

P - クロロニトロベンゼンのラット及びマウスを用いた
経口（混餌）によるがん原性試験結果報告書

APPENDIX

（A1- 1 ～A5 - 3）

急性試験 STUDY NO. 0032 ; 0033

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APPENDIX A 1-1

CLINICAL OBSERVATION (ACUTE STUDIES: SUMMARY)

RAT: MALE

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
| | | 0-0 1 | 0-0 2 | 0-0 3 | 0-0 4 | 1-1 1 | 1-2 1 | 1-3 1 | 1-4 1 | 1-5 1 | 1-6 1 | 1-7 1 | 2-1 1 | 2-2 1 | 2-3 1 |
| DEATH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 0 | 1 | 7 | 8 | 8 | 8 | 8 | 8 | 8 | 8 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 | 1 | 5 | 8 | 9 | 9 | 9 | 9 | 9 | 9 | 9 |
| | 2030 mg/kg | 0 | 0 | 0 | 0 | 5 | 10 | - | - | - | - | - | - | - | - |
| LOCOMOTOR MOVEMENT DECR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 2 | 10 | 9 | 2 | 1 | 1 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 1 | 7 | 7 | 5 | 2 | 1 | 1 | 1 | 0 | 0 | 0 |
| | 2030 mg/kg | 0 | 1 | 3 | 3 | 9 | 5 | - | - | - | - | - | - | - | - |
| PRONE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | 0 | 0 | 0 | 0 | 1 | 1 | - | - | - | - | - | - | - | - |
| LATERAL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 | 1 | 3 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | 0 | 0 | 0 | 0 | 6 | 4 | - | - | - | - | - | - | - | - |
| HUNCHBACK POSITION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 5 | 6 | 2 | 2 | 2 | 1 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 8 | 10 | 9 | 3 | 2 | 2 | 1 | 1 | 1 | 1 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 | 7 | 8 | 5 | 2 | 1 | 1 | 1 | 1 | 1 | 0 |
| | 2030 mg/kg | 0 | 0 | 0 | 0 | 3 | 2 | - | - | - | - | - | - | - | - |

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | |
|-------------------------|------------|-------------------------|-----|-----|-----|
| | | 2-4 | 2-5 | 2-6 | 2-7 |
| | | 1 | 1 | 1 | 1 |
| DEATH | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 8 | 8 | 8 | 8 |
| | 1350 mg/kg | 9 | 9 | 9 | 9 |
| | 2030 mg/kg | - | - | - | - |
| LOCOMOTOR MOVEMENT DECR | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | - | - | - | - |
| PRONE | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | - | - | - | - |
| LATERAL | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | - | - | - | - |
| HUNCHBACK POSITION | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | - | - | - | - |

STUDY NO. : 0032
ANIMAL : RAT F344
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CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

PAGE : 3

| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|------------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | | 0-0 | 0-0 | 0-0 | 0-0 | 1-1 | 1-2 | 1-3 | 1-4 | 1-5 | 1-6 | 1-7 | 2-1 | 2-2 | 2-3 |
| | | 1 | 2 | 3 | 4 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| ATAXIC GAIT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 1 | 3 | 4 | 2 | 1 | 1 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 | 2 | 3 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | 0 | 0 | 0 | 1 | 3 | 1 | - | - | - | - | - | - | - | - |
| PARALYTIC GAIT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - | - |
| EXCITEMENT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - | - |
| RIGHTING REPLEX REDUCE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - | - |
| WEAKNESS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 0 | 1 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 | 2 | 1 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | 0 | 0 | 0 | 0 | 6 | 3 | - | - | - | - | - | - | - | - |

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | |
|------------------------|------------|-------------------------|-----|-----|-----|
| | | 2-4 | 2-5 | 2-6 | 2-7 |
| | | 1 | 1 | 1 | 1 |
| ATAXIC GAIT | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | - | - | - | - |
| PARALYTIC GAIT | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | - | - | - | - |
| EXCITEMENT | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | - | - | - | - |
| RIGHTING REPLEX REDUCE | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | - | - | - | - |
| WEAKNESS | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | - | - | - | - |

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-----------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | | 0-0 | 0-0 | 0-0 | 0-0 | 1-1 | 1-2 | 1-3 | 1-4 | 1-5 | 1-6 | 1-7 | 2-1 | 2-2 | 2-3 |
| | | 1 | 2 | 3 | 4 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| COLORED | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 6 | 6 | 6 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 2 | 2 | 8 | 9 | 4 | 3 | 1 | 1 | 1 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 1 | 3 | 3 | 10 | 10 | 9 | 3 | 2 | 2 | 2 | 1 | 1 | 1 |
| | 1350 mg/kg | 0 | 3 | 6 | 6 | 10 | 8 | 5 | 2 | 1 | 1 | 1 | 0 | 0 | 0 |
| | 2030 mg/kg | 0 | 2 | 6 | 6 | 10 | 5 | - | - | - | - | - | - | - | - |
| PILOERECTION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 9 | 5 | 5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 4 | 4 | 10 | 10 | 10 | 8 | 5 | 7 | 3 | 1 | 1 | 1 |
| | 900 mg/kg | 0 | 8 | 9 | 9 | 10 | 10 | 9 | 3 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 1350 mg/kg | 0 | 10 | 10 | 10 | 10 | 8 | 5 | 2 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 2030 mg/kg | 0 | 10 | 10 | 10 | 10 | 5 | - | - | - | - | - | - | - | - |
| TRAUMA | Control | 0 | 2 | 2 | 2 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - | - |
| SOILED PERI GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 3 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 2 | 2 | 5 | 5 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 1 | 3 | 3 | 6 | 7 | 9 | 3 | 2 | 2 | 1 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 4 | 4 | 4 | 8 | 7 | 5 | 2 | 1 | 1 | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | 0 | 3 | 6 | 4 | 10 | 5 | - | - | - | - | - | - | - | - |
| LACRYMATION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 2 | 5 | 7 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 1 | 2 | 3 | 2 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | 0 | 0 | 1 | 2 | 9 | 4 | - | - | - | - | - | - | - | - |

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | |
|-----------------------|------------|-------------------------|-----|-----|-----|
| | | 2-4 | 2-5 | 2-6 | 2-7 |
| | | 1 | 1 | 1 | 1 |
| COLORED | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 1 | 1 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | - | - | - | - |
| PILOERECTION | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 2 | 2 | 2 | 2 |
| | 1350 mg/kg | 1 | 1 | 1 | 1 |
| | 2030 mg/kg | - | - | - | - |
| TRAUMA | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 1 | 0 |
| | 600 mg/kg | 1 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | - | - | - | - |
| SOILED PERI GENITALIA | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 1 | 0 | 0 | 0 |
| | 1350 mg/kg | 1 | 0 | 0 | 0 |
| | 2030 mg/kg | - | - | - | - |
| LACRYMATION | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | - | - | - | - |

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | | 0-0 | 0-0 | 0-0 | 0-0 | 1-1 | 1-2 | 1-3 | 1-4 | 1-5 | 1-6 | 1-7 | 2-1 | 2-2 | 2-3 |
| | | 1 | 2 | 3 | 4 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| GUM | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - | - |
| EYE HEMORRHAGIC DISCHA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 7 | 3 | 2 | 2 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | 0 | 0 | 1 | 0 | 2 | 0 | - | - | - | - | - | - | - | - |
| EYE OPACITY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - | - |
| NOSE HEMORRHAGIC DISCHA | Control | 0 | 2 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 1 | 4 | 4 | 1 | 9 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 2 | 4 | 10 | 10 | 10 | 2 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 4 | 7 | 10 | 7 | 10 | 10 | 9 | 2 | 1 | 1 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 9 | 10 | 9 | 9 | 10 | 8 | 5 | 2 | 1 | 1 | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | 7 | 8 | 9 | 8 | 9 | 5 | - | - | - | - | - | - | - | - |
| NOSE SEROUS DISCHARGE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 2 | 1 | 6 | 7 | 7 | 2 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 2 | 1 | 7 | 6 | 3 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | 0 | 1 | 3 | 3 | 10 | 5 | - | - | - | - | - | - | - | - |

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | |
|-------------------------|------------|-------------------------|-----|-----|-----|
| | | 2-4 | 2-5 | 2-6 | 2-7 |
| | | 1 | 1 | 1 | 1 |
| GUM | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 1 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | - | - | - | - |
| EYE HEMORRHAGIC DISCHA | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | - | - | - | - |
| EYE OPACITY | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | - | - | - | - |
| NOSE HEMORRHAGIC DISCHA | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | - | - | - | - |
| NOSE SEROUS DISCHARGE | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | - | - | - | - |

STUDY NO. : 0032
ANIMAL : RAT F344
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CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

PAGE : 9

| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|------------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | | 0-0 | 0-0 | 0-0 | 0-0 | 1-1 | 1-2 | 1-3 | 1-4 | 1-5 | 1-6 | 1-7 | 2-1 | 2-2 | 2-3 |
| | | 1 | 2 | 3 | 4 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| RESPIRATORY INHIBITION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | 0 | 0 | 0 | 0 | 1 | 0 | - | - | - | - | - | - | - | - |
| IRREGULAR BREATHING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - | - |
| DIARRHEA | Control | 0 | 2 | 2 | 3 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - | - |
| LOOSE STOOL | Control | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - | - |
| SUBNORMAL TEMP | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 | 1 | 1 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | 0 | 0 | 0 | 0 | 5 | 2 | - | - | - | - | - | - | - | - |

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | |
|------------------------|------------|-------------------------|-----|-----|-----|
| | | 2-4 | 2-5 | 2-6 | 2-7 |
| | | 1 | 1 | 1 | 1 |
| RESPIRATORY INHIBITION | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | - | - | - | - |
| IRREGULAR BREATHING | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | - | - | - | - |
| DIARRHEA | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | - | - | - | - |
| LOOSE STOOL | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | - | - | - | - |
| SUBNORMAL TEMP | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | - | - | - | - |

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

PAGE : 11

| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|---------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | | 0-0 | 0-0 | 0-0 | 0-0 | 1-1 | 1-2 | 1-3 | 1-4 | 1-5 | 1-6 | 1-7 | 2-1 | 2-2 | 2-3 |
| | | 1 | 2 | 3 | 4 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| SALIVATION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 1 | 0 | 0 | 0 | 3 | 3 | 4 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 | 2 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | 2 | 2 | 1 | 1 | 8 | 4 | - | - | - | - | - | - | - | - |

(HAN190)

BAIS 2

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

PAGE : 12

| Clinical sign | Group Name | Administration Week-day | | | |
|---------------|------------|-------------------------|-----|-----|-----|
| | | 2-4 | 2-5 | 2-6 | 2-7 |
| | | 1 | 1 | 1 | 1 |
| SALIVATION | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 |
| | 2030 mg/kg | - | - | - | - |

(HAN190)

BAIS2

APPENDIX A 1-2

CLINICAL OBSERVATION (ACUTE STUDIES: SUMMARY)

RAT: FEMALE

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

PAGE : 13

| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| | | 0-0 | 0-0 | 0-0 | 0-0 | 1-1 | 1-2 | 1-3 | 1-4 | 1-5 | 1-6 | 1-7 | 2-1 | 2-2 | 2-3 | |
| | | 1 | 2 | 3 | 4 | 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 | |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 0 | 1 | 6 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | |
| | 1350 mg/kg | 0 | 0 | 0 | 0 | 2 | 10 | - | - | - | - | - | - | - | - | |
| | 2030 mg/kg | 0 | 0 | 0 | 0 | 3 | 9 | 9 | 10 | - | - | - | - | - | - | |
| LOCOMOTOR MOVEMENT DECR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 4 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 6 | 6 | 5 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | |
| | 1350 mg/kg | 0 | 0 | 1 | 9 | 10 | 6 | - | - | - | - | - | - | - | - | |
| | 2030 mg/kg | 0 | 0 | 0 | 10 | 10 | 5 | 1 | 1 | - | - | - | - | - | - | |
| PRONE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | |
| | 1350 mg/kg | 0 | 0 | 0 | 0 | 2 | 1 | - | - | - | - | - | - | - | - | |
| | 2030 mg/kg | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | - | - | - | - | - | - | |
| LATERAL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | |
| | 1350 mg/kg | 0 | 0 | 0 | 0 | 3 | 5 | - | - | - | - | - | - | - | - | |
| | 2030 mg/kg | 0 | 0 | 0 | 0 | 4 | 5 | 1 | 1 | - | - | - | - | - | - | |
| HUNCHBACK POSITION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 10 | 9 | 4 | 4 | 4 | 3 | 0 | 0 | 0 | 0 | |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 10 | 10 | 9 | 4 | 2 | 2 | 1 | 0 | 0 | 0 | |
| | 1350 mg/kg | 0 | 0 | 1 | 8 | 9 | 5 | - | - | - | - | - | - | - | - | |
| | 2030 mg/kg | 0 | 0 | 10 | 10 | 10 | 5 | 1 | 1 | - | - | - | - | - | - | |

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

PAGE : 14

| Clinical sign | Group Name | Administration Week-day | | | |
|-------------------------|------------|-------------------------|-----|-----|-----|
| | | 2-4 | 2-5 | 2-6 | 2-7 |
| | | 1 | 1 | 1 | 1 |
| DEATH | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 8 | 8 | 8 | 8 |
| | 1350 mg/kg | - | - | - | - |
| | 2030 mg/kg | - | - | - | - |
| LOCOMOTOR MOVEMENT DECR | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | - | - | - | - |
| | 2030 mg/kg | - | - | - | - |
| PRONE | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | - | - | - | - |
| | 2030 mg/kg | - | - | - | - |
| LATERAL | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | - | - | - | - |
| | 2030 mg/kg | - | - | - | - |
| HUNCHBACK POSITION | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | - | - | - | - |
| | 2030 mg/kg | - | - | - | - |

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|---------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | | 0-0 | 0-0 | 0-0 | 0-0 | 1-1 | 1-2 | 1-3 | 1-4 | 1-5 | 1-6 | 1-7 | 2-1 | 2-2 | 2-3 |
| | | 1 | 2 | 3 | 4 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| ATAXIC GAIT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 | 2 | 2 | - | - | - | - | - | - | - | - |
| | 2030 mg/kg | 0 | 0 | 0 | 0 | 2 | 2 | 0 | 0 | - | - | - | - | - | - |
| WEAKNESS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 | 3 | 3 | - | - | - | - | - | - | - | - |
| | 2030 mg/kg | 0 | 0 | 0 | 0 | 3 | 1 | 0 | 0 | - | - | - | - | - | - |
| COLORED | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 6 | 7 | 7 | 7 | 5 | 2 | 2 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 5 | 8 | 9 | 5 | 3 | 3 | 3 | 1 | 0 | 0 | 1 |
| | 900 mg/kg | 0 | 0 | 0 | 2 | 9 | 10 | 9 | 4 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 1350 mg/kg | 0 | 0 | 0 | 8 | 9 | 5 | - | - | - | - | - | - | - | - |
| | 2030 mg/kg | 0 | 0 | 0 | 5 | 10 | 5 | 1 | 1 | - | - | - | - | - | - |
| PILOERECTION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 1 | 10 | 10 | 10 | 9 | 6 | 6 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 1 | 10 | 10 | 10 | 9 | 9 | 9 | 9 | 1 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 10 | 10 | 10 | 9 | 4 | 2 | 2 | 2 | 2 | 2 | 2 |
| | 1350 mg/kg | 0 | 0 | 8 | 10 | 10 | 6 | - | - | - | - | - | - | - | - |
| | 2030 mg/kg | 0 | 0 | 10 | 10 | 10 | 5 | 1 | 1 | - | - | - | - | - | - |
| TRAUMA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - | - |
| | 2030 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - |

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | |
|---------------|------------|-------------------------|-----|-----|-----|
| | | 2-4 | 2-5 | 2-6 | 2-7 |
| | | 1 | 1 | 1 | 1 |
| ATAXIC GAIT | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | - | - | - | - |
| | 2030 mg/kg | - | - | - | - |
| WEAKNESS | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | - | - | - | - |
| | 2030 mg/kg | - | - | - | - |
| COLORED | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 1 | 2 | 0 | 0 |
| | 900 mg/kg | 1 | 1 | 0 | 0 |
| | 1350 mg/kg | - | - | - | - |
| | 2030 mg/kg | - | - | - | - |
| PILOERECTION | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 1 | 1 | 1 | 1 |
| | 1350 mg/kg | - | - | - | - |
| | 2030 mg/kg | - | - | - | - |
| TRAUMA | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | - | - | - | - |
| | 2030 mg/kg | - | - | - | - |

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | | 0-0 | 0-0 | 0-0 | 0-0 | 1-1 | 1-2 | 1-3 | 1-4 | 1-5 | 1-6 | 1-7 | 2-1 | 2-2 | 2-3 |
| | | 1 | 2 | 3 | 4 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| SOILED PERI GENITALIA | Control | 1 | 3 | 3 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 2 | 6 | 7 | 1 | 1 | 2 | 2 | 2 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 2 | 5 | 5 | 5 | 1 | 2 | 2 | 2 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 2 | 6 | 9 | 8 | 3 | 1 | 1 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 1 | 7 | 9 | 5 | - | - | - | - | - | - | - | - |
| | 2030 mg/kg | 0 | 0 | 1 | 5 | 9 | 5 | 1 | 1 | - | - | - | - | - | - |
| LACRYMATION | Control | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 1 | 2 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 1 | 1 | 1 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 4 | 7 | 7 | 5 | - | - | - | - | - | - | - | - |
| | 2030 mg/kg | 0 | 1 | 3 | 6 | 9 | 4 | 1 | 1 | - | - | - | - | - | - |
| EYE HEMORRHAGIC DISCHA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 0 | 5 | 5 | 2 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - | - |
| | 2030 mg/kg | 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 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 | 1 | 1 | - | - | - | - | - | - | - | - |
| | 2030 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - |
| NOSE HEMORRHAGIC DISCHA | Control | 0 | 3 | 4 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 3 | 7 | 7 | 10 | 10 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 1 | 5 | 8 | 9 | 10 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 6 | 9 | 10 | 10 | 10 | 10 | 8 | 2 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 7 | 10 | 10 | 10 | 10 | 6 | - | - | - | - | - | - | - | - |
| | 2030 mg/kg | 9 | 10 | 10 | 10 | 10 | 5 | 1 | 1 | - | - | - | - | - | - |

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | |
|-------------------------|------------|-------------------------|-----|-----|-----|
| | | 2-4 | 2-5 | 2-6 | 2-7 |
| | | 1 | 1 | 1 | 1 |
| SOILED PERI GENITALIA | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 1 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | - | - | - | - |
| | 2030 mg/kg | - | - | - | - |
| LACRYMATION | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | - | - | - | - |
| | 2030 mg/kg | - | - | - | - |
| EYE HEMORRHAGIC DISCHA | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | - | - | - | - |
| | 2030 mg/kg | - | - | - | - |
| EYE OPACITY | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | - | - | - | - |
| | 2030 mg/kg | - | - | - | - |
| NOSE HEMORRHAGIC DISCHA | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | - | - | - | - |
| | 2030 mg/kg | - | - | - | - |

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

PAGE : 19

| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|------------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | | 0-0 | 0-0 | 0-0 | 0-0 | 1-1 | 1-2 | 1-3 | 1-4 | 1-5 | 1-6 | 1-7 | 2-1 | 2-2 | 2-3 |
| | | 1 | 2 | 3 | 4 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| NOSE SEROUS DISCHARGE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 1 | 0 | 0 | 0 | 5 | 3 | 4 | 2 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 2 | 2 | 2 | 2 | 10 | 6 | - | - | - | - | - | - | - | - |
| | 2030 mg/kg | 0 | 0 | 0 | 0 | 10 | 5 | 1 | 1 | - | - | - | - | - | - |
| CYANOSIS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 | 1 | 0 | - | - | - | - | - | - | - | - |
| | 2030 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - |
| RESPIRATORY INHIBITION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 | 2 | 2 | - | - | - | - | - | - | - | - |
| | 2030 mg/kg | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | - | - | - | - | - | - |
| DIARRHEA | Control | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - | - |
| | 2030 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - |
| LOOSE STOOL | Control | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - | - |
| | 2030 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - |

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

PAGE : 20

| Clinical sign | Group Name | Administration Week-day | | | |
|------------------------|------------|-------------------------|-----|-----|-----|
| | | 2-4 | 2-5 | 2-6 | 2-7 |
| | | 1 | 1 | 1 | 1 |
| NOSE SEROUS DISCHARGE | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | - | - | - | - |
| | 2030 mg/kg | - | - | - | - |
| CYANOSIS | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | - | - | - | - |
| | 2030 mg/kg | - | - | - | - |
| RESPIRATORY INHIBITION | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | - | - | - | - |
| | 2030 mg/kg | - | - | - | - |
| DIARRHEA | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | - | - | - | - |
| | 2030 mg/kg | - | - | - | - |
| LOOSE STOOL | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | - | - | - | - |
| | 2030 mg/kg | - | - | - | - |

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

PAGE : 21

| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|----------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | | 0-0 | 0-0 | 0-0 | 0-0 | 1-1 | 1-2 | 1-3 | 1-4 | 1-5 | 1-6 | 1-7 | 2-1 | 2-2 | 2-3 |
| | | 1 | 2 | 3 | 4 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| SUBNORMAL TEMP | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 0 | 0 | 0 | 0 | 2 | 2 | - | - | - | - | - | - | - | - |
| | 2030 mg/kg | 0 | 0 | 0 | 0 | 3 | 1 | 0 | 0 | - | - | - | - | - | - |
| SALIVATION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 1 | 0 | 1 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | 3 | 2 | 3 | 3 | 6 | 2 | - | - | - | - | - | - | - | - |
| | 2030 mg/kg | 2 | 2 | 4 | 2 | 7 | 2 | 0 | 0 | - | - | - | - | - | - |

(HAN190)

BAIS 2

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

PAGE : 22

| Clinical sign | Group Name | Administration Week-day | | | |
|----------------|------------|-------------------------|-----|-----|-----|
| | | 2-4 | 2-5 | 2-6 | 2-7 |
| | | 1 | 1 | 1 | 1 |
| SUBNORMAL TEMP | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | - | - | - | - |
| | 2030 mg/kg | - | - | - | - |
| SALIVATION | Control | 0 | 0 | 0 | 0 |
| | 400 mg/kg | 0 | 0 | 0 | 0 |
| | 600 mg/kg | 0 | 0 | 0 | 0 |
| | 900 mg/kg | 0 | 0 | 0 | 0 |
| | 1350 mg/kg | - | - | - | - |
| | 2030 mg/kg | - | - | - | - |

(HAN190)

BAIS2

APPENDIX A 1-3

CLINICAL OBSERVATION (ACUTE STUDIES: SUMMARY)

MOUSE: MALE

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

PAGE : 1

| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | | 0-0 | 0-0 | 0-0 | 0-0 | 1-1 | 1-2 | 1-3 | 1-4 | 1-5 | 1-6 | 1-7 | 2-1 | 2-2 | 2-3 |
| | | 1 | 2 | 3 | 4 | 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 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 | 0 | 1 | 3 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| | 2500 mg/kg | 0 | 0 | 0 | 0 | 0 | 7 | 9 | 10 | - | - | - | - | - | - |
| | 4000 mg/kg | 1 | 1 | 1 | 1 | 1 | 9 | 10 | - | - | - | - | - | - | - |
| LOCOMOTOR MOVEMENT DECR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 7 | 7 | 8 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 10 | 10 | 10 | 7 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 10 | 10 | 10 | 10 | 10 | 7 | 4 | 2 | 1 | 1 | 1 | 1 | 0 | 0 |
| | 2500 mg/kg | 10 | 10 | 10 | 10 | 9 | 10 | 3 | 1 | - | - | - | - | - | - |
| | 4000 mg/kg | 9 | 9 | 9 | 9 | 9 | 5 | 1 | - | - | - | - | - | - | - |
| PRONE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 3 | 2 | 3 | 2 | 3 | 3 | 0 | 0 | - | - | - | - | - | - |
| | 4000 mg/kg | 5 | 2 | 5 | 5 | 5 | 2 | 0 | - | - | - | - | - | - | - |
| LATERAL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 0 | 1 | 0 | 2 | 4 | 4 | 0 | 0 | - | - | - | - | - | - |
| | 4000 mg/kg | 2 | 5 | 2 | 3 | 3 | 2 | 0 | - | - | - | - | - | - | - |
| HUNCHBACK POSITION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 8 | 9 | 10 | 4 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 10 | 10 | 10 | 9 | 9 | 8 | 8 | 6 | 3 | 1 | 1 | 1 | 1 | 0 |
| | 2500 mg/kg | 6 | 6 | 7 | 5 | 6 | 7 | 3 | 1 | - | - | - | - | - | - |
| | 4000 mg/kg | 4 | 4 | 4 | 4 | 4 | 4 | 1 | - | - | - | - | - | - | - |

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

PAGE : 2

| Clinical sign | Group Name | Administration Week-day | | | |
|-------------------------|------------|-------------------------|-----|-----|-----|
| | | 2-4 | 2-5 | 2-6 | 2-7 |
| | | 1 | 1 | 1 | 1 |
| DEATH | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 5 | 5 | 5 | 5 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| LOCOMOTOR MOVEMENT DECR | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| PRONE | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| LATERAL | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| HUNCHBACK POSITION | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

PAGE : 3

| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|----------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | | 0-0 | 0-0 | 0-0 | 0-0 | 1-1 | 1-2 | 1-3 | 1-4 | 1-5 | 1-6 | 1-7 | 2-1 | 2-2 | 2-3 |
| | | 1 | 2 | 3 | 4 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| ATAXIC GAIT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 1 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 1 | 2 | 2 | 0 | 1 | 2 | 2 | 1 | 1 | 1 | 1 | 0 | 0 | 0 |
| | 2500 mg/kg | 1 | 1 | 1 | 2 | 3 | 4 | 2 | 0 | - | - | - | - | - | - |
| | 4000 mg/kg | 2 | 2 | 2 | 2 | 2 | 2 | 1 | - | - | - | - | - | - | - |
| PARALYTIC GAIT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 1 | 1 | 1 | 0 | 1 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 0 | 0 | 1 | 0 | 1 | 1 | 0 | 0 | - | - | - | - | - | - |
| | 4000 mg/kg | 1 | 1 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - |
| CONVULSION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - |
| | 4000 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - |
| TREMOR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | 2500 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - |
| | 4000 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - |
| STRAUB TAIL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - |
| | 4000 mg/kg | 4 | 1 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - |

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

PAGE : 4

| Clinical sign | Group Name | Administration Week-day | | | |
|----------------|------------|-------------------------|-----|-----|-----|
| | | 2-4 | 2-5 | 2-6 | 2-7 |
| | | 1 | 1 | 1 | 1 |
| ATAXIC GAIT | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| PARALYTIC GAIT | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| CONVULSION | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| TREMOR | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| STRAUB TAIL | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

PAGE : 5

| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|---------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | | 0-0 | 0-0 | 0-0 | 0-0 | 1-1 | 1-2 | 1-3 | 1-4 | 1-5 | 1-6 | 1-7 | 2-1 | 2-2 | 2-3 |
| | | 1 | 2 | 3 | 4 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| WEAKNESS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | 2500 mg/kg | 0 | 0 | 0 | 2 | 6 | 6 | 0 | 0 | - | - | - | - | - | - |
| | 4000 mg/kg | 0 | 0 | 0 | 7 | 8 | 4 | 0 | - | - | - | - | - | - | - |
| SOILED | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 | 1 | 3 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 |
| | 2500 mg/kg | 0 | 0 | 0 | 0 | 1 | 1 | 2 | 1 | - | - | - | - | - | - |
| | 4000 mg/kg | 0 | 0 | 0 | 0 | 1 | 1 | 1 | - | - | - | - | - | - | - |
| COLORED | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 6 | 9 | 6 | 5 | 5 | 4 | 2 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 | 8 | 9 | 9 | 6 | 4 | 4 | 4 | 1 | 1 | 1 |
| | 2500 mg/kg | 0 | 0 | 0 | 0 | 10 | 10 | 3 | 1 | - | - | - | - | - | - |
| | 4000 mg/kg | 1 | 1 | 1 | 1 | 6 | 5 | 1 | - | - | - | - | - | - | - |
| PILOERECTION | Control | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | 610 mg/kg | 8 | 5 | 3 | 1 | 10 | 7 | 7 | 5 | 5 | 3 | 3 | 1 | 1 | 3 |
| | 977 mg/kg | 3 | 0 | 0 | 1 | 9 | 10 | 9 | 10 | 10 | 7 | 6 | 0 | 0 | 0 |
| | 1560 mg/kg | 4 | 3 | 3 | 5 | 10 | 10 | 9 | 7 | 5 | 5 | 4 | 1 | 1 | 1 |
| | 2500 mg/kg | 6 | 4 | 4 | 4 | 8 | 8 | 3 | 1 | - | - | - | - | - | - |
| | 4000 mg/kg | 6 | 6 | 6 | 6 | 6 | 3 | 1 | - | - | - | - | - | - | - |
| LOSS OF HAIR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - |
| | 4000 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - |

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

PAGE : 6

| Clinical sign | Group Name | Administration Week-day | | | |
|---------------|------------|-------------------------|-----|-----|-----|
| | | 2-4 | 2-5 | 2-6 | 2-7 |
| | | 1 | 1 | 1 | 1 |
| WEAKNESS | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| SOILED | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 1 | 1 | 1 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| COLORED | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 1 | 1 | 1 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| PILOERECTION | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 2 | 0 | 1 | 1 |
| | 977 mg/kg | 0 | 0 | 0 | 1 |
| | 1560 mg/kg | 1 | 1 | 1 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| LOSS OF HAIR | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 1 | 1 | 1 | 2 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

PAGE : 7

| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-----------------------|------------|-------------------------|---|-----|---|-----|----|-----|---|-----|---|-----|---|-----|---|
| | | 0-0 | | 0-0 | | 0-0 | | 0-0 | | 1-1 | | 1-2 | | 1-3 | |
| | | 1 | 2 | 3 | 4 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| TRAUMA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - |
| | 4000 mg/kg | 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 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 1 | 0 | 5 | 2 | 1 | 2 | 0 | 2 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 1 | 1 | 0 | 0 | 7 | 9 | 7 | 5 | 3 | 2 | 2 | 1 | 1 | 1 |
| | 2500 mg/kg | 0 | 1 | 0 | 0 | 9 | 10 | 3 | 1 | - | - | - | - | - | - |
| | 4000 mg/kg | 1 | 1 | 0 | 0 | 6 | 5 | 1 | - | - | - | - | - | - | - |
| LACRYMATION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 2 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 1 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | - | - | - | - | - | - |
| | 4000 mg/kg | 2 | 1 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - |
| GUM | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 | 0 | 1 | 2 | 2 | 1 | 1 | 1 | 1 | 0 | 0 |
| | 2500 mg/kg | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | - | - | - | - | - | - |
| | 4000 mg/kg | 0 | 0 | 0 | 0 | 0 | 1 | 1 | - | - | - | - | - | - | - |
| NOSE SEROUS DISCHARGE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 4 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 9 | 3 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 10 | 0 | 0 | 0 | 2 | 2 | 0 | 0 | - | - | - | - | - | - |
| | 4000 mg/kg | 10 | 1 | 1 | 0 | 4 | 2 | 0 | - | - | - | - | - | - | - |

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

PAGE : 8

| Clinical sign | Group Name | Administration Week-day | | | |
|-----------------------|------------|-------------------------|-----|-----|-----|
| | | 2-4 | 2-5 | 2-6 | 2-7 |
| | | 1 | 1 | 1 | 1 |
| TRAUMA | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| SOILED PERI GENITALIA | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 1 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| LACRYMATION | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| GUM | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| NOSE SEROUS DISCHARGE | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

PAGE : 9

| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|------------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | | 0-0 | 0-0 | 0-0 | 0-0 | 1-1 | 1-2 | 1-3 | 1-4 | 1-5 | 1-6 | 1-7 | 2-1 | 2-2 | 2-3 |
| | | 1 | 2 | 3 | 4 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| NOSE FORMY DISCHARGE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - |
| | 4000 mg/kg | 0 | 0 | 0 | 0 | 1 | 0 | 0 | - | - | - | - | - | - | - |
| RESPIRATORY INHIBITION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | 2500 mg/kg | 0 | 0 | 0 | 0 | 1 | 2 | 2 | 0 | - | - | - | - | - | - |
| | 4000 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - |
| IRREGULAR BREATHING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 1 | 1 | 3 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 6 | 5 | 6 | 7 | 7 | 7 | 1 | 1 | - | - | - | - | - | - |
| | 4000 mg/kg | 8 | 7 | 8 | 8 | 8 | 4 | 1 | - | - | - | - | - | - | - |
| NOISY | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - |
| | 4000 mg/kg | 1 | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - |
| SUBNORMAL TEMP | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 0 | 0 | 2 | 2 | 3 | 3 | 0 | 0 | - | - | - | - | - | - |
| | 4000 mg/kg | 0 | 0 | 3 | 7 | 7 | 3 | 0 | - | - | - | - | - | - | - |

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

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| Clinical sign | Group Name | Administration Week-day | | | |
|------------------------|------------|-------------------------|-----|-----|-----|
| | | 2-4 | 2-5 | 2-6 | 2-7 |
| | | 1 | 1 | 1 | 1 |
| NOSE FORMY DISCHARGE | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| RESPIRATORY INHIBITION | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| IRREGULAR BREATHING | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| NOISY | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| SUBNORMAL TEMP | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

PAGE : 11

| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|---------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | | 0-0 | 0-0 | 0-0 | 0-0 | 1-1 | 1-2 | 1-3 | 1-4 | 1-5 | 1-6 | 1-7 | 2-1 | 2-2 | 2-3 |
| | | 1 | 2 | 3 | 4 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| SALIVATION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 1 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 3 | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 6 | 0 | 0 | 0 | 2 | 2 | 1 | 0 | - | - | - | - | - | - |
| | 4000 mg/kg | 10 | 2 | 0 | 1 | 2 | 1 | 1 | - | - | - | - | - | - | - |

(HAN190)

BAIS2

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

PAGE : 12

| Clinical sign | Group Name | Administration Week-day | | | |
|---------------|------------|-------------------------|-----|-----|-----|
| | | 2-4 | 2-5 | 2-6 | 2-7 |
| | | 1 | 1 | 1 | 1 |
| SALIVATION | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |

(HAN190)

BAIS 2

APPENDIX A 1-4

CLINICAL OBSERVATION (ACUTE STUDIES: SUMMARY)

MOUSE: FEMALE

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

PAGE : 13

| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-------------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | | 0-0 | 0-0 | 0-0 | 0-0 | 1-1 | 1-2 | 1-3 | 1-4 | 1-5 | 1-6 | 1-7 | 2-1 | 2-2 | 2-3 |
| | | 1 | 2 | 3 | 4 | 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 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 | 0 | 1 | 6 | 6 | 7 | 7 | 7 | 7 | 7 | 7 |
| | 2500 mg/kg | 0 | 0 | 0 | 0 | 1 | 8 | 10 | - | - | - | - | - | - | - |
| | 4000 mg/kg | 1 | 2 | 2 | 2 | 3 | 10 | - | - | - | - | - | - | - | - |
| LOCOMOTOR MOVEMENT DECR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 4 | 4 | 10 | 10 | 6 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 6 | 7 | 10 | 10 | 8 | 8 | 7 | 2 | 1 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 8 | 8 | 10 | 10 | 10 | 9 | 2 | - | - | - | - | - | - | - |
| | 4000 mg/kg | 10 | 9 | 8 | 8 | 8 | 6 | - | - | - | - | - | - | - | - |
| LOCOMOTOR MOVEMENT INCR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - |
| | 4000 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - | - |
| PRONE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 3 | 1 | 1 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 2 | 1 | 2 | 2 | 4 | 4 | 0 | - | - | - | - | - | - | - |
| | 4000 mg/kg | 6 | 6 | 5 | 3 | 3 | 3 | - | - | - | - | - | - | - | - |
| LATERAL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 1 | 0 | 0 | 1 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 3 | 1 | 1 | 1 | 1 | 2 | 1 | - | - | - | - | - | - | - |
| | 4000 mg/kg | 1 | 1 | 1 | 5 | 5 | 3 | - | - | - | - | - | - | - | - |

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

PAGE : 14

| Clinical sign | Group Name | Administration Week-day | | | |
|-------------------------|------------|-------------------------|-----|-----|-----|
| | | 2-4 | 2-5 | 2-6 | 2-7 |
| | | 1 | 1 | 1 | 1 |
| DEATH | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 1 | 1 | 1 | 1 |
| | 1560 mg/kg | 7 | 7 | 7 | 7 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| LOCOMOTOR MOVEMENT DECR | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| LOCOMOTOR MOVEMENT INCR | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| PRONE | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| LATERAL | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|--------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | | 0-0 | 0-0 | 0-0 | 0-0 | 1-1 | 1-2 | 1-3 | 1-4 | 1-5 | 1-6 | 1-7 | 2-1 | 2-2 | 2-3 |
| | | 1 | 2 | 3 | 4 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| HUNCHBACK POSITION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 3 | 4 | 6 | 7 | 9 | 3 | 2 | 4 | 2 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 5 | 9 | 9 | 9 | 9 | 9 | 9 | 4 | 1 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 5 | 10 | 10 | 10 | 10 | 9 | 2 | - | - | - | - | - | - | - |
| | 4000 mg/kg | 2 | 6 | 6 | 7 | 6 | 6 | - | - | - | - | - | - | - | - |
| BODY SAG | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 2 | 1 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - |
| | 4000 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - | - |
| ATAXIC GAIT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 1 | 1 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 2 | 3 | 1 | 1 | 4 | 2 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 1 | 2 | 5 | 5 | 4 | 4 | 1 | - | - | - | - | - | - | - |
| | 4000 mg/kg | 1 | 1 | 1 | 1 | 1 | 1 | - | - | - | - | - | - | - | - |
| PARALYTIC GAIT | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 | 2 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 0 | 0 | 0 | 0 | 1 | 0 | 0 | - | - | - | - | - | - | - |
| | 4000 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - | - |
| CONVULSION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 5 | 1 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - |
| | 4000 mg/kg | 6 | 1 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - | - |

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

PAGE : 16

| Clinical sign | Group Name | Administration Week-day | | | |
|--------------------|------------|-------------------------|-----|-----|-----|
| | | 2-4 | 2-5 | 2-6 | 2-7 |
| | | 1 | 1 | 1 | 1 |
| HUNCHBACK POSITION | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| BODY SAG | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| ATAXIC GAIT | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| PARALYTIC GAIT | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| CONVULSION | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

PAGE : 17

| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|---------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | | 0-0 | 0-0 | 0-0 | 0-0 | 1-1 | 1-2 | 1-3 | 1-4 | 1-5 | 1-6 | 1-7 | 2-1 | 2-2 | 2-3 |
| | | 1 | 2 | 3 | 4 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| STRAUB TAIL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 3 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 3 | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - |
| | 4000 mg/kg | 4 | 1 | 1 | 0 | 0 | 0 | - | - | - | - | - | - | - | - |
| WEAKNESS | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 0 | 0 | 0 | 0 | 4 | 6 | 1 | - | - | - | - | - | - | - |
| | 4000 mg/kg | 0 | 0 | 0 | 0 | 7 | 6 | - | - | - | - | - | - | - | - |
| SOILED | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 3 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 | 2 | 3 | 3 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - |
| | 4000 mg/kg | 0 | 0 | 0 | 0 | 1 | 1 | - | - | - | - | - | - | - | - |
| COLORED | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 1 | 3 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 | 5 | 10 | 8 | 3 | 3 | 2 | 2 | 0 | 0 | 0 |
| | 2500 mg/kg | 0 | 0 | 0 | 0 | 8 | 9 | 2 | - | - | - | - | - | - | - |
| | 4000 mg/kg | 0 | 0 | 0 | 0 | 7 | 6 | - | - | - | - | - | - | - | - |
| PILOERECTION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 1 | 0 | 7 | 1 | 2 | 2 | 3 | 3 | 2 | 2 | 2 | 2 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 4 | 10 | 10 | 10 | 9 | 9 | 8 | 6 | 1 | 1 | 0 |
| | 1560 mg/kg | 1 | 3 | 1 | 5 | 9 | 9 | 9 | 4 | 3 | 2 | 1 | 0 | 0 | 0 |
| | 2500 mg/kg | 1 | 4 | 5 | 8 | 8 | 8 | 2 | - | - | - | - | - | - | - |
| | 4000 mg/kg | 1 | 2 | 2 | 1 | 4 | 4 | - | - | - | - | - | - | - | - |

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | |
|---------------|------------|-------------------------|-----|-----|-----|
| | | 2-4 | 2-5 | 2-6 | 2-7 |
| | | 1 | 1 | 1 | 1 |
| STRAUB TAIL | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| WEAKNESS | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| SOILED | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| COLORED | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| PILOERECTION | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|-----------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | | 0-0 | 0-0 | 0-0 | 0-0 | 1-1 | 1-2 | 1-3 | 1-4 | 1-5 | 1-6 | 1-7 | 2-1 | 2-2 | 2-3 |
| | | 1 | 2 | 3 | 4 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| TRAUMA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - |
| | 4000 mg/kg | 1 | 1 | 1 | 1 | 1 | 1 | - | - | - | - | - | - | - | - |
| SOILED PERI GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 4 | 4 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 | 4 | 10 | 8 | 1 | 1 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 0 | 0 | 0 | 0 | 7 | 9 | 1 | - | - | - | - | - | - | - |
| | 4000 mg/kg | 0 | 0 | 0 | 0 | 7 | 6 | - | - | - | - | - | - | - | - |
| LACRYMATION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 | 0 | 1 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 0 | 0 | 0 | 0 | 1 | 0 | 0 | - | - | - | - | - | - | - |
| | 4000 mg/kg | 0 | 0 | 0 | 0 | 4 | 3 | - | - | - | - | - | - | - | - |
| GUM | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - |
| | 4000 mg/kg | 0 | 0 | 0 | 0 | 2 | 2 | - | - | - | - | - | - | - | - |
| NOSE SEROUS DISCHARGE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 1 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 3 | 3 | 0 | 0 | 2 | 0 | 0 | - | - | - | - | - | - | - |
| | 4000 mg/kg | 2 | 3 | 1 | 0 | 4 | 4 | - | - | - | - | - | - | - | - |

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | |
|-----------------------|------------|-------------------------|-----|-----|-----|
| | | 2-4 | 2-5 | 2-6 | 2-7 |
| | | 1 | 1 | 1 | 1 |
| TRAUMA | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| SOILED PERI GENITALIA | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| LACRYMATION | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| GUM | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| NOSE SEROUS DISCHARGE | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | | | | | | | | | | | |
|------------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | | 0-0 | 0-0 | 0-0 | 0-0 | 1-1 | 1-2 | 1-3 | 1-4 | 1-5 | 1-6 | 1-7 | 2-1 | 2-2 | 2-3 |
| | | 1 | 2 | 3 | 4 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| RESPIRATORY INHIBITION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 | 0 | 5 | 5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 0 | 0 | 0 | 0 | 2 | 5 | 2 | - | - | - | - | - | - | - |
| | 4000 mg/kg | 0 | 1 | 0 | 0 | 6 | 5 | - | - | - | - | - | - | - | - |
| IRREGULAR BREATHING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 3 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 1 | 1 | 0 | 1 | 5 | 4 | 0 | - | - | - | - | - | - | - |
| | 4000 mg/kg | 3 | 3 | 3 | 3 | 2 | 1 | - | - | - | - | - | - | - | - |
| LOOSE STOOL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - |
| | 4000 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | - | - | - | - | - | - | - | - |
| SUBNORMAL TEMP | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 0 | 0 | 0 | 0 | 4 | 4 | 0 | - | - | - | - | - | - | - |
| | 4000 mg/kg | 0 | 1 | 0 | 0 | 6 | 5 | - | - | - | - | - | - | - | - |
| SALIVATION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | 3 | 3 | 0 | 0 | 7 | 4 | 0 | - | - | - | - | - | - | - |
| | 4000 mg/kg | 4 | 3 | 0 | 0 | 5 | 3 | - | - | - | - | - | - | - | - |

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

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| Clinical sign | Group Name | Administration Week-day | | | |
|------------------------|------------|-------------------------|-----|-----|-----|
| | | 2-4 | 2-5 | 2-6 | 2-7 |
| | | 1 | 1 | 1 | 1 |
| RESPIRATORY INHIBITION | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| IRREGULAR BREATHING | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| LOOSE STOOL | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| SUBNORMAL TEMP | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |
| SALIVATION | Control | 0 | 0 | 0 | 0 |
| | 610 mg/kg | 0 | 0 | 0 | 0 |
| | 977 mg/kg | 0 | 0 | 0 | 0 |
| | 1560 mg/kg | 0 | 0 | 0 | 0 |
| | 2500 mg/kg | - | - | - | - |
| | 4000 mg/kg | - | - | - | - |

APPENDIX A 2-1

BODY WEIGHT CHANGES (ACUTE STUDIES: SUMMARY)

RAT: MALE

STUDY NO. : 0032
 ANIMAL : RAT F344
 UNIT : g
 REPORT TYPE : A1 2
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 1

| Group Name | Administration | | week-day | | | | | | | | | | | |
|------------|----------------|---|----------|-----|------|-----|------|------|------|------|------|------|------|------|
| | 0-0 | | 1-1 | | 1-2 | | 1-4 | | 1-7 | | 2-3 | | 2-7 | |
| Control | 109± | 4 | 122± | 4 | 129± | 4 | 141± | 5 | 160± | 6 | 179± | 7 | 202± | 7 |
| 400 mg/kg | 109± | 4 | 107± | 3** | 112± | 4 | 126± | 4** | 146± | 7** | 169± | 7 | 196± | 8 |
| 600 mg/kg | 109± | 4 | 102± | 4** | 100± | 7** | 114± | 9** | 135± | 10** | 159± | 11** | 188± | 13* |
| 900 mg/kg | 109± | 4 | 99± | 3** | 90± | 3** | 86± | 13** | 108± | 18** | 133± | 23** | 165± | 24** |
| 1350 mg/kg | 109± | 4 | 98± | 4** | 92± | 4** | 89± | 7** | 111± | 0 | 138± | 0 | 175± | 0 |
| 2030 mg/kg | 109± | 4 | 97± | 4** | 94± | 0** | - | | - | | - | | - | |

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

Test of Dunnett

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BAIS 2

APPENDIX A 2-2

BODY WEIGHT CHANGES (ACUTE STUDIES: SUMMARY)

RAT: FEMALE

STUDY NO. : 0032
 ANIMAL : RAT F344
 UNIT : g
 REPORT TYPE : A1 2
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 2

| Group Name | Administration | | week-day | | | | | | | | | | | |
|------------|----------------|---|----------|-----|-----|-----|------|------|------|-----|------|----|------|---|
| | 0-0 | | 1-1 | | 1-2 | | 1-4 | | 1-7 | | 2-3 | | 2-7 | |
| Control | 84± | 2 | 92± | 6 | 95± | 9 | 100± | 13 | 111± | 7 | 122± | 5 | 133± | 5 |
| 400 mg/kg | 84± | 2 | 83± | 5 | 86± | 3 | 95± | 4 | 106± | 4 | 120± | 4 | 134± | 4 |
| 600 mg/kg | 84± | 2 | 80± | 4* | 80± | 3 | 91± | 3** | 104± | 3** | 120± | 3 | 135± | 4 |
| 900 mg/kg | 84± | 2 | 77± | 2** | 73± | 4** | 73± | 11** | 92± | 7** | 112± | 6* | 134± | 3 |
| 1350 mg/kg | 84± | 2 | 77± | 3** | 73± | 1** | - | | - | | - | | - | |
| 2030 mg/kg | 84± | 2 | 76± | 2** | 74± | 3** | - | | - | | - | | - | |

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

Test of Dunnett

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BAIS 2

APPENDIX A 2-3

BODY WEIGHT CHANGES (ACUTE STUDIES: SUMMARY)

MOUSE: MALE

STUDY NO. : 0033
 ANIMAL : MOUSE BDF1
 UNIT : g
 REPORT TYPE : A1 2
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 1

| Group Name | Administration week-day | | | | | | |
|------------|-------------------------|-------------|-------------|-------------|-----------|-----------|-----------|
| | 0-0 | 1-1 | 1-2 | 1-4 | 1-7 | 2-3 | 2-7 |
| Control | 20.7± 0.8 | 23.2± 0.7 | 24.0± 0.8 | 24.7± 0.9 | 25.0± 0.8 | 25.3± 0.9 | 26.2± 0.8 |
| 610 mg/kg | 20.7± 0.8 | 20.4± 1.1** | 22.8± 1.4* | 24.4± 1.4 | 25.2± 1.6 | 25.3± 1.6 | 26.5± 1.7 |
| 977 mg/kg | 20.8± 0.8 | 19.6± 1.1** | 21.5± 0.9** | 23.2± 1.3 | 25.2± 1.2 | 25.6± 1.1 | 26.6± 1.0 |
| 1560 mg/kg | 20.8± 0.8 | 19.3± 0.9** | 18.3± 1.0** | 18.2± 1.9** | 21.1± 5.0 | 24.5± 3.0 | 26.1± 2.0 |
| 2500 mg/kg | 20.7± 0.9 | 19.2± 0.8** | 18.6± 0.9** | 18.2± 0.0 | - | - | - |
| 4000 mg/kg | 20.8± 0.8 | 19.9± 0.7** | 19.0± 0.7** | - | - | - | - |

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

Test of Dunnett

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BAIS 2

APPENDIX A 2-4

BODY WEIGHT CHANGES (ACUTE STUDIES: SUMMARY)

MOUSE: FEMALE

STUDY NO. : 0033
 ANIMAL : MOUSE BDF1
 UNIT : g
 REPORT TYPE : A1 2
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 2

| Group Name | Administration week-day | | | | | | |
|------------|-------------------------|-------------|-------------|-------------|-----------|-----------|-----------|
| | 0-0 | 1-1 | 1-2 | 1-4 | 1-7 | 2-3 | 2-7 |
| Control | 15.9± 0.7 | 18.1± 0.8 | 18.3± 0.8 | 18.9± 0.9 | 19.0± 0.8 | 19.0± 0.8 | 19.6± 0.8 |
| 610 mg/kg | 15.8± 0.7 | 15.5± 0.9** | 17.2± 0.8* | 18.6± 0.8 | 19.1± 1.0 | 19.0± 0.9 | 19.7± 0.8 |
| 977 mg/kg | 15.9± 0.6 | 14.8± 0.6** | 15.7± 1.0** | 17.2± 0.9** | 19.5± 1.2 | 20.0± 0.8 | 20.2± 0.7 |
| 1560 mg/kg | 15.9± 0.6 | 14.5± 0.5** | 13.7± 0.8** | 15.1± 2.2** | 19.7± 0.7 | 19.3± 0.8 | 19.8± 0.4 |
| 2500 mg/kg | 15.9± 0.6 | 14.7± 0.5** | 14.0± 0.6** | - | - | - | - |
| 4000 mg/kg | 15.9± 0.7 | 15.0± 0.6** | 14.8± 0.5** | - | - | - | - |

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HAN260)

BAIS2

APPENDIX A 3-1

GROSS FINDINGS (ACUTE STUDIES: SUMMARY)

RAT: MALE: DEAD AND MORIBUND ANIMALS

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

PAGE : 1

| Organ | Findings | Group Name NO. of Animals | Control 0 (%) | 400 mg/kg 0 (%) | 600 mg/kg 0 (%) | 900 mg/kg 8 (%) |
|-------------|-------------|------------------------------|------------------|--------------------|--------------------|--------------------|
| subcutis | black zone | | - (-) | - (-) | - (-) | 1 (13) |
| lung | red | | - (-) | - (-) | - (-) | 0 (0) |
| | brown | | - (-) | - (-) | - (-) | 6 (75) |
| thymus | atrophic | | - (-) | - (-) | - (-) | 7 (88) |
| | red | | - (-) | - (-) | - (-) | 1 (13) |
| | red zone | | - (-) | - (-) | - (-) | 4 (50) |
| heart | red zone | | - (-) | - (-) | - (-) | 5 (63) |
| rectum | red zone | | - (-) | - (-) | - (-) | 1 (13) |
| large intes | fluid:red | | - (-) | - (-) | - (-) | 0 (0) |
| liver | enlarged | | - (-) | - (-) | - (-) | 0 (0) |
| | herniation | | - (-) | - (-) | - (-) | 1 (13) |
| urin bladd | urine:red | | - (-) | - (-) | - (-) | 4 (50) |
| | urine:brown | | - (-) | - (-) | - (-) | 3 (38) |
| testis | red | | - (-) | - (-) | - (-) | 2 (25) |
| brain | hemorrhage | | - (-) | - (-) | - (-) | 1 (13) |
| eye | red | | - (-) | - (-) | - (-) | 2 (25) |
| | white zone | | - (-) | - (-) | - (-) | 2 (25) |
| other | blood:brown | | - (-) | - (-) | - (-) | 7 (88) |

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

PAGE : 2

| Organ | Findings | Group Name NO. of Animals | 1350 mg/kg 9 (%) | 2030 mg/kg 10 (%) |
|-------------|-------------|------------------------------|---------------------|----------------------|
| subcutis | black zone | | 0 (0) | 0 (0) |
| lung | red | | 0 (0) | 2 (20) |
| | brown | | 6 (67) | 8 (80) |
| thymus | atrophic | | 4 (44) | 0 (0) |
| | red | | 2 (22) | 0 (0) |
| | red zone | | 6 (67) | 9 (90) |
| heart | red zone | | 2 (22) | 0 (0) |
| rectum | red zone | | 0 (0) | 0 (0) |
| large intes | fluid:red | | 1 (11) | 0 (0) |
| liver | enlarged | | 1 (11) | 0 (0) |
| | herniation | | 0 (0) | 0 (0) |
| urin bladd | urine:red | | 2 (22) | 2 (20) |
| | urine:brown | | 4 (44) | 8 (80) |
| testis | red | | 2 (22) | 0 (0) |
| brain | hemorrhage | | 0 (0) | 0 (0) |
| eye | red | | 0 (0) | 0 (0) |
| | white zone | | 3 (33) | 0 (0) |
| other | blood:brown | | 8 (89) | 8 (80) |

APPENDIX A 3-2

GROSS FINDINGS (ACUTE STUDIES: SUMMARY)

RAT: FEMALE: DEAD AND MORIBUND ANIMALS

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

PAGE : 3

| Organ | Findings | Group Name NO. of Animals | Control 0 (%) | 400 mg/kg 0 (%) | 600 mg/kg 0 (%) | 900 mg/kg 8 (%) |
|------------|----------------|------------------------------|------------------|--------------------|--------------------|--------------------|
| subcutis | jaundice | | - (-) | - (-) | - (-) | 1 (13) |
| lung | brown | | - (-) | - (-) | - (-) | 6 (75) |
| | red zone | | - (-) | - (-) | - (-) | 1 (13) |
| thymus | atrophic | | - (-) | - (-) | - (-) | 7 (88) |
| | red zone | | - (-) | - (-) | - (-) | 3 (38) |
| heart | red zone | | - (-) | - (-) | - (-) | 4 (50) |
| urin bladd | red patch/zone | | - (-) | - (-) | - (-) | 2 (25) |
| | red zone | | - (-) | - (-) | - (-) | 1 (13) |
| | urine:red | | - (-) | - (-) | - (-) | 4 (50) |
| | urine:brown | | - (-) | - (-) | - (-) | 2 (25) |
| pleura | red zone | | - (-) | - (-) | - (-) | 0 (0) |
| other | blood:brown | | - (-) | - (-) | - (-) | 7 (88) |

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2w)

PAGE : 4

| Organ | Findings | Group Name | 1350 mg/kg | 2030 mg/kg |
|------------|----------------|----------------|------------|------------|
| | | NO. of Animals | 10 (%) | 10 (%) |
| subcutis | jaundice | | 0 (0) | 0 (0) |
| lung | brown | | 4 (40) | 6 (60) |
| | red zone | | 0 (0) | 0 (0) |
| thymus | atrophic | | 1 (10) | 0 (0) |
| | red zone | | 9 (90) | 9 (90) |
| heart | red zone | | 2 (20) | 0 (0) |
| urin bladd | red patch/zone | | 0 (0) | 0 (0) |
| | red zone | | 0 (0) | 0 (0) |
| | urine:red | | 3 (30) | 3 (30) |
| | urine:brown | | 1 (10) | 2 (20) |
| pleura | red zone | | 1 (10) | 0 (0) |
| other | blood:brown | | 10 (100) | 8 (80) |

APPENDIX A 3-3

GROSS FINDINGS (ACUTE STUDIES: SUMMARY)

RAT: MALE: SACRIFICED ANIMALS

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

PAGE : 1

| Organ | Findings | Group Name | Control | 400 mg/kg | 600 mg/kg | 900 mg/kg |
|--------|----------|----------------|---------|-----------|-----------|-----------|
| | | NO. of Animals | 10 (%) | 10 (%) | 10 (%) | 2 (%) |
| thymus | red zone | | 0 (0) | 1 (10) | 0 (0) | 0 (0) |
| testis | atrophic | | 0 (0) | 0 (0) | 2 (20) | 2 (100) |
| eye | red zone | | 0 (0) | 0 (0) | 0 (0) | 1 (50) |

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BAIS 2

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

PAGE : 2

| Organ | Findings | Group Name | 1350 mg/kg | 2030 mg/kg |
|--------|----------|----------------|------------|------------|
| | | NO. of Animals | 1 (%) | 0 (%) |
| thymus | red zone | | 0 (0) | - (-) |
| testis | atrophic | | 1 (100) | - (-) |
| eye | red zone | | 0 (0) | - (-) |

(HPT080)

BAIS 2

APPENDIX A 3-4

GROSS FINDINGS (ACUTE STUDIES: SUMMARY)

RAT: FEMALE: SACRIFICED ANIMALS

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

PAGE : 3

| Organ | Findings | Group Name | Control | 400 mg/kg | 600 mg/kg | 900 mg/kg |
|--------|----------|----------------|---------|-----------|-----------|-----------|
| | | NO. of Animals | 10 (%) | 10 (%) | 10 (%) | 2 (%) |
| spleen | enlarged | | 0 (0) | 0 (0) | 0 (0) | 1 (50) |

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BAIS 2

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

PAGE : 4

| Organ | Findings | Group Name | 1350 mg/kg | 2030 mg/kg |
|--------|----------|----------------|------------|------------|
| | | NO. of Animals | 0 (%) | 0 (%) |
| spleen | enlarged | | - (-) | - (-) |

(HPT080)

BAIS 2

APPENDIX A 3-5

GROSS FINDINGS (ACUTE STUDIES: SUMMARY)

MOUSE: MALE: DEAD AND MORIBUND ANIMALS

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

PAGE : 1

| Organ | Findings | Group Name NO. of Animals | Control 0 (%) | 610 mg/kg 0 (%) | 977 mg/kg 0 (%) | 1560 mg/kg 5 (%) |
|-------------|----------------------|------------------------------|------------------|--------------------|--------------------|---------------------|
| lung | red | | - (-) | - (-) | - (-) | 0 (0) |
| | brown | | - (-) | - (-) | - (-) | 5 (100) |
| | red zone | | - (-) | - (-) | - (-) | 0 (0) |
| thymus | atrophic | | - (-) | - (-) | - (-) | 4 (80) |
| heart | red zone | | - (-) | - (-) | - (-) | 0 (0) |
| gl stomach | red zone | | - (-) | - (-) | - (-) | 0 (0) |
| stomach | fluid:black | | - (-) | - (-) | - (-) | 0 (0) |
| liver | enlarged | | - (-) | - (-) | - (-) | 0 (0) |
| | red | | - (-) | - (-) | - (-) | 1 (20) |
| | brown | | - (-) | - (-) | - (-) | 0 (0) |
| | soft | | - (-) | - (-) | - (-) | 1 (20) |
| urin bladd | red | | - (-) | - (-) | - (-) | 1 (20) |
| | urine:brown | | - (-) | - (-) | - (-) | 0 (0) |
| eye | turbid | | - (-) | - (-) | - (-) | 0 (0) |
| thoracic ca | fluid:test substance | | - (-) | - (-) | - (-) | 0 (0) |
| other | blood:brown | | - (-) | - (-) | - (-) | 1 (20) |

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

PAGE : 2

| Organ | Findings | Group Name | 2500 mg/kg | 4000 mg/kg |
|-------------|----------------------|----------------|------------|------------|
| | | NO. of Animals | 10 (%) | 10 (%) |
| lung | red | | 0 (0) | 1 (10) |
| | brown | | 8 (80) | 2 (20) |
| | red zone | | 2 (20) | 2 (20) |
| thymus | atrophic | | 3 (30) | 1 (10) |
| heart | red zone | | 0 (0) | 3 (30) |
| gl stomach | red zone | | 1 (10) | 0 (0) |
| stomach | fluid:black | | 0 (0) | 1 (10) |
| liver | enlarged | | 1 (10) | 1 (10) |
| | red | | 0 (0) | 0 (0) |
| | brown | | 3 (30) | 1 (10) |
| | soft | | 0 (0) | 2 (20) |
| urin bladd | red | | 1 (10) | 0 (0) |
| | urine:brown | | 1 (10) | 0 (0) |
| eye | turbid | | 0 (0) | 1 (10) |
| thoracic ca | fluid:test substance | | 0 (0) | 1 (10) |
| other | blood:brown | | 5 (50) | 5 (50) |

APPENDIX A 3-6

GROSS FINDINGS (ACUTE STUDIES: SUMMARY)

MOUSE: FEMALE: DEAD AND MORIBUND ANIMALS

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

PAGE : 3

| Organ | Findings | Group Name NO. of Animals | Control 0 (%) | 610 mg/kg 0 (%) | 977 mg/kg 1 (%) | 1560 mg/kg 7 (%) |
|-------------|-------------|------------------------------|------------------|--------------------|--------------------|---------------------|
| lung | red | | - (-) | - (-) | 0 (0) | 3 (43) |
| | brown | | - (-) | - (-) | 1 (100) | 4 (57) |
| | red zone | | - (-) | - (-) | 0 (0) | 0 (0) |
| | edema | | - (-) | - (-) | 0 (0) | 0 (0) |
| thymus | atrophic | | - (-) | - (-) | 1 (100) | 6 (86) |
| heart | red zone | | - (-) | - (-) | 0 (0) | 0 (0) |
| gl stomach | red | | - (-) | - (-) | 0 (0) | 1 (14) |
| | fluid:black | | - (-) | - (-) | 0 (0) | 1 (14) |
| stomach | fluid:black | | - (-) | - (-) | 0 (0) | 0 (0) |
| liver | red | | - (-) | - (-) | 0 (0) | 0 (0) |
| | brown | | - (-) | - (-) | 1 (100) | 1 (14) |
| | soft | | - (-) | - (-) | 0 (0) | 0 (0) |
| eye | turbid | | - (-) | - (-) | 0 (0) | 0 (0) |
| thoracic ca | hemorrhage | | - (-) | - (-) | 0 (0) | 0 (0) |
| other | blood:brown | | - (-) | - (-) | 0 (0) | 0 (0) |

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

PAGE : 4

| Organ | Findings | Group Name NO. of Animals | 2500 mg/kg 10 (%) | 4000 mg/kg 10 (%) |
|-------------|-------------|------------------------------|----------------------|----------------------|
| lung | red | | 0 (0) | 3 (30) |
| | brown | | 7 (70) | 3 (30) |
| | red zone | | 2 (20) | 2 (20) |
| | edema | | 0 (0) | 1 (10) |
| thymus | atrophic | | 3 (30) | 0 (0) |
| heart | red zone | | 1 (10) | 0 (0) |
| gl stomach | red | | 0 (0) | 0 (0) |
| | fluid:black | | 0 (0) | 0 (0) |
| stomach | fluid:black | | 0 (0) | 1 (10) |
| liver | red | | 1 (10) | 0 (0) |
| | brown | | 0 (0) | 0 (0) |
| | soft | | 1 (10) | 0 (0) |
| eye | turbid | | 1 (10) | 0 (0) |
| thoracic ca | hemorrhage | | 0 (0) | 1 (10) |
| other | blood:brown | | 7 (70) | 6 (60) |

APPENDIX A 3-7

GROSS FINDINGS (ACUTE STUDIES: SUMMARY)

MOUSE: MALE: SACRIFICED ANIMALS

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

PAGE : 1

| Organ | Findings | Group Name | Control | 610 mg/kg | 977 mg/kg | 1560 mg/kg |
|--------|----------|----------------|---------|-----------|-----------|------------|
| | | NO. of Animals | 10 (%) | 10 (%) | 10 (%) | 5 (%) |
| Lung | red | | 0 (0) | 0 (0) | 1 (10) | 0 (0) |
| thymus | atrophic | | 0 (0) | 0 (0) | 2 (20) | 0 (0) |
| spleen | black | | 0 (0) | 7 (70) | 10 (100) | 5 (100) |
| testis | atrophic | | 0 (0) | 0 (0) | 0 (0) | 1 (20) |

(HPT080)

BAIS 2

△
STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

PAGE : 2

| Organ | Findings | Group Name | 2500 mg/kg | 4000 mg/kg |
|--------|----------|----------------|------------|------------|
| | | NO. of Animals | 0 (%) | 0 (%) |
| lung | red | | - (-) | - (-) |
| thymus | atrophic | | - (-) | - (-) |
| spleen | black | | - (-) | - (-) |
| testis | atrophic | | - (-) | - (-) |

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BAIS 2

APPENDIX A 3-8

GROSS FINDINGS (ACUTE STUDIES: SUMMARY)

MOUSE: FEMALE: SACRIFICED ANIMALS

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

PAGE : 3

| Organ | Findings | Group Name | Control | 610 mg/kg | 977 mg/kg | 1560 mg/kg |
|--------|----------------|----------------|---------|-----------|-----------|------------|
| | | NO. of Animals | 10 (%) | 10 (%) | 9 (%) | 3 (%) |
| thymus | atrophic | | 0 (0) | 1 (10) | 5 (56) | 0 (0) |
| spleen | black | | 1 (10) | 10 (100) | 9 (100) | 3 (100) |
| | black zone | | 1 (10) | 0 (0) | 0 (0) | 0 (0) |
| kidney | hydronephrosis | | 0 (0) | 0 (0) | 1 (11) | 0 (0) |

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BAIS2

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

PAGE : 4

| Organ | Findings | Group Name | 2500 mg/kg | 4000 mg/kg |
|--------|----------------|----------------|------------|------------|
| | | NO. of Animals | 0 (%) | 0 (%) |
| thymus | atrophic | | - (-) | - (-) |
| spleen | black | | - (-) | - (-) |
| | black zone | | - (-) | - (-) |
| kidney | hydronephrosis | | - (-) | - (-) |

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BAIS 2

APPENDIX A 4-1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (ACUTE STUDIES : SUMMARY)

RAT : MALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

PAGE : 1

| Organ | Findings | Group Name | Control | | | | 400 mg/kg | | | | 600 mg/kg | | | | 900 mg/kg | | | |
|------------------------|------------------|----------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|-------------|-------------|-------------|------------|--|
| | | No. of Animals | 0 | | | | 0 | | | | 0 | | | | 3 | | | |
| | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| lung/branch | hemorrhage | | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | 1 (33) | 0 (0) | 1 (33) | 0 (0) | |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| thymus | atrophy | | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | 0 (0) | 2 (67) | 0 (0) | 0 (0) | |
| | hemorrhage | | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | 1 (33) | 0 (0) | 2 (67) | 0 (0) | |
| | karyorrhexis | | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | 0 (0) | 0 (0) | 1 (33) | 0 (0) | |
| spleen | congestion | | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | 1 (33) | 2 (67) | 0 (0) | 0 (0) | |
| [Circulatory system] | | | | | | | | | | | | | | | | | | |
| heart | hemorrhage | | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | 1 (33) | 1 (33) | 1 (33) | 0 (0) | |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| liver | necrosis:central | | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | 0 (0) | 1 (33) | 2 (67) | 0 (0) | |
| [Reproductive system] | | | | | | | | | | | | | | | | | | |
| testis | atrophy | | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | 0 (0) | 2 (67) | 0 (0) | 0 (0) | |

<1>:Slight <2>:Moderate <3>:Marked <4>:Severe

STUDY NO. : 0032
 ANIMAL : RAT F344
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0- 2W)

PAGE : 2

| | | Group Name No. of Animals | | | | 1350 mg/kg 3 | | | | 2030 mg/kg 2 | | | |
|------------------------|------------------|------------------------------|------------|------------|------------|-----------------|------------|------------|------------|-----------------|--|--|--|
| Organ | Findings | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | | | | |
| [Respiratory system] | | | | | | | | | | | | | |
| lung/branch | hemorrhage | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (50) | 0 (0) | 0 (0) | 0 (0) | | | | |
| [Hematopoietic system] | | | | | | | | | | | | | |
| thymus | atrophy | 0 (0) | 1 (33) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | | | | |
| | hemorrhage | 0 (0) | 2 (67) | 1 (33) | 0 (0) | 2 (100) | 0 (0) | 0 (0) | 0 (0) | | | | |
| | karyorrhexis | 0 (0) | 0 (0) | 2 (67) | 0 (0) | 0 (0) | 2 (100) | 0 (0) | 0 (0) | | | | |
| spleen | congestion | 2 (67) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | | | | |
| [Circulatory system] | | | | | | | | | | | | | |
| heart | hemorrhage | 1 (33) | 2 (67) | 0 (0) | 0 (0) | 1 (50) | 1 (50) | 0 (0) | 0 (0) | | | | |
| [Digestive system] | | | | | | | | | | | | | |
| liver | necrosis:central | 0 (0) | 0 (0) | 2 (67) | 0 (0) | 0 (0) | 1 (50) | 0 (0) | 0 (0) | | | | |
| [Reproductive system] | | | | | | | | | | | | | |
| testis | atrophy | 1 (33) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | | | | |

<1>:Slight

<2>:Moderate

<3>:Marked

<4>:Severe

STUDY NO. : 0032
 ANIMAL : RAT F344
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0- 2W)

PAGE : 3

| Organ | Findings | Group Name | Control | | | | 400 mg/kg | | | | 600 mg/kg | | | | 900 mg/kg | | | | | | | |
|----------------------------------|------------|----------------|------------|--------------|------------|------------|-----------|------|------|------|-----------|------|------|------|-----------|-----|-----|-----|-------|-------|------|------|
| | | No. of Animals | 0 | | | | | 0 | | | | | 0 | | | | 3 | | | | | |
| | | | <1> | <2> | <3> | <4> | <1> | <2> | <3> | <4> | <1> | <2> | <3> | <4> | <1> | <2> | <3> | <4> | <1> | <2> | <3> | <4> |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| <hr/> | | | | | | | | | | | | | | | | | | | | | | |
| [Nervous system] | | | | | | | | | | | | | | | | | | | | | | |
| brain | hemorrhage | | - | - | - | - | - | - | - | - | - | - | - | - | 2 | 1 | 0 | 0 | (67) | (33) | (0) | (0) |
| | | | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | | | | | | | | |
| <hr/> | | | | | | | | | | | | | | | | | | | | | | |
| [Special sense organs/appandage] | | | | | | | | | | | | | | | | | | | | | | |
| eye | hemorrhage | | - | - | - | - | - | - | - | - | - | - | - | - | 0 | 2 | 0 | 0 | (0) | (67) | (0) | (0) |
| | | | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | | | | | | | | |
| <hr/> | | | | | | | | | | | | | | | | | | | | | | |
| | | | <1>:Slight | <2>:Moderate | <3>:Marked | <4>:Severe | | | | | | | | | | | | | | | | |

(HPT150)

BAIS2

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

PAGE : 4

| Organ | Findings | Group Name 1350 mg/kg No. of Animals 3 | | | | 2030 mg/kg 2 | | | |
|-------|----------|---|------------|------------|------------|-----------------|------------|------------|------------|
| | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |

[Nervous system]

| | | | | | | | | | |
|-------|------------|------------|-----------|-----------|-----------|------------|-----------|-----------|-----------|
| brain | hemorrhage | 1 (33) | 0 (0) | 0 (0) | 0 (0) | 1 (50) | 0 (0) | 0 (0) | 0 (0) |
|-------|------------|------------|-----------|-----------|-----------|------------|-----------|-----------|-----------|

[Special sense organs/appandage]

| | | | | | | | | | |
|-----|------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| eye | hemorrhage | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
|-----|------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|

<1>:Slight <2>:Moderate <3>:Marked <4>:Severe

(HPT150)

BAIS2

APPENDIX A 4-2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (ACUTE STUDIES : SUMMARY)

RAT : FEMALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

PAGE : 5

| | | Group Name No. of Animals | | | | Control 0 | | | | 400 mg/kg 0 | | | | 600 mg/kg 0 | | | | 900 mg/kg 3 | | | |
|------------------------|------------------|------------------------------|------------|------------|------------|--------------|------------|------------|------------|----------------|------------|------------|------------|----------------|-------------|--------------|------------|----------------|--|--|--|
| Organ | Findings | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | | | | |
| [Respiratory system] | | | | | | | | | | | | | | | | | | | | | |
| nasal cavit | thrombus | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | 1 (33) | 0 (0) | 0 (0) | 0 (0) | | | | |
| lung/branch | hemorrhage | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | 0 (0) | 0 (0) | 1 (33) | 0 (0) | | | | |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | | | | |
| thymus | atrophy | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | 0 (0) | 2 (67) | 0 (0) | 0 (0) | | | | |
| | hemorrhage | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | 1 (33) | 1 (33) | 0 (0) | 0 (0) | | | | |
| | karyorrhexis | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | 0 (0) | 1 (33) | 1 (33) | 0 (0) | | | | |
| spleen | congestion | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | 2 (67) | 1 (33) | 0 (0) | 0 (0) | | | | |
| [Circulatory system] | | | | | | | | | | | | | | | | | | | | | |
| heart | hemorrhage | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | 1 (33) | 2 (67) | 0 (0) | 0 (0) | | | | |
| [Digestive system] | | | | | | | | | | | | | | | | | | | | | |
| liver | necrosis:central | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | 0 (0) | 0 (0) | 3 (100) | 0 (0) | | | | |
| [Urinary system] | | | | | | | | | | | | | | | | | | | | | |
| kidney | tubular necrosis | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | 0 (0) | 1 (33) | 0 (0) | 0 (0) | | | | |

<1>:Slight <2>:Moderate <3>:Marked <4>:Severe

STUDY NO. : 0032
 ANIMAL : RAT F344
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0- 2W)

PAGE : 6

| | | Group Name No. of Animals | | | | 1350 mg/kg 2 | | | | 2030 mg/kg 3 | | | |
|------------------------|------------------|------------------------------|------------|------------|------------|-----------------|------------|------------|------------|-----------------|--|--|--|
| Organ | Findings | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | | | | |
| [Respiratory system] | | | | | | | | | | | | | |
| nasal cavit | thrombus | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | | | | |
| lung/branch | hemorrhage | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | | | | |
| [Hematopoietic system] | | | | | | | | | | | | | |
| thymus | atrophy | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | | | | |
| | hemorrhage | 0 (0) | 1 (50) | 1 (50) | 0 (0) | 0 (0) | 2 (67) | 0 (0) | 0 (0) | | | | |
| | karyorrhexis | 0 (0) | 0 (0) | 1 (50) | 0 (0) | 0 (0) | 0 (0) | 3 (100) | 0 (0) | | | | |
| spleen | congestion | 2 (100) | 0 (0) | 0 (0) | 0 (0) | 2 (67) | 0 (0) | 0 (0) | 0 (0) | | | | |
| [Circulatory system] | | | | | | | | | | | | | |
| heart | hemorrhage | 1 (50) | 1 (50) | 0 (0) | 0 (0) | 0 (0) | 2 (67) | 0 (0) | 0 (0) | | | | |
| [Digestive system] | | | | | | | | | | | | | |
| liver | necrosis:central | 0 (0) | 0 (0) | 1 (50) | 0 (0) | 0 (0) | 0 (0) | 1 (33) | 0 (0) | | | | |
| [Urinary system] | | | | | | | | | | | | | |
| kidney | tubular necrosis | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | | | | |

<1>:Slight

<2>:Moderate

<3>:Marked

<4>:Severe

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

PAGE : 7

| Organ | Findings | Group Name Control No. of Animals 0 | | | | 400 mg/kg 0 | | | | 600 mg/kg 0 | | | | 900 mg/kg 3 | | | |
|-------|----------|--|------------|------------|------------|----------------|------------|------------|------------|----------------|------------|------------|------------|----------------|------------|------------|------------|
| | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |

[Endocrine system]

| | | | | | | | | | | | | | | | | | |
|---------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|-------------|------------|------------|
| adrenal | hemorrhage | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | 0 (0) | 1 (33) | 0 (0) | 0 (0) |
|---------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|-------------|------------|------------|

[Nervous system]

| | | | | | | | | | | | | | | | | | |
|-------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|-------------|------------|------------|------------|
| brain | hemorrhage | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | 1 (33) | 0 (0) | 0 (0) | 0 (0) |
|-------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|-------------|------------|------------|------------|

<1>:Slight <2>:Moderate <3>:Marked <4>:Severe

(HPT150)

BAIS2

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

PAGE : 8

| Organ | Findings | Group Name 1350 mg/kg No. of Animals 2 | | | | 2030 mg/kg 3 | | | |
|-------|----------|---|------------|------------|------------|-----------------|------------|------------|------------|
| | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |

[Endocrine system]

| | | | | | | | | | |
|---------|------------|-----------|------------|-----------|-----------|-----------|-----------|-----------|-----------|
| adrenal | hemorrhage | 0 (0) | 1 (50) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
|---------|------------|-----------|------------|-----------|-----------|-----------|-----------|-----------|-----------|

[Nervous system]

| | | | | | | | | | |
|-------|------------|------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| brain | hemorrhage | 1 (50) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
|-------|------------|------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|

<1>:Slight <2>:Moderate <3>:Marked <4>:Severe

(HPT150)

BAIS2

APPENDIX A 4-3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (ACUTE STUDIES : SUMMARY)

RAT : MALE : SACRIFICED ANIMALS

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (2W)

PAGE : 1

| | | Group Name | Control | | | | 400 mg/kg | | | | 600 mg/kg | | | | 900 mg/kg | | | |
|------------------------|--------------------------|----------------|------------|------------|------------|------------|------------|------------|------------|------------|-------------|-------------|------------|------------|-------------|-------------|-------------|------------|
| | | No. of Animals | 2 | | | | 2 | | | | 2 | | | | 2 | | | |
| Organ | Findings | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| Lung/branch | hemorrhage | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (50) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| bone marrow | deposit of hemosiderin | | 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 (100) | 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) | 1 (50) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| spleen | congestion | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (100) | 0 (0) | 0 (0) | 0 (0) | 1 (50) | 0 (0) | 0 (0) | 0 (0) |
| | deposit of hemosiderin | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (100) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (100) | 0 (0) | 0 (0) | 1 (50) | 1 (50) | 0 (0) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| liver | deposit of hemosiderin | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (50) | 0 (0) | 0 (0) | 0 (0) | 2 (100) | 0 (0) | 0 (0) | 0 (0) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | deposit of hemosiderin | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (50) | 0 (0) | 0 (0) | 0 (0) | 2 (100) | 0 (0) | 0 (0) | 0 (0) |
| [Reproductive system] | | | | | | | | | | | | | | | | | | |
| testis | atrophy | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (50) | 1 (50) | 0 (0) | 0 (0) | 1 (50) | 1 (50) | 0 (0) | 0 (0) |

<1>:Slight <2>:Moderate <3>:Marked <4>:Severe

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (2W)

PAGE : 2

| Organ | Findings | Group Name No. of Animals | | | | 1350 mg/kg 1 | | | | 2030 mg/kg 0 | | | |
|------------------------|--------------------------|------------------------------|------------|--------------|------------|-----------------|------------|------------|------------|-----------------|------------|------------|------------|
| | | <1> | <2> | <3> | <4> | <1> | <2> | <3> | <4> | <1> | <2> | <3> | <4> |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Respiratory system] | | | | | | | | | | | | | |
| lung/branch | hemorrhage | 0 (0) | 0 (0) | 0 (0) | 0 (0) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) |
| [Hematopoietic system] | | | | | | | | | | | | | |
| bone marrow | deposit of hemosiderin | 0 (0) | 0 (0) | 0 (0) | 0 (0) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) |
| | erythropoiesis:increased | 0 (0) | 0 (0) | 0 (0) | 0 (0) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) |
| spleen | congestion | 0 (0) | 0 (0) | 0 (0) | 0 (0) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) |
| | deposit of hemosiderin | 0 (0) | 0 (0) | 1 (100) | 0 (0) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) |
| [Digestive system] | | | | | | | | | | | | | |
| liver | deposit of hemosiderin | 1 (100) | 0 (0) | 0 (0) | 0 (0) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) |
| [Urinary system] | | | | | | | | | | | | | |
| kidney | deposit of hemosiderin | 1 (100) | 0 (0) | 0 (0) | 0 (0) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) |
| [Reproductive system] | | | | | | | | | | | | | |
| testis | atrophy | 1 (100) | 0 (0) | 0 (0) | 0 (0) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) |

<1>:Slight <2>:Moderate <3>:Marked <4>:Severe

APPENDIX A 4-4

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (ACUTE STUDIES:SUMMARY)

RAT:FEMALE:SACRIFICED ANIMALS

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (2W)

PAGE : 3

| Organ | Findings | Group Name | Control | | | | 400 mg/kg | | | | 600 mg/kg | | | | 900 mg/kg | | | |
|------------------------|--------------------------|----------------|------------|------------|------------|------------|--------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|-----------|
| | | No. of Animals | 3 | | | | 2 | | | | 2 | | | | 2 | | | |
| | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| bone marrow | erythropoiesis:increased | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (100) | 0 (0) | 0 (0) | 0 (0) | 2 (100) | 0 (0) | 0 (0) | 0 (0) |
| spleen | congestion | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (100) | 0 (0) | 0 (0) | 0 (0) | 2 (100) | 0 (0) | 0 (0) | 0 (0) | 2 (100) | 0 (0) | 0 (0) | 0 (0) |
| | deposit of hemosiderin | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (100) | 0 (0) | 0 (0) | 0 (0) | 2 (100) | 0 (0) | 0 (0) | 0 (0) | 2 (100) | 0 (0) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| liver | deposit of hemosiderin | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (50) | 0 (0) | 0 (0) | 0 (0) | 2 (100) | 0 (0) | 0 (0) | 0 (0) | 2 (100) | 0 (0) | 0 (0) | 0 (0) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | deposit of hemosiderin | | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (50) | 0 (0) | 0 (0) | 0 (0) | 2 (100) | 0 (0) | 0 (0) | 0 (0) |
| | | | <1>:Slight | | | | <2>:Moderate | | | | <3>:Marked | | | | <4>:Severe | | | |

(HPT150)

BA1S2

STUDY NO. : 0032
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (2W)

PAGE : 4

| | | Group Name 1350 mg/kg | | | | 2030 mg/kg | | | |
|-------|----------|-----------------------|-----|-----|-----|------------|-----|-----|-----|
| | | 0 | | | | 0 | | | |
| | | <1> | <2> | <3> | <4> | <1> | <2> | <3> | <4> |
| Organ | Findings | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |

[Hematopoietic system]

| | | | | | | | | | | |
|-------------|---------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| bone marrow | erythropoiesis: increased | - | - | - | - | - | - | - | - | - |
| | | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) |
| spleen | congestion | - | - | - | - | - | - | - | - | - |
| | | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) |
| | deposit of hemosiderin | - | - | - | - | - | - | - | - | - |
| | | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) |

[Digestive system]

| | | | | | | | | | | |
|-------|------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| liver | deposit of hemosiderin | - | - | - | - | - | - | - | - | - |
| | | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) |

[Urinary system]

| | | | | | | | | | | |
|--------|------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| kidney | deposit of hemosiderin | - | - | - | - | - | - | - | - | - |
| | | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) |

<1>: Slight <2>: Moderate <3>: Marked <4>: Severe

APPENDIX A 4-5

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (ACUTE STUDIES : SUMMARY)

MOUSE : MALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

PAGE : 1

| Organ | Findings | Group Name | Control | | | | 610 mg/kg | | | | 977 mg/kg | | | | 1560 mg/kg | | | |
|------------------------|-----------------------------------|----------------|---------|-----|-----|-----|-----------|-----|-----|-----|-----------|-----|-----|-----|------------|-------|------|-----|
| | | No. of Animals | | | | | | | | | | | | | | | | |
| | | | <1> | <2> | <3> | <4> | <1> | <2> | <3> | <4> | <1> | <2> | <3> | <4> | <1> | <2> | <3> | <4> |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| nasal cavit | degeneration:olfactory epithelium | | - | - | - | - | - | - | - | - | - | - | - | - | 0 | 2 | 0 | 0 |
| | | | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (0) | (100) | (0) | (0) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| bone marrow | deposit of hemosiderin | | - | - | - | - | - | - | - | - | - | - | - | - | 1 | 0 | 0 | 0 |
| | | | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (50) | (0) | (0) | (0) |
| lymph node | karyorrhexis | | - | - | - | - | - | - | - | - | - | - | - | - | 0 | 0 | 0 | 0 |
| | | | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (0) | (0) | (0) | (0) |
| thymus | atrophy | | - | - | - | - | - | - | - | - | - | - | - | - | 0 | 2 | 0 | 0 |
| | | | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (0) | (100) | (0) | (0) |
| | karyorrhexis | | - | - | - | - | - | - | - | - | - | - | - | - | 0 | 0 | 0 | 0 |
| | | | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (0) | (0) | (0) | (0) |
| spleen | congestion | | - | - | - | - | - | - | - | - | - | - | - | - | 0 | 2 | 0 | 0 |
| | | | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (0) | (100) | (0) | (0) |
| | karyorrhexis | | - | - | - | - | - | - | - | - | - | - | - | - | 0 | 0 | 0 | 0 |
| | | | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (0) | (0) | (0) | (0) |
| | deposit of hemosiderin | | - | - | - | - | - | - | - | - | - | - | - | - | 1 | 0 | 0 | 0 |
| | | | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (50) | (0) | (0) | (0) |
| | extramedullary hematopoiesis | | - | - | - | - | - | - | - | - | - | - | - | - | 1 | 0 | 0 | 0 |
| | | | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (50) | (0) | (0) | (0) |
| [Reproductive system] | | | | | | | | | | | | | | | | | | |
| testis | atrophy | | - | - | - | - | - | - | - | - | - | - | - | - | 0 | 1 | 1 | 0 |
| | | | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (-) | (0) | (50) | (50) | (0) |

<1>:Slight

<2>:Moderate

<3>:Marked

<4>:Severe

STUDY NO. : 0033
 ANIMAL : MOUSE BDF1
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0- 2W)

PAGE : 2

| Organ | Findings | Group Name No. of Animals | | | | 2500 mg/kg 2 | | | | 4000 mg/kg 2 | | | |
|------------------------|-----------------------------------|------------------------------|--------|--------|-------|-----------------|--------|-------|-------|-----------------|-------|-------|-------|
| | | <1> | <2> | <3> | <4> | <1> | <2> | <3> | <4> | <1> | <2> | <3> | <4> |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Respiratory system] | | | | | | | | | | | | | |
| nasal cavit | degeneration:olfactory epithelium | 0 | 0 | 2 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (100) | (0) | (0) | (50) | (0) | (0) | (0) | (0) | (0) | (0) |
| [Hematopoietic system] | | | | | | | | | | | | | |
| bone marrow | deposit of hemosiderin | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| lymph node | karyorrhesis | 1 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (50) | (0) | (0) | (0) | (0) | (100) | (0) | (0) | (0) | (0) | (0) | (0) |
| thymus | atrophy | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (50) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | karyorrhesis | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (50) | (0) | (0) | (0) | (100) | (0) | (0) | (0) | (0) | (0) |
| spleen | congestion | 0 | 2 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (100) | (0) | (0) | (50) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | karyorrhesis | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (100) | (0) | (0) | (0) | (0) | (0) | (0) |
| | deposit of hemosiderin | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| | extramedullary hematopoiesis | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| [Reproductive system] | | | | | | | | | | | | | |
| testis | atrophy | 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>:Slight

<2>:Moderate

<3>:Marked

<4>:Severe

APPENDIX A 4-6

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (ACUTE STUDIES : SUMMARY)

MOUSE : FEMALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0033
 ANIMAL : MOUSE BDF1
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0- 2W)

PAGE : 3

| Organ | Findings | Group Name | Control | | | | 610 mg/kg | | | | 977 mg/kg | | | | 1560 mg/kg | | | | | | |
|------------------------|-----------------------------------|----------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| | | No. of Animals | 0 | | | | 0 | | | | 1 | | | | 1 | | | | | | |
| | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | | | | |
| [Respiratory system] | | | | | | | | | | | | | | | | | | | | | |
| nasal cavit | degeneration:olfactory epithelium | | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (100) | 0 (0) | 0 (0) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | | | | |
| lymph node | karyorrhexis | | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| thymus | atrophy | | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (100) | 0 (0) | 0 (0) |
| | karyorrhexis | | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| spleen | congestion | | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | 0 (0) | 1 (100) | 0 (0) | 0 (0) | 0 (0) | 1 (100) | 0 (0) | 0 (0) |
| | karyorrhexis | | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| [Digestive system] | | | | | | | | | | | | | | | | | | | | | |
| liver | fatty change | | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | 0 (0) | 1 (100) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| [Urinary system] | | | | | | | | | | | | | | | | | | | | | |
| kidney | fatty change | | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | 1 (100) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |

<1>:Slight <2>:Moderate <3>:Marked <4>:Severe

STUDY NO. : 0033
 ANIMAL : MOUSE BDF1
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0- 2W)

PAGE : 4

| | | Group Name No. of Animals | | | | 2500 mg/kg 2 | | | | 4000 mg/kg 3 | | | |
|------------------------|-----------------------------------|------------------------------|------------|------------|------------|-----------------|------------|------------|------------|-----------------|--|--|--|
| Organ_____ | Findings_____ | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | | | | |
| [Respiratory system] | | | | | | | | | | | | | |
| nasal cavit | degeneration:olfactory epithelium | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | | | | |
| [Hematopoietic system] | | | | | | | | | | | | | |
| lymph node | karyorrhexis | 1 (50) | 1 (50) | 0 (0) | 0 (0) | 1 (33) | 1 (33) | 0 (0) | 0 (0) | | | | |
| thymus | atrophy | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | | | | |
| | karyorrhexis | 0 (0) | 0 (0) | 2 (100) | 0 (0) | 0 (0) | 0 (0) | 2 (67) | 0 (0) | | | | |
| spleen | congestion | 1 (50) | 1 (50) | 0 (0) | 0 (0) | 1 (33) | 2 (67) | 0 (0) | 0 (0) | | | | |
| | karyorrhexis | 2 (100) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (33) | 0 (0) | 0 (0) | | | | |
| [Digestive system] | | | | | | | | | | | | | |
| liver | fatty change | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (33) | 0 (0) | 0 (0) | 0 (0) | | | | |
| [Urinary system] | | | | | | | | | | | | | |
| kidney | fatty change | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 1 (33) | 0 (0) | 0 (0) | 0 (0) | | | | |

<1>:Slight <2>:Moderate <3>:Marked <4>:Severe

APPENDIX A 4-7

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (ACUTE STUDIES : SUMMARY)

MOUSE : MALE : SACRIFICED ANIMALS

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (2W)

PAGE : 1

| Organ | Findings | Group Name Control | | | | 610 mg/kg | | | | 977 mg/kg | | | | 1560 mg/kg | | | |
|--------------------------|------------------------------|--------------------|-------|-------|-------|-----------|--------|-------|-------|-----------|--------|-------|-------|------------|--------|--------|-------|
| | | No. of Animals | | | | 2 | | | | 2 | | | | 2 | | | |
| | | <1> | <2> | <3> | <4> | <1> | <2> | <3> | <4> | <1> | <2> | <3> | <4> | <1> | <2> | <3> | <4> |
| | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | |
| bone marrow | deposit of hemosiderin | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (100) | (0) | (0) | (0) | (100) | (0) | (0) | (0) |
| spleen | congestion | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (50) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (100) | (0) | (0) | (0) |
| | deposit of hemosiderin | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (50) | (50) | (0) | (0) | (0) | (100) | (0) | (0) | (0) | (100) | (0) | (0) |
| | extramedullary hematopoiesis | 2 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 1 | 0 | 0 |
| | | (100) | (0) | (0) | (0) | (50) | (50) | (0) | (0) | (50) | (50) | (0) | (0) | (50) | (50) | (0) | (0) |
| [Digestive system] | | | | | | | | | | | | | | | | | |
| liver | deposit of hemosiderin | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (100) | (0) | (0) | (0) | (100) | (0) | (0) | (0) |
| | swelling:central | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (100) | (0) | (0) | (0) | (100) | (0) | (0) | (0) |
| [Urinary system] | | | | | | | | | | | | | | | | | |
| urin bladd | hemorrhage | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (50) | (0) | (0) | (0) | (0) | (0) | (0) | (0) |
| [Reproductive system] | | | | | | | | | | | | | | | | | |
| testis | atrophy | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| | | (0) | (0) | (0) | (0) | (50) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (0) | (50) | (0) |
| [Musculoskeletal system] | | | | | | | | | | | | | | | | | |
| muscle | necrosis | 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) | (50) | (0) | (0) | (0) |

<1>:Slight

<2>:Moderate

<3>:Marked

<4>:Severe

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (2W)

PAGE : 2

| | | Group Name | 2500 mg/kg | | | | 4000 mg/kg | | | |
|--------------------------|------------------------------|----------------|------------|------------|------------|------------|------------|------------|------------|------------|
| | | No. of Animals | 0 | | | | 0 | | | |
| Organ | Findings | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |
| [Hematopoietic system] | | | | | | | | | | |
| bone marrow | deposit of hemosiderin | | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) |
| spleen | congestion | | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) |
| | deposit of hemosiderin | | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) |
| | extramedullary hematopoiesis | | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) |
| [Digestive system] | | | | | | | | | | |
| liver | deposit of hemosiderin | | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) |
| | swelling:central | | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) |
| [Urinary system] | | | | | | | | | | |
| urin bladd | hemorrhage | | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) |
| [Reproductive system] | | | | | | | | | | |
| testis | atrophy | | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) |
| [Musculoskeletal system] | | | | | | | | | | |
| muscle | necrosis | | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) |

<1>:Slight <2>:Moderate <3>:Marked <4>:Severe

APPENDIX A 4-8

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (ACUTE STUDIES : SUMMARY)

MOUSE : FEMALE : SACRIFICED ANIMALS

STUDY NO. : 0033
 ANIMAL : MOUSE BDF1
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
 SACRIFICED ANIMALS (20)

PAGE : 3

| Organ | Findings | Group Name | Control | | | | 610 mg/kg | | | | 977 mg/kg | | | | 1560 mg/kg | | | |
|------------------------|------------------------------|----------------|--------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|--|
| | | No. of Animals | 2 | | | | 2 | | | | 2 | | | | 2 | | | |
| | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| bone marrow | deposit of hemosiderin | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (100) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | |
| spleen | deposit of hemosiderin | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (100) | 0 (0) | 0 (0) | 0 (0) | 2 (100) | 0 (0) | 0 (0) | 1 (50) | 1 (50) | 0 (0) | 0 (0) | |
| | extramedullary hematopoiesis | 2 (100) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (100) | 0 (0) | 0 (0) | 0 (0) | 2 (100) | 0 (0) | 0 (0) | 1 (50) | 1 (50) | 0 (0) | 0 (0) | |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| liver | deposit of hemosiderin | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 2 (100) | 0 (0) | 0 (0) | 0 (0) | 2 (100) | 0 (0) | 0 (0) | 0 (0) | |
| | | <1>:Slight | <2>:Moderate | <3>:Marked | <4>:Severe | | | | | | | | | | | | | |

<1>:Slight

<2>:Moderate

<3>:Marked

<4>:Severe

(HPT150)

BAIS2

STUDY NO. : 0033
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (2W)

PAGE : 4

| | | Group Name | 2500 mg/kg | | | | 4000 mg/kg | | | |
|------------------------|------------------------------|----------------|------------|------------|------------|------------|------------|------------|------------|------------|
| | | No. of Animals | 0 | | | | 0 | | | |
| Organ_____ | Findings_____ | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |
| <hr/> | | | | | | | | | | |
| [Hematopoietic system] | | | | | | | | | | |
| bone marrow | deposit of hemosiderin | | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) |
| spleen | deposit of hemosiderin | | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) |
| | extramedullary hematopoiesis | | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) |
| [Digestive system] | | | | | | | | | | |
| liver | deposit of hemosiderin | | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) | - (-) |

<1>:Slight

<2>:Moderate

<3>:Marked

<4>:Severe

(HPT150)

BAIS2

APPENDIX A 5-1

IDENTITY AND PURITY OF p-CNB

PERFORMED AT THE JAPAN BIOASSAY LABORATORY

(ACUTE STUDIES)

IDENTITY AND PURITY OF p-CNB PERFORMED AT THE JAPAN BIOASSAY LABORATORY
(ACUTE STUDIES)

Lot no. WKE1251

A. Spectral data

Infrared

Instrument : Hitachi 270-30

Cell : KBr

Slit : Medium

Results : Wave Number
(CM^{-1})

| | |
|------|------|
| 470 | 470 |
| 540 | 540 |
| 620 | |
| 670 | 680 |
| 740 | 740 |
| 840 | 850 |
| 1020 | 1020 |
| 1090 | 1100 |
| 1120 | 1120 |
| 1170 | 1180 |
| 1280 | 1280 |
| 1310 | 1320 |
| 1350 | 1350 |
| 1420 | 1420 |
| 1470 | 1480 |
| 1520 | 1520 |
| 1580 | 1580 |
| 1600 | 1610 |
| 3100 | 3100 |

(Sadtler handbook
by Sadtler Research
Laboratories, Inc.)

B. Gas Chromatography

Instrument : Shimadzu GC-9A
Column : THERM 1000, 50m, 0.25 ϕ
Column Temperature : 180°C
Flow Rate : 1ml/min
Detector : Flame Ionization Detector(FID)
Injection Volume : 1 μ l
Results : Only one major peak

| Peak No. | Retention Time(min) | Retention Time Relative to Major Peak | Area (percent of Major peak) |
|----------|---------------------|---------------------------------------|------------------------------|
| 1 | 4.703 | 1.00 | 100 |

C. Conclusions: The results of the infrared spectra agreed with the literature values. Impurity was not detected in test substance by Gas chromatography.

APPENDIX A 5-2

STABILITY OF p-CNB AT THE JAPAN BIOASSAY LABORATORY

(ACUTE STUDIES)

STABILITY OF p-CNB AT THE JAPAN BIOASSAY LABORATORY(ACUTE STUDIES)

Lot no.WKE1251

A.Sample storage: p-CNB were stored for about three days at 5°C.

| B.Spectral data | <u>Previous determined of test</u> (12/06/83) | <u>After determined of test</u> (12/08/83) |
|-----------------|--|---|
| Infrared | | |
| Instrument | : Hitachi 270-30 | |
| Cell | : KBr | |
| Slit | : Medium | |
| Results | : Wave Number (CM ⁻¹) | |
| | 470 | 470 |
| | 540 | 540 |
| | 680 | 680 |
| | 740 | 740 |
| | 850 | 850 |
| | 1020 | 1020 |
| | 1100 | 1100 |
| | 1120 | 1120 |
| | 1180 | 1180 |
| | 1280 | 1280 |
| | 1320 | 1320 |
| | 1350 | 1350 |
| | 1420 | 1420 |
| | 1480 | 1480 |
| | 1520 | 1520 |
| | 1580 | 1580 |
| | 1610 | 1610 |
| | 3100 | 3100 |

C. Gas Chromatography

Instrument : Shimadzu GC-9A
Column : THERM 1000, 50m, 0.25 ϕ
Column Temperature : 180°C
Flow Rate : 1ml/min
Detector : Flame Ionization Detector(FID)
Injection Volume : 1 μ l
Results : Only one major peak

| Date | Retention Time(min) | Retention Time Relative to Major Peak | Area (percent of Major peak) |
|----------|---------------------|---------------------------------------|------------------------------|
| 12/06/83 | 4.703 | 1.00 | 100 |
| 12/08/83 | 4.703 | 1.00 | 100 |

D. Conclusions: The results of the Infrared spectra agreed with the previous determine of test Values. Impurity was not detected in test substance by Gas chromatography.
Consequently, p-CNB was stable as the chemical when stored for about three days at temperatures to 5°C.

APPENDIX A 5-3

RESULTS OF ANALYSIS OF FORMULATED DIETS
IN THE ACUTE STUDIES OF p-CNB

RESULTS OF ANALYSIS OF FORMULATED DIETS IN THE ACUTE STUDIES OF p-CNB

(Rat)

| Date Mixed | Concentration of p-CNB in feed for Taget Concentration(ppm) | | | | |
|------------|---|----------------|----------------|-----------------|-----------------|
| | 40000 (a) | 60000 (a) | 90000 (a) | 135000 (a) | 203000 (a) |
| 12/06/83 | 38913.0(97.3) | 57625.0(96.0) | 83875.0(93.2) | 135013.0(100.0) | 206763.0(101.9) |

(Mouse)

| Date Mixed | Concentration of p-CNB in feed for Taget Concentration(ppm) | | | | |
|------------|---|----------------|----------------|-----------------|-----------------|
| | 30500 (a) | 48850 (a) | 78000 (a) | 125000 (a) | 200000 (a) |
| 12/07/83 | 32125.0(105.3) | 47725.0(97.7) | 77788.0(99.7) | 123025.0(98.4) | 193688.0(96.8) |

(a) Determined as a percent of taget