | 3 (8) | 0 (0) | 0 (0) | 0 (0) | 0 ** (0) | 3 (7) | 0 (0) | 0 (0) | 0 (0) | 0 ** (0) | 5 (17) | 0 (0) |
| | deposit of hemosiderin | | 42 (93) | 0 (0) | 0 (0) | 0 (0) | 37 (93) | 0 (0) | 0 (0) | 0 (0) | 41 (95) | 1 (2) | 0 (0) | 0 (0) | 30 (100) | 0 (0) | 0 (0) | 0 (0) |
| | eosinophilic body | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | chronic nephropathy | | 5 (11) | 22 (49) | 14 (31) | 3 (7) | 19 (48) | 19 (48) | 2 (5) | 0 ** (0) | 18 (42) | 17 (40) | 5 (12) | 0 (0) | 0 ** (0) | 18 (60) | 6 (20) | 5 (17) |
| | hydronephrosis | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| 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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 25

| | | Group Name No. of Animals on Study Grade | Control 45 | | | | 1000 ppm 40 | | | | 2000 ppm 43 | | | | 4000 ppm 30 | | | |
|--------------------|---|--|---------------|------------|------------|------------|----------------|-------------|------------|------------|----------------|------------|------------|--------------|----------------|------------|------------|------------|
| Organ_____ | Findings_____ | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | | | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | mineralization:cortico-medullary junction | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | mineralization:pelvis | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (7) | 0 (0) | 0 (0) | 0 (0) |
| [Endocrine system] | | | | | | | | | | | | | | | | | | |
| pituitary | | | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | angiectasis | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 6 (14) | 1 (2) | 0 (0) | 0 * (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | cyst | | 14 (31) | 2 (4) | 0 (0) | 0 (0) | 12 (30) | 4 (10) | 0 (0) | 0 (0) | 13 (30) | 3 (7) | 1 (2) | 0 (0) | 9 (30) | 2 (7) | 0 (0) | 0 (0) |
| | hyperplasia | | 13 (29) | 3 (7) | 1 (2) | 0 (0) | 6 (15) | 7 (18) | 0 (0) | 0 (0) | 13 (30) | 2 (5) | 0 (0) | 0 (0) | 5 (17) | 1 (3) | 1 (3) | 0 (0) |
| thyroid | | | <44> | | | | <40> | | | | <43> | | | | <30> | | | |
| | ultimibranhial body remanet | | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |

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. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 26

| Organ | Findings | Control No. of Animals on Study Grade | | | | 1000 ppm 40 | | | | 2000 ppm 43 | | | | 4000 ppm 30 | | | |
|--------------------|-----------------------------------|---|-------|------|------|----------------|-------|------|------|----------------|-------|------|------|----------------|-------|------|------|
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Endocrine system] | | | | | | | | | | | | | | | | | |
| thyroid | | <44> | | | | <40> | | | | <43> | | | | <30> | | | |
| | C-cell hyperplasia | 7 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 3 | 1 | 0 | 0 | 8 | 0 | 0 | 0 |
| | | (16) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (7) | (2) | (0) | (0) | (27) | (0) | (0) | (0) |
| | focal follicular cell hyperplasia | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (5) | (0) | (0) | (0) | (7) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| adrenal | | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | peliosis-like lesion | 26 | 15 | 0 | 0 | 27 | 9 | 0 | 0 | 22 | 16 | 0 | 0 | 16 | 11 | 1 | 0 |
| | | (58) | (33) | (0) | (0) | (68) | (23) | (0) | (0) | (51) | (37) | (0) | (0) | (53) | (37) | (3) | (0) |
| | extramedullary hematopoiesis | 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) | (7) | (0) | (0) | (0) |
| | hyperplasia:cortical cell | 3 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 5 | 1 | 0 | 0 | 4 | 0 | 0 | 0 |
| | | (7) | (0) | (0) | (0) | (13) | (0) | (0) | (0) | (12) | (2) | (0) | (0) | (13) | (0) | (0) | (0) |
| | hyperplasia:medulla | 3 | 1 | 0 | 0 | 5 | 0 | 0 | 0 | 4 | 1 | 0 | 0 | 4 | 1 | 0 | 0 |
| | | (7) | (2) | (0) | (0) | (13) | (0) | (0) | (0) | (9) | (2) | (0) | (0) | (13) | (3) | (0) | (0) |
| | focal fatty change:cortex | 9 | 3 | 0 | 0 | 6 | 2 | 0 | 0 | 5 | 3 | 0 | 0 | 12 | 3 | 0 | 0 |
| | | (20) | (7) | (0) | (0) | (15) | (5) | (0) | (0) | (12) | (7) | (0) | (0) | (40) | (10) | (0) | (0) |
| | focal hypertrophy:cortex | 1 | 0 | 0 | 0 | 4 | 1 | 0 | 0 | 3 | 1 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | (2) | (0) | (0) | (0) | (10) | (3) | (0) | (0) | (7) | (2) | (0) | (0) | (10) | (0) | (0) | (0) |

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

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 27

| Organ | Findings | Group Name No. of Animals on Study Grade | Control 45 | | | | 1000 ppm 40 | | | | 2000 ppm 43 | | | | 4000 ppm 30 | | | |
|-------|----------|--|---------------|-----|-----|-----|----------------|-----|-----|-----|----------------|-----|-----|-----|----------------|-----|-----|-----|
| | | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |

[Reproductive system]

| | | | | | | | | | | | | | | | | | |
|------------|--------------------------------|--------|-------|-------|-------|--------|-------|--------|-------|--------|-------|-------|-------|--------|-------|--------|-------|
| ovary | cyst | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (0) | (0) |
| uterus | cystic endometrial hyperplasia | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | | 13 | 0 | 0 | 0 | 4 | 2 | 4 | 1 * | 14 | 2 | 1 | 0 | 3 | 0 | 4 | 0 * |
| | | (29) | (0) | (0) | (0) | (10) | (5) | (10) | (3) | (33) | (5) | (2) | (0) | (10) | (0) | (13) | (0) |
| mammary gl | duct ectasia | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | (2) | (0) | (2) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (0) | (0) | (3) | (0) | (0) | (0) |
| | hyperplasia | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (4) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | galactoceles | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (2) | (0) | (3) | (0) | (0) |

[Special sense organs/appandage]

| | | | | | | | | | | | | | | | | | |
|-----|----------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| eye | cataract | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (2) | (0) | (0) | (0) | (5) | (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 ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 28

| Organ_____ | Findings_____ | Group Name No. of Animals on Study Grade | Control 45 | | | | 1000 ppm 40 | | | | 2000 ppm 43 | | | | 4000 ppm 30 | | | |
|----------------------------------|--------------------------|--|---------------|-----------|-----------|-----------|----------------|-----------|-----------|-----------|----------------|-----------|-----------|-------------|----------------|-----------|-----------|-----------|
| | | | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) | 1 (%) | 2 (%) | 3 (%) | 4 (%) |
| [Special sense organs/appandage] | | | | | | | | | | | | | | | | | | |
| eye | | | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | retinal atrophy | | 2 (4) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 3 (8) | 4 (9) | 0 (0) | 1 (2) | 1 (2) | 2 (7) | 0 (0) | 2 (7) | 0 (0) |
| | keratitis | | 2 (4) | 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) | 0 (0) |
| | degeneration:cornea | | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| | mineralization:cornea | | 1 (2) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) |
| Harder gl | | | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | degeneration | | 16 (36) | 0 (0) | 0 (0) | 0 (0) | 20 (50) | 0 (0) | 0 (0) | 0 (0) | 26 (60) | 0 (0) | 0 (0) | 0 (0) * | 15 (50) | 0 (0) | 0 (0) | 0 (0) |
| | lymphocytic infiltration | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (3) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| nasolacr d | | | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | inflammation | | 10 (22) | 0 (0) | 0 (0) | 0 (0) | 3 (8) | 0 (0) | 0 (0) | 0 (0) | 2 (5) | 0 (0) | 0 (0) | 0 (0) * | 6 (20) | 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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 29

| Organ_____ | Findings_____ | Group Name Control | | | | 1000 ppm | | | | 2000 ppm | | | | 4000 ppm | | | |
|------------|---------------|----------------------------|-----|-----|-----|----------|-----|-----|-----|----------|-----|-----|-----|----------|-----|-----|-----|
| | | No. of Animals on Study 45 | | | | 40 | | | | 43 | | | | 30 | | | |
| | | Grade | | | | | | | | | | | | | | | |
| | | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |

[Musculoskeletal system]

| | | | | | | | | | | | | | | | | | |
|------|----------------|-------|-------|------|------|-------|-------|------|------|-------|-------|------|------|-------|-------|------|------|
| bone | osteosclerosis | <45> | | | | <40> | | | | <43> | | | | <30> | | | |
| | | 13 | 6 | 0 | 0 | 12 | 7 | 2 | 0 | 15 | 6 | 2 | 0 | 7 | 4 | 0 | 0 |
| | | (29) | (13) | (0) | (0) | (30) | (18) | (5) | (0) | (35) | (14) | (5) | (0) | (23) | (13) | (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)

BAIS3

APPENDIX K 1

NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS-TIME RELATED
RAT: MALE
(2-YEAR STUDY)

STUDY NO. : 0278
 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 | 1000 ppm | 2000 ppm | 4000 ppm |
|-----------------------|-------------------------------------|------------|---------|----------|----------|----------|
| 0 - 52 | NO. OF EXAMINED ANIMALS | | 0 | 0 | 0 | 0 |
| | NO. OF ANIMALS WITH TUMORS | | 0 | 0 | 0 | 0 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 0 | 0 | 0 | 0 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 0 | 0 | 0 | 0 |
| | NO. OF BENIGN TUMORS | | 0 | 0 | 0 | 0 |
| | NO. OF MALIGNANT TUMORS | | 0 | 0 | 0 | 0 |
| | NO. OF TOTAL TUMORS | | 0 | 0 | 0 | 0 |
| 53 - 78 | NO. OF EXAMINED ANIMALS | | 2 | 1 | 1 | 4 |
| | NO. OF ANIMALS WITH TUMORS | | 2 | 1 | 1 | 4 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 0 | 0 | 0 | 2 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 2 | 1 | 1 | 2 |
| | NO. OF BENIGN TUMORS | | 2 | 1 | 1 | 2 |
| | NO. OF MALIGNANT TUMORS | | 3 | 1 | 1 | 4 |
| | NO. OF TOTAL TUMORS | | 5 | 2 | 2 | 6 |
| 79 - 104 | NO. OF EXAMINED ANIMALS | | 16 | 6 | 11 | 18 |
| | NO. OF ANIMALS WITH TUMORS | | 16 | 6 | 11 | 17 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 1 | 1 | 1 | 1 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 15 | 5 | 10 | 16 |
| | NO. OF BENIGN TUMORS | | 27 | 9 | 27 | 31 |
| | NO. OF MALIGNANT TUMORS | | 14 | 6 | 6 | 10 |
| | NO. OF TOTAL TUMORS | | 41 | 15 | 33 | 41 |
| 105 - 105 | NO. OF EXAMINED ANIMALS | | 32 | 43 | 38 | 28 |
| | NO. OF ANIMALS WITH TUMORS | | 32 | 43 | 38 | 28 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 7 | 14 | 9 | 4 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 25 | 29 | 29 | 24 |
| | NO. OF BENIGN TUMORS | | 68 | 87 | 80 | 71 |
| | NO. OF MALIGNANT TUMORS | | 6 | 8 | 12 | 13 |
| | NO. OF TOTAL TUMORS | | 74 | 95 | 92 | 84 |

STUDY NO. : 0278
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 | 1000 ppm | 2000 ppm | 4000 ppm |
|-----------------------|-------------------------------------|------------|---------|----------|----------|----------|
| 0 - 105 | NO. OF EXAMINED ANIMALS | | 50 | 50 | 50 | 50 |
| | NO. OF ANIMALS WITH TUMORS | | 50 | 50 | 50 | 49 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 8 | 15 | 10 | 7 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 42 | 35 | 40 | 42 |
| | NO. OF BENIGN TUMORS | | 97 | 97 | 108 | 104 |
| | NO. OF MALIGNANT TUMORS | | 23 | 15 | 19 | 27 |
| | NO. OF TOTAL TUMORS | | 120 | 112 | 127 | 131 |

(HPT070)

BAIS3

APPENDIX K 2

NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS-TIME RELATED
RAT: FEMALE
(2-YEAR STUDY)

STUDY NO. : 0278
 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 | 1000 ppm | 2000 ppm | 4000 ppm |
|-----------------------|-------------------------------------|------------|---------|----------|----------|----------|
| 0 - 52 | NO. OF EXAMINED ANIMALS | | 0 | 0 | 0 | 0 |
| | NO. OF ANIMALS WITH TUMORS | | 0 | 0 | 0 | 0 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 0 | 0 | 0 | 0 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 0 | 0 | 0 | 0 |
| | NO. OF BENIGN TUMORS | | 0 | 0 | 0 | 0 |
| | NO. OF MALIGNANT TUMORS | | 0 | 0 | 0 | 0 |
| | NO. OF TOTAL TUMORS | | 0 | 0 | 0 | 0 |
| | | | | | | |
| 53 - 78 | NO. OF EXAMINED ANIMALS | | 1 | 1 | 0 | 6 |
| | NO. OF ANIMALS WITH TUMORS | | 1 | 1 | 0 | 6 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 1 | 1 | 0 | 5 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 0 | 0 | 0 | 1 |
| | NO. OF BENIGN TUMORS | | 0 | 1 | 0 | 3 |
| | NO. OF MALIGNANT TUMORS | | 1 | 0 | 0 | 4 |
| | NO. OF TOTAL TUMORS | | 1 | 1 | 0 | 7 |
| | | | | | | |
| 79 - 104 | NO. OF EXAMINED ANIMALS | | 4 | 9 | 7 | 14 |
| | NO. OF ANIMALS WITH TUMORS | | 4 | 9 | 6 | 13 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 3 | 4 | 1 | 5 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 1 | 5 | 5 | 8 |
| | NO. OF BENIGN TUMORS | | 2 | 12 | 4 | 17 |
| | NO. OF MALIGNANT TUMORS | | 3 | 5 | 7 | 7 |
| | NO. OF TOTAL TUMORS | | 5 | 17 | 11 | 24 |
| | | | | | | |
| 105 - 105 | NO. OF EXAMINED ANIMALS | | 45 | 40 | 43 | 30 |
| | NO. OF ANIMALS WITH TUMORS | | 36 | 33 | 34 | 26 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 19 | 16 | 12 | 13 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 17 | 17 | 22 | 13 |
| | NO. OF BENIGN TUMORS | | 54 | 49 | 54 | 41 |
| | NO. OF MALIGNANT TUMORS | | 6 | 6 | 7 | 6 |
| | NO. OF TOTAL TUMORS | | 60 | 55 | 61 | 47 |
| | | | | | | |

STUDY NO. : 0278
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 | 1000 ppm | 2000 ppm | 4000 ppm |
|-----------------------|-------------------------------------|------------|---------|----------|----------|----------|
| 0 - 105 | NO. OF EXAMINED ANIMALS | | 50 | 50 | 50 | 50 |
| | NO. OF ANIMALS WITH TUMORS | | 41 | 43 | 40 | 45 |
| | NO. OF ANIMALS WITH SINGLE TUMORS | | 23 | 21 | 13 | 23 |
| | NO. OF ANIMALS WITH MULTIPLE TUMORS | | 18 | 22 | 27 | 22 |
| | NO. OF BENIGN TUMORS | | 56 | 62 | 58 | 61 |
| | NO. OF MALIGNANT TUMORS | | 10 | 11 | 14 | 17 |
| | NO. OF TOTAL TUMORS | | 66 | 73 | 72 | 78 |

(HPT070)

BAISS

APPENDIX L 1

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

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 1

| Organ | Findings | Group Name No. of animals on Study | Control 50 | 1000 ppm 50 | 2000 ppm 50 | 4000 ppm 50 |
|----------------------------------|--------------------------------|---------------------------------------|---------------|----------------|----------------|----------------|
| [Integumentary system/appandage] | | | | | | |
| skin/app | | | <50> | <50> | <50> | <50> |
| | squamous cell papilloma | | 1 (2%) | 0 (0%) | 1 (2%) | 0 (0%) |
| | schwannoma | | 1 (2%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | keratoacanthoma | | 2 (4%) | 4 (8%) | 1 (2%) | 2 (4%) |
| subcutis | | | <50> | <50> | <50> | <50> |
| | fibroma | | 1 (2%) | 4 (8%) | 7 (14%) | 12 (24%) |
| | lipoma | | 0 (0%) | 0 (0%) | 4 (8%) | 1 (2%) |
| | schwannoma | | 0 (0%) | 1 (2%) | 0 (0%) | 0 (0%) |
| | fibrosarcoma | | 0 (0%) | 0 (0%) | 1 (2%) | 0 (0%) |
| | schwannoma:malignant | | 0 (0%) | 1 (2%) | 1 (2%) | 2 (4%) |
| [Respiratory system] | | | | | | |
| lung | | | <50> | <50> | <50> | <50> |
| | bronchiolar-alveolar adenoma | | 2 (4%) | 0 (0%) | 1 (2%) | 1 (2%) |
| | bronchiolar-alveolar carcinoma | | 2 (4%) | 1 (2%) | 0 (0%) | 1 (2%) |
| [Hematopoietic system] | | | | | | |
| bone marrow | | | <50> | <50> | <50> | <50> |
| | osteoma | | 0 (0%) | 1 (2%) | 0 (0%) | 0 (0%) |

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

(HPT085)

BAIS3

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 2

| Organ | Findings | Group Name No. of animals on Study | Control 50 | 1000 ppm 50 | 2000 ppm 50 | 4000 ppm 50 |
|------------------------|---------------------------|---------------------------------------|-----------------|-----------------|-----------------|-----------------|
| [Hematopoietic system] | | | | | | |
| bone marrow | histiocytic sarcoma | | <50> 0 (0%) | <50> 1 (2%) | <50> 2 (4%) | <50> 0 (0%) |
| lymph node | malignant lymphoma | | <50> 1 (2%) | <50> 0 (0%) | <50> 2 (4%) | <50> 2 (4%) |
| spleen | hemangioma | | <50> 1 (2%) | <50> 1 (2%) | <50> 0 (0%) | <50> 0 (0%) |
| | mononuclear cell leukemia | | 3 (6%) | 3 (6%) | 8 (16%) | 4 (8%) |
| | hemangiosarcoma | | 0 (0%) | 1 (2%) | 0 (0%) | 0 (0%) |
| [Circulatory system] | | | | | | |
| heart | schwannoma | | <50> 1 (2%) | <50> 0 (0%) | <50> 2 (4%) | <50> 0 (0%) |
| [Digestive system] | | | | | | |
| tongue | squamous cell papilloma | | <50> 0 (0%) | <50> 1 (2%) | <50> 0 (0%) | <50> 0 (0%) |
| stomach | squamous cell papilloma | | <50> 0 (0%) | <50> 1 (2%) | <50> 0 (0%) | <50> 2 (4%) |
| | squamous cell carcinoma | | 1 (2%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | leiomyosarcoma | | 1 (2%) | 0 (0%) | 0 (0%) | 0 (0%) |
| liver | hepatocellular adenoma | | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) | <50> 1 (2%) |

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

(HPT085)

BAIS3

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 3

| Organ | Findings | Group Name No. of animals on Study | Control 50 | 1000 ppm 50 | 2000 ppm 50 | 4000 ppm 50 |
|--------------------|-----------------------------|---------------------------------------|-------------------|------------------|-------------------|-------------------|
| [Digestive system] | | | | | | |
| liver | histiocytic sarcoma | | <50> 1 (2%) | <50> 0 (0%) | <50> 0 (0%) | <50> 0 (0%) |
| | hepatocellular carcinoma | | 1 (2%) | 0 (0%) | 1 (2%) | 2 (4%) |
| pancreas | islet cell adenoma | | <50> 6 (12%) | <50> 2 (4%) | <50> 4 (8%) | <50> 3 (6%) |
| | islet cell adenocarcinoma | | 0 (0%) | 2 (4%) | 0 (0%) | 0 (0%) |
| [Urinary system] | | | | | | |
| kidney | renal cell carcinoma | | <50> 2 (4%) | <50> 0 (0%) | <50> 0 (0%) | <50> 0 (0%) |
| | nephroblastoma | | 0 (0%) | 1 (2%) | 0 (0%) | 1 (2%) |
| urin bladd | transitional cell papilloma | | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) | <49> 0 (0%) |
| | transitional cell carcinoma | | 0 (0%) | 0 (0%) | 1 (2%) | 0 (0%) |
| | liposarcoma | | 0 (0%) | 0 (0%) | 0 (0%) | 1 (2%) |
| [Endocrine system] | | | | | | |
| pituitary | adenoma | | <50> 18 (36%) | <50> 7 (14%) | <50> 10 (20%) | <50> 12 (24%) |
| | adenocarcinoma | | 1 (2%) | 0 (0%) | 0 (0%) | 0 (0%) |

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

(HPT085)

BAIS3

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 4

| Organ | Findings | Group Name No. of animals on Study | Control 50 | 1000 ppm 50 | 2000 ppm 50 | 4000 ppm 50 |
|-----------------------|---------------------------|---------------------------------------|---------------|----------------|----------------|----------------|
| [Endocrine system] | | | | | | |
| thyroid | | | <50> | <48> | <49> | <50> |
| | C-cell adenoma | | 9 (18%) | 5 (10%) | 7 (14%) | 4 (8%) |
| | follicular adenoma | | 0 (0%) | 4 (8%) | 0 (0%) | 1 (2%) |
| | C-cell carcinoma | | 1 (2%) | 0 (0%) | 1 (2%) | 2 (4%) |
| | follicular adenocarcinoma | | 2 (4%) | 2 (4%) | 0 (0%) | 4 (8%) |
| adrenal | | | <50> | <50> | <50> | <50> |
| | pheochromocytoma | | 8 (16%) | 13 (26%) | 14 (28%) | 9 (18%) |
| [Reproductive system] | | | | | | |
| testis | | | <49> | <50> | <50> | <50> |
| | interstitial cell tumor | | 45 (92%) | 49 (98%) | 48 (96%) | 46 (92%) |
| mammary gl | | | <50> | <50> | <50> | <50> |
| | adenoma | | 1 (2%) | 0 (0%) | 0 (0%) | 0 (0%) |
| | fibroadenoma | | 1 (2%) | 2 (4%) | 3 (6%) | 8 (16%) |
| | adenocarcinoma | | 1 (2%) | 0 (0%) | 0 (0%) | 0 (0%) |
| prep/cli gl | | | <50> | <50> | <50> | <50> |
| | adenoma | | 0 (0%) | 2 (4%) | 4 (8%) | 1 (2%) |
| | adenocarcinoma | | 0 (0%) | 1 (2%) | 0 (0%) | 0 (0%) |
| [Nervous system] | | | | | | |
| brain | | | <50> | <50> | <50> | <50> |
| | glioma | | 1 (2%) | 0 (0%) | 1 (2%) | 0 (0%) |

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

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 5

| Organ | Findings | Group Name No. of animals on Study | Control 50 | 1000 ppm 50 | 2000 ppm 50 | 4000 ppm 50 |
|----------------------------------|-------------------------|---------------------------------------|-----------------|-----------------|-----------------|-----------------|
| [Special sense organs/appandage] | | | | | | |
| Zymbal gl | squamous cell carcinoma | | <50> 1 (2%) | <50> 1 (2%) | <50> 0 (0%) | <50> 0 (0%) |
| [Musculoskeletal system] | | | | | | |
| bone | osteosarcoma | | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) | <50> 0 (0%) |
| [Body cavities] | | | | | | |
| peritoneum | tumor:benign:NOS | | <50> 0 (0%) | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) |
| | mesothelioma | | 3 (6%) | 1 (2%) | 0 (0%) | 7 (14%) |
| | sarcoma:NOS | | 1 (2%) | 0 (0%) | 0 (0%) | 0 (0%) |
| retroperit | schwannoma:malignant | | <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

(HPT085)

BATS3

APPENDIX L 2

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

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 6

| Organ | Findings | Group Name No. of animals on Study | Control 50 | 1000 ppm 50 | 2000 ppm 50 | 4000 ppm 50 |
|----------------------------------|------------------------------|---------------------------------------|---------------|----------------|----------------|----------------|
| [Integumentary system/appandage] | | | | | | |
| skin/app | | | <50> | <50> | <50> | <50> |
| | squamous cell papilloma | | 1 (2%) | 0 (0%) | 1 (2%) | 0 (0%) |
| subcutis | | | <50> | <50> | <50> | <50> |
| | fibroma | | 0 (0%) | 2 (4%) | 0 (0%) | 1 (2%) |
| | lipoma | | 0 (0%) | 1 (2%) | 0 (0%) | 0 (0%) |
| | schwannoma | | 0 (0%) | 0 (0%) | 0 (0%) | 1 (2%) |
| [Respiratory system] | | | | | | |
| nasal cavit | | | <50> | <50> | <50> | <50> |
| | chondroma | | 0 (0%) | 1 (2%) | 0 (0%) | 0 (0%) |
| nasopharynx | | | <50> | <50> | <50> | <50> |
| | squamous cell papilloma | | 0 (0%) | 0 (0%) | 0 (0%) | 1 (2%) |
| lung | | | <50> | <50> | <50> | <50> |
| | bronchiolar-alveolar adenoma | | 2 (4%) | 1 (2%) | 2 (4%) | 1 (2%) |
| | adenosquamous carcinoma | | 1 (2%) | 0 (0%) | 0 (0%) | 0 (0%) |
| [Hematopoietic system] | | | | | | |
| lymph node | | | <50> | <50> | <50> | <50> |
| | malignant lymphoma | | 1 (2%) | 2 (4%) | 2 (4%) | 2 (4%) |
| spleen | | | <50> | <50> | <50> | <50> |
| | mononuclear cell leukemia | | 2 (4%) | 4 (8%) | 8 (16%) | 7 (14%) |
| [Circulatory system] | | | | | | |
| heart | | | <50> | <50> | <50> | <50> |
| | schwannoma | | 1 (2%) | 0 (0%) | 0 (0%) | 0 (0%) |

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

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 7

| Organ | Findings | Group Name No. of animals on Study | Control 50 | 1000 ppm 50 | 2000 ppm 50 | 4000 ppm 50 |
|--------------------|-----------------------------|---------------------------------------|---------------|----------------|----------------|----------------|
| [Digestive system] | | | | | | |
| oral cavity | | | <50> | <50> | <50> | <50> |
| | sarcoma:NOS | | 1 (2%) | 0 (0%) | 0 (0%) | 0 (0%) |
| stomach | | | <50> | <50> | <50> | <50> |
| | squamous cell papilloma | | 1 (2%) | 1 (2%) | 0 (0%) | 0 (0%) |
| liver | | | <50> | <50> | <50> | <50> |
| | hepatocellular adenoma | | 2 (4%) | 0 (0%) | 0 (0%) | 3 (6%) |
| | histiocytic sarcoma | | 0 (0%) | 0 (0%) | 1 (2%) | 0 (0%) |
| pancreas | | | <50> | <50> | <50> | <50> |
| | islet cell adenoma | | 1 (2%) | 1 (2%) | 0 (0%) | 1 (2%) |
| | islet cell adenocarcinoma | | 1 (2%) | 0 (0%) | 0 (0%) | 0 (0%) |
| [Urinary system] | | | | | | |
| kidney | | | <50> | <50> | <50> | <50> |
| | renal cell carcinoma | | 0 (0%) | 0 (0%) | 0 (0%) | 1 (2%) |
| urin bladd | | | <49> | <50> | <50> | <49> |
| | transitional cell papilloma | | 2 (4%) | 0 (0%) | 0 (0%) | 0 (0%) |
| [Endocrine system] | | | | | | |
| pituitary | | | <50> | <50> | <50> | <50> |
| | adenoma | | 18 (36%) | 28 (56%) | 24 (48%) | 19 (38%) |
| | adenocarcinoma | | 1 (2%) | 1 (2%) | 0 (0%) | 0 (0%) |
| thyroid | | | <49> | <50> | <50> | <50> |
| | C-cell adenoma | | 5 (10%) | 3 (6%) | 7 (14%) | 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. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 8

| Organ | Findings | Group Name No. of animals on Study | Control 50 | 1000 ppm 50 | 2000 ppm 50 | 4000 ppm 50 |
|-----------------------|--------------------------------------|---------------------------------------|-----------------|-----------------|-----------------|-----------------|
| [Endocrine system] | | | | | | |
| thyroid | follicular adenoma | | <49> 0 (0%) | <50> 1 (2%) | <50> 1 (2%) | <50> 1 (2%) |
| | C-cell carcinoma | | 0 (0%) | 1 (2%) | 1 (2%) | 1 (2%) |
| | follicular adenocarcinoma | | 2 (4%) | 1 (2%) | 0 (0%) | 0 (0%) |
| parathyroid | adenoma | | <50> 0 (0%) | <50> 1 (2%) | <50> 1 (2%) | <50> 0 (0%) |
| | | | | | | |
| adrenal | pheochromocytoma | | <50> 4 (8%) | <50> 2 (4%) | <50> 4 (8%) | <50> 2 (4%) |
| | cortical adenoma | | 1 (2%) | 0 (0%) | 0 (0%) | 0 (0%) |
| [Reproductive system] | | | | | | |
| ovary | granulosa-theca cell tumor | | <50> 1 (2%) | <50> 0 (0%) | <50> 0 (0%) | <50> 0 (0%) |
| | granulosa-theca cell tumor:malignant | | 0 (0%) | 0 (0%) | 0 (0%) | 1 (2%) |
| uterus | leiomyoma | | <50> 0 (0%) | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) |
| | endometrial stromal polyp | | 8 (16%) | 11 (22%) | 6 (12%) | 9 (18%) |
| | adenocarcinoma | | 0 (0%) | 0 (0%) | 1 (2%) | 0 (0%) |
| | leiomyosarcoma | | 0 (0%) | 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

(HPT085)

BAIS3

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 9

| Organ | Findings | Group Name No. of animals on Study | Control 50 | 1000 ppm 50 | 2000 ppm 50 | 4000 ppm 50 |
|--------------------------|-----------------------------|---------------------------------------|-----------------|-----------------|-----------------|-----------------|
| [Reproductive system] | | | | | | |
| uterus | endometrial stromal sarcoma | | <50> 0 (0%) | <50> 0 (0%) | <50> 0 (0%) | <50> 2 (4%) |
| vagina | squamous cell papilloma | | <50> 0 (0%) | <50> 0 (0%) | <50> 2 (4%) | <50> 0 (0%) |
| mammary gl | adenoma | | <50> 0 (0%) | <50> 2 (4%) | <50> 1 (2%) | <50> 0 (0%) |
| | fibroadenoma | | 7 (14%) | 7 (14%) | 9 (18%) | 14 (28%) |
| | adenocarcinoma | | 0 (0%) | 2 (4%) | 0 (0%) | 1 (2%) |
| prep/cli gl | squamous cell papilloma | | <50> 1 (2%) | <50> 0 (0%) | <50> 0 (0%) | <50> 0 (0%) |
| | adenoma | | 1 (2%) | 0 (0%) | 0 (0%) | 0 (0%) |
| [Nervous system] | | | | | | |
| brain | glioma | | <50> 1 (2%) | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) |
| [Musculoskeletal system] | | | | | | |
| bone | osteosarcoma | | <50> 0 (0%) | <50> 0 (0%) | <50> 1 (2%) | <50> 0 (0%) |
| [Body cavities] | | | | | | |
| adipose | lipoma | | <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

APPENDIX M 1

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANALYSIS, RAT: MALE

(2-YEAR STUDY)

STUDY No. : 0278
ANIMAL : RAT F344/DuCrj
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 1

| Group Name | Control | 1000 ppm | 2000 ppm | 4000 ppm |
|--|--------------|------------|-------------|--------------|
| SITE : skin/appendage TUMOR : keratoacanthoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 2/50(4.0) | 4/50(8.0) | 1/50(2.0) | 2/50(4.0) |
| Adjusted rates(b) | 6.25 | 9.30 | 2.13 | 7.14 |
| Terminal rates(c) | 2/32(6.3) | 4/43(9.3) | 0/38(0.0) | 2/28(7.1) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.6142 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.6865 | | | |
| Fisher Exact test(e) | | P = 0.3389 | P = 0.5000 | P = 0.3088 |
| SITE : subcutis TUMOR : fibroma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 1/50(2.0) | 4/50(8.0) | 7/50(14.0) | 12/50(24.0) |
| Adjusted rates(b) | 3.13 | 9.30 | 15.56 | 36.67 |
| Terminal rates(c) | 1/32(3.1) | 4/43(9.3) | 5/38(13.2) | 10/28(35.7) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.0799 ? | | | |
| Prevalence method(d) | P = 0.0001** | | | |
| Combined analysis(d) | P < 0.0001** | | | |
| Cochran-Armitage test(e) | P = 0.0004** | | | |
| Fisher Exact test(e) | | P = 0.1811 | P = 0.0297* | P = 0.0009** |
| SITE : subcutis TUMOR : lipoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 0/50(0.0) | 0/50(0.0) | 4/50(8.0) | 1/50(2.0) |
| Adjusted rates(b) | 0.0 | 0.0 | 8.51 | 3.57 |
| Terminal rates(c) | 0/32(0.0) | 0/43(0.0) | 2/38(5.3) | 1/28(3.6) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.1510 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.3196 | | | |
| Fisher Exact test(e) | | P = 0.5000 | P = 0.0587 | P = 0.4999 |

STUDY No. : 0278
ANIMAL : RAT F344/DuCrj
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 2

| Group Name | Control | 1000 ppm | 2000 ppm | 4000 ppm |
|---|--------------|------------|-------------|--------------|
| SITE : subcutis TUMOR : fibroma,fibrosarcoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 1/50(2.0) | 4/50(8.0) | 8/50(16.0) | 12/50(24.0) |
| Adjusted rates(b) | 3.13 | 9.30 | 17.78 | 36.67 |
| Terminal rates(c) | 1/32(3.1) | 4/43(9.3) | 6/38(15.8) | 10/28(35.7) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.0799 ? | | | |
| Prevalence method(d) | P = 0.0001** | | | |
| Combined analysis(d) | P < 0.0001** | | | |
| Cochran-Armitage test(e) | P = 0.0005** | | | |
| Fisher Exact test(e) | | P = 0.1811 | P = 0.0154* | P = 0.0009** |
| SITE : spleen TUMOR : mononuclear cell leukemia | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 3/50(6.0) | 3/50(6.0) | 8/50(16.0) | 4/50(8.0) |
| Adjusted rates(b) | 2.56 | 6.82 | 10.53 | 7.14 |
| Terminal rates(c) | 0/32(0.0) | 2/43(4.7) | 4/38(10.5) | 2/28(7.1) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.2510 | | | |
| Prevalence method(d) | P = 0.3346 | | | |
| Combined analysis(d) | P = 0.2248 | | | |
| Cochran-Armitage test(e) | P = 0.5587 | | | |
| Fisher Exact test(e) | | P = 0.3388 | P = 0.0999 | P = 0.4998 |
| SITE : liver TUMOR : hepatocellular adenoma,hepatocellular carcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 1/50(2.0) | 0/50(0.0) | 2/50(4.0) | 3/50(6.0) |
| Adjusted rates(b) | 3.13 | 0.0 | 5.26 | 10.71 |
| Terminal rates(c) | 1/32(3.1) | 0/43(0.0) | 2/38(5.3) | 3/28(10.7) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.0371* | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.1232 | | | |
| Fisher Exact test(e) | | P = 0.4999 | P = 0.5000 | P = 0.3086 |

STUDY No. : 0278
 ANIMAL : RAT F344/DuCrj
 SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 3

| Group Name | Control | 1000 ppm | 2000 ppm | 4000 ppm |
|--|--------------|--------------|--------------|--------------|
| SITE : pancreas TUMOR : islet cell adenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 6/50(12.0) | 2/50(4.0) | 4/50(8.0) | 3/50(6.0) |
| Adjusted rates(b) | 15.63 | 4.65 | 10.53 | 7.89 |
| Terminal rates(c) | 5/32(15.6) | 2/43(4.7) | 4/38(10.5) | 2/28(7.1) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.7386 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.4405 | | | |
| Fisher Exact test(e) | | P = 0.1344 | P = 0.3705 | P = 0.2436 |
| SITE : pancreas TUMOR : islet cell adenoma, islet cell adenocarcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 6/50(12.0) | 4/50(8.0) | 4/50(8.0) | 3/50(6.0) |
| Adjusted rates(b) | 15.63 | 6.98 | 10.53 | 7.89 |
| Terminal rates(c) | 5/32(15.6) | 3/43(7.0) | 4/38(10.5) | 2/28(7.1) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.5972 | | | |
| Prevalence method(d) | P = 0.7741 | | | |
| Combined analysis(d) | P = 0.8052 | | | |
| Cochran-Armitage test(e) | P = 0.3243 | | | |
| Fisher Exact test(e) | | P = 0.3705 | P = 0.3705 | P = 0.2436 |
| SITE : pituitary gland TUMOR : adenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 18/50(36.0) | 7/50(14.0) | 10/50(20.0) | 12/50(24.0) |
| Adjusted rates(b) | 35.56 | 16.28 | 18.75 | 37.93 |
| Terminal rates(c) | 11/32(34.4) | 7/43(16.3) | 5/38(13.2) | 10/28(35.7) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.5900 | | | |
| Prevalence method(d) | P = 0.7219 | | | |
| Combined analysis(d) | P = 0.7419 | | | |
| Cochran-Armitage test(e) | P = 0.4137 | | | |
| Fisher Exact test(e) | | P = 0.0099** | P = 0.0592 | P = 0.1378 |

STUDY No. : 0278
 ANIMAL : RAT F344/DuCrj
 SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 4

| Group Name | Control | 1000 ppm | 2000 ppm | 4000 ppm |
|--|--------------|--------------|--------------|--------------|
| SITE : pituitary gland TUMOR : adenoma,adenocarcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 19/50(38.0) | 7/50(14.0) | 10/50(20.0) | 12/50(24.0) |
| Adjusted rates(b) | 35.56 | 16.28 | 18.75 | 37.93 |
| Terminal rates(c) | 11/32(34.4) | 7/43(16.3) | 5/38(13.2) | 10/28(35.7) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.7744 | | | |
| Prevalence method(d) | P = 0.7219 | | | |
| Combined analysis(d) | P = 0.7984 | | | |
| Cochran-Armitage test(e) | P = 0.3137 | | | |
| Fisher Exact test(e) | | P = 0.0057** | P = 0.0385* | P = 0.0973 |
| SITE : thyroid TUMOR : C-cell adenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 9/50(18.0) | 5/48(10.4) | 7/49(14.3) | 4/50(8.0) |
| Adjusted rates(b) | 21.95 | 10.64 | 17.50 | 9.76 |
| Terminal rates(c) | 6/32(18.8) | 4/43(9.3) | 6/37(16.2) | 2/28(7.1) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.9082 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.2001 | | | |
| Fisher Exact test(e) | | P = 0.2174 | P = 0.4104 | P = 0.1169 |
| SITE : thyroid TUMOR : follicular adenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 0/50(0.0) | 4/48(8.3) | 0/49(0.0) | 1/50(2.0) |
| Adjusted rates(b) | 0.0 | 9.30 | 0.0 | 3.03 |
| Terminal rates(c) | 0/32(0.0) | 4/43(9.3) | 0/37(0.0) | 0/28(0.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.5241 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.8119 | | | |
| Fisher Exact test(e) | | P = 0.0539 | P = 0.5000 | P = 0.4999 |

STUDY No. : 0278
 ANIMAL : RAT F344/DuCrj
 SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 5

| Group Name | Control | 1000 ppm | 2000 ppm | 4000 ppm |
|--|--------------|-------------|-------------|-------------|
| SITE : thyroid TUMOR : follicular adenocarcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 2/50(4.0) | 2/48(4.2) | 0/49(0.0) | 4/50(8.0) |
| Adjusted rates(b) | 5.56 | 2.33 | 0.0 | 14.29 |
| Terminal rates(c) | 1/32(3.1) | 1/43(2.3) | 0/37(0.0) | 4/28(14.3) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.5868 | | | |
| Prevalence method(d) | P = 0.0671 | | | |
| Combined analysis(d) | P = 0.1126 | | | |
| Cochran-Armitage test(e) | P = 0.3381 | | | |
| Fisher Exact test(e) | | P = 0.3243 | P = 0.2525 | P = 0.3389 |
| SITE : thyroid TUMOR : C-cell adenoma,C-cell carcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 10/50(20.0) | 5/48(10.4) | 8/49(16.3) | 6/50(12.0) |
| Adjusted rates(b) | 21.95 | 10.64 | 20.00 | 13.95 |
| Terminal rates(c) | 6/32(18.8) | 4/43(9.3) | 7/37(18.9) | 3/28(10.7) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ——— | | | |
| Prevalence method(d) | P = 0.7351 | | | |
| Combined analysis(d) | P = ——— | | | |
| Cochran-Armitage test(e) | P = 0.4227 | | | |
| Fisher Exact test(e) | | P = 0.1501 | P = 0.4166 | P = 0.2071 |
| SITE : thyroid TUMOR : follicular adenoma,follicular adenocarcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 2/50(4.0) | 6/48(12.5) | 0/49(0.0) | 5/50(10.0) |
| Adjusted rates(b) | 5.56 | 11.63 | 0.0 | 15.15 |
| Terminal rates(c) | 1/32(3.1) | 5/43(11.6) | 0/37(0.0) | 4/28(14.3) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.5868 | | | |
| Prevalence method(d) | P = 0.1455 | | | |
| Combined analysis(d) | P = 0.1943 | | | |
| Cochran-Armitage test(e) | P = 0.5413 | | | |
| Fisher Exact test(e) | | P = 0.1213 | P = 0.2525 | P = 0.2181 |

STUDY No. : 0278
ANIMAL : RAT F344/DuCrj
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 6

| Group Name | Control | 1000 ppm | 2000 ppm | 4000 ppm |
|--|--------------|--------------|--------------|--------------|
| SITE : adrenal gland TUMOR : pheochromocytoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 8/50(16.0) | 13/50(26.0) | 14/50(28.0) | 9/50(18.0) |
| Adjusted rates(b) | 18.18 | 27.27 | 31.71 | 24.24 |
| Terminal rates(c) | 5/32(15.6) | 11/43(25.6) | 11/38(28.9) | 5/28(17.9) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.4229 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 1.0000 | | | |
| Fisher Exact test(e) | | P = 0.1634 | P = 0.1137 | P = 0.4995 |
| SITE : testis TUMOR : interstitial cell tumor | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 45/49(91.8) | 49/50(98.0) | 48/50(96.0) | 46/50(92.0) |
| Adjusted rates(b) | 97.30 | 100.00 | 100.00 | 97.56 |
| Terminal rates(c) | 31/32(96.9) | 43/43(100.0) | 38/38(100.0) | 27/28(96.4) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.4959 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.7285 | | | |
| Fisher Exact test(e) | | P = 0.1748 | P = 0.3292 | P = 0.3459 |
| SITE : mammary gland TUMOR : fibroadenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 1/50(2.0) | 2/50(4.0) | 3/50(6.0) | 8/50(16.0) |
| Adjusted rates(b) | 3.13 | 4.65 | 6.12 | 25.00 |
| Terminal rates(c) | 1/32(3.1) | 2/43(4.7) | 2/38(5.3) | 7/28(25.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.0923 | | | |
| Prevalence method(d) | P = 0.0020** | | | |
| Combined analysis(d) | P = 0.0007** | | | |
| Cochran-Armitage test(e) | P = 0.0037** | | | |
| Fisher Exact test(e) | | P = 0.5000 | P = 0.3086 | P = 0.0154* |

STUDY No. : 0278
ANIMAL : RAT F344/DuCrj
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 7

| Group Name | Control | 1000 ppm | 2000 ppm | 4000 ppm |
|---|--------------|------------|------------|-------------|
| SITE : mammary gland TUMOR : adenoma,fibroadenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 2/50(4.0) | 2/50(4.0) | 3/50(6.0) | 8/50(16.0) |
| Adjusted rates(b) | 6.25 | 4.65 | 6.12 | 25.00 |
| Terminal rates(c) | 2/32(6.3) | 2/43(4.7) | 2/38(5.3) | 7/28(25.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.0923 | | | |
| Prevalence method(d) | P = 0.0068** | | | |
| Combined analysis(d) | P = 0.0026** | | | |
| Cochran-Armitage test(e) | P = 0.0126* | | | |
| Fisher Exact test(e) | | P = 0.3088 | P = 0.4999 | P = 0.0458* |
| SITE : mammary gland TUMOR : adenoma,fibroadenoma,adenocarcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 3/50(6.0) | 2/50(4.0) | 3/50(6.0) | 8/50(16.0) |
| Adjusted rates(b) | 6.25 | 4.65 | 6.12 | 25.00 |
| Terminal rates(c) | 2/32(6.3) | 2/43(4.7) | 2/38(5.3) | 7/28(25.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.3854 | | | |
| Prevalence method(d) | P = 0.0068** | | | |
| Combined analysis(d) | P = 0.0086** | | | |
| Cochran-Armitage test(e) | P = 0.0345* | | | |
| Fisher Exact test(e) | | P = 0.4999 | P = 0.3388 | P = 0.0999 |
| SITE : preputial/clitoral gland TUMOR : adenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 0/50(0.0) | 2/50(4.0) | 4/50(8.0) | 1/50(2.0) |
| Adjusted rates(b) | 0.0 | 4.65 | 9.76 | 3.57 |
| Terminal rates(c) | 0/32(0.0) | 2/43(4.7) | 3/38(7.9) | 1/28(3.6) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.2418 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.6489 | | | |
| Fisher Exact test(e) | | P = 0.2475 | P = 0.0587 | P = 0.4999 |

STUDY No. : 0278
 ANIMAL : RAT F344/DuCrj
 SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 8

| Group Name | Control | 1000 ppm | 2000 ppm | 4000 ppm |
|---|-------------|------------|------------|-------------|
| SITE : preputial/clitoral gland TUMOR : adenoma,adenocarcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 0/50(0.0) | 3/50(6.0) | 4/50(8.0) | 1/50(2.0) |
| Adjusted rates(b) | 0.0 | 6.98 | 9.76 | 3.57 |
| Terminal rates(c) | 0/32(0.0) | 3/43(7.0) | 3/38(7.9) | 1/28(3.6) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.3085 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.8073 | | | |
| Fisher Exact test(e) | | P = 0.1212 | P = 0.0587 | P = 0.4999 |
| SITE : peritoneum TUMOR : mesothelioma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 3/50(6.0) | 1/50(2.0) | 0/50(0.0) | 7/50(14.0) |
| Adjusted rates(b) | 5.13 | 0.0 | 0.0 | 14.29 |
| Terminal rates(c) | 1/32(3.1) | 0/43(0.0) | 0/38(0.0) | 4/28(14.3) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.0960 | | | |
| Prevalence method(d) | P = 0.0568 | | | |
| Combined analysis(d) | P = 0.0198* | | | |
| Cochran-Armitage test(e) | P = 0.0409* | | | |
| Fisher Exact test(e) | | P = 0.3086 | P = 0.1212 | P = 0.1590 |

(HPT360A)

BAIS3

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

APPENDIX M 2

NEOPLASTIC LESIONS - INCIDENCE AND STATISTICAL ANALYSIS, RAT: FEMALE

(2-YEAR STUDY)

STUDY No. : 0278
 ANIMAL : RAT F344/DuCrj
 SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 9

| Group Name | Control | 1000 ppm | 2000 ppm | 4000 ppm |
|---|-------------|------------|-------------|-------------|
| SITE : lung TUMOR : bronchiolar-alveolar adenoma,adenosquamous carcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 3/50(6.0) | 1/50(2.0) | 2/50(4.0) | 1/50(2.0) |
| Adjusted rates(b) | 6.67 | 2.50 | 4.08 | 3.03 |
| Terminal rates(c) | 3/45(6.7) | 1/40(2.5) | 1/43(2.3) | 0/30(0.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.7590 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.3979 | | | |
| Fisher Exact test(e) | | P = 0.3086 | P = 0.4999 | P = 0.3086 |
| SITE : spleen TUMOR : mononuclear cell leukemia | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 2/50(4.0) | 4/50(8.0) | 8/50(16.0) | 7/50(14.0) |
| Adjusted rates(b) | 2.22 | 7.50 | 9.30 | 10.00 |
| Terminal rates(c) | 1/45(2.2) | 3/40(7.5) | 4/43(9.3) | 3/30(10.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.0375* | | | |
| Prevalence method(d) | P = 0.1001 | | | |
| Combined analysis(d) | P = 0.0151* | | | |
| Cochran-Armitage test(e) | P = 0.0793 | | | |
| Fisher Exact test(e) | | P = 0.3389 | P = 0.0458* | P = 0.0798 |
| SITE : liver TUMOR : hepatocellular adenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 2/50(4.0) | 0/50(0.0) | 0/50(0.0) | 3/50(6.0) |
| Adjusted rates(b) | 4.44 | 0.0 | 0.0 | 9.68 |
| Terminal rates(c) | 2/45(4.4) | 0/40(0.0) | 0/43(0.0) | 2/30(6.7) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.1002 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.3196 | | | |
| Fisher Exact test(e) | | P = 0.2475 | P = 0.2475 | P = 0.4999 |

STUDY No. : 0278
ANIMAL : RAT F344/DuCrj
SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 10

| Group Name | Control | 1000 ppm | 2000 ppm | 4000 ppm |
|--|--------------|--------------|--------------|--------------|
| SITE : liver TUMOR : hepatocellular adenoma, hepatocellular carcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 2/50(4.0) | 0/50(0.0) | 0/50(0.0) | 3/50(6.0) |
| Adjusted rates(b) | 4.44 | 0.0 | 0.0 | 9.68 |
| Terminal rates(c) | 2/45(4.4) | 0/40(0.0) | 0/43(0.0) | 2/30(6.7) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.1002 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.3196 | | | |
| Fisher Exact test(e) | | P = 0.2475 | P = 0.2475 | P = 0.4999 |
| SITE : pituitary gland TUMOR : adenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 18/50(36.0) | 28/50(56.0) | 24/50(48.0) | 19/50(38.0) |
| Adjusted rates(b) | 37.78 | 53.19 | 51.16 | 42.42 |
| Terminal rates(c) | 17/45(37.8) | 19/40(47.5) | 22/43(51.2) | 12/30(40.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.1991 | | | |
| Prevalence method(d) | P = 0.5048 | | | |
| Combined analysis(d) | P = 0.3817 | | | |
| Cochran-Armitage test(e) | P = 0.7183 | | | |
| Fisher Exact test(e) | | P = 0.0353* | P = 0.1558 | P = 0.4991 |
| SITE : pituitary gland TUMOR : adenoma, adenocarcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 19/50(38.0) | 29/50(58.0) | 24/50(48.0) | 19/50(38.0) |
| Adjusted rates(b) | 37.78 | 55.32 | 51.16 | 42.42 |
| Terminal rates(c) | 17/45(37.8) | 20/40(50.0) | 22/43(51.2) | 12/30(40.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.3387 | | | |
| Prevalence method(d) | P = 0.5659 | | | |
| Combined analysis(d) | P = 0.4988 | | | |
| Cochran-Armitage test(e) | P = 0.5485 | | | |
| Fisher Exact test(e) | | P = 0.0356* | P = 0.2101 | P = 0.4173 |

STUDY No. : 0278
ANIMAL : RAT F344/DuCrj
SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 11

| Group Name | Control | 1000 ppm | 2000 ppm | 4000 ppm |
|---|-------------|-------------|-------------|-------------|
| SITE : thyroid TUMOR : C-cell adenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 5/49(10.2) | 3/50(6.0) | 7/50(14.0) | 6/50(12.0) |
| Adjusted rates(b) | 11.36 | 7.50 | 16.28 | 15.00 |
| Terminal rates(c) | 5/44(11.4) | 3/40(7.5) | 7/43(16.3) | 3/30(10.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.1628 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.5255 | | | |
| Fisher Exact test(e) | | P = 0.3462 | P = 0.3945 | P = 0.4852 |
| SITE : thyroid TUMOR : C-cell adenoma,C-cell carcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 5/49(10.2) | 4/50(8.0) | 8/50(16.0) | 7/50(14.0) |
| Adjusted rates(b) | 11.36 | 10.00 | 18.60 | 15.00 |
| Terminal rates(c) | 5/44(11.4) | 4/40(10.0) | 8/43(18.6) | 3/30(10.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.1069 | | | |
| Prevalence method(d) | P = 0.1758 | | | |
| Combined analysis(d) | P = 0.1069 | | | |
| Cochran-Armitage test(e) | P = 0.3937 | | | |
| Fisher Exact test(e) | | P = 0.4873 | P = 0.2902 | P = 0.3945 |
| SITE : adrenal gland TUMOR : pheochromocytoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 4/50(8.0) | 2/50(4.0) | 4/50(8.0) | 2/50(4.0) |
| Adjusted rates(b) | 8.89 | 5.00 | 8.51 | 4.76 |
| Terminal rates(c) | 4/45(8.9) | 2/40(5.0) | 3/43(7.0) | 1/30(3.3) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.6688 | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.5459 | | | |
| Fisher Exact test(e) | | P = 0.3389 | P = 0.3573 | P = 0.3389 |

STUDY No. : 0278
ANIMAL : RAT F344/DuCrj
SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 12

| Group Name | Control | 1000 ppm | 2000 ppm | 4000 ppm |
|--|---------------|--------------|-------------|--------------|
| SITE : uterus TUMOR : endometrial stromal polyp | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 8/50(16.0) | 11/50(22.0) | 6/50(12.0) | 9/50(18.0) |
| Adjusted rates(b) | 17.39 | 21.28 | 13.95 | 20.00 |
| Terminal rates(c) | 7/45(15.6) | 8/40(20.0) | 6/43(14.0) | 6/30(20.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.0152* | | | |
| Prevalence method(d) | P = 0.6589 | | | |
| Combined analysis(d) | P = 0.3162 | | | |
| Cochran-Armitage test(e) | P = 0.9493 | | | |
| Fisher Exact test(e) | | P = 0.3059 | P = 0.3875 | P = 0.4995 |
| SITE : uterus TUMOR : endometrial stromal sarcoma, leiomyosarcoma | | | | |
| 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 | 0.0 |
| Terminal rates(c) | 0/45(0.0) | 0/40(0.0) | 0/43(0.0) | 0/30(0.0) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.0034**? | | | |
| Prevalence method(d) | P = ----- | | | |
| Combined analysis(d) | P = 0.0034**? | | | |
| Cochran-Armitage test(e) | P = 0.0079** | | | |
| Fisher Exact test(e) | | P = 0.5000 | P = 0.5000 | P = 0.1212 |
| SITE : mammary gland TUMOR : fibroadenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 7/50(14.0) | 7/50(14.0) | 9/50(18.0) | 14/50(28.0) |
| Adjusted rates(b) | 15.56 | 15.00 | 20.93 | 43.33 |
| Terminal rates(c) | 7/45(15.6) | 6/40(15.0) | 9/43(20.9) | 13/30(43.3) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.0029** | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.0454* | | | |
| Fisher Exact test(e) | | P = 0.3866 | P = 0.3932 | P = 0.0699 |

STUDY No. : 0278
ANIMAL : RAT F344/DuCrj
SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 13

| Group Name | Control | 1000 ppm | 2000 ppm | 4000 ppm |
|---|--------------|-------------|--------------|--------------|
| SITE : mammary gland TUMOR : adenoma,fibroadenoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 7/50(14.0) | 8/50(16.0) | 10/50(20.0) | 14/50(28.0) |
| Adjusted rates(b) | 15.56 | 17.50 | 23.26 | 43.33 |
| Terminal rates(c) | 7/45(15.6) | 7/40(17.5) | 10/43(23.3) | 13/30(43.3) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = ----- | | | |
| Prevalence method(d) | P = 0.0035** | | | |
| Combined analysis(d) | P = ----- | | | |
| Cochran-Armitage test(e) | P = 0.0574 | | | |
| Fisher Exact test(e) | | P = 0.4996 | P = 0.2980 | P = 0.0699 |
| SITE : mammary gland TUMOR : adenoma,fibroadenoma,adenocarcinoma | | | | |
| Tumor rate | | | | |
| Overall rates(a) | 7/50(14.0) | 9/50(18.0) | 10/50(20.0) | 14/50(28.0) |
| Adjusted rates(b) | 15.56 | 18.18 | 23.26 | 43.33 |
| Terminal rates(c) | 7/45(15.6) | 7/40(17.5) | 10/43(23.3) | 13/30(43.3) |
| Statistical analysis | | | | |
| Peto test | | | | |
| Standard method(d) | P = 0.5814 | | | |
| Prevalence method(d) | P = 0.0038** | | | |
| Combined analysis(d) | P = 0.0056** | | | |
| Cochran-Armitage test(e) | P = 0.0730 | | | |
| Fisher Exact test(e) | | P = 0.3932 | P = 0.2980 | P = 0.0699 |

(HPT360A)

BAIS3

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

APPENDIX N 1

HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR: SUMMARY,
RAT: MALE: ALL ANIMALS
(2-YEAR STUDY)

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 1

| Organ | Findings | Group Name No. of Animals on Study | Control 50 | 1000 ppm 50 | 2000 ppm 50 | 4000 ppm 50 |
|----------------------------------|------------------------------|---------------------------------------|---------------|----------------|----------------|----------------|
| [Integumentary system/appandage] | | | | | | |
| subcutis | Leukemic cell infiltration | | <50> 0 | <50> 0 | <50> 1 | <50> 0 |
| [Respiratory system] | | | | | | |
| nasal cavit | Leukemic cell infiltration | | <50> 1 | <50> 1 | <50> 4 | <50> 0 |
| lung | Leukemic cell infiltration | | <50> 2 | <50> 2 | <50> 3 | <50> 2 |
| | metastasis:liver tumor | | 1 | 0 | 0 | 0 |
| | metastasis:thyroid tumor | | 1 | 0 | 0 | 1 |
| | metastasis:peritoneum tumor | | 1 | 0 | 0 | 1 |
| | metastasis:subcutis tumor | | 0 | 0 | 1 | 1 |
| | metastasis:bone tumor | | 0 | 0 | 1 | 0 |
| [Hematopoietic system] | | | | | | |
| bone marrow | Leukemic cell infiltration | | <50> 2 | <50> 0 | <50> 5 | <50> 3 |
| lymph node | Leukemic cell infiltration | | <50> 2 | <50> 1 | <50> 2 | <50> 1 |
| | metastasis:bone marrow tumor | | 0 | 1 | 0 | 0 |
| spleen | Leukemic cell infiltration | | <50> 1 | <50> 0 | <50> 1 | <50> 0 |

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

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 2

| Group Name | | Control | 1000 ppm | 2000 ppm | 4000 ppm |
|-------------------------|--|-----------|-----------|-----------|-----------|
| No. of Animals on Study | | 50 | 50 | 50 | 50 |
| Organ | Findings | | | | |
| [Hematopoietic system] | | | | | |
| spleen | metastasis:liver tumor | <50> 1 | <50> 0 | <50> 0 | <50> 0 |
| | metastasis:peritoneum tumor | 0 | 0 | 0 | 2 |
| | metastasis:bone marrow tumor | 0 | 1 | 0 | 0 |
| [Circulatory system] | | | | | |
| heart | leukemic cell infiltration | <50> 0 | <50> 0 | <50> 0 | <50> 1 |
| | | | | | |
| [Digestive system] | | | | | |
| salivary gl | leukemic cell infiltration | <50> 0 | <50> 0 | <50> 1 | <50> 0 |
| | metastasis:peritoneum tumor | 0 | 0 | 0 | 1 |
| stomach | leukemic cell infiltration | <50> 0 | <50> 0 | <50> 1 | <50> 0 |
| | metastasis:peritoneum tumor | 1 | 0 | 0 | 2 |
| small intes | leukemic cell infiltration | <50> 0 | <50> 0 | <50> 1 | <50> 0 |
| | metastasis:peritoneum tumor | 1 | 0 | 0 | 0 |
| large intes | leukemic cell infiltration | <50> 0 | <50> 0 | <50> 1 | <50> 1 |
| | metastasis:peritoneum tumor | 1 | 0 | 0 | 0 |
| < a > | a : Number of animals examined at the site | | | | |
| b | b : Number of animals with lesion | | | | |

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 3

| Group Name No. of Animals on Study | | Control 50 | 1000 ppm 50 | 2000 ppm 50 | 4000 ppm 50 |
|---------------------------------------|------------------------------|---------------|----------------|----------------|----------------|
| Organ | Findings | | | | |
| [Digestive system] | | | | | |
| liver | leukemic cell infiltration | <50> 2 | <50> 3 | <50> 8 | <50> 4 |
| | metastasis:peritoneum tumor | 0 | 0 | 0 | 1 |
| | metastasis:bone marrow tumor | 0 | 1 | 0 | 0 |
| pancreas | leukemic cell infiltration | <50> 0 | <50> 0 | <50> 1 | <50> 0 |
| | metastasis:peritoneum tumor | 2 | 0 | 0 | 5 |
| [Urinary system] | | | | | |
| kidney | leukemic cell infiltration | <50> 0 | <50> 1 | <50> 4 | <50> 1 |
| | metastasis:peritoneum tumor | 0 | 0 | 0 | 1 |
| urin bladd | leukemic cell infiltration | <50> 1 | <50> 0 | <50> 0 | <49> 0 |
| [Endocrine system] | | | | | |
| pituitary | leukemic cell infiltration | <50> 1 | <50> 1 | <50> 1 | <50> 0 |
| | leukemic cell infiltration | <50> 0 | <50> 0 | <50> 0 | <50> 1 |
| adrenal | leukemic cell infiltration | <50> 1 | <50> 1 | <50> 1 | <50> 0 |
| | metastasis:liver tumor | 1 | 0 | 0 | 0 |

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

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 4

| Organ | Findings | Group Name No. of Animals on Study | Control 50 | 1000 ppm 50 | 2000 ppm 50 | 4000 ppm 50 |
|----------------------------------|-----------------------------|---------------------------------------|---------------|----------------|----------------|----------------|
| [Endocrine system] | | | | | | |
| adrenal | metastasis:peritoneum tumor | | <50> 0 | <50> 0 | <50> 0 | <50> 1 |
| [Reproductive system] | | | | | | |
| testis | leukemic cell infiltration | | <50> 2 | <50> 0 | <50> 3 | <50> 1 |
| epididymis | leukemic cell infiltration | | <50> 0 | <50> 0 | <50> 1 | <50> 0 |
| prostate | leukemic cell infiltration | | <50> 0 | <50> 0 | <50> 2 | <50> 0 |
| [Nervous system] | | | | | | |
| brain | leukemic cell infiltration | | <50> 1 | <50> 1 | <50> 1 | <50> 0 |
| | metastasis:pituitary tumor | | 1 | 0 | 0 | 0 |
| spinal cord | leukemic cell infiltration | | <50> 1 | <50> 0 | <50> 0 | <50> 0 |
| [Special sense organs/appandage] | | | | | | |
| Harder gl | leukemic cell infiltration | | <50> 0 | <50> 0 | <50> 0 | <50> 1 |
| [Body cavities] | | | | | | |
| pleura | metastasis:subcutis tumor | | <50> 0 | <50> 0 | <50> 1 | <50> 0 |

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

STUDY NO. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 5

| | | Group Name | Control | 1000 ppm | 2000 ppm | 4000 ppm |
|-----------------|--|-------------------------|-----------|-----------|-----------|-----------|
| | | No. of Animals on Study | 50 | 50 | 50 | 50 |
| Organ | Findings | | | | | |
| [Body cavities] | | | | | | |
| pleura | metastasis:lung tumor | | <50> 1 | <50> 0 | <50> 0 | <50> 0 |
| mediastinum | metastasis:peritoneum tumor | | <50> 1 | <50> 0 | <50> 0 | <50> 0 |
| retroperit | leukemic cell infiltration | | <50> 0 | <50> 0 | <50> 1 | <50> 0 |
| < a > | a : Number of animals examined at the site | | | | | |
| b | b : Number of animals with lesion | | | | | |

(JPT150)

BAIS3

APPENDIX N 2

HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR: SUMMARY,
RAT: MALE: DEAD AND MORIBUND ANIMALS
(2-YEAR STUDY)

STUDY NO. : 0278
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 1

| Organ | Findings | Group Name No. of Animals on Study | Control 18 | 1000 ppm 7 | 2000 ppm 12 | 4000 ppm 22 |
|----------------------------------|--|---------------------------------------|---------------|---------------|----------------|----------------|
| [Integumentary system/appandage] | | | | | | |
| subcutis | leukemic cell infiltration | | <18> 0 | < 7> 0 | <12> 1 | <22> 0 |
| [Respiratory system] | | | | | | |
| nasal cavit | leukemic cell infiltration | | <18> 1 | < 7> 1 | <12> 3 | <22> 0 |
| lung | leukemic cell infiltration | | <18> 2 | < 7> 1 | <12> 2 | <22> 2 |
| | metastasis:liver tumor | | 1 | 0 | 0 | 0 |
| | metastasis:peritoneum tumor | | 1 | 0 | 0 | 1 |
| | metastasis:subcutis tumor | | 0 | 0 | 1 | 1 |
| [Hematopoietic system] | | | | | | |
| bone marrow | leukemic cell infiltration | | <18> 2 | < 7> 0 | <12> 4 | <22> 2 |
| lymph node | leukemic cell infiltration | | <18> 2 | < 7> 0 | <12> 1 | <22> 1 |
| | metastasis:bone marrow tumor | | 0 | 1 | 0 | 0 |
| spleen | leukemic cell infiltration | | <18> 1 | < 7> 0 | <12> 1 | <22> 0 |
| | metastasis:liver tumor | | 1 | 0 | 0 | 0 |
| | metastasis:peritoneum tumor | | 0 | 0 | 0 | 1 |
| < a > | a : Number of animals examined at the site | | | | | |
| b | b : Number of animals with lesion | | | | | |

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 2

| Group Name No. of Animals on Study | | Control 18 | 1000 ppm 7 | 2000 ppm 12 | 4000 ppm 22 |
|---------------------------------------|------------------------------|---------------|---------------|----------------|----------------|
| Organ | Findings | | | | |
| [Hematopoietic system] | | | | | |
| spleen | metastasis:bone marrow tumor | <18> 0 | < 7> 1 | <12> 0 | <22> 0 |
| [Circulatory system] | | | | | |
| heart | leukemic cell infiltration | <18> 0 | < 7> 0 | <12> 0 | <22> 1 |
| [Digestive system] | | | | | |
| salivary gl | leukemic cell infiltration | <18> 0 | < 7> 0 | <12> 1 | <22> 0 |
| stomach | leukemic cell infiltration | <18> 0 | < 7> 0 | <12> 1 | <22> 0 |
| | metastasis:peritoneum tumor | 1 | 0 | 0 | 1 |
| small intes | leukemic cell infiltration | <18> 0 | < 7> 0 | <12> 1 | <22> 0 |
| | metastasis:peritoneum tumor | 1 | 0 | 0 | 0 |
| large intes | leukemic cell infiltration | <18> 0 | < 7> 0 | <12> 1 | <22> 1 |
| | metastasis:peritoneum tumor | 1 | 0 | 0 | 0 |
| liver | leukemic cell infiltration | <18> 2 | < 7> 1 | <12> 5 | <22> 3 |
| | metastasis:bone marrow tumor | 0 | 1 | 0 | 0 |
| pancreas | leukemic cell infiltration | <18> 0 | < 7> 0 | <12> 1 | <22> 0 |

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

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 3

| Organ | Findings | Group Name No. of Animals on Study | Control 18 | 1000 ppm 7 | 2000 ppm 12 | 4000 ppm 22 |
|-----------------------|-----------------------------|---------------------------------------|---------------|---------------|----------------|----------------|
| [Digestive system] | | | | | | |
| pancreas | metastasis:peritoneum tumor | | <18> 2 | < 7> 0 | <12> 0 | <22> 3 |
| [Urinary system] | | | | | | |
| kidney | leukemic cell infiltration | | <18> 0 | < 7> 1 | <12> 3 | <22> 1 |
| | metastasis:peritoneum tumor | | 0 | 0 | 0 | 1 |
| urin bladd | leukemic cell infiltration | | <18> 1 | < 7> 0 | <12> 0 | <22> 0 |
| [Endocrine system] | | | | | | |
| pituitary | leukemic cell infiltration | | <18> 1 | < 7> 1 | <12> 1 | <22> 0 |
| thyroid | leukemic cell infiltration | | <18> 0 | < 5> 0 | <12> 0 | <22> 1 |
| adrenal | leukemic cell infiltration | | <18> 1 | < 7> 1 | <12> 1 | <22> 0 |
| | metastasis:liver tumor | | 1 | 0 | 0 | 0 |
| | metastasis:peritoneum tumor | | 0 | 0 | 0 | 1 |
| [Reproductive system] | | | | | | |
| testis | leukemic cell infiltration | | <18> 2 | < 7> 0 | <12> 3 | <22> 0 |

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

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 4

| Group Name No. of Animals on Study | | Control 18 | 1000 ppm 7 | 2000 ppm 12 | 4000 ppm 22 |
|---------------------------------------|-----------------------------|---------------|---------------|----------------|----------------|
| Organ | Findings | | | | |
| [Reproductive system] | | | | | |
| epididymis | leukemic cell infiltration | <18> 0 | < 7> 0 | <12> 1 | <22> 0 |
| prostate | leukemic cell infiltration | <18> 0 | < 7> 0 | <12> 1 | <22> 0 |
| [Nervous system] | | | | | |
| brain | leukemic cell infiltration | <18> 1 | < 7> 1 | <12> 1 | <22> 0 |
| | metastasis:pituitary tumor | 1 | 0 | 0 | 0 |
| spinal cord | leukemic cell infiltration | <18> 1 | < 7> 0 | <12> 0 | <22> 0 |
| [Special sense organs/appandage] | | | | | |
| Harder gl | leukemic cell infiltration | <18> 0 | < 7> 0 | <12> 0 | <22> 1 |
| [Body cavities] | | | | | |
| pleura | metastasis:subcutis tumor | <18> 0 | < 7> 0 | <12> 1 | <22> 0 |
| | metastasis:lung tumor | 1 | 0 | 0 | 0 |
| mediastinum | metastasis:peritoneum tumor | <18> 1 | < 7> 0 | <12> 0 | <22> 0 |

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

APPENDIX N 3

HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR: SUMMARY,
RAT: MALE: SACRIFICED ANIMALS
(2-YEAR STUDY)

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 1

| Organ | Findings | Group Name No. of Animals on Study | Control 32 | 1000 ppm 43 | 2000 ppm 38 | 4000 ppm 28 |
|------------------------|-----------------------------|---------------------------------------|---------------|----------------|----------------|----------------|
| [Respiratory system] | | | | | | |
| nasal cavit | | | <32> | <43> | <38> | <28> |
| | leukemic cell infiltration | | 0 | 0 | 1 | 0 |
| lung | | | <32> | <43> | <38> | <28> |
| | leukemic cell infiltration | | 0 | 1 | 1 | 0 |
| | metastasis:thyroid tumor | | 1 | 0 | 0 | 1 |
| | metastasis:bone tumor | | 0 | 0 | 1 | 0 |
| [Hematopoietic system] | | | | | | |
| bone marrow | | | <32> | <43> | <38> | <28> |
| | leukemic cell infiltration | | 0 | 0 | 1 | 1 |
| lymph node | | | <32> | <43> | <38> | <28> |
| | leukemic cell infiltration | | 0 | 1 | 1 | 0 |
| spleen | | | <32> | <43> | <38> | <28> |
| | metastasis:peritoneum tumor | | 0 | 0 | 0 | 1 |
| [Digestive system] | | | | | | |
| salivary gl | | | <32> | <43> | <38> | <28> |
| | metastasis:peritoneum tumor | | 0 | 0 | 0 | 1 |
| stomach | | | <32> | <43> | <38> | <28> |
| | metastasis:peritoneum tumor | | 0 | 0 | 0 | 1 |
| liver | | | <32> | <43> | <38> | <28> |
| | leukemic cell infiltration | | 0 | 2 | 3 | 1 |
| | metastasis:peritoneum tumor | | 0 | 0 | 0 | 1 |

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

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 2

| Group Name No. of Animals on Study | | Control 32 | 1000 ppm 43 | 2000 ppm 38 | 4000 ppm 28 |
|---------------------------------------|-----------------------------|--|----------------|----------------|----------------|
| Organ | Findings | | | | |
| [Digestive system] | | | | | |
| pancreas | metastasis:peritoneum tumor | <32> 0 | <43> 0 | <38> 0 | <28> 2 |
| [Urinary system] | | | | | |
| kidney | leukemic cell infiltration | <32> 0 | <43> 0 | <38> 1 | <28> 0 |
| [Reproductive system] | | | | | |
| testis | leukemic cell infiltration | <32> 0 | <43> 0 | <38> 0 | <28> 1 |
| prostate | leukemic cell infiltration | <32> 0 | <43> 0 | <38> 1 | <28> 0 |
| [Body cavities] | | | | | |
| retroperit | leukemic cell infiltration | <32> 0 | <43> 0 | <38> 1 | <28> 0 |
| < a > | | a : Number of animals examined at the site | | | |
| b | | b : Number of animals with lesion | | | |

(JPT150)

BAIS3

APPENDIX N 4

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

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 6

| Organ | Findings | Group Name No. of Animals on Study | Control 50 | 1000 ppm 50 | 2000 ppm 50 | 4000 ppm 50 |
|------------------------|----------------------------|---------------------------------------|---------------|----------------|----------------|----------------|
| [Respiratory system] | | | | | | |
| nasal cavit | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 0 | 0 | 0 | 1 |
| trachea | | | <50> | <50> | <50> | <50> |
| | metastasis:thyroid tumor | | 0 | 0 | 0 | 1 |
| lung | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 2 | 4 | 5 | 3 |
| | metastasis:uterus tumor | | 0 | 0 | 0 | 1 |
| | metastasis:thyroid tumor | | 0 | 0 | 0 | 1 |
| | metastasis:bone tumor | | 0 | 0 | 1 | 0 |
| [Hematopoietic system] | | | | | | |
| bone marrow | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 1 | 3 | 5 | 8 |
| | metastasis:liver tumor | | 0 | 0 | 1 | 0 |
| lymph node | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 0 | 1 | 2 | 1 |
| | metastasis:uterus tumor | | 0 | 0 | 0 | 1 |
| | metastasis:bone tumor | | 0 | 0 | 1 | 0 |
| spleen | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 0 | 1 | 1 | 0 |
| | metastasis:liver tumor | | 0 | 0 | 1 | 0 |
| [Circulatory system] | | | | | | |
| heart | | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | | 0 | 1 | 1 | 0 |

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

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 7

| Group Name | | Control | 1000 ppm | 2000 ppm | 4000 ppm |
|-------------------------|----------------------------|---------|----------|----------|----------|
| No. of Animals on Study | | 50 | 50 | 50 | 50 |
| Organ | Findings | | | | |
| [Digestive system] | | | | | |
| stomach | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | 0 | 1 | 2 | 0 |
| small intes | | <50> | <50> | <50> | <50> |
| | metastasis:uterus tumor | 0 | 0 | 0 | 1 |
| liver | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | 2 | 5 | 7 | 6 |
| | | | | | |
| | metastasis:uterus tumor | 0 | 0 | 0 | 1 |
| pancreas | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | 0 | 2 | 1 | 0 |
| [Urinary system] | | | | | |
| kidney | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | 0 | 3 | 4 | 1 |
| urin bladd | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | 0 | 0 | 1 | 0 |
| [Endocrine system] | | | | | |
| pituitary | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | 0 | 0 | 5 | 1 |
| thyroid | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | 0 | 0 | 1 | 0 |
| adrenal | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | 0 | 2 | 5 | 3 |
| [Reproductive system] | | | | | |
| ovary | | <50> | <50> | <50> | <50> |
| | leukemic cell infiltration | 0 | 0 | 3 | 0 |

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

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 8

| Organ | Findings | Group Name No. of Animals on Study | Control 50 | 1000 ppm 50 | 2000 ppm 50 | 4000 ppm 50 |
|----------------------------------|----------------------------|---------------------------------------|---------------|----------------|----------------|----------------|
| [Reproductive system] | | | | | | |
| ovary | metastasis:uterus tumor | | <50> 0 | <50> 0 | <50> 0 | <50> 1 |
| uterus | leukemic cell infiltration | | <50> 0 | <50> 1 | <50> 1 | <50> 0 |
| vagina | leukemic cell infiltration | | <50> 0 | <50> 0 | <50> 1 | <50> 0 |
| [Nervous system] | | | | | | |
| brain | leukemic cell infiltration | | <50> 0 | <50> 2 | <50> 1 | <50> 0 |
| | metastasis:pituitary tumor | | 1 | 1 | 0 | 0 |
| spinal cord | leukemic cell infiltration | | <50> 0 | <50> 0 | <50> 2 | <50> 0 |
| [Special sense organs/appandage] | | | | | | |
| eye | leukemic cell infiltration | | <50> 0 | <50> 0 | <50> 1 | <50> 0 |
| Harder gl | leukemic cell infiltration | | <50> 0 | <50> 0 | <50> 1 | <50> 1 |
| [Body cavities] | | | | | | |
| peritoneum | metastasis:uterus tumor | | <50> 0 | <50> 0 | <50> 0 | <50> 1 |

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

APPENDIX N 5

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

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 5

| Organ | Findings | Group Name No. of Animals on Study | Control 5 | 1000 ppm 10 | 2000 ppm 7 | 4000 ppm 20 |
|------------------------|--|---------------------------------------|--------------|----------------|---------------|----------------|
| [Respiratory system] | | | | | | |
| nasal cavit | | | < 5> | <10> | < 7> | <20> |
| | leukemic cell infiltration | | 0 | 0 | 0 | 1 |
| trachea | | | < 5> | <10> | < 7> | <20> |
| | metastasis:thyroid tumor | | 0 | 0 | 0 | 1 |
| lung | | | < 5> | <10> | < 7> | <20> |
| | leukemic cell infiltration | | 2 | 3 | 4 | 3 |
| | metastasis:uterus tumor | | 0 | 0 | 0 | 1 |
| | metastasis:thyroid tumor | | 0 | 0 | 0 | 1 |
| | metastasis:bone tumor | | 0 | 0 | 1 | 0 |
| [Hematopoietic system] | | | | | | |
| bone marrow | | | < 5> | <10> | < 7> | <20> |
| | leukemic cell infiltration | | 0 | 2 | 3 | 5 |
| | metastasis:liver tumor | | 0 | 0 | 1 | 0 |
| lymph node | | | < 5> | <10> | < 7> | <20> |
| | leukemic cell infiltration | | 0 | 0 | 2 | 0 |
| | metastasis:uterus tumor | | 0 | 0 | 0 | 1 |
| | metastasis:bone tumor | | 0 | 0 | 1 | 0 |
| spleen | | | < 5> | <10> | < 7> | <20> |
| | leukemic cell infiltration | | 0 | 1 | 0 | 0 |
| | metastasis:liver tumor | | 0 | 0 | 1 | 0 |
| [Circulatory system] | | | | | | |
| heart | | | < 5> | <10> | < 7> | <20> |
| | leukemic cell infiltration | | 0 | 1 | 0 | 0 |
| < a > | a : Number of animals examined at the site | | | | | |
| b | b : Number of animals with lesion | | | | | |

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 6

| Group Name No. of Animals on Study | | Control 5 | 1000 ppm 10 | 2000 ppm 7 | 4000 ppm 20 |
|---------------------------------------|----------------------------|--------------|----------------|---------------|----------------|
| Organ | Findings | | | | |
| [Digestive system] | | | | | |
| stomach | | < 5> | <10> | < 7> | <20> |
| | leukemic cell infiltration | 0 | 1 | 1 | 0 |
| small intes | | < 5> | <10> | < 7> | <20> |
| | metastasis:uterus tumor | 0 | 0 | 0 | 1 |
| liver | | < 5> | <10> | < 7> | <20> |
| | leukemic cell infiltration | 1 | 3 | 4 | 4 |
| | metastasis:uterus tumor | 0 | 0 | 0 | 1 |
| pancreas | | < 5> | <10> | < 7> | <20> |
| | leukemic cell infiltration | 0 | 2 | 0 | 0 |
| [Urinary system] | | | | | |
| kidney | | < 5> | <10> | < 7> | <20> |
| | leukemic cell infiltration | 0 | 3 | 3 | 1 |
| [Endocrine system] | | | | | |
| pituitary | | < 5> | <10> | < 7> | <20> |
| | leukemic cell infiltration | 0 | 0 | 4 | 1 |
| thyroid | | < 5> | <10> | < 7> | <20> |
| | leukemic cell infiltration | 0 | 0 | 1 | 0 |
| adrenal | | < 5> | <10> | < 7> | <20> |
| | leukemic cell infiltration | 0 | 1 | 4 | 2 |
| [Reproductive system] | | | | | |
| ovary | | < 5> | <10> | < 7> | <20> |
| | leukemic cell infiltration | 0 | 0 | 2 | 0 |

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

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 7

| Group Name No. of Animals on Study | | Control 5 | 1000 ppm 10 | 2000 ppm 7 | 4000 ppm 20 |
|---------------------------------------|----------------------------|--------------|----------------|---------------|----------------|
| Organ | Findings | | | | |
| [Reproductive system] | | | | | |
| ovary | | < 5> | <10> | < 7> | <20> |
| | metastasis:uterus tumor | 0 | 0 | 0 | 1 |
| uterus | | < 5> | <10> | < 7> | <20> |
| | leukemic cell infiltration | 0 | 1 | 0 | 0 |
| [Nervous system] | | | | | |
| brain | | < 5> | <10> | < 7> | <20> |
| | leukemic cell infiltration | 0 | 2 | 1 | 0 |
| | metastasis:pituitary tumor | 1 | 0 | 0 | 0 |
| spinal cord | | < 5> | <10> | < 7> | <20> |
| | leukemic cell infiltration | 0 | 0 | 2 | 0 |
| [Special sense organs/appandage] | | | | | |
| Harder gl | | < 5> | <10> | < 7> | <20> |
| | leukemic cell infiltration | 0 | 0 | 0 | 1 |
| [Body cavities] | | | | | |
| peritoneum | | < 5> | <10> | < 7> | <20> |
| | metastasis:uterus tumor | 0 | 0 | 0 | 1 |

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

(JPT150)

BAIS3

APPENDIX N 6

HISTOLOGICAL FINDINGS: METASTASIS OF TUMOR: SUMMARY,
RAT: FEMALE: SACRIFICED ANIMALS
(2-YEAR STUDY)

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 3

| Organ | Findings | Group Name No. of Animals on Study | Control 45 | 1000 ppm 40 | 2000 ppm 43 | 4000 ppm 30 |
|------------------------|----------------------------|---------------------------------------|---------------|----------------|----------------|----------------|
| [Respiratory system] | | | | | | |
| lung | leukemic cell infiltration | | <45> 0 | <40> 1 | <43> 1 | <30> 0 |
| [Hematopoietic system] | | | | | | |
| bone marrow | leukemic cell infiltration | | <45> 1 | <40> 1 | <43> 2 | <30> 3 |
| lymph node | leukemic cell infiltration | | <45> 0 | <40> 1 | <43> 0 | <30> 1 |
| spleen | leukemic cell infiltration | | <45> 0 | <40> 0 | <43> 1 | <30> 0 |
| [Circulatory system] | | | | | | |
| heart | leukemic cell infiltration | | <45> 0 | <40> 0 | <43> 1 | <30> 0 |
| [Digestive system] | | | | | | |
| stomach | leukemic cell infiltration | | <45> 0 | <40> 0 | <43> 1 | <30> 0 |
| liver | leukemic cell infiltration | | <45> 1 | <40> 2 | <43> 3 | <30> 2 |
| pancreas | leukemic cell infiltration | | <45> 0 | <40> 0 | <43> 1 | <30> 0 |
| [Urinary system] | | | | | | |
| kidney | leukemic cell infiltration | | <45> 0 | <40> 0 | <43> 1 | <30> 0 |

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

STUDY NO. : 0278
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 4

| Group Name No. of Animals on Study | | Control 45 | 1000 ppm 40 | 2000 ppm 43 | 4000 ppm 30 |
|---------------------------------------|--|---------------|----------------|----------------|----------------|
| Organ | Findings | | | | |
| [Urinary system] | | | | | |
| urin bladd | leukemic cell infiltration | <45> 0 | <40> 0 | <43> 1 | <30> 0 |
| [Endocrine system] | | | | | |
| pituitary | leukemic cell infiltration | <45> 0 | <40> 0 | <43> 1 | <30> 0 |
| adrenal | leukemic cell infiltration | <45> 0 | <40> 1 | <43> 1 | <30> 1 |
| [Reproductive system] | | | | | |
| ovary | leukemic cell infiltration | <45> 0 | <40> 0 | <43> 1 | <30> 0 |
| uterus | leukemic cell infiltration | <45> 0 | <40> 0 | <43> 1 | <30> 0 |
| vagina | leukemic cell infiltration | <45> 0 | <40> 0 | <43> 1 | <30> 0 |
| [Nervous system] | | | | | |
| brain | metastasis:pituitary tumor | <45> 0 | <40> 1 | <43> 0 | <30> 0 |
| [Special sense organs/appandage] | | | | | |
| eye | leukemic cell infiltration | <45> 0 | <40> 0 | <43> 1 | <30> 0 |
| < a > | a : Number of animals examined at the site | | | | |
| b | b : Number of animals with lesion | | | | |

STUDY NO. : 0278
ANIMAL : RAT F344/DuGrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 5

| | | Group Name | Control | 1000 ppm | 2000 ppm | 4000 ppm |
|----------------------------------|--|-------------------------|-----------|-----------|-----------|-----------|
| | | No. of Animals on Study | 45 | 40 | 43 | 30 |
| Organ | Findings | | | | | |
| [Special sense organs/appandage] | | | | | | |
| Harder gl | leukemic cell infiltration | | <45> 0 | <40> 0 | <43> 1 | <30> 0 |
| < a > | a : Number of animals examined at the site | | | | | |
| b | b : Number of animals with lesion | | | | | |

(JPT150)

BA1S3

APPENDIX O 1

IDENTITY OF DICHLOROMETHANE IN THE 2-YEAR
INHALATION STUDY

IDENTITY OF DICHLOROMETHANE IN THE 2-YEAR INHALATION STUDY

Test Substance : Dichloromethane (Wako Pure Chemical Industries, LTD.)

A. Lot No. : APR5260

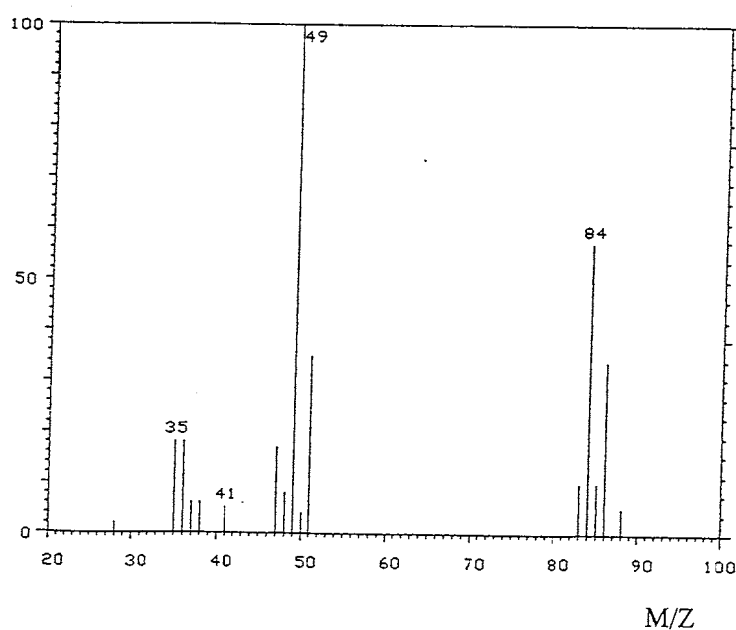
1. Spectral data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Results: The mass spectrum was consistent with literature spectrum.

Determines

Fragment Peak (M/Z)

35

49

84

Literature Values*

Fragment Peak (M/Z)

35

49

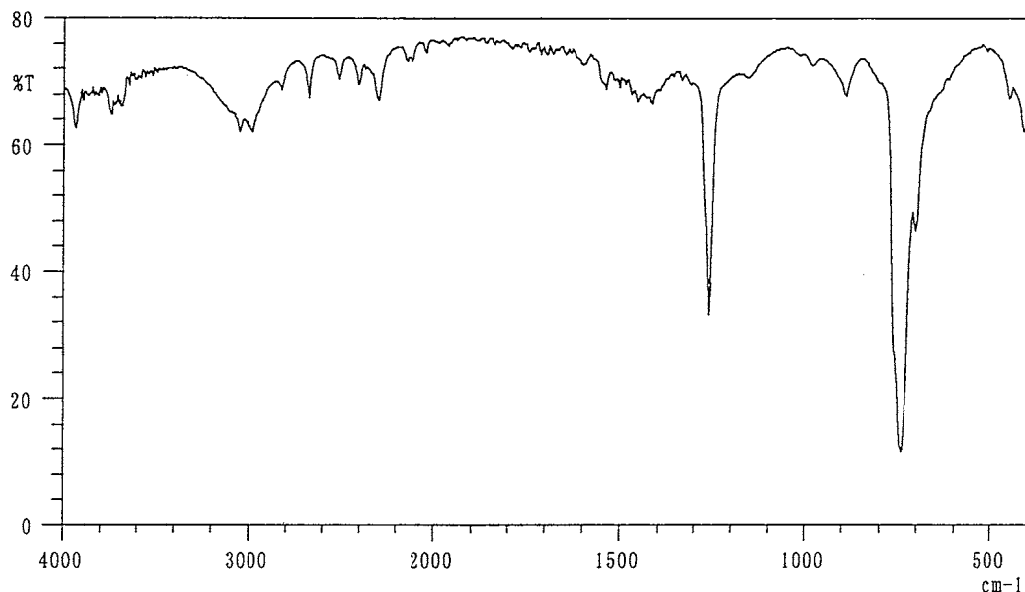
84

(* EPA/NIH Mass Spectral
Data Base (1978) Vol. 1, p. 33.)

Infrared Spectrometry

Instrument : Shimadzu FT-IR 8200PC Infrared Spectrometer

Cell : KBr



Infrared Spectrum of Test Substance

Results: The infrared spectrum was consistent with literature spectrum.

| <u>Determined Values</u> | <u>Literature Values</u> * |
|---------------------------------|---------------------------------|
| Wave Number (cm ⁻¹) | Wave Number (cm ⁻¹) |
| 650~840 | 650~850 |
| 870~940 | 870~940 |
| 970~1000 | 970~1000 |
| 1120~1180 | 1130~1180 |
| 1200~1340 | 1200~1350 |
| 1370~1500 | 1380~1500 |
| 1530~1570 | 1540~1570 |
| 1580~1630 | 1580~1630 |
| 2040~2090 | 2050~2090 |
| 2100~2190 | 2120~2190 |
| 2250~2360 | 2280~2370 |
| 2380~2460 | 2400~2460 |
| 2500~2550 | 2500~2560 |
| 2650~2730 | 2650~2730 |
| 2800~2860 | 2800~2860 |
| 2900~3200 | 2900~3200 |
| 3650~3730 | 3670~3750 |
| 3730~3800 | 3750~3800 |
| 3900~4000 | 3900~4000 |

(*Performed by the WAKO PURE
CHEMICAL INDUSTRIES, LTD.)

2. Conclusions: The test substance was identified as dichloromethane, by the mass spectrum and the infrared spectrum.

B. Lot No. : KCH4634

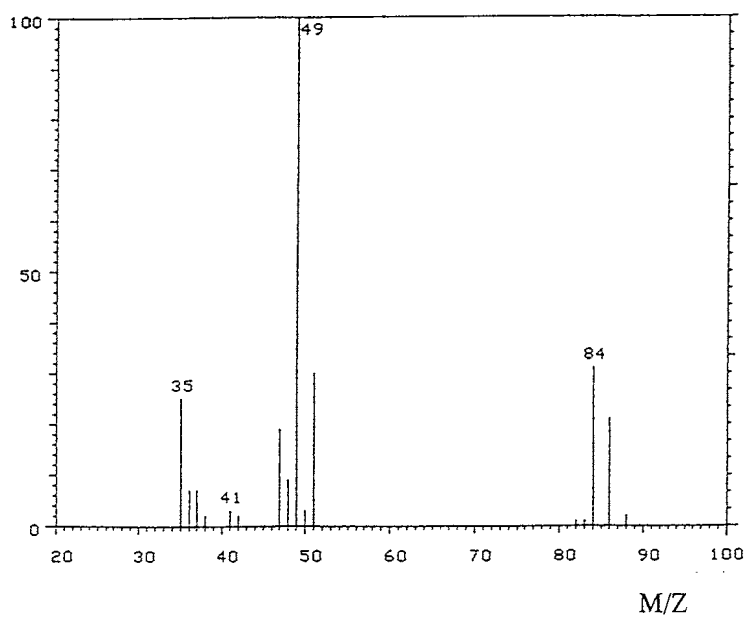
1. Spectral data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Results: The mass spectrum was consistent with literature spectrum.

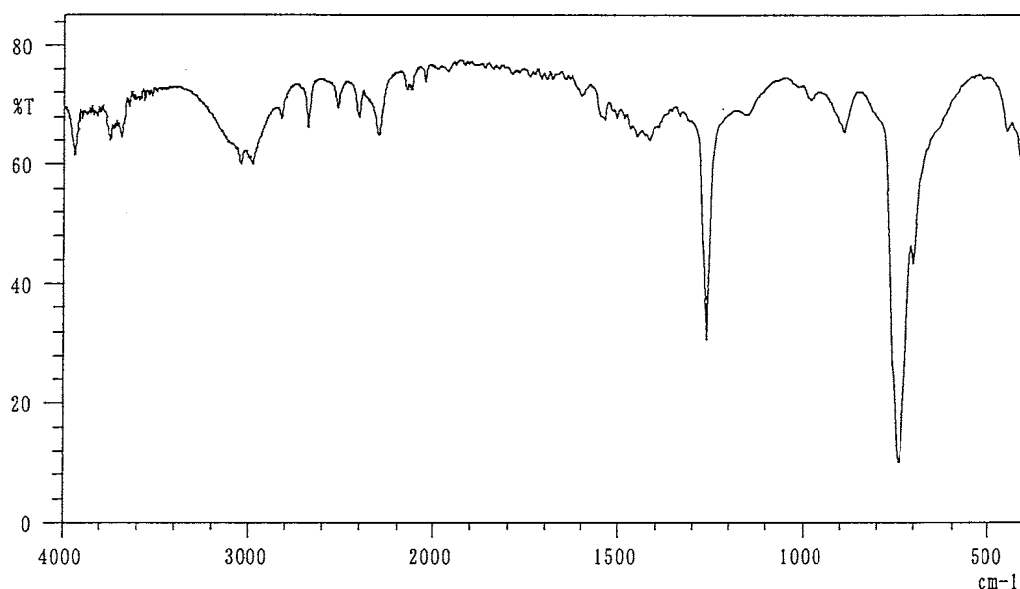
| <u>Determines</u> | <u>Literature Values</u> [*] |
|---------------------|---------------------------------------|
| Fragment Peak (M/Z) | Fragment Peak (M/Z) |
| 35 | 35 |
| 49 | 49 |
| 84 | 84 |

(^{*} EPA/NIH Mass Spectral
Data Base (1978) Vol. 1, p. 33.)

Infrared Spectrometry

Instrument : Shimadzu FT-IR 8200PC Infrared Spectrometer

Cell : KBr



Infrared Spectrum of Test Substance

Results: The infrared spectrum was consistent with literature spectrum.

| <u>Determined Values</u> | <u>Literature Values</u> [*] |
|---------------------------------|---------------------------------------|
| Wave Number (cm ⁻¹) | Wave Number (cm ⁻¹) |
| 650~ 840 | 650~ 850 |
| 870~ 940 | 870~ 940 |
| 970~1000 | 970~1000 |
| 1120~1180 | 1130~1180 |
| 1200~1340 | 1200~1350 |
| 1370~1500 | 1380~1500 |
| 1530~1570 | 1540~1570 |
| 1580~1630 | 1580~1630 |
| 2040~2090 | 2050~2090 |
| 2100~2190 | 2120~2190 |
| 2250~2360 | 2280~2370 |
| 2380~2460 | 2400~2460 |
| 2500~2550 | 2500~2560 |
| 2650~2730 | 2650~2730 |
| 2800~2860 | 2800~2860 |
| 2900~3200 | 2900~3200 |
| 3650~3730 | 3670~3750 |
| 3730~3800 | 3750~3800 |
| 3900~4000 | 3900~4000 |

(*Performed by the WAKO PURE
CHEMICAL INDUSTRIES, LTD.)

2. Conclusions: The test substance was identified as dichloromethane, by the mass spectrum and the infrared spectrum.

C. Lot No. : ESR7256

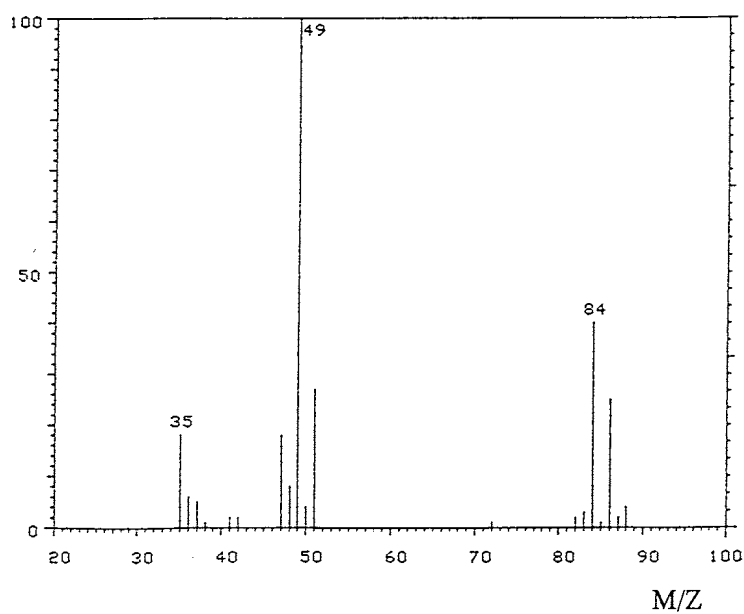
1. Spectral data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Results: The mass spectrum was consistent with literature spectrum.

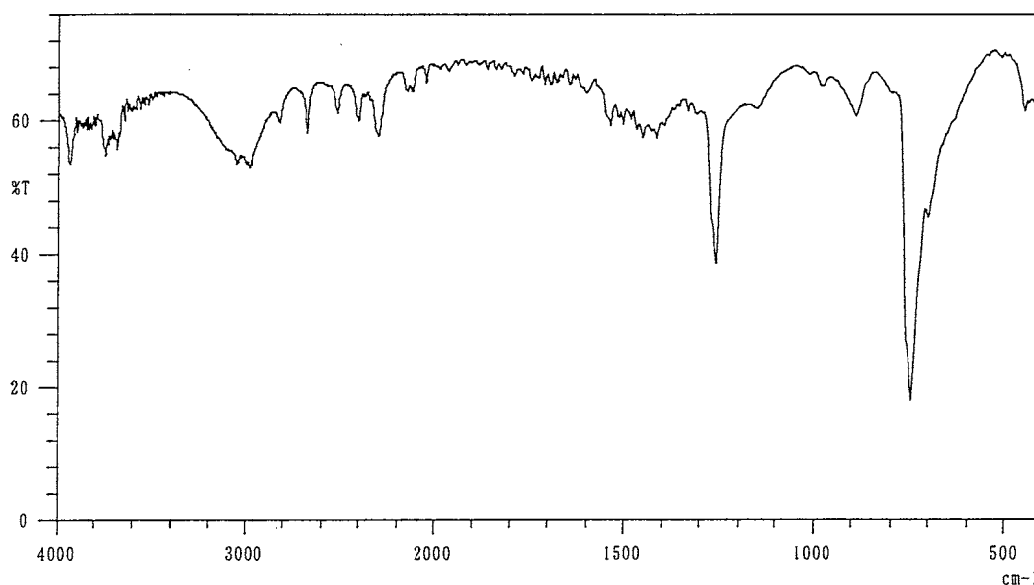
| <u>Determines</u> | <u>Literature Values*</u> |
|---------------------|---------------------------|
| Fragment Peak (M/Z) | Fragment Peak (M/Z) |
| 35 | 35 |
| 49 | 49 |
| 84 | 84 |

(* EPA/NIH Mass Spectral
Data Base (1978) Vol. 1, p. 33.)

Infrared Spectrometry

Instrument : Shimadzu FT-IR 8200PC Infrared Spectrometer

Cell : KBr



Infrared Spectrum of Test Substance

Results: The infrared spectrum was consistent with literature spectrum.

| <u>Determined Values</u> | <u>Literature Values*</u> |
|---------------------------------|--------------------------------|
| Wave Number (cm ⁻¹) | Wave Number(cm ⁻¹) |
| 650~ 840 | 650~ 850 |
| 870~ 940 | 870~ 940 |
| 970~1000 | 970~1000 |
| 1120~1180 | 1130~1180 |
| 1200~1340 | 1200~1350 |
| 1370~1500 | 1380~1500 |
| 1530~1570 | 1540~1570 |
| 1580~1630 | 1580~1630 |
| 2040~2090 | 2050~2090 |
| 2100~2190 | 2120~2190 |
| 2250~2360 | 2280~2370 |
| 2380~2460 | 2400~2460 |
| 2500~2550 | 2500~2560 |
| 2650~2730 | 2650~2730 |
| 2800~2860 | 2800~2860 |
| 2900~3200 | 2900~3200 |
| 3650~3730 | 3670~3750 |
| 3730~3800 | 3750~3800 |
| 3900~4000 | 3900~4000 |

(*Performed by the WAKO PURE
CHEMICAL INDUSTRIES, LTD.)

2. Conclusions: The test substance was identified as dichloromethane, by the mass spectrum and the infrared spectrum.

D. Lot No. : ESM2924

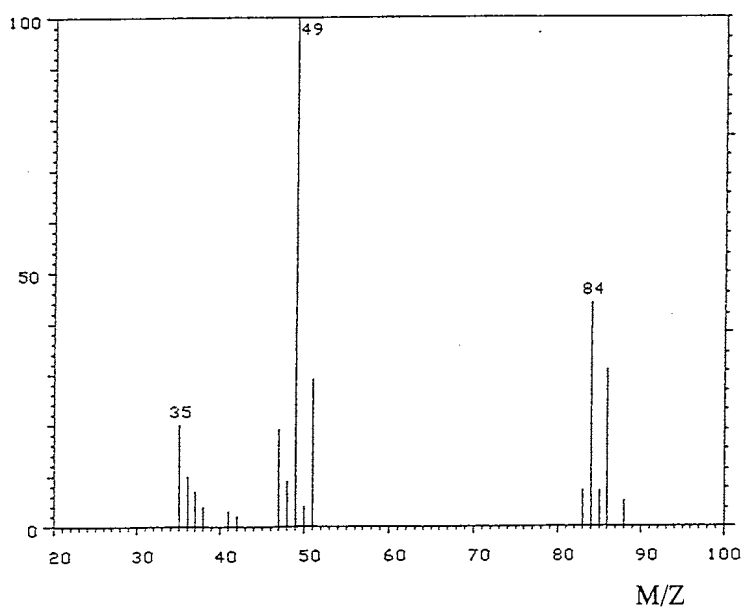
1. Spectral data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Results: The mass spectrum was consistent with literature spectrum.

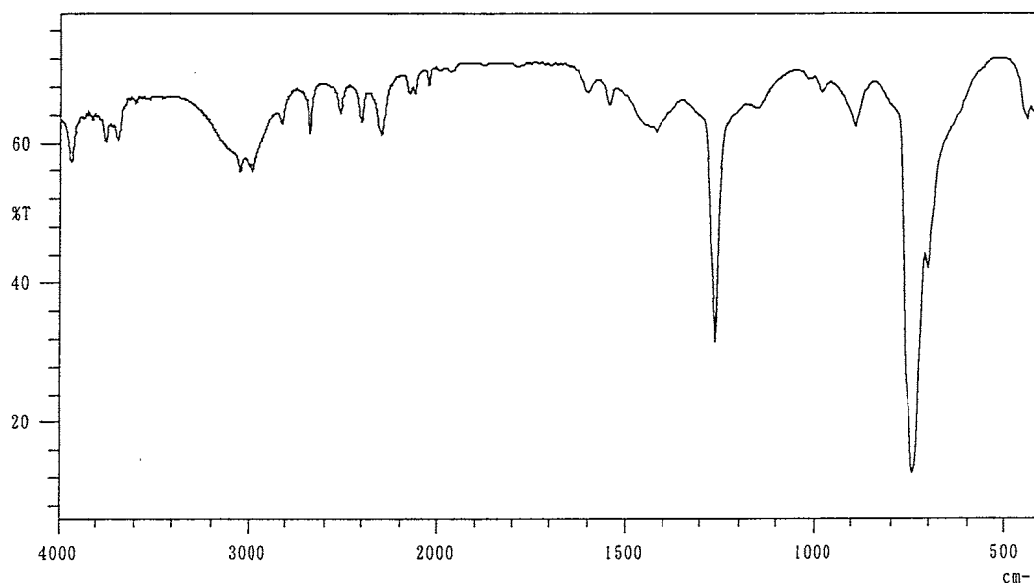
| <u>Determines</u> | <u>Literature Values</u> * |
|---------------------|----------------------------|
| Fragment Peak (M/Z) | Fragment Peak (M/Z) |
| 35 | 35 |
| 49 | 49 |
| 84 | 84 |

(* EPA/NIH Mass Spectral
Data Base (1978) Vol. 1, p. 33.)

Infrared Spectrometry

Instrument : Shimadzu FT-IR 8200PC Infrared Spectrometer

Cell : KBr



Infrared Spectrum of Test Substance

Results: The infrared spectrum was consistent with literature spectrum.

| <u>Determined Values</u> | <u>Literature Values*</u> |
|----------------------------------|----------------------------------|
| Wave Number (cm^{-1}) | Wave Number (cm^{-1}) |
| 650~840 | 650~850 |
| 870~940 | 870~940 |
| 970~1000 | 970~1000 |
| 1120~1180 | 1130~1180 |
| 1200~1340 | 1200~1350 |
| 1370~1500 | 1380~1500 |
| 1530~1570 | 1540~1570 |
| 1580~1630 | 1580~1630 |
| 2040~2090 | 2050~2090 |
| 2100~2190 | 2120~2190 |
| 2250~2360 | 2280~2370 |
| 2380~2460 | 2400~2460 |
| 2500~2550 | 2500~2560 |
| 2650~2730 | 2650~2730 |
| 2800~2860 | 2800~2860 |
| 2900~3200 | 2900~3200 |
| 3650~3730 | 3670~3750 |
| 3730~3800 | 3750~3800 |
| 3900~4000 | 3900~4000 |

(*Performed by the WAKO PURE
CHEMICAL INDUSTRIES, LTD.)

2. Conclusions: The test substance was identified as dichloromethane, by the mass spectrum and the infrared spectrum.

E. Lot No. : ESJ4826

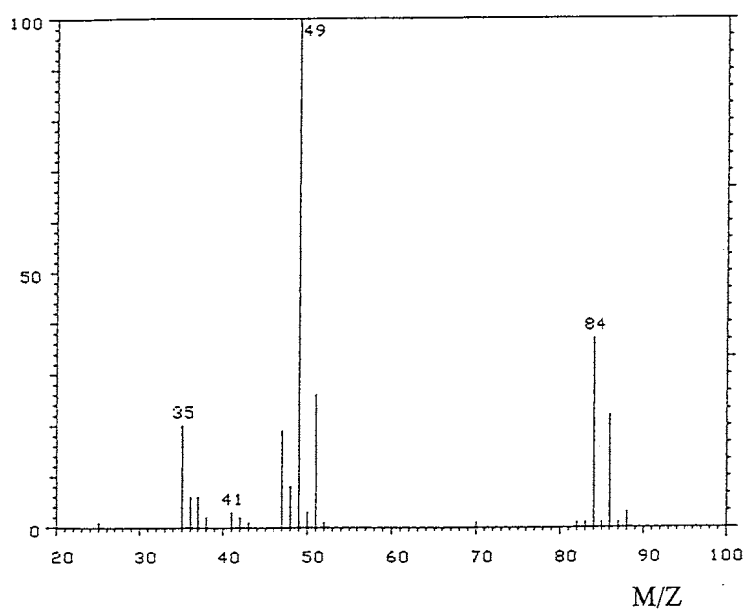
1. Spectral data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Results: The mass spectrum was consistent with literature spectrum.

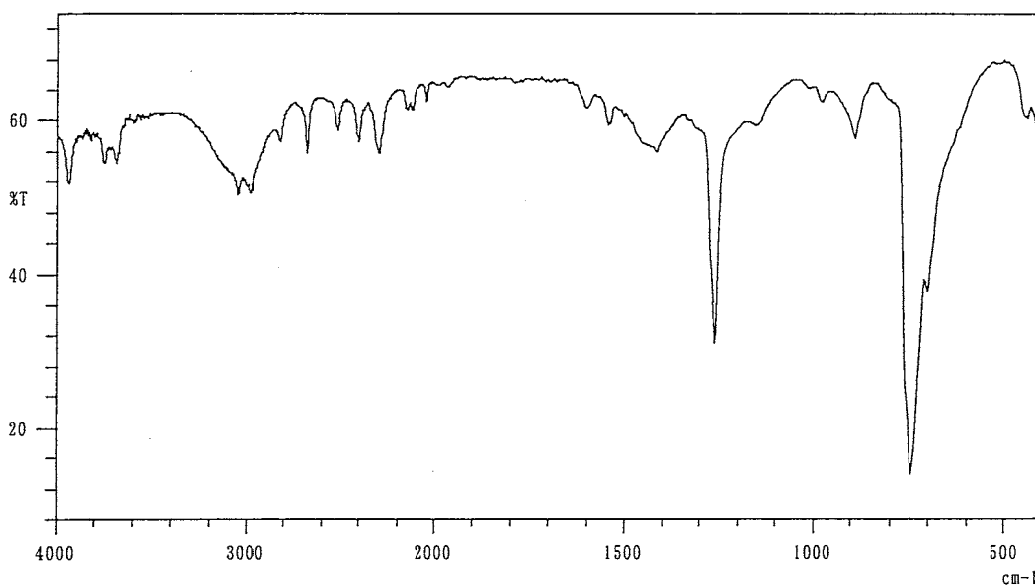
| <u>Determines</u> | <u>Literature Values*</u> |
|---------------------|---------------------------|
| Fragment Peak (M/Z) | Fragment Peak (M/Z) |
| 35 | 35 |
| 49 | 49 |
| 84 | 84 |

(* EPA/NIH Mass Spectral
Data Base (1978) Vol. 1, p. 33.)

Infrared Spectrometry

Instrument : Shimadzu FT-IR 8200PC Infrared Spectrometer

Cell : KBr



Infrared Spectrum of Test Substance

Results: The infrared spectrum was consistent with literature spectrum.

| <u>Determined Values</u> | <u>Literature Values</u> * |
|---------------------------------|---------------------------------|
| Wave Number (cm ⁻¹) | Wave Number (cm ⁻¹) |
| 650~840 | 650~850 |
| 870~940 | 870~940 |
| 970~1000 | 970~1000 |
| 1120~1180 | 1130~1180 |
| 1200~1340 | 1200~1350 |
| 1370~1500 | 1380~1500 |
| 1530~1570 | 1540~1570 |
| 1580~1630 | 1580~1630 |
| 2040~2090 | 2050~2090 |
| 2100~2190 | 2120~2190 |
| 2250~2360 | 2280~2370 |
| 2380~2460 | 2400~2460 |
| 2500~2550 | 2500~2560 |
| 2650~2730 | 2650~2730 |
| 2800~2860 | 2800~2860 |
| 2900~3200 | 2900~3200 |
| 3650~3730 | 3670~3750 |
| 3730~3800 | 3750~3800 |
| 3900~4000 | 3900~4000 |

(*Performed by the WAKO PURE
CHEMICAL INDUSTRIES, LTD.)

2. Conclusions: The test substance was identified as dichloromethane, by the mass spectrum and the infrared spectrum.

F. Lot No. : ESF6669

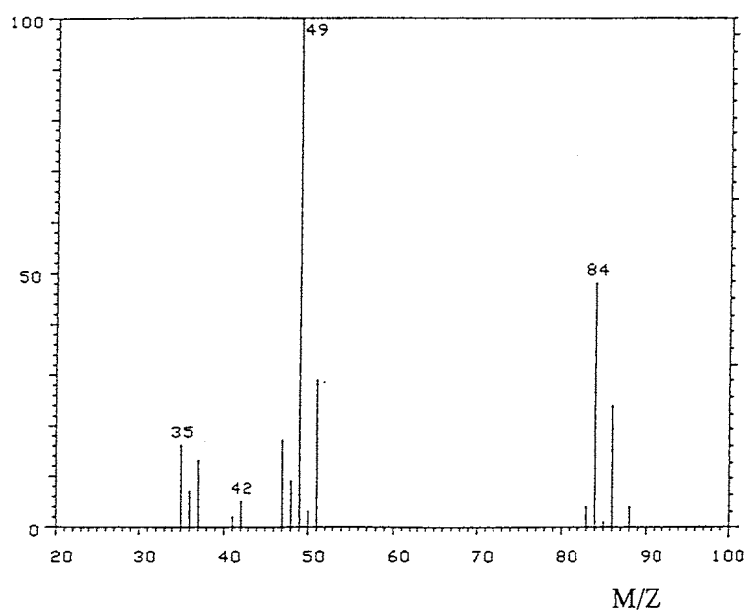
1. Spectral data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Results: The mass spectrum was consistent with literature spectrum.

Determines

Fragment Peak (M/Z)

35

49

84

Literature Values*

Fragment Peak (M/Z)

35

49

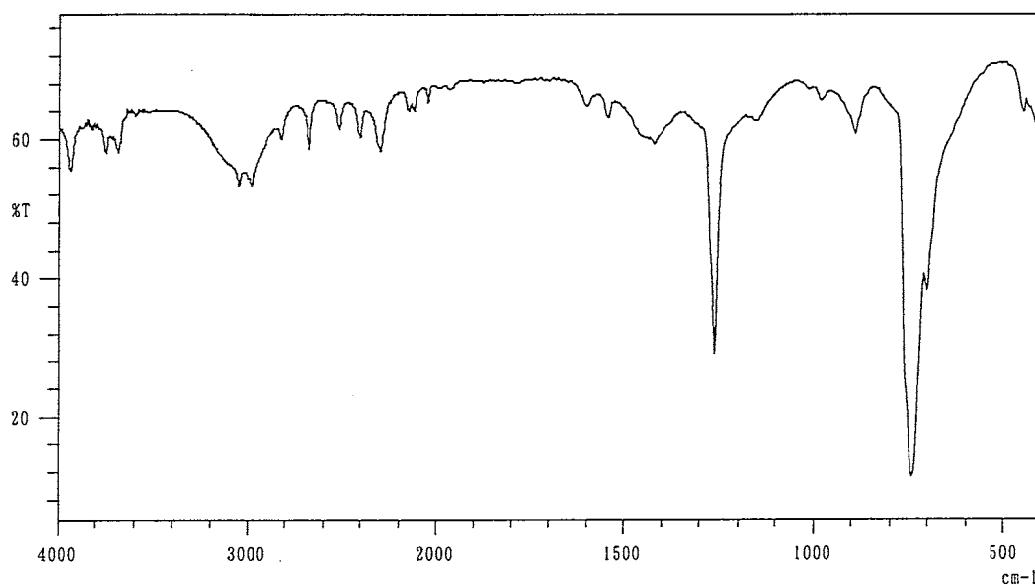
84

(* EPA/NIH Mass Spectral
Data Base (1978) Vol. 1, p. 33.)

Infrared Spectrometry

Instrument : Shimadzu FT-IR 8200PC Infrared Spectrometer

Cell : KBr



Infrared Spectrum of Test Substance

Results: The infrared spectrum was consistent with literature spectrum.

| <u>Determined Values</u> | <u>Literature Values*</u> |
|---------------------------------|---------------------------------|
| Wave Number (cm ⁻¹) | Wave Number (cm ⁻¹) |
| 650~840 | 650~850 |
| 870~940 | 870~940 |
| 970~1000 | 970~1000 |
| 1120~1180 | 1130~1180 |
| 1200~1340 | 1200~1350 |
| 1370~1500 | 1380~1500 |
| 1530~1570 | 1540~1570 |
| 1580~1630 | 1580~1630 |
| 2040~2090 | 2050~2090 |
| 2100~2190 | 2120~2190 |
| 2250~2360 | 2280~2370 |
| 2380~2460 | 2400~2460 |
| 2500~2550 | 2500~2560 |
| 2650~2730 | 2650~2730 |
| 2800~2860 | 2800~2860 |
| 2900~3200 | 2900~3200 |
| 3650~3730 | 3670~3750 |
| 3730~3800 | 3750~3800 |
| 3900~4000 | 3900~4000 |

(*Performed by the WAKO PURE
CHEMICAL INDUSTRIES, LTD.)

2. Conclusions: The test substance was identified as dichloromethane, by the mass spectrum and the infrared spectrum.

G. Lot No. : DLP1873

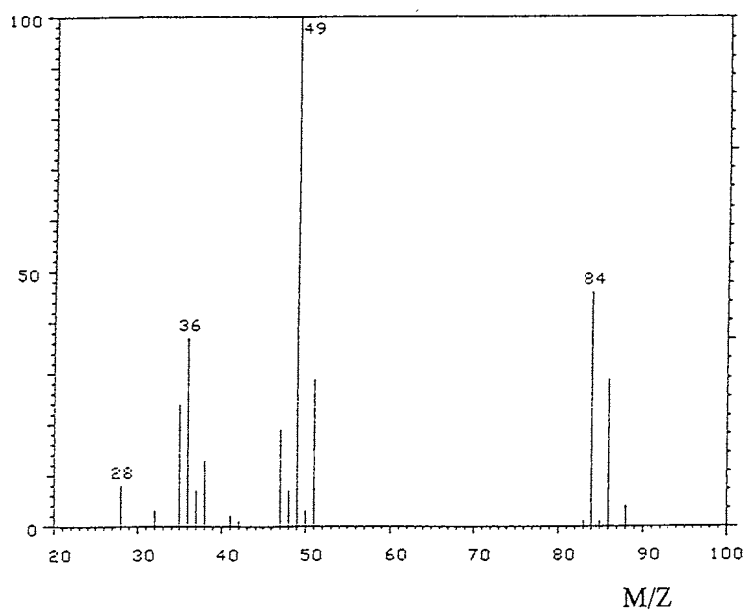
1. Spectral data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Results: The mass spectrum was consistent with literature spectrum.

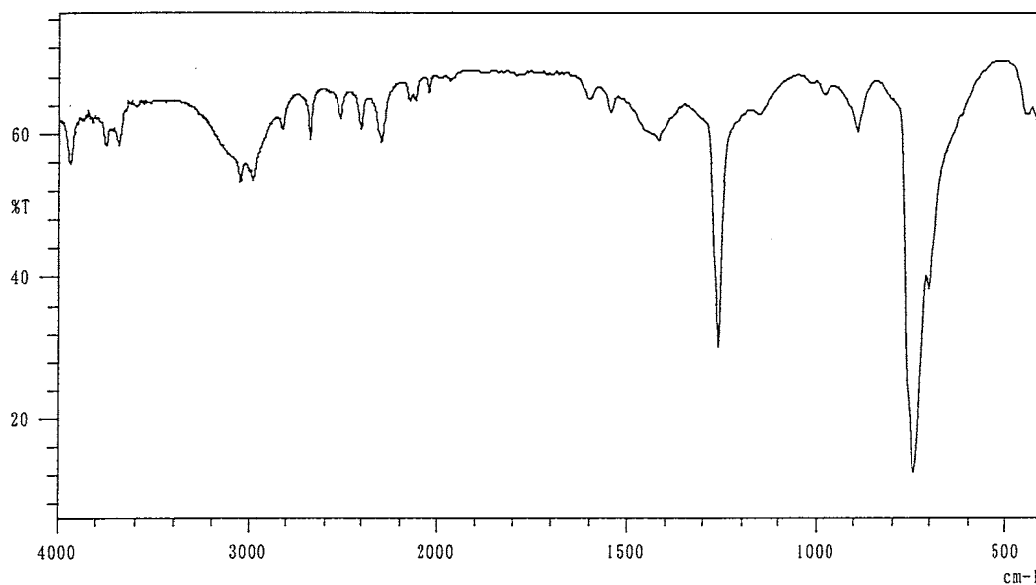
| <u>Determines</u> | <u>Literature Values</u> * |
|---------------------|----------------------------|
| Fragment Peak (M/Z) | Fragment Peak (M/Z) |
| 35 | 35 |
| 49 | 49 |
| 84 | 84 |

* EPA/NIH Mass Spectral
Data Base (1978) Vol. 1, p. 33.)

Infrared Spectrometry

Instrument : Shimadzu FT-IR 8200PC Infrared Spectrometer

Cell : KBr



Infrared Spectrum of Test Substance

Results: The infrared spectrum was consistent with literature spectrum.

| <u>Determined Values</u> | <u>Literature Values</u> * |
|---------------------------------|---------------------------------|
| Wave Number (cm ⁻¹) | Wave Number (cm ⁻¹) |
| 650~840 | 650~850 |
| 870~940 | 870~940 |
| 970~1000 | 970~1000 |
| 1120~1180 | 1130~1180 |
| 1200~1340 | 1200~1350 |
| 1370~1500 | 1380~1500 |
| 1530~1570 | 1540~1570 |
| 1580~1630 | 1580~1630 |
| 2040~2090 | 2050~2090 |
| 2100~2190 | 2120~2190 |
| 2250~2360 | 2280~2370 |
| 2380~2460 | 2400~2460 |
| 2500~2550 | 2500~2560 |
| 2650~2730 | 2650~2730 |
| 2800~2860 | 2800~2860 |
| 2900~3200 | 2900~3200 |
| 3650~3730 | 3670~3750 |
| 3730~3800 | 3750~3800 |
| 3900~4000 | 3900~4000 |

(*Performed by the WAKO PURE
CHEMICAL INDUSTRIES, LTD.)

2. Conclusions: The test substance was identified as dichloromethane, by the mass spectrum and the infrared spectrum.

H. Lot No. : DLL3810

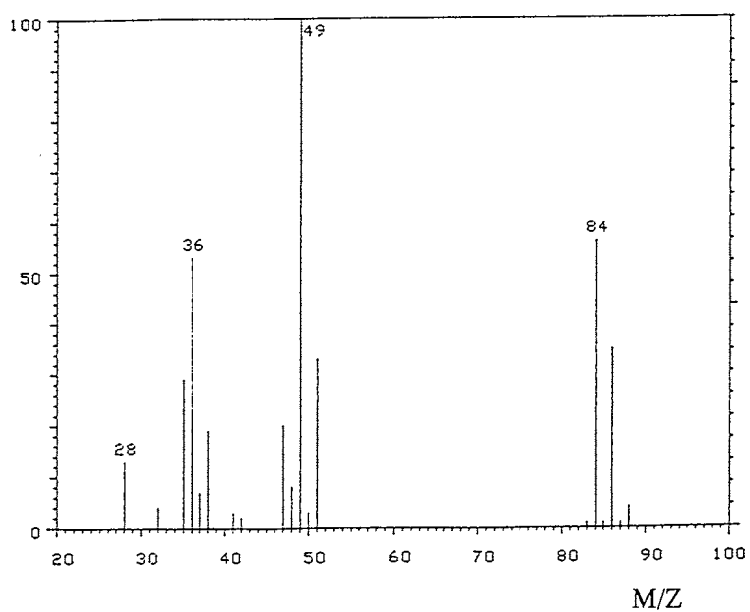
1. Spectral data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Results: The mass spectrum was consistent with literature spectrum.

Determines

Fragment Peak (M/Z)

35

49

84

Literature Values*

Fragment Peak (M/Z)

35

49

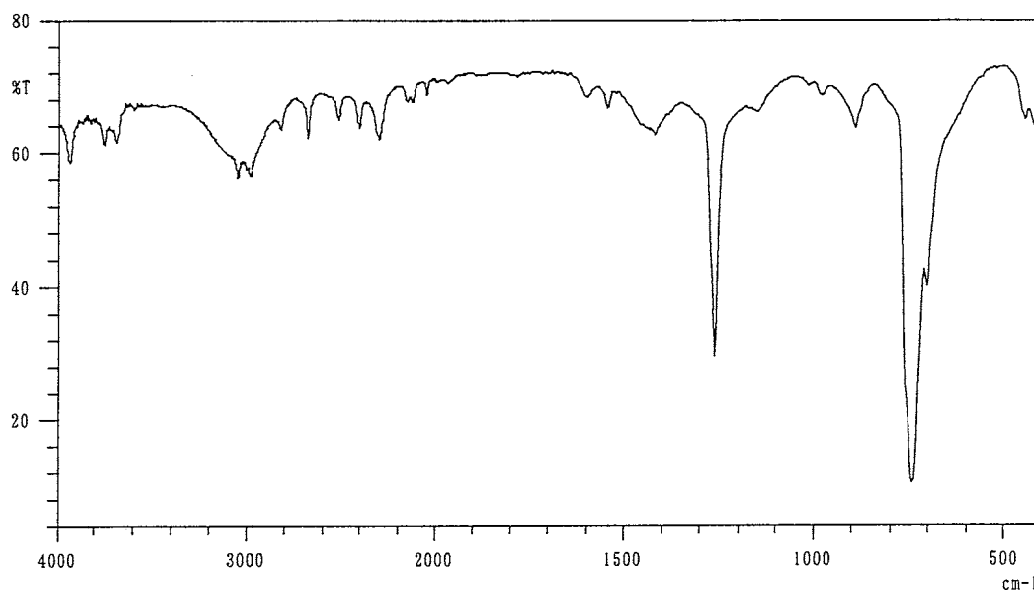
84

* EPA/NIH Mass Spectral
Data Base (1978) Vol. 1, p. 33.)

Infrared Spectrometry

Instrument : Shimadzu FT-IR 8200PC Infrared Spectrometer

Cell : KBr



Infrared Spectrum of Test Substance

Results: The infrared spectrum was consistent with literature spectrum.

| <u>Determined Values</u> | <u>Literature Values*</u> |
|---------------------------------|---------------------------------|
| Wave Number (cm ⁻¹) | Wave Number (cm ⁻¹) |
| 650~840 | 650~850 |
| 870~940 | 870~940 |
| 970~1000 | 970~1000 |
| 1120~1180 | 1130~1180 |
| 1200~1340 | 1200~1350 |
| 1370~1500 | 1380~1500 |
| 1530~1570 | 1540~1570 |
| 1580~1630 | 1580~1630 |
| 2040~2090 | 2050~2090 |
| 2100~2190 | 2120~2190 |
| 2250~2360 | 2280~2370 |
| 2380~2460 | 2400~2460 |
| 2500~2550 | 2500~2560 |
| 2650~2730 | 2650~2730 |
| 2800~2860 | 2800~2860 |
| 2900~3200 | 2900~3200 |
| 3650~3730 | 3670~3750 |
| 3730~3800 | 3750~3800 |
| 3900~4000 | 3900~4000 |

(*Performed by the WAKO PURE
CHEMICAL INDUSTRIES, LTD.)

2. Conclusions: The test substance was identified as dichloromethane, by the mass spectrum and the infrared spectrum.

I. Lot No. : DLH5609

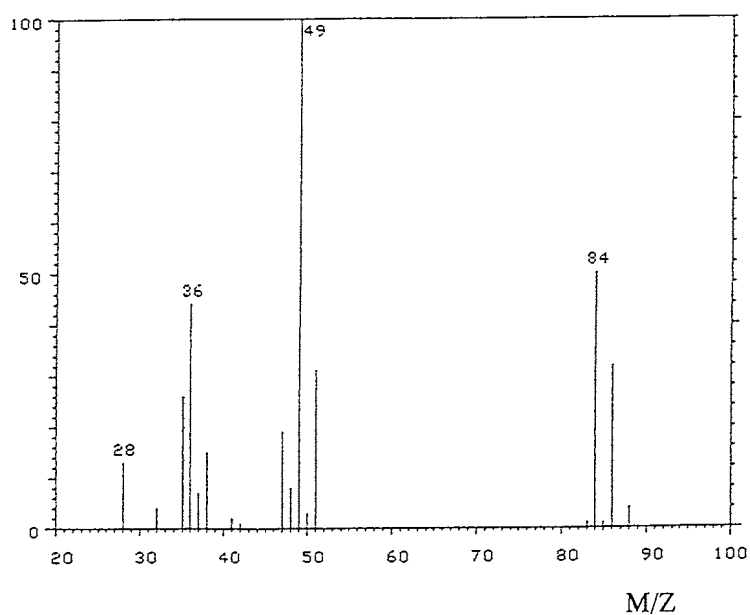
1. Spectral data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Results: The mass spectrum was consistent with literature spectrum.

Determines

Fragment Peak (M/Z)

35

49

84

Literature Values*

Fragment Peak (M/Z)

35

49

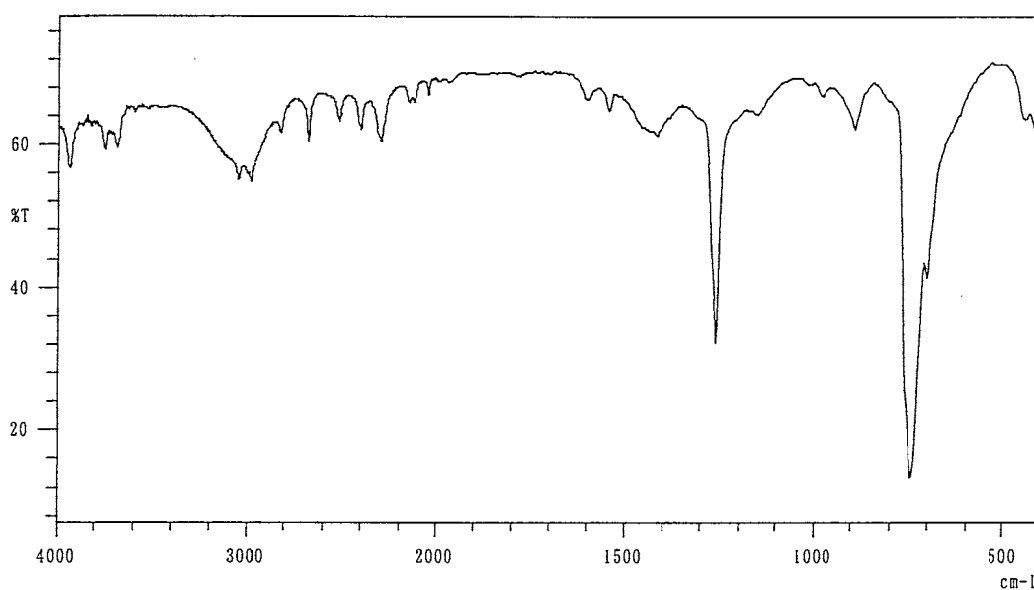
84

(* EPA/NIH Mass Spectral
Data Base (1978) Vol. 1, p. 33.)

Infrared Spectrometry

Instrument : Shimadzu FT-IR 8200PC Infrared Spectrometer

Cell : KBr



Infrared Spectrum of Test Substance

Results: The infrared spectrum was consistent with literature spectrum.

| <u>Determined Values</u> | <u>Literature Values</u> * |
|----------------------------------|----------------------------------|
| Wave Number (cm^{-1}) | Wave Number (cm^{-1}) |
| 650~840 | 650~850 |
| 870~940 | 870~940 |
| 970~1000 | 970~1000 |
| 1120~1180 | 1130~1180 |
| 1200~1340 | 1200~1350 |
| 1370~1500 | 1380~1500 |
| 1530~1570 | 1540~1570 |
| 1580~1630 | 1580~1630 |
| 2040~2090 | 2050~2090 |
| 2100~2190 | 2120~2190 |
| 2250~2360 | 2280~2370 |
| 2380~2460 | 2400~2460 |
| 2500~2550 | 2500~2560 |
| 2650~2730 | 2650~2730 |
| 2800~2860 | 2800~2860 |
| 2900~3200 | 2900~3200 |
| 3650~3730 | 3670~3750 |
| 3730~3800 | 3750~3800 |
| 3900~4000 | 3900~4000 |

(*Performed by the WAKO PURE
CHEMICAL INDUSTRIES, LTD.)

2. Conclusions: The test substance was identified as dichloromethane, by the mass spectrum and the infrared spectrum.

APPENDIX O 2
STABILITY OF DICHLOROMETHANE IN THE 2-YEAR
INHALATION STUDY

STABILITY OF DICHLOROMETHANE IN THE 2-YEAR INHALATION STUDY

Test Substance : Dichloromethane (Wako Pure Chemical Industries, LTD.)

A. Lot No. : APR5260

1. Sample : This lot was used from 1994.10.20 to 1995.1.9. Test substance was stored at room temperature.

2. Infrared Spectrometry

Instrument : Shimadzu FT-IR 8200PC Infrared Spectrometer

Cell : KBr

Results: The result of infrared spectrum did not change when before and after studies.

| <u>1994.10.07 (date analyzed)</u> | <u>1995.01.09 (date analyzed)</u> |
|-----------------------------------|-----------------------------------|
| Wave Number(cm^{-1}) | Wave Number (cm^{-1}) |
| 650~840 | 650~840 |
| 870~940 | 870~940 |
| 970~1000 | 970~1000 |
| 1120~1180 | 1120~1180 |
| 1200~1340 | 1200~1340 |
| 1370~1500 | 1370~1500 |
| 1530~1570 | 1530~1570 |
| 1580~1630 | 1580~1630 |
| 2040~2090 | 2040~2090 |
| 2100~2190 | 2100~2190 |
| 2250~2360 | 2250~2360 |
| 2380~2460 | 2380~2460 |
| 2500~2550 | 2500~2550 |
| 2650~2730 | 2650~2730 |
| 2800~2860 | 2800~2860 |
| 2900~3200 | 2900~3200 |
| 3650~3730 | 3650~3730 |
| 3730~3800 | 3730~3800 |
| 3900~4000 | 3900~4000 |

3. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : Methyl Silicone (0.2mm ϕ \times 50m)

Column Temperature : 60° C

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μ L

Results: Gas chromatography indicated one major peak (peak No.1) and one impurity (peak No.2 < 1% of total area) analyzed at 1994.10.7 and one major peak (peak No.1) and one impurity (peak No.2 < 1% of total area) analyzed at 1995.1.9. It was identified only by comparing its gas chromatograph with that of the amylene (peak No.2) in the dichloromethane, the amount in the test substance were 0.0008% at 1994.10.7. No new trace impurity peak in the test substance analyzed at 1995.1.9 was detected.

| Date | Peak No. | Retention Time (min) | Area (%) |
|------------|----------|-------------------------|-------------|
| 1994.10.07 | 1 | 3.302 | 99.99 |
| | 2 | 3.403 | 0.01 |
| 1995.01.09 | 1 | 3.305 | 99.99 |
| | 2 | 3.407 | 0.01 |

4. Conclusions: The test substance was stable for about 3 months in the dark at room temperature.

B. Lot No. : KCH4634

1. Sample : This lot was used from 1995.1.7 to 1995.4.3. Test substance was stored at room temperature.

2. Infrared Spectrometry

Instrument : Shimadzu FT-IR 8200PC Infrared Spectrometer

Cell : KBr

Slit : Medium

1994.12.27 (date analyzed)

Wave Number (cm^{-1})

650~ 840

870~ 940

970~1000

1120~1180

1200~1340

1370~1500

1530~1570

1580~1630

2040~2090

2100~2190

2250~2360

2380~2460

2500~2550

2650~2730

2800~2860

2900~3200

3650~3730

3730~3800

3900~4000

1995.04.03 (date analyzed)

Wave Number (cm^{-1})

650~ 840

870~ 940

970~1000

1120~1180

1200~1340

1370~1500

1530~1570

1580~1630

2040~2090

2100~2190

2250~2360

2380~2460

2500~2550

2650~2730

2800~2860

2900~3200

3650~3730

3730~3800

3900~4000

3. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : Methyl Silicone (0.2mm ϕ \times 50m)

Column Temperature : 60° C

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μ L

Results: Gas chromatography indicated one major peak (peak No.1) and one impurity (peak No.2 < 1% of total area) analyzed at 1994.12.27 and one major peak (peak No.1) and one impurity (peak No.2 < 1% of total area) analyzed at 1995.4.3. It was identified only by comparing its gas chromatograph with that of the amylene (peak No.2) in the dichloromethane, the amount in the test substance were 0.0008% at 1995.4.3. No new trace impurity peak in the test substance analyzed at 1995.1.9 was detected.

| Date | Peak No. | Retention Time (min) | Area (%) |
|------------|----------|-------------------------|-------------|
| 1994.12.27 | 1 | 3.3 | 99.98 |
| | 2 | 3.407 | 0.02 |
| 1995.04.03 | 1 | 3.307 | 99.99 |
| | 2 | 3.407 | 0.01 |

4. Conclusions: The test substance was stable for about 3 months in the dark at room temperature.

C. Lot No. : ESR7256

1. Sample : This lot was used from 1995.4.4 to 1995.6.28. Test substance was stored at room temperature.

2. Infrared Spectrometry

Instrument : Shimadzu FT-IR 8200PC Infrared Spectrometer

Cell : KBr

Results: The result of infrared spectrum did not change when before and after studies.

| <u>1995.03.27 (date analyzed)</u> | <u>1995.06.28 (date analyzed)</u> |
|-----------------------------------|-----------------------------------|
| Wave Number(cm^{-1}) | Wave Number (cm^{-1}) |
| 650~ 840 | 650~ 840 |
| 870~ 940 | 870~ 940 |
| 970~1000 | 970~1000 |
| 1120~1180 | 1120~1180 |
| 1200~1340 | 1200~1340 |
| 1370~1500 | 1370~1500 |
| 1530~1570 | 1530~1570 |
| 1580~1630 | 1580~1630 |
| 2040~2090 | 2040~2090 |
| 2100~2190 | 2100~2190 |
| 2250~2360 | 2250~2360 |
| 2380~2460 | 2380~2460 |
| 2500~2550 | 2500~2550 |
| 2650~2730 | 2650~2730 |
| 2800~2860 | 2800~2860 |
| 2900~3200 | 2900~3200 |
| 3650~3730 | 3650~3730 |
| 3730~3800 | 3730~3800 |
| 3900~4000 | 3900~4000 |

3. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : Methyl Silicone (0.2mm ϕ \times 50m)

Column Temperature : 60° C

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μ L

Results: Gas chromatography indicated one major peak (peak No.1) and one impurity (peak No.2 < 1% of total area) analyzed at 1995.3.27 and one major peak (peak No.1) and one impurity (peak No.2 < 1% of total area) analyzed at 1995.6.28. It was identified only by comparing its gas chromatograph with that of the amylene (peak No.2) in the dichloromethane, the amount in the test substance were 0.0008% at 1995.3.27. No new trace impurity peak in the test substance analyzed at 1995.6.28 was detected.

| Date | Peak No. | Retention Time (min) | Area (%) |
|------------|----------|-------------------------|-------------|
| 1995.03.27 | 1 | 3.302 | 99.98 |
| | 2 | 3.407 | 0.02 |
| 1995.06.28 | 1 | 3.302 | 99.81 |
| | 2 | 3.405 | 0.19 |

4. Conclusions: The test substance was stable for about 3 months in the dark at room temperature.

D. Lot No. : ESM2924

1. Sample : This lot was used from 1995.6.28 to 1995.9.22. Test substance was stored at room temperature.

2. Infrared Spectrometry

Instrument : Shimadzu FT-IR 8200PC Infrared Spectrometer

Cell : KBr

Results: The result of infrared spectrum did not change when before and after studies.

| <u>1995.06.26 (date analyzed)</u> | <u>1995.10.02 (date analyzed)</u> |
|-----------------------------------|-----------------------------------|
| Wave Number (cm^{-1}) | Wave Number (cm^{-1}) |
| 650~840 | 650~840 |
| 870~940 | 870~940 |
| 970~1000 | 970~1000 |
| 1120~1180 | 1120~1180 |
| 1200~1340 | 1200~1340 |
| 1370~1500 | 1370~1500 |
| 1530~1570 | 1530~1570 |
| 1580~1630 | 1580~1630 |
| 2040~2090 | 2040~2090 |
| 2100~2190 | 2100~2190 |
| 2250~2360 | 2250~2360 |
| 2380~2460 | 2380~2460 |
| 2500~2550 | 2500~2550 |
| 2650~2730 | 2650~2730 |
| 2800~2860 | 2800~2860 |
| 2900~3200 | 2900~3200 |
| 3650~3730 | 3650~3730 |
| 3730~3800 | 3730~3800 |
| 3900~4000 | 3900~4000 |

3. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : Methyl Silicone (0.2mm ϕ \times 50m)

Column Temperature : 60° C

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μ L

Results: Gas chromatography indicated one major peak (peak No.1) and one impurity (peak No.2 < 1% of total area) analyzed at 1995.6.26 and one major peak (peak No.1) and one impurity (peak No.2 < 1% of total area) analyzed at 1995.10.2. It was identified only by comparing its gas chromatograph with that of the amylene (peak No.2) in the dichloromethane, the amount in the test substance were 0.0008% at 1995.6.26. No new trace impurity peak in the test substance analyzed at 1995.10.2 was detected.

| Date | Peak No. | Retention Time (min) | Area (%) |
|------------|----------|-------------------------|-------------|
| 1995.06.26 | 1 | 3.302 | 99.99 |
| | 2 | 3.405 | 0.01 |
| 1995.10.02 | 1 | 3.302 | 99.99 |
| | 2 | 3.405 | 0.01 |

4. Conclusions: The test substance was stable for about 4 months in the dark at room temperature.

E. Lot No. : ESJ4826

1. Sample : This lot was used from 1995.9.22 to 1995.12.25. Test substance was stored at room temperature.

2. Infrared Spectrometry

Instrument : Shimadzu FT-IR 8200PC Infrared Spectrometer

Cell : KBr

Results: The result of infrared spectrum did not change when before and after studies.

| <u>1995.09.14 (date analyzed)</u> | <u>1995.12.25 (date analyzed)</u> |
|-----------------------------------|-----------------------------------|
| Wave Number (cm^{-1}) | Wave Number (cm^{-1}) |
| 650~840 | 650~840 |
| 870~940 | 870~940 |
| 970~1000 | 970~1000 |
| 1120~1180 | 1120~1180 |
| 1200~1340 | 1200~1340 |
| 1370~1500 | 1370~1500 |
| 1530~1570 | 1530~1570 |
| 1580~1630 | 1580~1630 |
| 2040~2090 | 2040~2090 |
| 2100~2190 | 2100~2190 |
| 2250~2360 | 2250~2360 |
| 2380~2460 | 2380~2460 |
| 2500~2550 | 2500~2550 |
| 2650~2730 | 2650~2730 |
| 2800~2860 | 2800~2860 |
| 2900~3200 | 2900~3200 |
| 3650~3730 | 3650~3730 |
| 3730~3800 | 3730~3800 |
| 3900~4000 | 3900~4000 |

3. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : Methyl Silicone (0.2mm ϕ \times 50m)

Column Temperature : 60° C

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μ L

Results: Gas chromatography indicated one major peak (peak No.2) and one impurity (peak No.2 and peak No.2 < 1% of total area) analyzed at 1995.9.14 and one major peak (peak No.1) and one impurity (peak No.2 < 1% of total area) analyzed at 1995.12.25. It was identified only by comparing its gas chromatograph with that of the amylene (peak No.3) in the dichloromethane, the amount in the test substance were 0.0004% at 1995.9.14. No new trace impurity peak in the test substance analyzed at 1995.12.25 was detected.

| Date | Peak No. | Retention Time (min) | Area (%) |
|------------|----------|-------------------------|-------------|
| 1995.09.14 | 1 | 3.27 | 0.001 |
| | 2 | 3.305 | 99.987 |
| | 3 | 3.408 | 0.012 |
| 1995.12.25 | 1 | 3.302 | 99.99 |
| | 2 | 3.407 | 0.01 |

4. Conclusions: The test substance was stable for about 3 months in the dark at room temperature.

F. Lot No. : ESF6669

1. Sample : This lot was used from 1995.12.25 to 1996.4.1. Test substance was stored at room temperature.

2. Infrared Spectrometry

Instrument : Shimadzu FT-IR 8200PC Infrared Spectrometer

Cell : KBr

Results: The result of infrared spectrum did not change when before and after studies.

| <u>1995.12.22 (date analyzed)</u> | <u>1996.04.02 (date analyzed)</u> |
|-----------------------------------|-----------------------------------|
| Wave Number (cm^{-1}) | Wave Number (cm^{-1}) |
| 650~840 | 650~840 |
| 870~940 | 870~940 |
| 970~1000 | 970~1000 |
| 1120~1180 | 1120~1180 |
| 1200~1340 | 1200~1340 |
| 1370~1500 | 1370~1500 |
| 1530~1570 | 1530~1570 |
| 1580~1630 | 1580~1630 |
| 2040~2090 | 2040~2090 |
| 2100~2190 | 2100~2190 |
| 2250~2360 | 2250~2360 |
| 2380~2460 | 2380~2460 |
| 2500~2550 | 2500~2550 |
| 2650~2730 | 2650~2730 |
| 2800~2860 | 2800~2860 |
| 2900~3200 | 2900~3200 |
| 3650~3730 | 3650~3730 |
| 3730~3800 | 3730~3800 |
| 3900~4000 | 3900~4000 |

3. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : Methyl Silicone (0.2mm ϕ \times 50m)

Column Temperature : 60° C

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μ L

Results: Gas chromatography indicated one major peak (peak No.1) and one impurity (peak No.2 < 1% of total area) analyzed at 1995.12.22 and one major peak (peak No.1) and one impurity (peak No.2 < 1% of total area) analyzed at 1996.4.2. It was identified only by comparing its gas chromatograph with that of the amylene (peak No.2) in the dichloromethane, the amount in the test substance were 0.0007 % at 1995.12.22. No new trace impurity peak in the test substance analyzed at 1996.4.2 was detected.

| Date | Peak No. | Retention Time (min) | Area (%) |
|------------|----------|-------------------------|-------------|
| 1995.12.22 | 1 | 3.302 | 99.83 |
| | 2 | 3.405 | 0.17 |
| 1996.04.02 | 1 | 3.302 | 99.99 |
| | 2 | 3.405 | 0.01 |

4. Conclusions: The test substance was stable for about 4 months in the dark at room temperature.

G. Lot No. : DLP1873

1. Sample : This lot was used from 1996.4.1 to 1996.6.27. Test substance was stored at room temperature.

2. Infrared Spectrometry

Instrument : Shimadzu FT-IR 8200PC Infrared Spectrometer

Cell : KBr

Results: The result of infrared spectrum did not change when before and after studies.

| <u>1996.03.25 (date analyzed)</u> | <u>1996.06.28 (date analyzed)</u> |
|-----------------------------------|-----------------------------------|
| Wave Number (cm^{-1}) | Wave Number (cm^{-1}) |
| 650~840 | 650~840 |
| 870~940 | 870~940 |
| 970~1000 | 970~1000 |
| 1120~1180 | 1120~1180 |
| 1200~1340 | 1200~1340 |
| 1370~1500 | 1370~1500 |
| 1530~1570 | 1530~1570 |
| 1580~1630 | 1580~1630 |
| 2040~2090 | 2040~2090 |
| 2100~2190 | 2100~2190 |
| 2250~2360 | 2250~2360 |
| 2380~2460 | 2380~2460 |
| 2500~2550 | 2500~2550 |
| 2650~2730 | 2650~2730 |
| 2800~2860 | 2800~2860 |
| 2900~3200 | 2900~3200 |
| 3650~3730 | 3650~3730 |
| 3730~3800 | 3730~3800 |
| 3900~4000 | 3900~4000 |

3. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : Methyl Silicone(0.2mm ϕ \times 50m)

Column Temperature : 60° C

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μ L

Results: Gas chromatography indicated one major peak (peak No.1) and one impurity (peak No.2 < 1% of total area) analyzed at 1996.3.25 and one major peak (peak No.1) and one impurity (peak No.2 < 1% of total area) analyzed at 1996.6.28. It was identified only by comparing its gas chromatograph with that of the amylene (peak No.2) in the dichloromethane, the amount in the test substance were 0.0006% at 1996.3.25. No new trace impurity peak in the test substance analyzed at 1996.6.28 was detected.

| Date | Peak No. | Retention Time (min) | Area (%) |
|------------|----------|-------------------------|-------------|
| 1996.03.25 | 1 | 3.302 | 99.98 |
| | 2 | 3.407 | 0.02 |
| 1996.06.28 | 1 | 3.302 | 99.98 |
| | 2 | 3.407 | 0.02 |

4. Conclusions: The test substance was stable for about 3 months in the dark at room temperature.

H. Lot No. : DLL3810

1. Sample : This lot was used from 1996.6.28 to 1996.9.26. Test substance was stored at room temperature.

2. Infrared Spectrometry

Instrument : Shimadzu FT-IR 8200PC Infrared Spectrometer

Cell : KBr

Results: The result of infrared spectrum did not change when before and after studies.

| <u>1996.06.26 (date analyzed)</u> | <u>1996.09.26 (date analyzed)</u> |
|-----------------------------------|-----------------------------------|
| Wave Number (cm^{-1}) | Wave Number (cm^{-1}) |
| 650~840 | 650~840 |
| 870~940 | 870~940 |
| 970~1000 | 970~1000 |
| 1120~1180 | 1120~1180 |
| 1200~1340 | 1200~1340 |
| 1370~1500 | 1370~1500 |
| 1530~1570 | 1530~1570 |
| 1580~1630 | 1580~1630 |
| 2040~2090 | 2040~2090 |
| 2100~2190 | 2100~2190 |
| 2250~2360 | 2250~2360 |
| 2380~2460 | 2380~2460 |
| 2500~2550 | 2500~2550 |
| 2650~2730 | 2650~2730 |
| 2800~2860 | 2800~2860 |
| 2900~3200 | 2900~3200 |
| 3650~3730 | 3650~3730 |
| 3730~3800 | 3730~3800 |
| 3900~4000 | 3900~4000 |

3. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : Methyl Silicone (0.2mm ϕ \times 50m)

Column Temperature : 60° C

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μ L

Results: Gas chromatography indicated one major peak (peak No.1) and one impurity (peak No.2 < 1% of total area) analyzed at 1996.6.26 and one major peak (peak No.1) and one impurity(peak No.2 < 1% of total area) analyzed at 1996.9.26. It was identified only by comparing its gas chromatograph with that of the amylene (peak No.2) in the dichloromethane, the amount in the test substance were 0.0007% at 1996.6.26. No new trace impurity peak in the test substance analyzed at 1996.9.26 was detected.

| Date | Peak No. | Retention Time (min) | Area (%) |
|------------|----------|-------------------------|-------------|
| 1996.06.26 | 1 | 3.302 | 99.98 |
| | 2 | 3.407 | 0.02 |
| 1996.09.26 | 1 | 3.302 | 99.99 |
| | 2 | 3.407 | 0.01 |

4. Conclusions: The test substance was stable for about 3 months in the dark at room temperature.

I. Lot No. : DLH5609

1. Sample : This lot was used from 1996.9.27 to 1996.10.16. Test substance was stored at room temperature.

2. Infrared Spectrometry

Instrument : Shimadzu FT-IR 8200PC Infrared Spectrometer

Cell : KBr

Results: The result of infrared spectrum did not change when before and after studies.

| <u>1996.09.25 (date analyzed)</u> | <u>1996.11.25 (date analyzed)</u> |
|-----------------------------------|-----------------------------------|
| Wave Number (cm^{-1}) | Wave Number (cm^{-1}) |
| 650~840 | 650~840 |
| 870~940 | 870~940 |
| 970~1000 | 970~1000 |
| 1120~1180 | 1120~1180 |
| 1200~1340 | 1200~1340 |
| 1370~1500 | 1370~1500 |
| 1530~1570 | 1530~1570 |
| 1580~1630 | 1580~1630 |
| 2040~2090 | 2040~2090 |
| 2100~2190 | 2100~2190 |
| 2250~2360 | 2250~2360 |
| 2380~2460 | 2380~2460 |
| 2500~2550 | 2500~2550 |
| 2650~2730 | 2650~2730 |
| 2800~2860 | 2800~2860 |
| 2900~3200 | 2900~3200 |
| 3650~3730 | 3650~3730 |
| 3730~3800 | 3730~3800 |
| 3900~4000 | 3900~4000 |

3. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : Methyl Silicone(0.2mm ϕ \times 50m)

Column Temperature : 60° C

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μ L

Results: Gas chromatography indicated one major peak (peak No.1) and one impurity (peak No.2 < 1% of total area) analyzed at 1996.9.25 and one major peak (peak No.1) and one impurity (peak No.2 < 1% of total area) analyzed at 1996.11.25. It was identified only by comparing its gas chromatograph with that of the amylene (peak No.2) in the dichloromethane, the amount in the test substance were 0.0008% at 1996.9.25. No new trace impurity peak in the test substance analyzed at 1996.11.25 was detected.

| Date | Peak No. | Retention Time (min) | Area (%) |
|------------|----------|-------------------------|-------------|
| 1996.09.25 | 1 | 3.302 | 99.99 |
| | 2 | 3.407 | 0.01 |
| 1996.11.25 | 1 | 3.303 | 99.98 |
| | 2 | 3.407 | 0.02 |

4. Conclusions: The test substance was stable for about 3 months in the dark at room temperature.

APPENDIX P 1

CONCENTRATION OF DICHLOROMETHANE IN THE INHALATION CHAMBER
OF THE 2-YEAR INHALATION STUDY

CONCENTRATION OF DICHLROMETHANE IN THE INHALATION CHAMBER
OF THE 2-YEAR INHALATION STUDY

| Group Name | Concentration (ppm) |
|------------|---------------------|
| | Mean \pm S.D. |
| Control | 0.0 \pm 0.0 |
| 1000ppm | 999.9 \pm 6.5 |
| 2000ppm | 2003.2 \pm 9.0 |
| 4000ppm | 3988.5 \pm 25.7 |

APPENDIX P 2

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 2-YEAR
INHALATION STUDY OF DICHLOROMETHANE

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 2-YEAR INHALATION STUDY OF DICHLOROMETHANE

| Group Name | Temperature(°C) Mean ± S.D. | Humidity(%) Mean ± S.D. | Ventilation Rate(L/min) Mean ± S.D. | Air Changes(time/h) Mean |
|------------|--------------------------------|----------------------------|--|-----------------------------|
| Control | 22.4 ± 0.2 | 54.8 ± 1.4 | 1831.0 ± 9.2 (916.4 ± 3.3) | 12.1 (6.0) |
| 1000ppm | 22.2 ± 0.2 | 54.5 ± 1.5 | 1825.4 ± 8.9 (917.9 ± 2.8) | 12.0 (6.0) |
| 2000ppm | 22.2 ± 0.1 | 55.6 ± 1.4 | 1826.0 ± 8.6 (915.9 ± 2.3) | 12.0 (6.0) |
| 4000ppm | 22.2 ± 0.1 | 55.0 ± 1.6 | 1830.1 ± 8.2 (916.1 ± 2.5) | 12.1 (6.0) |

():during exposure

APPENDIX Q 1

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS IN THE 2-YEAR INHALATION STUDY OF DICHLOROMERHANE

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS
IN THE 2-YEAR INHALATION STUDY OF DICHLOROMETHANE

| Item | Method |
|--|--|
| Hematology | |
| Red blood cell (RBC) | Light scattering method ¹⁾ |
| Hemoglobin (Hgb) | Cyanmethemoglobin method ¹⁾ |
| Hematocrit (Hct) | Calculated as $RBC \times MCV/10$ ¹⁾ |
| Mean corpuscular volume (MCV) | Light scattering method ¹⁾ |
| Mean corpuscular hemoglobin (MCH) | Calculated as $Hgb/RBC \times 10$ ¹⁾ |
| Mean corpuscular hemoglobin concentration (MCHC) | Calculated as $Hgb/Hct \times 100$ ¹⁾ |
| Platelet | Light scattering method ¹⁾ |
| White blood cell (WBC) | Light scattering method ¹⁾ |
| Differential WBC | Pattern recognition method ²⁾ (May-Grunwald-Giemsa staining) |
| Biochemistry | |
| Total protein (TP) | Biuret method ³⁾ |
| Albumin (Alb) | BCG method ³⁾ |
| A/G ratio | Calculated as $Alb/(TP - Alb)$ ³⁾ |
| T-bilirubin | Alkaline azobilirubin method ³⁾ |
| Glucose | Enzymatic method (GLK·G-6-PDH) ³⁾ |
| T-cholesterol | Enzymatic method (CE·COD·POD) ³⁾ |
| Triglyceride | Enzymatic method (LPL·GK·GPO·POD) ³⁾ |
| Phospholipid | Enzymatic method (PLD·COD·POD) ³⁾ |
| Glutamic oxaloacetic transaminase (GOT) | UV·Rate method ³⁾ |
| Glutamic pyruvic transaminase (GPT) | UV·Rate method ³⁾ |
| Lactate dehydrogenase (LDH) | UV·Rate method ³⁾ |
| Alkaline phosphatase (ALP) | p-Nitrophenylphosphate method ³⁾ |
| γ -Glutamyl transpeptidase (γ -GTP) | L- γ -Glutamyl-p-nitroanilide method ³⁾ |
| Creatine phosphokinase (CPK) | UV·Rate method ³⁾ |
| Urea nitrogen | Enzymatic method (Urease·GLDH) ³⁾ |
| Creatinine | Jaffe method ³⁾ |
| Sodium | Ion selective electrode method ³⁾ |
| Potassium | Ion selective electrode method ³⁾ |
| Chloride | Ion selective electrode method ³⁾ |
| Calcium | OCPC method ³⁾ |
| Inorganic phosphorus | Enzymatic method (PNP·XOD·POD) ³⁾ |
| Urinalysis | |
| PH, Protein, Glucose, Ketone body, Bilirubin, Occult Blood, Urobilinogen | Urinalysis reagent paper method ⁴⁾ |

1) Automatic blood cell analyzer (Technicon H·1 : Technicon Instruments Corporation, USA)

2) Automatic blood cell differential analyzer (Hitachi 8200 : Hitachi, Ltd., Japan)

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

4) Ames reagent strips for urinalysis (Multistix : Bayer-Sankyo Co., Ltd., Japan)

APPENDIX Q 2

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY
IN THE 2-YEAR INHALATION STUDY OF DICHLOROMETHANE

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY
IN THE 2-YEAR INHALATION STUDY OF DICHLOROMETHANE

| Item | Unit | Decimal place |
|--|---------------------------|---------------|
| Hematology | | |
| Red blood cell (RBC) | $\times 10^6/\mu\text{L}$ | 2 |
| Hemoglobin | g/dL | 1 |
| Hematocrit | % | 1 |
| Mean corpuscular volume (MCV) | fL | 1 |
| Mean corpuscular hemoglobin (MCH) | pg | 1 |
| Mean corpuscular hemoglobin concentration (MCHC) | g/dL | 1 |
| Platelet | $\times 10^3/\mu\text{L}$ | 0 |
| White blood cell (WBC) | $\times 10^3/\mu\text{L}$ | 2 |
| Differential WBC | % | 0 |
| Biochemistry | | |
| Total protein | g/dL | 1 |
| Albumin | g/dL | 1 |
| A/G ratio | — | 1 |
| T-bilirubin | mg/dL | 2 |
| Glucose | mg/dL | 0 |
| T-cholesterol | mg/dL | 0 |
| Triglyceride | mg/dL | 0 |
| Phospholipid | mg/dL | 0 |
| Glutamic oxaloacetic transminase (GOT) | IU/L | 0 |
| Glutamic pyruvic transaminase (GPT) | IU/L | 0 |
| Lactate dehydrogenase (LDH) | IU/L | 0 |
| Alkaline phosphatase (ALP) | IU/L | 0 |
| γ -Glutamyl transpeptidase (γ -GTP) | IU/L | 0 |
| Creatine phosphokinase (CPK) | IU/L | 0 |
| Urea nitrogen | mg/dL | 1 |
| Creatinine | mg/dL | 1 |
| Sodium | mEq/L | 0 |
| Potassium | mEq/L | 1 |
| Chloride | mEq/L | 0 |
| Calcium | mg/dL | 1 |
| Inorganic phosphorus | mg/dL | 1 |