ビフェニルのラット及びマウスを用いた
経口投与によるがん原性予備試験(混餌試験)報告書

# APPENDIX

(A1-1～A7-4)
2 週間試験：ラット/0179；マウス/0180

# APPENDIXES

APPENDIXES (CONTINUED)

APPENDIX A 1-1

# CLINICAL OBSERVATION (TWO-WEEK STUDY: SUMMARY)

RAT : MALE

STUDY NO. : 0179
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE



| Clinical sign | Group Name | Administration Week-day 1-1 | 1-2 | 1-3 | 1-4 | 1-5 | 1-6 | 1-7 | 2-1 | 2-2 | 2-3 | 2-4 | 2-5 | 2-6 | 2-7 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| PILOERECTION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 40000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 4 | 4 | 4 | 7 | 7 | 7 | 7 |
| SOILED PERI GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 40000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 |
| OLIGO-STOOL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 40000 ppm | 0 | 0 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 4 | 1 | 0 | 0 |

APPENDIX A 1-2

# CLINICAL OBSERVATION (TWO-WEEK STUDY: SUMMARY)

RAT : FEMALE

STUDY NO. : 0179
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE



| Clinical sign | Group Name | Administration Week-day 1-1 | 1-2 | 1-3 | 1-4 | 1-5 | 1-6 | 1-7 | 2-1 | 2-2 | 2-3 | 2-4 | 2-5 | 2-6 | 2-7 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| PILOERECTION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 40000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| OLIGO-STOOL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 40000 ppm | 0 | 0 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 5 | 2 | 2 | 0 |

APPENDIX A 1-3

CLINICAL OBSERVATION (TWO-WEEK STUDY: SUMMARY)

MOSUE : MALE

STUDY NO. : 0180
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE



| Clinical sign | Group Name | Administration Week-day 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 | 2-4 1 | 2-5 1 | 2-6 1 | 2-7 1 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| DEATH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1250 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 20000 ppm | 0 | 0 | 0 | 1 | 3 | 5 | 6 | 7 | 7 | 7 | 7 | 7 | 7 | 7 |
| LOCOMOTOR MOVEMENT DECR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1250 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000 ppm | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000 ppm | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PRONE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1250 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000 ppm | 0 | 0 | 0 | 1 | 2 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| LATERAL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1250 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000 ppm | 0 | 0 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| HUNCHBACK POSITION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1250 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000 ppm | 0 | 0 | 0 | 10 | 7 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000 ppm | 0 | 0 | 0 | 9 | 7 | 5 | 3 | 2 | 2 | 1 | 0 | 0 | 0 | 0 |

STUDY NO. : 0180
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE



| Clinical sign | Group Name | Administration Week-day 1-1 | 1-2 | 1-3 | 1-4 | 1-5 | 1-6 | 1-7 | 2-1 | 2-2 | 2-3 | 2-4 | 2-5 | 2-6 | 2-7 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| PILOERECTION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1250 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000 ppm | 0 | 0 | 0 | 10 | 10 | 5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000 ppm | 0 | 0 | 0 | 9 | 7 | 5 | 3 | 2 | 2 | 2 | 2 | 2 | 2 | 1 |
| SMALL STOOL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1250 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000 ppm | 0 | 0 | 0 | 10 | 10 | 8 | 3 | 1 | 1 | 0 | 0 | 0 | 0 | 0 |
| | 20000 ppm | 0 | 0 | 0 | 8 | 7 | 7 | 4 | 3 | 2 | 2 | 2 | 2 | 2 | 2 |
| OLIGO-STOOL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1250 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000 ppm | 10 | 10 | 10 | 10 | 10 | 10 | 8 | 5 | 1 | 0 | 0 | 0 | 0 | 0 |
| | 20000 ppm | 10 | 10 | 10 | 10 | 9 | 7 | 5 | 4 | 3 | 2 | 2 | 2 | 2 | 1 |

APPENDIX A 1-4

CLINICAL OBSERVATION (TWO-WEEK STUDY: SUMMARY)

MOSUE: FEMALE

STUDY NO. : 0180
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE



| Clinical sign | Group Name | Administration Week-day 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 | 2-4 1 | 2-5 1 | 2-6 1 | 2-7 1 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| DEATH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1250 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000 ppm | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| | 20000 ppm | 0 | 0 | 0 | 1 | 3 | 4 | 4 | 5 | 6 | 6 | 6 | 6 | 6 | 6 |
| LOCOMOTOR MOVEMENT DECR | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1250 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000 ppm | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000 ppm | 0 | 0 | 0 | 6 | 2 | 2 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| PRONE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1250 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000 ppm | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000 ppm | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| LATERAL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1250 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000 ppm | 0 | 0 | 0 | 1 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| HUNCHBACK POSITION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1250 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000 ppm | 0 | 0 | 0 | 6 | 5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000 ppm | 0 | 0 | 0 | 9 | 7 | 6 | 6 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0180
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE



| Clinical sign | Group Name | Administration Week-day 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 | 2-4 1 | 2-5 1 | 2-6 1 | 2-7 1 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| SOILED | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1250 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000 ppm | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| PILOERECTION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1250 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000 ppm | 0 | 0 | 0 | 6 | 5 | 3 | 2 | 1 | 1 | 0 | 0 | 0 | 0 | 0 |
| | 20000 ppm | 0 | 0 | 0 | 9 | 7 | 6 | 6 | 4 | 0 | 0 | 0 | 0 | 0 | 0 |
| IRREGULAR BREATHING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1250 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000 ppm | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRATION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1250 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000 ppm | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| SMALL STOOL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1250 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000 ppm | 0 | 0 | 0 | 4 | 4 | 6 | 4 | 4 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000 ppm | 0 | 0 | 0 | 9 | 8 | 7 | 6 | 6 | 4 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0180
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE



| Clinical sign | Group Name | Administration Week-day 1-1 | 1-2 | 1-3 | 1-4 | 1-5 | 1-6 | 1-7 | 2-1 | 2-2 | 2-3 | 2-4 | 2-5 | 2-6 | 2-7 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| OLIGO-STOOL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1250 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000 ppm | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000 ppm | 10 | 10 | 9 | 8 | 8 | 7 | 4 | 4 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000 ppm | 10 | 10 | 10 | 10 | 9 | 7 | 6 | 6 | 5 | 4 | 4 | 4 | 4 | 0 |

APPENDIX A 2-1

# BODY WEIGHT CHANGES (TWO-WEEK STUDY:SUMMARY)

RAT : MALE

STUDY NO. : 0179
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day 0-0 | 1-1 | 1-2 | 1-4 | 1-7 | 2-4 | 2-7 |
|---|---|---|---|---|---|---|---|
| Control | 125± 5 | 130± 5 | 136± 4 | 147± 5 | 162± 6 | 183± 6 | 199± 9 |
| 2500 ppm | 125± 5 | 125± 7 | 135± 5 | 146± 6 | 161± 7 | 179± 6 | 194± 7 |
| 5000 ppm | 125± 5 | 125± 5 | 133± 6 | 143± 7 | 159± 6 | 178± 6 | 192± 7 |
| 10000 ppm | 125± 5 | 116± 4** | 118± 5** | 131± 5** | 146± 6** | 161± 6** | 175± 7** |
| 20000 ppm | 125± 5 | 111± 4** | 108± 4** | 113± 6** | 126± 6** | 140± 7** | 151± 7** |
| 40000 ppm | 125± 5 | 109± 4** | 104± 4** | 93± 6** | 93± 5** | 97± 7** | 102± 8** |

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX A 2-2

# BODY WEIGHT CHANGES (TWO-WEEK STUDY: SUMMARY)

## RAT : FEMALE

STUDY NO. : 0179
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day 0-0 | 1-1 | 1-2 | 1-4 | 1-7 | 2-4 | 2-7 |
|---|---|---|---|---|---|---|---|
| Control | 103± 3 | 106± 3 | 109± 3 | 113± 3 | 121± 4 | 126± 3 | 135± 4 |
| 2500 ppm | 103± 3 | 105± 4 | 108± 4 | 112± 4 | 121± 4 | 125± 5 | 133± 5 |
| 5000 ppm | 103± 3 | 100± 3** | 104± 3** | 110± 4 | 116± 5* | 122± 4 | 130± 4 |
| 10000 ppm | 103± 3 | 94± 3** | 96± 3** | 103± 3** | 111± 2** | 118± 3** | 124± 4** |
| 20000 ppm | 103± 3 | 93± 3** | 91± 3** | 94± 2** | 101± 3** | 110± 4** | 117± 5** |
| 40000 ppm | 103± 3 | 90± 3** | 85± 3** | 81± 4** | 80± 4** | 84± 4** | 88± 5** |

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX A 2-3

BODY WEIGHT CHANGES(TWO-WEEK STUDY:SUMMARY)

MOSUE : MALE

STUDY NO. : 0180
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day 0-0 | 1-1 | 1-2 | 1-4 | 1-7 | 2-4 | 2-7 |
|---|---|---|---|---|---|---|---|
| Control | 22.9± 0.9 | 22.5± 1.1 | 22.8± 1.3 | 22.8± 1.1 | 23.1± 1.2 | 24.7± 1.4 | 24.2± 1.8 |
| 1250 ppm | 22.9± 0.9 | 22.2± 1.1 | 22.8± 1.1 | 23.0± 1.0 | 23.4± 1.0 | 24.7± 1.0 | 24.5± 1.0 |
| 2500 ppm | 22.8± 1.0 | 22.2± 1.1 | 22.5± 0.8 | 22.8± 0.8 | 23.2± 0.9 | 24.4± 1.0 | 24.3± 1.0 |
| 5000 ppm | 22.9± 0.9 | 21.1± 0.9** | 21.2± 1.1** | 21.8± 1.1 | 22.4± 0.7 | 24.0± 1.1 | 24.0± 1.0 |
| 10000 ppm | 22.9± 0.9 | 19.5± 0.8** | 18.2± 0.7** | 17.0± 0.8** | 17.5± 1.0** | 20.1± 1.5** | 21.3± 1.3** |
| 20000 ppm | 22.9± 0.9 | 19.4± 0.7** | 17.7± 0.8** | 15.8± 1.0** | 15.1± 1.2** | 16.9± 2.9** | 18.2± 3.4* |

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX A 2-4

BODY WEIGHT CHANGES (TWO-WEEK STUDY: SUMMARY)

MOSUE: FEMALE

STUDY NO. : 0180
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day 0-0 | 1-1 | 1-2 | 1-4 | 1-7 | 2-4 | 2-7 |
|---|---|---|---|---|---|---|---|
| Control | 18.8± 0.6 | 18.4± 0.8 | 18.5± 0.7 | 18.4± 0.8 | 18.8± 0.8 | 20.0± 0.8 | 19.8± 0.8 |
| 1250 ppm | 18.9± 0.6 | 18.2± 0.7 | 18.4± 0.9 | 18.6± 0.6 | 18.8± 0.8 | 19.9± 0.9 | 19.9± 0.7 |
| 2500 ppm | 18.9± 0.6 | 18.2± 0.7 | 18.2± 0.8 | 18.5± 0.8 | 18.4± 0.9 | 19.6± 0.9 | 19.6± 1.0 |
| 5000 ppm | 18.8± 0.6 | 17.3± 0.6** | 17.5± 0.5* | 17.9± 0.4 | 18.6± 0.5 | 19.4± 0.7 | 19.4± 0.7 |
| 10000 ppm | 18.9± 0.6 | 15.9± 0.6** | 14.8± 0.8** | 14.1± 1.7** | 15.4± 1.5** | 17.4± 1.0** | 18.3± 1.1** |
| 20000 ppm | 18.8± 0.6 | 15.4± 0.4** | 13.8± 0.5** | 12.5± 0.9** | 12.8± 1.6** | 15.2± 1.6** | 16.6± 1.0** |

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX A 3-1

# FOOD CONSUMPTION CHANGES (TWO-WEEK STUDY: SUMMARY)

RAT : MALE

STUDY NO. : 0179
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day(effective) 1-4(4) | 1-7(3) | 2-4(4) | 2-7(3) |
|---|---|---|---|---|
| Control | 14.3± 0.6 | 15.0± 0.9 | 14.6± 0.7 | 16.2± 1.1 |
| 2500 ppm | 13.6± 1.2 | 14.9± 0.9 | 13.9± 0.9 | 15.9± 1.1 |
| 5000 ppm | 12.3± 0.7 | 14.3± 0.7 | 13.6± 0.6* | 15.6± 0.8 |
| 10000 ppm | 10.0± 3.9** | 13.3± 0.9** | 13.0± 0.8** | 14.7± 0.9** |
| 20000 ppm | 6.2± 2.1** | 11.0± 0.8** | 11.7± 0.9** | 13.0± 1.0** |
| 40000 ppm | 5.6± 7.7** | 7.1± 1.6** | 7.0± 0.4** | 8.6± 0.9** |

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX A 3-2

# FOOD CONSUMPTION CHANGES (TWO-WEEK STUDY: SUMMARY)

RAT : FEMALE

STUDY NO. : 0179
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day(effective) 1-4(4) | 1-7(3) | 2-4(4) | 2-7(3) |
|---|---|---|---|---|
| Control | 11.2± 0.6 | 11.3± 0.5 | 10.1± 0.5 | 11.5± 0.6 |
| 2500 ppm | 10.7± 0.6 | 11.2± 0.4 | 9.6± 0.3 | 11.5± 0.7 |
| 5000 ppm | 9.5± 0.9 | 10.6± 0.6 | 9.5± 0.6 | 11.3± 0.5 |
| 10000 ppm | 7.0± 1.3** | 10.3± 0.5 | 9.5± 0.6 | 11.2± 1.8 |
| 20000 ppm | 4.9± 1.3** | 9.2± 0.6** | 9.1± 0.5** | 10.1± 0.9* |
| 40000 ppm | 4.2± 4.8** | 8.3± 5.1** | 8.6± 7.0** | 7.9± 0.7** |

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX A 3-3

FOOD CONSUMPTION CHANGES (TWO-WEEK STUDY: SUMMARY)

MOSUE : MALE

STUDY NO. : 0180
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day(effective) 1-4(4) | 1-7(3) | 2-4(4) | 2-7(3) |
|---|---|---|---|---|
| Control | 4.5± 0.4 | 4.7± 0.5 | 4.7± 0.6 | 4.3± 0.6 |
| 1250 ppm | 4.6± 0.4 | 4.6± 0.3 | 4.5± 0.4 | 4.6± 0.4 |
| 2500 ppm | 4.5± 0.7 | 4.9± 0.6 | 4.5± 0.6 | 4.6± 0.6 |
| 5000 ppm | 4.8± 0.9 | 5.8± 0.9 | 5.0± 0.7 | 4.9± 0.5 |
| 10000 ppm | 3.5± 1.0 | 5.9± 1.1 | 7.8± 1.8** | 7.3± 1.1** |
| 20000 ppm | 2.7± 1.4* | 3.7± 2.4 | 6.1± 3.6 | 6.9± 3.2 |

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX A 3-4

FOOD CONSUMPTION CHANGES(TWO-WEEK STUDY: SUMMARY)

MOSUE : FEMALE

STUDY NO. : 0180
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day(effective) 1-4(4) | 1-7(3) | 2-4(4) | 2-7(3) |
|---|---|---|---|---|
| Control | 4.3± 0.3 | 4.6± 0.3 | 4.2± 0.6 | 4.2± 1.0 |
| 1250 ppm | 4.4± 0.8 | 4.7± 0.6 | 4.4± 0.2 | 4.5± 0.6 |
| 2500 ppm | 4.2± 0.5 | 4.7± 0.6 | 4.1± 0.5 | 4.6± 0.6 |
| 5000 ppm | 5.6± 1.6 | 6.0± 0.7* | 4.4± 0.7 | 4.4± 0.8 |
| 10000 ppm | 3.6± 1.2 | 7.6± 2.7* | 6.8± 1.6** | 5.7± 1.0** |
| 20000 ppm | 2.1± 0.9** | 3.4± 1.5 | 5.5± 2.8 | 6.4± 1.4** |

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX A 4-1

# CHEMICAL INTAKE CHANGES (TWO-WEEK STUDY: SUMMARY)

## RAT : MALE

STUDY NO. : 0179
ANIMAL : RAT F344
UNIT : g／kg／d a y
REPORT TYPE : A1 2
SEX : MALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration (weeks) 1 | 2 |
|---|---|---|
| Control | 0.000± 0.000 | 0.000± 0.000 |
| 2500 ppm | 0.231± 0.006 | 0.204± 0.008 |
| 5000 ppm | 0.448± 0.020 | 0.406± 0.018 |
| 10000 ppm | 0.913± 0.040 | 0.841± 0.035 |
| 20000 ppm | 1.747± 0.066 | 1.722± 0.080 |
| 40000 ppm | 3.049± 0.655 | 3.377± 0.305 |

APPENDIX A 4-2

# CHEMICAL INTAKE CHANGES (TWO-WEEK STUDY: SUMMARY)

## RAT : FEMALE

STUDY NO. : 0179
ANIMAL : RAT F344
UNIT : g／kg／d a y
REPORT TYPE : A1 2
SEX : FEMALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration (weeks) 1 | 2 |
|---|---|---|
| Control | 0.000± 0.000 | 0.000± 0.000 |
| 2500 ppm | 0.231± 0.005 | 0.215± 0.008 |
| 5000 ppm | 0.455± 0.017 | 0.433± 0.021 |
| 10000 ppm | 0.930± 0.049 | 0.899± 0.122 |
| 20000 ppm | 1.806± 0.096 | 1.733± 0.111 |
| 40000 ppm | 4.190± 2.663 | 3.591± 0.359 |

APPENDIX A 4-3

# CHEMICAL INTAKE CHANGES (TWO-WEEK STUDY: SUMMARY)

## MOSUE : MALE

STUDY NO. : 0180
ANIMAL : MOUSE BDF1
UNIT : g／kg／d a y
REPORT TYPE : A1 2
SEX : MALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration (weeks) 1 | 2 |
|---|---|---|
| Control | 0.000± 0.000 | 0.000± 0.000 |
| 1250 ppm | 0.244± 0.020 | 0.234± 0.022 |
| 2500 ppm | 0.525± 0.054 | 0.473± 0.063 |
| 5000 ppm | 1.293± 0.206 | 1.025± 0.107 |
| 10000 ppm | 3.463± 0.601 | 3.422± 0.495 |
| 20000 ppm | 6.431± 4.426 | 7.680± 3.978 |

APPENDIX A 4-4

# CHEMICAL INTAKE CHANGES (TWO-WEEK STUDY: SUMMARY)

## MOSUE : FEMALE

STUDY NO. : 0180
ANIMAL : MOUSE BDF1
UNIT : g/kg/day
REPORT TYPE : A1 2
SEX : FEMALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration (weeks) 1 | 2 |
|---|---|---|
| Control | 0.000± 0.000 | 0.000± 0.000 |
| 1250 ppm | 0.312± 0.035 | 0.283± 0.039 |
| 2500 ppm | 0.637± 0.065 | 0.584± 0.061 |
| 5000 ppm | 1.612± 0.193 | 1.129± 0.194 |
| 10000 ppm | 5.369± 1.794 | 3.168± 0.672 |
| 20000 ppm | 5.737± 2.047 | 7.681± 1.493 |

APPENDIX A 5-1

GROSS FINDINGS (TWO-WEEK STUDY: SUMMARY)

RAT : MALE : SACRIFICED ANIMALS

STUDY NO. : 0179
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS ( 2W)



| Organ | Findings | Group Name / NO. of Animals | Control 10 (%) | 2500 ppm 10 (%) | 5000 ppm 10 (%) | 10000 ppm 10 (%) |
|---|---|---|---|---|---|---|
| thymus | atrophic | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

STUDY NO. : 0179
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS ( 2W)



| Organ | Findings | Group Name / NO. of Animals | 20000 ppm 10 (%) | 40000 ppm 10 (%) |
|---|---|---|---|---|
| thymus | atrophic | | 0 ( 0) | 2 ( 20) |

APPENDIX A 5-2

GROSS FINDINGS (TWO-WEEK STUDY: SUMMARY)

RAT : FEMALE : SACRIFICED ANIMALS

STUDY NO. : 0179
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS ( 2W)



| Organ | Findings | Group Name / NO. of Animals | Control 10 (%) | 2500 ppm 10 (%) | 5000 ppm 10 (%) | 10000 ppm 10 (%) |
|---|---|---|---|---|---|---|
| thymus | atrophic | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| liver | herniation | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

STUDY NO. : 0179
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS ( 2W)



| Organ | Findings | Group Name / NO. of Animals | 20000 ppm 10 (%) | 40000 ppm 10 (%) |
|---|---|---|---|---|
| thymus | atrophic | | 0 ( 0) | 1 ( 10) |
| liver | herniation | | 1 ( 10) | 0 ( 0) |

APPENDIX A 5-3

GROSS FINDINGS (TWO-WEEK STUDY: SUMMARY)

MOUSE: MALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0180
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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



| Organ | Findings | Group Name / NO. of Animals | Control 0 (%) | 1250 ppm 0 (%) | 2500 ppm 0 (%) | 5000 ppm 0 (%) |
|---|---|---|---|---|---|---|
| thymus | atrophic | | - ( -) | - ( -) | - ( -) | - ( -) |
| whole body | wasting | | - ( -) | - ( -) | - ( -) | - ( -) |

STUDY NO. : 0180
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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



| Organ | Findings | Group Name<br>NO. of Animals | 10000 ppm<br>1 (%) | 20000 ppm<br>7 (%) |
|---|---|---|---|---|
| thymus | atrophic | | 0 ( 0) | 1 ( 14) |
| whole body | wasting | | 1 (100) | 4 ( 57) |

APPENDIX A 5-4

GROSS FINDINGS (TWO-WEEK STUDY: SUMMARY)

MOUSE: FEMALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0180
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

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



| Organ | Findings | Group Name / NO. of Animals | Control 0 (%) | 1250 ppm 0 (%) | 2500 ppm 0 (%) | 5000 ppm 0 (%) |
|---|---|---|---|---|---|---|
| thymus | atrophic | | - ( -) | - ( -) | - ( -) | - ( -) |
| whole body | wasting | | - ( -) | - ( -) | - ( -) | - ( -) |

STUDY NO. : 0180
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

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



| Organ | Findings | Group Name<br>NO. of Animals | 10000 ppm<br>1 (%) | 20000 ppm<br>6 (%) |
|---|---|---|---|---|
| thymus | atrophic | | 0 ( 0) | 2 ( 33) |
| whole body | wasting | | 1 (100) | 5 ( 83) |

APPENDIX A 5-5

GROSS FINDINGS (TWO-WEEK STUDY: SUMMARY)

MOUSE: MALE : SACRIFICED ANIMALS

STUDY NO. : 0180
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS ( 2W)



| Organ | Findings | Group Name / NO. of Animals | Control 10 (%) | 1250 ppm 10 (%) | 2500 ppm 10 (%) | 5000 ppm 10 (%) |
|---|---|---|---|---|---|---|
| thymus | atrophic | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| spleen | black zone | | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| kidney | hydronephrosis | | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

STUDY NO. : 0180
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS ( 2W)



| Organ | Findings | Group Name<br>NO. of Animals | 10000 ppm<br>9 (%) | 20000 ppm<br>3 (%) |
|---|---|---|---|---|
| thymus | atrophic | | 0 ( 0) | 1 ( 33) |
| spleen | black zone | | 0 ( 0) | 0 ( 0) |
| kidney | hydronephrosis | | 0 ( 0) | 0 ( 0) |

APPENDIX A 5-6

GROSS FINDINGS (TWO-WEEK STUDY: SUMMARY)

MOUSE: FEMALE : SACRIFICED ANIMALS

STUDY NO. : 0180
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS ( 2W)



| Organ | Findings | Group Name / NO. of Animals | Control 10 (%) | 1250 ppm 10 (%) | 2500 ppm 10 (%) | 5000 ppm 10 (%) |
|---|---|---|---|---|---|---|
| thymus | atrophic | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| spleen | black zone | | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) |
| ovary | cyst | | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) |

STUDY NO. : 0180
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS ( 2W)



| Organ | Findings | Group Name<br>NO. of Animals | 10000 ppm<br>9 (%) | 20000 ppm<br>4 (%) |
|---|---|---|---|---|
| thymus | atrophic | | 1 ( 11) | 1 ( 25) |
| spleen | black zone | | 0 ( 0) | 0 ( 0) |
| ovary | cyst | | 0 ( 0) | 0 ( 0) |

APPENDIX A 6-1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

RAT : MALE : SACRIFICED ANIMALS

STUDY NO. : 0179
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

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



| Organ | Findings | Group Name | Control | | | | 2500 ppm | | | | 5000 ppm | | | | 10000 ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 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 | hypoplasia | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| thymus | 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) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | basophilic change | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | hyaline cast | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | desquamation:pelvis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Endocrine system] | | | | | | | | | | | | | | | | | | |
| adrenal | increased lipid:cortex | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [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) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

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

| Organ | Findings | Group Name | 20000 ppm | | | | 40000 ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals | 2 | | | | 2 | | | |
| | | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |
| [Hematopoietic system] | | | | | | | | | | |
| bone marrow | hypoplasia | | 2 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 (100) | 0 ( 0) | 0 ( 0) |
| thymus | atrophy | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 50) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Urinary system] | | | | | | | | | | |
| kidney | basophilic change | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | hyaline cast | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 50) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | desquamation:pelvis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Endocrine system] | | | | | | | | | | |
| adrenal | increased lipid:cortex | | 0 ( 0) | 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) | 2 (100) | 0 ( 0) | 0 ( 0) |

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

APPENDIX A 6-2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

RAT : FEMALE : SACRIFICED ANIMALS

| Organ | Findings | Group Name | Control | | | | 2500 ppm | | | | 5000 ppm | | | | 10000 ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 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 | hypoplasia | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| stomach | dilated glands | | 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) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | basophilic change | | 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) |
| | mineralization:cortico-medullary junction | | 1 ( 50) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 50) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | dilatation:tubular lumen | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | desquamation:pelvis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Endocrine system] | | | | | | | | | | | | | | | | | | |
| pituitary | Rathke pouch | | 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) |

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

| Organ | Findings | Group Name | 20000 ppm | | | | 40000 ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals | 2 | | | | 2 | | | |
| | | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |
| [Hematopoietic system] | | | | | | | | | | |
| bone marrow | hypoplasia | | 1 ( 50) | 1 ( 50) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 (100) | 0 ( 0) | 0 ( 0) |
| [Digestive system] | | | | | | | | | | |
| stomach | dilated glands | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 50) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Urinary system] | | | | | | | | | | |
| kidney | basophilic change | | 1 ( 50) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 50) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | mineralization:cortico-medullary junction | | 1 ( 50) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | dilatation:tubular lumen | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 50) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | desquamation:pelvis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Endocrine system] | | | | | | | | | | |
| pituitary | Rathke pouch | | 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 6-3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

MOUSE: MALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0180
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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



| Organ | Findings | Group Name | Control | | | | 1250 ppm | | | | 2500 ppm | | | | 5000 ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals | 0 | | | | 0 | | | | 0 | | | | 0 | | | |
| | | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| spleen | atrophy | | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| liver | atrophy | | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) |
| | necrosis:focal | | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) |

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

| Organ | Findings | Group Name | 10000 ppm | | | | 20000 ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals | 1 | | | | 2 | | | |
| | | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |
| [Hematopoietic system] | | | | | | | | | | |
| spleen | atrophy | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 50) | 1 ( 50) | 0 ( 0) | 0 ( 0) |
| [Digestive system] | | | | | | | | | | |
| liver | atrophy | | 0 ( 0) | 1 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 (100) | 0 ( 0) | 0 ( 0) |
| | necrosis:focal | | 1 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

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

APENDIX A 6-4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

MOUSE: FEMALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0180
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

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



| Organ | Findings | Group Name | Control | | | | 1250 ppm | | | | 2500 ppm | | | | 5000 ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals | 0 | | | | 0 | | | | 0 | | | | 0 | | | |
| | | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| thymus | atrophy | | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) |
| spleen | atrophy | | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| liver | atrophy | | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) |
| | necrosis:central | | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) |
| | necrosis:focal | | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) |

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

| Organ | Findings | Group Name | 10000 ppm | | | | 20000 ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals | 1 | | | | 2 | | | |
| | | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |
| [Hematopoietic system] | | | | | | | | | | |
| thymus | atrophy | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 50) | 0 ( 0) | 0 ( 0) |
| spleen | atrophy | | 1 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Digestive system] | | | | | | | | | | |
| liver | atrophy | | 0 ( 0) | 1 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 50) | 0 ( 0) | 0 ( 0) |
| | necrosis:central | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 50) | 0 ( 0) | 0 ( 0) |
| | necrosis:focal | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 50) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

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

APPENDIX A 6-5

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

MOUSE: MALE : SACRIFICED ANIMALS

STUDY NO. : 0180
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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



| Organ | Findings | Group Name | Control | | | | 1250 ppm | | | | 2500 ppm | | | | 5000 ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals | 2 | | | | 2 | | | | 2 | | | | 2 | | | |
| | | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| liver | swelling | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | necrosis:focal | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | granulation | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | basophilic change | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Reproductive system] | | | | | | | | | | | | | | | | | | |
| epididymis | spermatogenic granuloma | | 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 ( 50) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Musculoskeletal system] | | | | | | | | | | | | | | | | | | |
| muscle | necrosis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

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

| Organ | Findings | Group Name | 10000 ppm | | | | 20000 ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals | 2 | | | | 2 | | | |
| | | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |
| [Digestive system] | | | | | | | | | | |
| liver | swelling | | 2 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | necrosis:focal | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | granulation | | 2 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 50) | 0 ( 0) | 0 ( 0) |
| [Urinary system] | | | | | | | | | | |
| kidney | basophilic change | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 50) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Reproductive system] | | | | | | | | | | |
| epididymis | spermatogenic granuloma | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Musculoskeletal system] | | | | | | | | | | |
| muscle | necrosis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 50) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

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

APPENDIX A 6-6

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

MOUSE: FEMALE : SACRIFICED ANIMALS

| Organ | Findings | Group Name | Control | | | | 1250 ppm | | | | 2500 ppm | | | | 5000 ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals | 2 | | | | 2 | | | | 2 | | | | 2 | | | |
| | | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| stomach | intestinal metaplasia | | 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) |
| liver | swelling | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | necrosis:focal | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | granulation | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 50) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 50) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

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

| Organ | Findings | Group Name | 10000 ppm | | | | 20000 ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals | 2 | | | | 2 | | | |
| | | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |
| [Digestive system] | | | | | | | | | | |
| stomach | intestinal metaplasia | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| liver | swelling | | 2 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | necrosis:focal | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | granulation | | 0 ( 0) | 1 ( 50) | 0 ( 0) | 0 ( 0) | 1 ( 50) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

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

APPENDIX A 7-1

# IDENTITY AND PURITY OF BIPHENYL

# PERFORMED AT THE JAPAN BIOASSAY LABORATORY

# (TWO-WEEK STUDY)

IDENTITY AND PURITY OF BIPHENYL PERFORMED AT THE JAPANBIOASSAY LABORATORY (TWO-WEEK STUDIES)

Lot no.DSQ3708

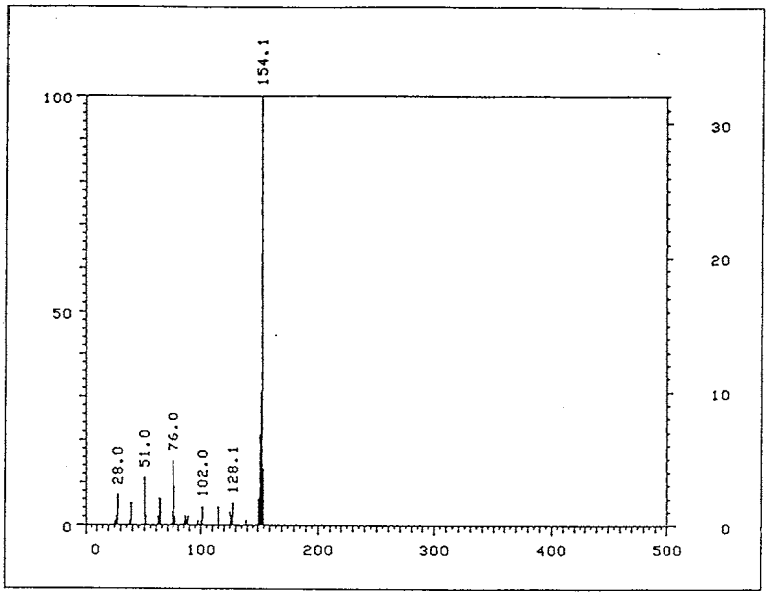
1. Spectral data

Mass Spectrometry

Instrument: Hitachi M-80B

Ionization: EI(Electron Ionization)

Ionization Voltage: 70eV




Mass Spectrum of BIPHENYL

Result:

| | Molecule Weight |
|---|---|
| Theoretical Value | 154.1(Calculated) |
| Determined | 154.1 |

ULTRA VIOLET SPECTRUM

Instrument: SHIMADZU UV-240

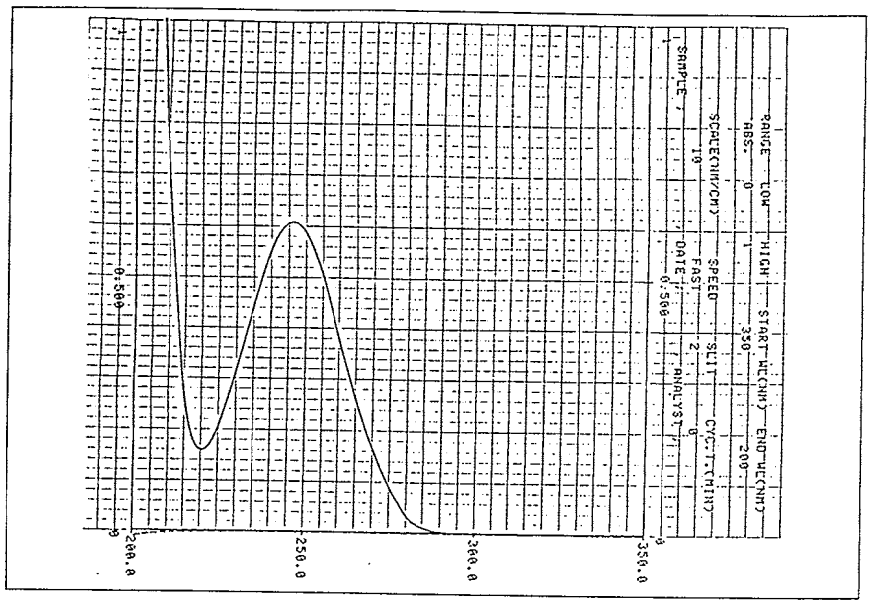
Cell: 1 mm Cell

Solvent: Methanol

Slit: 2 nm

Range: 0-1

Concentration(mg/l): 50




Ultra Violet Spectrum of BIPHENYL

| Results: | Determined | Literature Value (Sadtler handbook by Sadtler Research Laboratories, Inc.) |
|---|---|---|
| Wave Length (nm) | 246.5 | 246.5 |

2. Gas Chromatography

| | |
|---|---|
| Instrument: | Hewlett Packard 5890A |
| Column: | Methyl Silicone(0.2mm$\phi$ × 50m) |
| Column Temperature: | 180°C |
| Flow Rate: | 1 ml/min |
| Detector: | FID(Hydrogen Flame Ionization) |
| Injection Volume: | 1 $\mu$l |

Results: Only major peak(except solvent peak)

| Peak No. | Retention Time(min) | Retention Time Relative to Major Peak | AREA (percent of major peak) |
|---|---|---|---|
| 1 | 3.27 | 1.00 | 100 |

3. Conclusions: The result of the Mass spectrum agreed with the theoretical value and the ultra violet spectrum agreed with the literature values. Gas chromtography indicated only the major peak.

APPENDIX A 7-2

# STABILITY OF BIPHENYL AT THE JAPAN BIOASSAY LABORATORY

## (TWO-WEEK STUDY)

STABILITY OF BIPHENYL AT THE JAPAN BIOASSAY LABORATORY(TWO-WEEK STUDIES)

Lot no. DSQ3708

1. Sample storage: Biphenyl were stored for about 2 weeks at 5°C.

2. Gas Chromatography

| | |
|---|---|
| Instrument: | Hewlett Packard 5890A |
| Column: | Methyl Silicone(0.2mm$\phi$ × 50m) |
| Column Temperature: | 180°C |
| Flow Rate: | 1 ml/min |
| Detector: | FID(Hydrogen Flame Ionization) |
| Injection Volume: | 1 $\mu$l |

Results: Only major peak(except solvent peak)

| Date | Retention Time(min) | Retention Time Relative to Major Peak | Area (percent of Major peak) |
|---|---|---|---|
| 08/30/91 | 3.27 | 1.00 | 100 |
| 10/14/91 | 3.27 | 1.00 | 100 |

3. Conclusions: Gas chromatography indicates only the major peak. Consequently, Biphenyl was stable as the chemical when stored for about 2 weeks at 5°C.

# APPENDIX A 7-3

# ANALYSYS OF BIPHENYL CONCENTRATION IN FORMULATED DIETS

# OF THE TOW-WEEK STUDIES

ANALYSIS OF BIPHENYL CONCENTRATION IN FORMULATED DIETS OF THE TWO-WEEK STUDIES

(Rat)

| Concentration of BIPHENYL in feed for Target Concentration(ppm) | | | | |
|---|---|---|---|---|
| 2500 ( a ) | 5000 ( a ) | 10000 ( a ) | 20000 ( a ) | 40000 ( a ) |
| 2572.9(102.9) | 4461.1( 89.2) | 9138.1( 91.4) | 19843.3( 99.2) | 40182.0(100.5) |

(Mouse)

| Concentration of BIPHENYL in feed for Target Concentration(ppm) | | | | |
|---|---|---|---|---|
| 1250 ( a ) | 2500 ( a ) | 5000 ( a ) | 10000 ( a ) | 20000 ( a ) |
| 1220.0( 97.6) | 2572.9(102.9) | 4461.1( 89.2) | 9138.1( 91.4) | 19843.3( 99.2) |

(a) Determined as a percent of target concentration

# APPENDIX A 7-4

# STABILITY OF BIPHENYL IN FORMULATED DIETS

# OF THE TOW-WEEK STUDIES

STABILITY OF BIPHENYL IN FORMULATED DIETS OF THE TWO-WEEK STUDIES

(Rat)(Mouse)

| | Concentration of BIPHENYL in feed for Target Concentration(ppm) | |
|---|---|---|
| Date Mixed | 1250 ( a ) | 40000 ( a ) |
| 08/26/91 | 1177.7 | 37454.5 |
| 09/02/91 | 1097.8( 93.2) | 37763.7(100.8) |

(a) Determined as a percent of target concentration