1,3,5,7-テトラアザトリシクロ〔3.3.1.1 $^{3,7}$〕デカンの
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（混水試験）報告書

# APPENDIXES

（B1-1～C2）
13 週間試験：ラット/0201；マウス/0202

# APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

# APPENDIXES (CONTINUED)

# APPENDIXES (CONTINUED)

# APPENDIX B 1-1

## CLINICAL OBSERVATION (THIRTEEN−WEEK STUDY: SUMMARY)

## RAT: MALE

STUDY NO. : 0201
ANIMAL : RAT F344
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE



| Clinical sign | Group Name | Administration Week-day 1-7 | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 | 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 1 | 1 | 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 |
| | 2500 ppm | 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 |
| | 10000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000 ppm | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 4 | 4 | 4 | 4 | 6 |
| | 40000 ppm | 0 | 0 | 0 | 0 | 0 | 8 | 8 | 8 | 10 | 10 | 10 | 10 | 10 |

APPENDIX B 1-2

# CLINICAL OBSERVATION (THIRTEEN−WEEK STUDY: SUMMARY)

## RAT: FEMALE

| Clinical sign | Group Name | Administration Week-day 1-7 | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 | 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 1 | 1 | 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 |
| | 2500 ppm | 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 |
| | 10000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000 ppm | 0 | 0 | 0 | 0 | 0 | 3 | 3 | 3 | 3 | 4 | 5 | 6 | 7 |
| | 40000 ppm | 0 | 0 | 0 | 0 | 0 | 6 | 6 | 6 | 9 | 9 | 9 | 9 | 10 |
| SOILED PERI GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| | 5000 ppm | 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 |
| | 20000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | 40000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 |
| SMALL STOOL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2500 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| | 5000 ppm | 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 |
| | 20000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | 40000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| OLIGO-STOOL | Control | 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 |
| | 5000 ppm | 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 |
| | 20000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | 40000 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

APPENDIX B 1-3

# CLINICAL OBSERVATION (THIRTEEN−WEEK STUDY: SUMMARY)

## MOUSE: MALE

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE



| Clinical sign | Group Name | Administration Week-day 1-7 | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 | 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| MORIBUND SACRIFICE | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 40000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 80000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 |
| HUNCHBACK POSITION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 40000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 80000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| PILOERECTION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 40000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 80000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| IRREGULAR BREATHING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 40000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 80000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| ABNORMAL RESPIRATION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 40000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 80000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE



| Clinical sign | Group Name | Administration Week-day 1-7 | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 | 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 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 |
| | 5000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 40000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 80000ppm | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |

APPENDIX B 1-4

# CLINICAL OBSERVATION (THIRTEEN−WEEK STUDY: SUMMARY)

## MOUSE: FEMALE

| Clinical sign | Group Name | Administration Week-day 1-7 | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 | 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| DEATH | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 40000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 80000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| HUNCHBACK POSITION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 40000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 80000ppm | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 |
| WASTING | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 40000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 80000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 |
| PILOERECTION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 40000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 80000ppm | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 |
| OLIGO-STOOL | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 5000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 10000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 20000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 40000ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 80000ppm | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |

APPENDIX B 2-1

# BODY WEIGHT CHANGES (THIRTEEN−WEEK STUDY:SUMMARY)

RAT : MALE

STUDY NO. : 0201
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day 0-0 | 1-7 | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 |
|---|---|---|---|---|---|---|---|
| Control | 134± 4 | 167± 6 | 199± 7 | 225± 6 | 243± 8 | 261± 8 | 273± 10 |
| 2500 ppm | 134± 4 | 166± 5 | 196± 7 | 220± 9 | 236± 12 | 251± 15 | 261± 17 |
| 5000 ppm | 134± 4 | 164± 5 | 192± 6 | 216± 8 | 233± 11 | 247± 13 | 259± 17 |
| 10000 ppm | 134± 4 | 163± 4 | 191± 7 | 212± 8** | 227± 11* | 241± 14** | 251± 16* |
| 20000 ppm | 134± 4 | 162± 5 | 190± 8* | 212± 10** | 227± 12** | 243± 13* | 253± 15* |
| 40000 ppm | 134± 4 | 155± 5** | 180± 7** | 199± 10** | 212± 13** | 226± 16** | 237± 19** |

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

STUDY NO. : 0201
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 |
|---|---|---|---|---|---|---|---|
| Control | 286± 11 | 300± 12 | 310± 13 | 316± 14 | 325± 13 | 335± 14 | 343± 14 |
| 2500 ppm | 272± 18 | 285± 20 | 292± 22 | 300± 23 | 308± 23 | 317± 22 | 324± 21 |
| 5000 ppm | 270± 17 | 283± 19 | 290± 20 | 298± 21 | 308± 23 | 315± 24 | 323± 23 |
| 10000 ppm | 263± 18* | 276± 21* | 284± 22* | 291± 23* | 301± 23 | 310± 24 | 318± 23* |
| 20000 ppm | 265± 16* | 276± 17* | 285± 19* | 293± 20 | 302± 21 | 311± 21 | 316± 21* |
| 40000 ppm | 249± 23** | 260± 24** | 267± 25** | 275± 25** | 284± 25** | 293± 24** | 299± 24** |

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

APPENDIX B 2-2

# BODY WEIGHT CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

RAT : FEMALE

STUDY NO. : 0201
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day 0-0 | 1-7 | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 |
|---|---|---|---|---|---|---|---|
| Control | 101± 3 | 118± 4 | 133± 4 | 145± 6 | 154± 6 | 161± 6 | 166± 9 |
| 2500 ppm | 102± 3 | 118± 4 | 133± 5 | 144± 5 | 152± 6 | 160± 8 | 164± 8 |
| 5000 ppm | 101± 3 | 117± 4 | 132± 5 | 143± 7 | 151± 6 | 159± 8 | 163± 7 |
| 10000 ppm | 101± 3 | 116± 5 | 131± 5 | 140± 6 | 148± 6 | 154± 7 | 157± 9 |
| 20000 ppm | 102± 3 | 116± 4 | 131± 3 | 141± 4 | 147± 5 | 154± 6 | 157± 7 |
| 40000 ppm | 102± 3 | 111± 3** | 124± 4** | 134± 4** | 141± 5** | 147± 5** | 151± 6** |

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

STUDY NO. : 0201
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 |
|---|---|---|---|---|---|---|---|
| Control | 173± 12 | 176± 12 | 181± 13 | 186± 13 | 190± 13 | 192± 12 | 196± 13 |
| 2500 ppm | 171± 9 | 175± 9 | 175± 9 | 181± 8 | 186± 10 | 189± 10 | 191± 8 |
| 5000 ppm | 167± 11 | 173± 7 | 177± 8 | 181± 8 | 185± 9 | 189± 7 | 191± 7 |
| 10000 ppm | 162± 9* | 165± 10* | 170± 11 | 172± 10** | 176± 11* | 180± 12* | 181± 11** |
| 20000 ppm | 163± 9 | 167± 8 | 171± 9 | 174± 10* | 174± 14* | 181± 11 | 183± 11* |
| 40000 ppm | 157± 6** | 160± 6** | 164± 6** | 166± 7** | 169± 9** | 173± 9** | 174± 8** |

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

APPENDIX B 2-3

# BODY WEIGHT CHANGES (THIRTEEN−WEEK STUDY:SUMMARY)

MOSUE : MALE

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day 0-0 | 1-7 | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 |
|---|---|---|---|---|---|---|---|
| Control | 24.1± 0.9 | 24.9± 1.1 | 26.0± 1.0 | 26.7± 0.8 | 27.7± 0.7 | 28.5± 1.0 | 29.6± 1.2 |
| 5000ppm | 24.1± 0.9 | 25.3± 1.1 | 26.4± 1.1 | 27.4± 1.2 | 28.1± 1.6 | 29.3± 1.3 | 30.3± 1.2 |
| 10000ppm | 24.1± 0.9 | 25.1± 0.9 | 26.2± 1.2 | 27.2± 1.2 | 28.0± 1.5 | 29.1± 1.6 | 30.3± 1.8 |
| 20000ppm | 24.1± 0.9 | 24.9± 1.1 | 26.3± 1.1 | 27.2± 1.1 | 28.2± 1.4 | 29.0± 1.3 | 30.1± 1.5 |
| 40000ppm | 24.1± 1.0 | 25.2± 1.1 | 26.3± 0.8 | 27.1± 1.4 | 28.0± 1.2 | 28.9± 1.1 | 29.8± 1.6 |
| 80000ppm | 24.1± 1.0 | 23.2± 0.9** | 24.7± 1.3* | 25.2± 1.5* | 26.0± 2.0* | 26.5± 2.8 | 27.0± 3.4 |

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

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 |
|---|---|---|---|---|---|---|---|
| Control | 30.3± 1.4 | 31.7± 1.5 | 32.7± 1.6 | 33.8± 1.9 | 34.4± 1.8 | 35.3± 2.0 | 35.9± 2.1 |
| 5000ppm | 31.0± 1.8 | 32.2± 1.9 | 33.5± 1.8 | 34.6± 2.0 | 35.4± 2.3 | 36.2± 2.7 | 36.7± 2.6 |
| 10000ppm | 30.8± 1.8 | 32.1± 2.1 | 33.0± 2.3 | 34.2± 2.5 | 34.7± 2.4 | 35.6± 2.5 | 36.3± 2.5 |
| 20000ppm | 30.6± 1.9 | 31.7± 2.0 | 32.5± 2.1 | 33.0± 2.0 | 33.8± 1.8 | 34.5± 1.9 | 35.5± 2.1 |
| 40000ppm | 30.1± 1.7 | 31.4± 2.1 | 32.0± 2.3 | 33.2± 2.5 | 33.6± 2.6 | 34.5± 2.7 | 35.4± 2.8 |
| 80000ppm | 26.6± 4.1** | 29.1± 1.2* | 29.7± 1.0** | 30.5± 1.3** | 31.0± 1.5** | 31.7± 1.6** | 32.5± 1.2** |

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

APPENDIX B 2-4

# BODY WEIGHT CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

## MOSUE: FEMALE

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day 0-0 | 1-7 | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 |
|---|---|---|---|---|---|---|---|
| Control | 18.9± 0.7 | 20.1± 0.9 | 20.6± 0.5 | 20.8± 0.8 | 21.4± 0.8 | 22.0± 0.8 | 22.4± 0.9 |
| 5000ppm | 19.0± 0.6 | 19.2± 0.6 | 20.4± 0.7 | 20.2± 0.8 | 21.1± 0.7 | 21.6± 1.0 | 22.0± 0.8 |
| 10000ppm | 19.0± 0.7 | 19.5± 1.1 | 20.7± 1.1 | 20.9± 0.7 | 21.2± 1.1 | 21.7± 1.1 | 22.2± 1.1 |
| 20000ppm | 19.0± 0.7 | 19.6± 0.9 | 20.2± 0.9 | 20.3± 0.8 | 20.9± 0.7 | 21.9± 1.1 | 21.8± 0.8 |
| 40000ppm | 19.0± 0.7 | 19.5± 0.5 | 20.2± 0.5 | 20.6± 1.4 | 20.9± 1.1 | 21.5± 0.6 | 22.0± 0.9 |
| 80000ppm | 19.0± 0.7 | 17.3± 1.5** | 19.4± 1.0** | 19.4± 0.7** | 19.9± 1.2** | 20.2± 2.3 | 20.0± 2.6** |

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

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 |
|---|---|---|---|---|---|---|---|
| Control | 22.4± 1.0 | 23.2± 0.4 | 23.7± 0.9 | 23.3± 0.7 | 23.8± 0.4 | 23.7± 1.6 | 24.6± 1.3 |
| 5000ppm | 21.8± 0.9 | 22.8± 0.8 | 23.7± 1.5 | 23.2± 1.1 | 23.4± 1.2 | 23.8± 1.1 | 24.1± 1.3 |
| 10000ppm | 22.1± 1.2 | 23.2± 1.2 | 23.1± 1.1 | 23.7± 1.4 | 23.4± 1.6 | 23.9± 1.5 | 23.6± 1.7 |
| 20000ppm | 21.9± 1.1 | 23.3± 0.8 | 22.9± 0.5 | 22.8± 0.9 | 23.7± 1.3 | 23.8± 1.0 | 23.9± 1.3 |
| 40000ppm | 22.1± 1.0 | 22.8± 0.8 | 23.2± 0.8 | 22.9± 0.8 | 23.0± 1.1 | 23.6± 1.0 | 23.3± 0.7 |
| 80000ppm | 20.4± 2.9 | 21.4± 2.7 | 21.7± 2.8 | 21.5± 2.9 | 22.0± 3.4 | 23.2± 1.4 | 22.9± 1.0 |

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

APPENDIX B 3-1

# WATER CONSUMPTION CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

RAT : MALE

STUDY NO. : 0201
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day(effective) 1-7(4) | 2-7(4) | 3-7(4) | 4-7(4) | 5-7(4) | 6-7(4) | 7-7(4) |
|---|---|---|---|---|---|---|---|
| Control | 18.3± 1.0 | 20.4± 1.8 | 21.1± 1.4 | 21.7± 1.7 | 20.7± 1.3 | 20.1± 1.5 | 19.6± 1.6 |
| 2500 ppm | 19.4± 1.2 | 21.3± 1.3 | 21.1± 1.1 | 21.6± 1.7 | 20.4± 2.1 | 19.7± 2.3 | 19.5± 2.6 |
| 5000 ppm | 19.2± 1.2 | 21.1± 0.9 | 21.2± 0.7 | 22.0± 1.2 | 20.5± 1.0 | 20.5± 1.7 | 20.1± 1.8 |
| 10000 ppm | 19.8± 1.4 | 22.2± 1.7 | 21.9± 1.6 | 21.7± 2.2 | 19.9± 1.9 | 19.2± 1.6 | 18.8± 1.8 |
| 20000 ppm | 21.5± 1.6** | 22.9± 2.5* | 22.8± 2.4 | 23.6± 4.2 | 23.2± 3.7 | 21.4± 1.9 | 21.2± 1.5 |
| 40000 ppm | 17.6± 2.0 | 18.6± 0.9 | 19.3± 1.9 | 18.7± 2.0* | 18.3± 2.6 | 17.4± 2.1** | 17.9± 2.7 |

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

STUDY NO. : 0201
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day(effective) 8-7(4) | 9-7(4) | 10-7(4) | 11-7(4) | 12-7(4) | 13-7(4) |
|---|---|---|---|---|---|---|
| Control | 19.8± 2.2 | 19.4± 1.4 | 18.5± 1.3 | 18.2± 1.3 | 18.2± 1.3 | 18.7± 1.4 |
| 2500 ppm | 19.7± 2.3 | 19.2± 2.2 | 19.0± 2.6 | 18.6± 2.2 | 18.4± 2.2 | 18.5± 2.1 |
| 5000 ppm | 20.4± 2.0 | 19.4± 1.9 | 19.3± 2.0 | 19.3± 1.9 | 18.4± 1.8 | 18.9± 1.8 |
| 10000 ppm | 19.3± 2.0 | 18.4± 1.8 | 18.3± 1.4 | 18.2± 1.5 | 18.3± 1.8 | 18.6± 1.5 |
| 20000 ppm | 21.0± 1.9 | 21.1± 2.9 | 20.6± 2.4 | 20.9± 1.8** | 20.0± 2.6 | 20.0± 2.3 |
| 40000 ppm | 18.5± 1.8 | 17.5± 2.1 | 17.1± 1.8 | 18.6± 1.8 | 17.7± 1.4 | 18.1± 1.9 |

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

APPENDIX B 3-2

# WATER CONSUMPTION CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

## RAT : FEMALE

STUDY NO. : 0201
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day(effective) 1-7(4) | 2-7(4) | 3-7(4) | 4-7(4) | 5-7(4) | 6-7(4) | 7-7(4) |
|---|---|---|---|---|---|---|---|
| Control | 15.9± 0.7 | 16.8± 0.9 | 17.0± 0.9 | 16.7± 1.1 | 16.8± 1.6 | 19.1± 8.7 | 17.2± 2.8 |
| 2500 ppm | 18.5± 5.9 | 17.1± 1.2 | 17.7± 2.0 | 18.6± 5.2 | 18.5± 6.0 | 19.0± 6.7 | 21.8± 11.4 |
| 5000 ppm | 16.5± 1.5 | 17.7± 1.8 | 17.3± 1.6 | 17.3± 1.5 | 17.5± 1.6 | 18.6± 6.0 | 19.3± 8.6 |
| 10000 ppm | 17.2± 1.4 | 18.0± 2.1 | 19.1± 6.7 | 17.4± 2.6 | 17.2± 2.5 | 16.5± 2.6 | 16.2± 2.3 |
| 20000 ppm | 18.0± 1.0* | 18.7± 1.5* | 17.9± 1.3 | 17.4± 1.6 | 17.0± 1.6 | 16.2± 1.9 | 16.7± 2.4 |
| 40000 ppm | 15.0± 1.4 | 15.3± 1.2 | 24.0± 17.8 | 20.4± 9.6 | 14.8± 2.1 | 14.4± 3.0 | 14.6± 2.4 |

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

STUDY NO. : 0201
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day(effective) 8-7(4) | 9-7(4) | 10-7(4) | 11-7(4) | 12-7(4) | 13-7(4) |
|---|---|---|---|---|---|---|
| Control | 18.1± 4.5 | 18.5± 5.5 | 18.4± 5.0 | 18.8± 7.7 | 17.3± 3.9 | 16.9± 3.8 |
| 2500 ppm | 22.4± 12.0 | 15.3± 8.2 | 17.3± 3.4 | 18.4± 7.9 | 17.4± 5.4 | 20.4± 8.8 |
| 5000 ppm | 19.6± 8.8 | 18.5± 7.4 | 19.1± 9.6 | 18.5± 5.1 | 18.0± 7.3 | 18.4± 5.9 |
| 10000 ppm | 16.5± 2.5 | 17.1± 3.3 | 16.8± 3.5 | 19.1± 6.5 | 18.0± 4.3 | 18.1± 6.3 |
| 20000 ppm | 16.7± 1.4 | 16.2± 1.7 | 15.8± 1.5 | 19.0± 10.1 | 18.0± 5.9 | 22.1± 18.1 |
| 40000 ppm | 15.1± 2.9 | 13.9± 2.9* | 13.4± 3.5** | 13.8± 2.9 | 13.3± 3.1 | 13.4± 2.3 |

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

APPENDIX B 3-3

# WATER CONSUMPTION CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

## MOSUE : MALE

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day(effective) 1-7(4) | 2-7(4) | 3-7(4) | 4-7(4) | 5-7(4) | 6-7(4) | 7-7(4) |
|---|---|---|---|---|---|---|---|
| Control | 5.1± 1.4 | 4.9± 1.0 | 4.6± 0.8 | 4.4± 0.8 | 4.6± 1.3 | 4.3± 1.0 | 4.3± 1.1 |
| 5000ppm | 5.2± 0.8 | 4.7± 0.8 | 4.7± 0.7 | 4.7± 1.1 | 4.8± 1.4 | 4.6± 1.0 | 4.7± 0.9 |
| 10000ppm | 5.2± 0.7 | 5.0± 0.7 | 4.8± 0.5 | 4.7± 0.5 | 4.5± 0.5 | 4.7± 0.4 | 4.6± 0.6 |
| 20000ppm | 5.5± 0.8 | 5.2± 0.8 | 5.2± 1.0 | 5.0± 0.8 | 4.9± 0.8 | 4.7± 0.6 | 4.8± 0.9 |
| 40000ppm | 6.4± 0.9** | 5.7± 0.7* | 5.6± 0.8* | 5.3± 0.6* | 5.1± 0.5 | 5.3± 0.3* | 5.2± 0.4* |
| 80000ppm | 7.9± 2.0** | 6.7± 2.4* | 7.5± 3.2** | 7.5± 3.3** | 7.5± 3.7** | 7.4± 3.7** | 7.1± 2.0** |

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

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day(effective) 8-7(4) | 9-7(4) | 10-7(4) | 11-7(4) | 12-7(4) | 13-7(4) |
|---|---|---|---|---|---|---|
| Control | 4.3± 0.9 | 4.0± 0.6 | 3.9± 0.7 | 3.7± 0.5 | 3.6± 0.4 | 3.6± 0.5 |
| 5000ppm | 4.4± 1.0 | 4.1± 0.4 | 4.2± 0.5 | 4.0± 0.6 | 3.9± 0.4 | 3.8± 0.3 |
| 10000ppm | 4.6± 0.5 | 4.2± 0.5 | 4.3± 0.5 | 4.1± 0.6 | 4.0± 0.4 | 3.9± 0.5 |
| 20000ppm | 5.1± 1.5 | 4.6± 1.1 | 4.4± 0.7 | 4.3± 0.8 | 4.3± 0.7 | 4.2± 0.6 |
| 40000ppm | 5.1± 0.4 | 4.9± 0.3* | 4.9± 0.5** | 4.6± 0.4* | 4.6± 0.3** | 4.5± 0.2** |
| 80000ppm | 6.3± 2.0** | 6.0± 1.8** | 6.2± 2.1** | 6.0± 1.8** | 5.8± 1.7** | 5.6± 1.4** |

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

APPENDIX B 3-4

# WATER CONSUMPTION CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

## MOSUE : FEMALE

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day(effective) 1-7(4) | 2-7(4) | 3-7(4) | 4-7(4) | 5-7(4) | 6-7(4) | 7-7(4) |
|---|---|---|---|---|---|---|---|
| Control | 4.9± 0.8 | 4.7± 0.5 | 4.6± 0.6 | 5.0± 1.1 | 5.5± 1.8 | 5.2± 1.5 | 5.5± 1.5 |
| 5000ppm | 5.0± 0.7 | 5.2± 0.8 | 5.0± 1.1 | 5.2± 1.0 | 5.5± 1.3 | 5.5± 1.5 | 5.5± 0.9 |
| 10000ppm | 5.0± 0.7 | 5.2± 0.9 | 4.8± 0.5 | 4.9± 0.3 | 4.5± 0.3 | 4.8± 0.5 | 5.0± 0.5 |
| 20000ppm | 5.4± 0.5 | 5.3± 0.9 | 6.0± 2.7 | 5.7± 1.1 | 5.9± 2.2 | 5.6± 1.5 | 6.3± 1.3 |
| 40000ppm | 5.7± 0.3* | 5.6± 0.6 | 6.0± 1.0** | 6.0± 1.1* | 6.6± 2.2 | 5.9± 1.0 | 6.2± 1.0 |
| 80000ppm | 7.2± 2.4** | 7.3± 1.0** | 9.2± 2.7** | 9.6± 3.3** | 9.9± 1.9** | 9.7± 2.8** | 9.7± 2.3** |

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

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day(effective) 8-7(4) | 9-7(4) | 10-7(4) | 11-7(4) | 12-7(4) | 13-7(4) |
|---|---|---|---|---|---|---|
| Control | 5.8± 2.6 | 6.8± 2.9 | 6.1± 2.8 | 6.7± 3.1 | 6.6± 3.5 | 5.9± 2.5 |
| 5000ppm | 5.5± 1.2 | 5.3± 0.6 | 4.8± 0.5 | 4.8± 0.6 | 4.7± 0.5 | 4.8± 0.6 |
| 10000ppm | 4.9± 0.6 | 4.8± 0.5 | 4.7± 0.3 | 4.8± 0.6 | 4.7± 0.7 | 5.1± 1.7 |
| 20000ppm | 5.9± 1.5 | 6.5± 3.8 | 5.9± 1.5 | 5.9± 1.9 | 5.7± 1.7 | 5.9± 2.0 |
| 40000ppm | 6.0± 0.8 | 5.6± 0.5 | 5.7± 0.8 | 5.7± 1.2 | 5.5± 1.1 | 5.5± 0.9 |
| 80000ppm | 9.5± 3.5** | 10.1± 4.6* | 10.3± 4.6** | 10.7± 7.0* | 8.6± 2.2 | 7.3± 0.7* |

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

APPENDIX B 4-1

# FOOD CONSUMPTION CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

RAT : MALE

STUDY NO. : 0201
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day(effective) 1-7(7) | 2-7(7) | 3-7(7) | 4-7(7) | 5-7(7) | 6-7(7) | 7-7(7) |
|---|---|---|---|---|---|---|---|
| Control | 15.0± 1.1 | 16.3± 1.0 | 17.1± 0.8 | 17.3± 1.0 | 17.1± 0.6 | 16.6± 0.8 | 16.5± 1.0 |
| 2500 ppm | 14.9± 0.5 | 16.1± 0.7 | 16.7± 0.9 | 16.6± 0.8 | 16.0± 1.2 | 15.3± 1.1 | 15.5± 1.3 |
| 5000 ppm | 14.9± 0.7 | 15.6± 0.8 | 16.0± 0.9 | 16.6± 1.4 | 16.0± 1.2 | 15.5± 1.4 | 15.3± 1.6 |
| 10000 ppm | 14.5± 0.5 | 16.0± 0.9 | 16.0± 1.1 | 16.4± 1.6 | 15.4± 1.4* | 14.8± 1.6* | 15.1± 1.8 |
| 20000 ppm | 14.5± 0.8 | 15.7± 0.8 | 16.2± 1.1 | 16.4± 1.2 | 16.0± 1.4 | 15.2± 1.2 | 15.7± 1.1 |
| 40000 ppm | 12.7± 0.9** | 14.7± 0.8** | 15.0± 1.2** | 14.9± 1.1** | 14.3± 1.5** | 14.0± 1.5** | 14.4± 1.7 |

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

STUDY NO. : 0201
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day(effective) 8-7(7) | 9-7(7) | 10-7(7) | 11-7(7) | 12-7(7) | 13-7(7) |
|---|---|---|---|---|---|---|
| Control | 16.4± 0.9 | 16.5± 1.0 | 16.3± 1.1 | 16.6± 0.6 | 16.3± 1.0 | 16.4± 0.9 |
| 2500 ppm | 15.3± 1.3 | 15.1± 1.4 | 15.2± 1.4 | 15.5± 1.2 | 14.7± 1.1 | 15.4± 0.6 |
| 5000 ppm | 15.4± 1.6 | 15.0± 1.6 | 15.2± 1.6 | 15.4± 1.4 | 14.7± 1.8 | 15.1± 1.5 |
| 10000 ppm | 14.8± 1.8 | 14.7± 1.8 | 14.7± 1.4 | 15.1± 1.4* | 14.6± 1.4* | 15.2± 1.3 |
| 20000 ppm | 15.4± 1.2 | 15.3± 1.2 | 15.4± 1.4 | 15.8± 1.2 | 15.2± 1.5 | 15.5± 1.2 |
| 40000 ppm | 14.1± 1.8** | 14.5± 1.9 | 14.0± 1.4** | 14.6± 1.3** | 14.4± 1.2* | 14.9± 1.1 |

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

APPENDIX B 4-2

# FOOD CONSUMPTION CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

RAT : FEMALE

STUDY NO. : 0201
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day(effective) 1-7(7) | 2-7(7) | 3-7(7) | 4-7(7) | 5-7(7) | 6-7(7) | 7-7(7) |
|---|---|---|---|---|---|---|---|
| Control | 12.0± 0.7 | 12.8± 0.8 | 12.9± 0.9 | 12.7± 0.5 | 12.3± 0.8 | 11.6± 1.4 | 12.2± 1.5 |
| 2500 ppm | 11.4± 0.7 | 12.1± 0.8 | 12.4± 1.0 | 12.3± 0.9 | 11.8± 1.0 | 11.3± 1.1 | 11.9± 1.0 |
| 5000 ppm | 11.4± 0.6 | 12.4± 0.9 | 12.2± 0.8 | 12.2± 0.8 | 11.9± 0.8 | 11.3± 0.7 | 11.4± 0.9 |
| 10000 ppm | 11.0± 0.5** | 11.8± 1.0* | 11.5± 0.8** | 11.6± 1.0* | 11.1± 0.9* | 10.5± 1.3 | 10.7± 1.1* |
| 20000 ppm | 11.1± 0.3** | 11.9± 0.4* | 11.8± 0.7* | 11.4± 0.7** | 11.2± 0.8 | 10.4± 1.1 | 10.7± 1.1* |
| 40000 ppm | 10.1± 0.7** | 11.2± 0.7** | 11.2± 0.7** | 11.2± 1.0** | 10.9± 1.2** | 10.1± 1.2* | 10.6± 1.2* |

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

STUDY NO. : 0201
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day(effective) 8-7(7) | 9-7(7) | 10-7(7) | 11-7(7) | 12-7(7) | 13-7(7) |
|---|---|---|---|---|---|---|
| Control | 11.6± 1.2 | 11.5± 1.0 | 11.7± 1.4 | 11.7± 1.0 | 11.5± 0.9 | 11.5± 0.9 |
| 2500 ppm | 11.3± 1.0 | 10.6± 1.4 | 11.1± 1.1 | 11.5± 1.3 | 11.3± 1.1 | 10.9± 0.7 |
| 5000 ppm | 11.4± 0.9 | 11.0± 0.9 | 11.1± 0.8 | 11.4± 1.0 | 11.2± 0.9 | 11.0± 0.8 |
| 10000 ppm | 10.4± 0.9* | 10.2± 1.1* | 10.0± 0.9** | 10.3± 1.1 | 10.4± 1.1 | 10.0± 0.9** |
| 20000 ppm | 10.7± 0.9 | 10.2± 1.0* | 10.2± 1.1* | 10.0± 1.6* | 10.6± 1.0 | 10.4± 1.0* |
| 40000 ppm | 10.3± 1.0* | 9.9± 1.2** | 9.7± 1.4** | 10.1± 1.1* | 9.9± 1.0** | 9.6± 1.0** |

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

APPENDIX B 4-3

FOOD CONSUMPTION CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : MALE

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day(effective) 1-7(7) | 2-7(7) | 3-7(7) | 4-7(7) | 5-7(7) | 6-7(7) | 7-7(7) |
|---|---|---|---|---|---|---|---|
| Control | 3.9± 0.3 | 3.9± 0.3 | 3.9± 0.3 | 4.0± 0.3 | 3.9± 0.3 | 4.0± 0.3 | 3.9± 0.3 |
| 5000ppm | 4.0± 0.3 | 4.0± 0.2 | 3.9± 0.2 | 4.0± 0.2 | 3.9± 0.2 | 4.1± 0.2 | 4.1± 0.3 |
| 10000ppm | 3.9± 0.1 | 4.0± 0.2 | 3.9± 0.2 | 4.0± 0.2 | 4.0± 0.2 | 4.2± 0.2 | 4.0± 0.2 |
| 20000ppm | 4.1± 0.3 | 4.1± 0.4 | 4.0± 0.4 | 4.2± 0.4 | 4.1± 0.3 | 4.2± 0.3 | 4.1± 0.3 |
| 40000ppm | 4.1± 0.2 | 4.0± 0.2 | 3.9± 0.2 | 4.1± 0.1 | 4.0± 0.2 | 4.1± 0.2 | 4.0± 0.2 |
| 80000ppm | 3.4± 0.3** | 4.0± 0.3 | 3.8± 0.3 | 3.9± 0.3 | 3.8± 0.4 | 3.8± 0.4 | 3.6± 0.5 |

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

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day(effective) 8-7(7) | 9-7(7) | 10-7(7) | 11-7(7) | 12-7(7) | 13-7(7) |
|---|---|---|---|---|---|---|
| Control | 4.2± 0.3 | 4.1± 0.4 | 4.2± 0.3 | 4.1± 0.2 | 4.2± 0.2 | 4.0± 0.3 |
| 5000ppm | 4.2± 0.2 | 4.3± 0.3 | 4.4± 0.3 | 4.2± 0.3 | 4.3± 0.3 | 4.1± 0.2 |
| 10000ppm | 4.2± 0.3 | 4.2± 0.2 | 4.3± 0.2 | 4.2± 0.2 | 4.2± 0.2 | 4.1± 0.2 |
| 20000ppm | 4.2± 0.2 | 4.2± 0.3 | 4.2± 0.2 | 4.1± 0.2 | 4.2± 0.2 | 4.2± 0.3 |
| 40000ppm | 4.2± 0.2 | 4.1± 0.1 | 4.3± 0.2 | 4.1± 0.2 | 4.2± 0.2 | 4.2± 0.2 |
| 80000ppm | 4.0± 0.2 | 4.0± 0.3 | 4.1± 0.4 | 3.9± 0.3 | 4.1± 0.3 | 4.0± 0.3 |

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

APPENDIX B 4-4

# FOOD CONSUMPTION CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : FEMALE

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day(effective) 1-7(7) | 2-7(7) | 3-7(7) | 4-7(7) | 5-7(7) | 6-7(7) | 7-7(7) |
|---|---|---|---|---|---|---|---|
| Control | 3.6± 0.1 | 3.4± 0.2 | 3.5± 0.2 | 3.7± 0.2 | 3.8± 0.3 | 3.8± 0.2 | 3.8± 0.3 |
| 5000ppm | 3.4± 0.2 | 3.5± 0.2 | 3.5± 0.2 | 3.7± 0.2 | 3.8± 0.2 | 3.7± 0.2 | 3.8± 0.2 |
| 10000ppm | 3.5± 0.2 | 3.5± 0.2 | 3.4± 0.2 | 3.6± 0.2 | 3.7± 0.2 | 3.7± 0.2 | 3.8± 0.3 |
| 20000ppm | 3.4± 0.3 | 3.4± 0.2 | 3.4± 0.2 | 3.6± 0.2 | 3.8± 0.3 | 3.7± 0.2 | 3.9± 0.3 |
| 40000ppm | 3.4± 0.2 | 3.5± 0.2 | 3.5± 0.2 | 3.7± 0.2 | 3.8± 0.2 | 3.7± 0.3 | 3.9± 0.2 |
| 80000ppm | 3.0± 0.3** | 3.4± 0.1 | 3.4± 0.2 | 3.6± 0.2 | 3.6± 0.4 | 3.5± 0.3 | 3.6± 0.4 |

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

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week-day(effective) 8-7(7) | 9-7(7) | 10-7(7) | 11-7(7) | 12-7(7) | 13-7(7) |
|---|---|---|---|---|---|---|
| Control | 4.0± 0.2 | 4.1± 0.3 | 3.9± 0.2 | 3.9± 0.2 | 3.9± 0.3 | 4.0± 0.3 |
| 5000ppm | 4.1± 0.2 | 4.1± 0.3 | 3.9± 0.2 | 3.9± 0.2 | 4.0± 0.2 | 3.9± 0.3 |
| 10000ppm | 3.9± 0.2 | 3.9± 0.3 | 4.0± 0.3 | 3.8± 0.3 | 3.9± 0.3 | 3.7± 0.2 |
| 20000ppm | 4.0± 0.3 | 3.9± 0.3 | 3.8± 0.3 | 3.9± 0.3 | 3.9± 0.3 | 3.9± 0.3 |
| 40000ppm | 4.0± 0.3 | 4.0± 0.2 | 3.9± 0.2 | 3.8± 0.2 | 4.0± 0.2 | 3.8± 0.1 |
| 80000ppm | 3.7± 0.4 | 3.7± 0.5 | 3.7± 0.4 | 3.5± 0.8 | 3.6± 0.7 | 3.6± 0.3** |

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

APPENDIX B 5-1

# CHEMICAL INTAKE CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

## RAT : MALE

STUDY NO. : 0201
ANIMAL : RAT F344
UNIT : g/kg/day
REPORT TYPE : A1 13
SEX : MALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration (weeks) 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| Control | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 |
| 2500 ppm | 0.292± 0.013 | 0.271± 0.013 | 0.240± 0.008 | 0.229± 0.013 | 0.203± 0.014 | 0.191± 0.018 | 0.179± 0.018 |
| 5000 ppm | 0.584± 0.033 | 0.548± 0.019 | 0.491± 0.021 | 0.474± 0.015 | 0.415± 0.014 | 0.396± 0.025 | 0.373± 0.029 |
| 10000 ppm | 1.211± 0.067 | 1.158± 0.061 | 1.031± 0.047 | 0.952± 0.065 | 0.825± 0.039 | 0.765± 0.049 | 0.713± 0.042 |
| 20000 ppm | 2.648± 0.129 | 2.411± 0.267 | 2.153± 0.220 | 2.083± 0.372 | 1.912± 0.304 | 1.697± 0.129 | 1.606± 0.083 |
| 40000 ppm | 4.559± 0.428 | 4.149± 0.195 | 3.891± 0.316 | 3.540± 0.277 | 3.228± 0.297 | 2.945± 0.269 | 2.873± 0.277 |

STUDY NO. : 0201
ANIMAL : RAT F344
UNIT : g／kg／d a y
REPORT TYPE : A1 13
SEX : MALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration (weeks) 8 | 9 | 10 | 11 | 12 | 13 |
|---|---|---|---|---|---|---|
| Control | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 |
| 2500 ppm | 0.173± 0.015 | 0.164± 0.015 | 0.159± 0.019 | 0.151± 0.016 | 0.146± 0.017 | 0.143± 0.015 |
| 5000 ppm | 0.360± 0.018 | 0.335± 0.019 | 0.323± 0.018 | 0.313± 0.020 | 0.292± 0.017 | 0.292± 0.018 |
| 10000 ppm | 0.700± 0.038 | 0.650± 0.031 | 0.628± 0.032 | 0.605± 0.023 | 0.589± 0.028 | 0.585± 0.026 |
| 20000 ppm | 1.518± 0.122 | 1.482± 0.191 | 1.406± 0.131 | 1.386± 0.068 | 1.284± 0.123 | 1.264± 0.105 |
| 40000 ppm | 2.848± 0.112 | 2.622± 0.205 | 2.494± 0.221 | 2.624± 0.227 | 2.427± 0.190 | 2.427± 0.197 |

APPENDIX B 5-2

# CHEMICAL INTAKE CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

## RAT : FEMALE

STUDY NO. : 0201
ANIMAL : RAT F344
UNIT : g/kg/day
REPORT TYPE : A1 13
SEX : FEMALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration (weeks) 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| Control | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 |
| 2500 ppm | 0.392± 0.126 | 0.321± 0.018 | 0.308± 0.038 | 0.307± 0.094 | 0.290± 0.089 | 0.290± 0.099 | 0.321± 0.174 |
| 5000 ppm | 0.701± 0.048 | 0.669± 0.047 | 0.606± 0.038 | 0.573± 0.034 | 0.552± 0.048 | 0.574± 0.202 | 0.590± 0.325 |
| 10000 ppm | 1.475± 0.094 | 1.375± 0.122 | 1.370± 0.476 | 1.177± 0.141 | 1.118± 0.137 | 1.043± 0.127 | 0.996± 0.111 |
| 20000 ppm | 3.094± 0.143 | 2.856± 0.210 | 2.534± 0.123 | 2.363± 0.160 | 2.195± 0.159 | 2.048± 0.165 | 2.051± 0.218 |
| 40000 ppm | 5.430± 0.424 | 4.927± 0.347 | 7.181± 5.335 | 5.785± 2.757 | 4.040± 0.503 | 3.808± 0.678 | 3.717± 0.488 |

STUDY NO. : 0201
ANIMAL : RAT F344
UNIT : g／kg／d a y
REPORT TYPE : A1 13
SEX : FEMALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration (weeks) 8 | 9 | 10 | 11 | 12 | 13 |
|---|---|---|---|---|---|---|
| Control | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 |
| 2500 ppm | 0.324± 0.182 | 0.215± 0.109 | 0.240± 0.046 | 0.247± 0.102 | 0.231± 0.073 | 0.270± 0.126 |
| 5000 ppm | 0.570± 0.272 | 0.524± 0.224 | 0.533± 0.294 | 0.506± 0.173 | 0.476± 0.197 | 0.481± 0.158 |
| 10000 ppm | 0.997± 0.106 | 1.000± 0.178 | 0.971± 0.176 | 1.080± 0.329 | 0.999± 0.200 | 0.989± 0.283 |
| 20000 ppm | 2.000± 0.118 | 1.896± 0.154 | 1.818± 0.134 | 2.246± 1.478 | 1.973± 0.542 | 2.407± 1.939 |
| 40000 ppm | 3.746± 0.599 | 3.390± 0.587 | 3.210± 0.700 | 3.228± 0.528 | 3.050± 0.540 | 3.067± 0.412 |

APPENDIX B 5-3

# CHEMICAL INTAKE CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

## MOSUE : MALE

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
UNIT : g/kg/day
REPORT TYPE : A1 13
SEX : MALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration (weeks) 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| Control | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 |
| 5000ppm | 1.034± 0.219 | 0.892± 0.190 | 0.869± 0.155 | 0.851± 0.256 | 0.825± 0.279 | 0.754± 0.180 | 0.766± 0.184 |
| 10000ppm | 2.085± 0.344 | 1.890± 0.257 | 1.764± 0.188 | 1.677± 0.201 | 1.558± 0.196 | 1.546± 0.158 | 1.482± 0.209 |
| 20000ppm | 4.442± 0.729 | 3.963± 0.609 | 3.807± 0.751 | 3.529± 0.595 | 3.369± 0.647 | 3.097± 0.425 | 3.174± 0.734 |
| 40000ppm | 10.240± 1.591 | 8.696± 1.096 | 8.311± 1.034 | 7.633± 0.982 | 7.139± 0.791 | 7.091± 0.623 | 6.969± 0.716 |
| 80000ppm | 27.286± 7.411 | 19.163± 3.776 | 24.202± 12.555 | 23.671± 13.492 | 24.209± 17.569 | 23.824± 18.905 | 22.788± 12.294 |

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
UNIT : g/kg/day
REPORT TYPE : A1 13
SEX : MALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration (weeks) 8 | 9 | 10 | 11 | 12 | 13 |
|---|---|---|---|---|---|---|
| Control | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 |
| 5000ppm | 0.684± 0.180 | 0.611± 0.097 | 0.610± 0.102 | 0.569± 0.125 | 0.541± 0.097 | 0.525± 0.081 |
| 10000ppm | 1.439± 0.178 | 1.289± 0.172 | 1.268± 0.173 | 1.184± 0.181 | 1.127± 0.133 | 1.073± 0.165 |
| 20000ppm | 3.281± 1.108 | 2.855± 0.773 | 2.672± 0.511 | 2.570± 0.614 | 2.507± 0.553 | 2.365± 0.458 |
| 40000ppm | 6.518± 0.716 | 6.118± 0.658 | 5.884± 0.796 | 5.449± 0.702 | 5.330± 0.715 | 5.150± 0.472 |
| 80000ppm | 17.353± 5.888 | 16.276± 5.005 | 16.258± 5.772 | 15.461± 4.650 | 14.750± 4.633 | 13.689± 3.439 |

APPENDIX B 5-4

# CHEMICAL INTAKE CHANGES (THIRTEEN−WEEK STUDY: SUMMARY)

## MOUSE: FEMALE

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
UNIT : g／kg／d a y
REPORT TYPE : A1 13
SEX : FEMALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration (weeks) 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| Control | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 |
| 5000ppm | 1.291± 0.157 | 1.286± 0.192 | 1.243± 0.303 | 1.223± 0.231 | 1.286± 0.323 | 1.264± 0.365 | 1.262± 0.253 |
| 10000ppm | 2.577± 0.469 | 2.530± 0.522 | 2.295± 0.241 | 2.294± 0.215 | 2.098± 0.178 | 2.171± 0.309 | 2.249± 0.273 |
| 20000ppm | 5.571± 0.520 | 5.264± 0.667 | 5.849± 2.543 | 5.456± 1.078 | 5.420± 1.905 | 5.187± 1.409 | 5.798± 1.473 |
| 40000ppm | 11.757± 0.697 | 11.155± 1.251 | 11.792± 2.732 | 11.490± 2.605 | 12.257± 4.362 | 10.693± 1.971 | 11.228± 2.201 |
| 80000ppm | 32.638± 10.770 | 30.110± 4.729 | 38.096± 12.501 | 39.285± 16.258 | 40.298± 12.745 | 41.062± 21.053 | 40.398± 20.548 |

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
UNIT : g／kg／d a y
REPORT TYPE : A1 13
SEX : FEMALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration (weeks) 8 | 9 | 10 | 11 | 12 | 13 |
|---|---|---|---|---|---|---|
| Control | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 | 0.000± 0.000 |
| 5000ppm | 1.198± 0.291 | 1.119± 0.175 | 1.036± 0.156 | 1.031± 0.166 | 0.994± 0.128 | 0.998± 0.163 |
| 10000ppm | 2.093± 0.252 | 2.081± 0.220 | 1.994± 0.145 | 2.062± 0.379 | 1.972± 0.341 | 2.214± 0.862 |
| 20000ppm | 5.052± 1.222 | 5.686± 3.273 | 5.178± 1.347 | 4.946± 1.434 | 4.748± 1.353 | 4.848± 1.281 |
| 40000ppm | 10.459± 1.380 | 9.723± 0.940 | 9.896± 1.372 | 9.969± 2.372 | 9.353± 1.678 | 9.413± 1.563 |
| 80000ppm | 37.972± 24.174 | 40.835± 31.308 | 42.301± 32.944 | 45.871± 51.738 | 27.377± 3.328 | 25.517± 2.819 |

APPENDIX B 6-1

# HEMATOLOGY (THIRTEEN−WEEK STUDY: SUMMARY)

RAT : MALE

STUDY NO. : 0201
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HEMATOLOGY(1) (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | RED BLOOD CELL $10^6/\mu\ell$ | | HEMOGLOBIN g/dℓ | | HEMATOCRIT % | | MCV f ℓ | | MCH p g | | MCHC g/dℓ | | PLATELET $10^3/\mu\ell$ | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Control | 10 | 9.85± | 0.15 | 16.6± | 0.2 | 47.1± | 0.8 | 47.8± | 0.4 | 16.9± | 0.2 | 35.3± | 0.4 | 738± | 36 |
| 2500 ppm | 10 | 9.75± | 0.15 | 16.7± | 0.3 | 46.7± | 0.8 | 47.9± | 0.5 | 17.2± | 0.2 | 35.8± | 0.4 | 731± | 36 |
| 5000 ppm | 10 | 9.66± | 0.40 | 16.4± | 0.7 | 46.2± | 1.8 | 47.9± | 0.8 | 17.0± | 0.3 | 35.5± | 0.6 | 741± | 46 |
| 10000 ppm | 10 | 9.74± | 0.21 | 16.6± | 0.3 | 46.7± | 1.1 | 48.0± | 0.8 | 17.1± | 0.3 | 35.6± | 0.5 | 725± | 45 |
| 20000 ppm | 10 | 9.83± | 0.18 | 16.6± | 0.3 | 46.6± | 0.9 | 47.4± | 0.7 | 16.9± | 0.3 | 35.5± | 0.6 | 736± | 35 |
| 40000 ppm | 10 | 9.74± | 0.31 | 16.7± | 0.3 | 46.8± | 1.1 | 48.1± | 0.8 | 17.1± | 0.4 | 35.7± | 0.5 | 726± | 35 |

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

STUDY NO. : 0201
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HEMATOLOGY(2) (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | WBC $10^3/\mu\ell$ | Differential WBC (%) N-BAND | N-SEG | EOSINO | BASO | MONO | LYMPHO | OTHER |
|---|---|---|---|---|---|---|---|---|---|
| Control | 10 | 5.14± 1.61 | 0± 0 | 30± 8 | 2± 1 | 0± 0 | 4± 1 | 65± 8 | 0± 0 |
| 2500 ppm | 10 | 4.91± 1.10 | 0± 0 | 29± 7 | 2± 1 | 0± 0 | 4± 2 | 65± 8 | 0± 0 |
| 5000 ppm | 10 | 4.84± 1.40 | 0± 1 | 28± 5 | 2± 1 | 0± 0 | 5± 1 | 65± 4 | 0± 0 |
| 10000 ppm | 10 | 4.93± 1.38 | 0± 0 | 34± 7 | 1± 1 | 0± 0 | 4± 1 | 60± 7 | 0± 0 |
| 20000 ppm | 10 | 4.36± 1.14 | 0± 0 | 30± 10 | 1± 1 | 0± 0 | 4± 2 | 64± 8 | 0± 0 |
| 40000 ppm | 10 | 5.92± 1.60 | 0± 0 | 28± 6 | 1± 1 | 0± 0 | 4± 1 | 68± 5 | 0± 0 |

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

APPENDIX B 6-2

# HEMATOLOGY (THIRTEEN−WEEK STUDY: SUMMARY)

## RAT: FEMALE

STUDY NO. : 0201
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HEMATOLOGY(1) (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | RED BLOOD CELL $10^6/\mu\ell$ | HEMOGLOBIN g/dℓ | HEMATOCRIT % | MCV f ℓ | MCH p g | MCHC g/dℓ | PLATELET $10^3/\mu\ell$ |
|---|---|---|---|---|---|---|---|---|
| Control | 9 | 9.19± 0.17 | 16.9± 0.3 | 47.2± 1.1 | 51.4± 0.4 | 18.3± 0.2 | 35.7± 0.4 | 822± 41 |
| 2500 ppm | 10 | 8.96± 0.37 | 16.6± 0.5 | 45.8± 2.0 | 51.1± 0.3 | 18.6± 0.7 | 36.3± 1.6 | 812± 47 |
| 5000 ppm | 10 | 9.04± 0.35 | 16.7± 0.4 | 46.3± 1.8 | 51.2± 0.5 | 18.5± 0.6 | 36.1± 1.2 | 799± 33 |
| 10000 ppm | 10 | 9.05± 0.30 | 16.5± 0.6 | 45.9± 1.5 | 50.7± 0.5* | 18.3± 0.3 | 36.0± 0.4 | 813± 61 |
| 20000 ppm | 10 | 9.11± 0.20 | 16.6± 0.3 | 46.4± 1.1 | 50.9± 0.5 | 18.3± 0.2 | 35.9± 0.5 | 805± 63 |
| 40000 ppm | 10 | 8.86± 0.22 | 16.1± 0.5** | 45.0± 0.9** | 50.8± 0.7* | 18.2± 0.2 | 35.9± 0.8 | 787± 42 |

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

STUDY NO. : 0201
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HEMATOLOGY(2) (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | WBC $10^3/\mu\ell$ | | Differential WBC (%) N-BAND | | N-SEG | | EOSINO | | BASO | | MONO | | LYMPHO | | OTHER | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Control | 9 | 3.55± | 0.78 | 0± | 0 | 25± | 6 | 2± | 1 | 0± | 0 | 4± | 1 | 69± | 6 | 0± | 0 |
| 2500 ppm | 10 | 3.56± | 1.28 | 0± | 0 | 28± | 8 | 2± | 2 | 0± | 0 | 4± | 1 | 65± | 9 | 0± | 0 |
| 5000 ppm | 10 | 2.66± | 0.61 | 1± | 1 | 28± | 6 | 2± | 2 | 0± | 0 | 4± | 2 | 65± | 8 | 0± | 0 |
| 10000 ppm | 10 | 3.15± | 1.09 | 0± | 0 | 25± | 4 | 2± | 1 | 0± | 0 | 5± | 1 | 68± | 4 | 0± | 0 |
| 20000 ppm | 10 | 3.13± | 0.97 | 1± | 1 | 28± | 6 | 2± | 1 | 0± | 0 | 4± | 1 | 66± | 7 | 0± | 0 |
| 40000 ppm | 10 | 3.05± | 0.52 | 0± | 0 | 25± | 4 | 2± | 1 | 0± | 0 | 5± | 2 | 69± | 4 | 0± | 0 |

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

APPENDIX B 6-3

# HEMATOLOGY (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : MALE

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HEMATOLOGY(1) (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | RED BLOOD CELL $10^6/\mu\ell$ | HEMOGLOBIN g/dℓ | HEMATOCRIT % | MCV fℓ | MCH pg | MCHC g/dℓ | PLATELET $10^3/\mu\ell$ |
|---|---|---|---|---|---|---|---|---|
| Control | 10 | 10.41± 0.24 | 15.5± 0.4 | 45.5± 1.1 | 43.8± 0.8 | 14.9± 0.2 | 34.0± 0.8 | 1342± 89 |
| 5000ppm | 10 | 10.61± 0.47 | 15.7± 0.7 | 46.6± 2.8 | 43.9± 1.1 | 14.8± 0.2 | 33.8± 0.7 | 1371± 165 |
| 10000ppm | 10 | 10.55± 0.41 | 15.7± 0.4 | 46.1± 2.0 | 43.7± 0.6 | 14.9± 0.3 | 34.1± 1.0 | 1372± 112 |
| 20000ppm | 10 | 10.63± 0.36 | 15.7± 0.6 | 46.3± 2.2 | 43.5± 0.9 | 14.8± 0.3 | 34.1± 0.7 | 1386± 117 |
| 40000ppm | 10 | 10.59± 0.25 | 15.7± 0.3 | 45.8± 0.8 | 43.2± 0.4 | 14.9± 0.3 | 34.4± 0.4 | 1442± 89 |
| 80000ppm | 9 | 10.47± 0.35 | 15.6± 0.3 | 45.2± 1.6 | 43.2± 0.5 | 14.9± 0.5 | 34.6± 1.1 | 1386± 106 |

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

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HEMATOLOGY(2) (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | WBC $10^3/\mu\ell$ | | Differential WBC (%) N-BAND | | N-SEG | | EOSINO | | BASO | | MONO | | LYMPHO | | OTHER | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Control | 10 | 1.30± | 0.72 | 1± | 1 | 14± | 4 | 2± | 1 | 0± | 0 | 4± | 1 | 80± | 5 | 0± | 0 |
| 5000ppm | 10 | 1.47± | 0.94 | 1± | 1 | 17± | 5 | 1± | 1 | 0± | 0 | 4± | 2 | 76± | 6 | 0± | 0 |
| 10000ppm | 10 | 1.79± | 0.95 | 1± | 1 | 13± | 4 | 1± | 1 | 0± | 0 | 4± | 1 | 81± | 3 | 0± | 0 |
| 20000ppm | 10 | 1.49± | 0.73 | 1± | 1 | 13± | 3 | 2± | 1 | 0± | 0 | 4± | 2 | 80± | 4 | 0± | 0 |
| 40000ppm | 10 | 1.20± | 0.51 | 0± | 0 | 14± | 3 | 2± | 1 | 0± | 0 | 4± | 2 | 80± | 3 | 0± | 0 |
| 80000ppm | 9 | 1.18± | 0.40 | 1± | 1 | 14± | 3 | 1± | 1 | 0± | 0 | 3± | 1 | 80± | 3 | 0± | 0 |

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

APPENDIX B 6-4

HEMATOLOGY (THIRTEEN−WEEK STUDY: SUMMARY )

MOSUE : FEMALE

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

HEMATOLOGY(1) (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | RED BLOOD CELL $10^6/\mu\ell$ | HEMOGLOBIN g/dℓ | HEMATOCRIT % | MCV f ℓ | MCH p g | MCHC g/dℓ | PLATELET $10^3/\mu\ell$ |
|---|---|---|---|---|---|---|---|---|
| Control | 10 | 10.62± 0.40 | 15.8± 0.7 | 45.5± 2.1 | 42.9± 0.9 | 14.9± 0.5 | 34.8± 1.0 | 1212± 75 |
| 5000ppm | 10 | 10.45± 0.47 | 15.6± 0.6 | 45.3± 2.2 | 43.4± 0.4 | 15.0± 0.2 | 34.5± 0.6 | 1198± 138 |
| 10000ppm | 10 | 10.51± 0.45 | 15.8± 0.7 | 45.7± 2.2 | 43.4± 0.4 | 15.0± 0.3 | 34.6± 0.6 | 1219± 124 |
| 20000ppm | 9 | 10.62± 0.43 | 15.9± 0.7 | 46.1± 1.6 | 43.4± 0.7 | 15.0± 0.2 | 34.5± 0.7 | 1227± 83 |
| 40000ppm | 10 | 10.46± 0.38 | 15.7± 0.5 | 45.5± 1.9 | 43.5± 0.4 | 15.0± 0.3 | 34.6± 0.9 | 1185± 101 |
| 80000ppm | 9 | 10.54± 0.43 | 15.8± 0.6 | 45.5± 2.0 | 43.2± 0.5 | 15.0± 0.3 | 34.8± 0.6 | 1195± 135 |

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

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

HEMATOLOGY(2) (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | WBC $10^3/\mu\ell$ | | Differential WBC (%) N-BAND | | N-SEG | | EOSINO | | BASO | | MONO | | LYMPHO | | OTHER | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Control | 10 | 0.97± | 0.67 | 0± | 1 | 15± | 5 | 1± | 1 | 0± | 0 | 3± | 1 | 81± | 4 | 0± | 0 |
| 5000ppm | 10 | 1.48± | 2.04 | 1± | 1 | 16± | 6 | 1± | 1 | 0± | 0 | 3± | 1 | 79± | 5 | 0± | 0 |
| 10000ppm | 10 | 1.28± | 1.38 | 1± | 1 | 16± | 5 | 1± | 1 | 0± | 0 | 3± | 0 | 80± | 6 | 0± | 0 |
| 20000ppm | 9 | 1.42± | 0.98 | 1± | 1 | 14± | 5 | 1± | 1 | 0± | 0 | 3± | 1 | 82± | 5 | 0± | 0 |
| 40000ppm | 10 | 1.22± | 0.88 | 1± | 2 | 16± | 10 | 1± | 1 | 0± | 0 | 3± | 1 | 79± | 13 | 0± | 0 |
| 80000ppm | 9 | 0.84± | 0.42 | 0± | 1 | 17± | 8 | 0± | 0 | 0± | 0 | 3± | 1 | 79± | 8 | 0± | 0 |

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

APPENDIX B 7-1

BIOCHEMISTRY (THIRTEEN−WEEK STUDY: SUMMARY)

RAT : MALE

STUDY NO. : 0201
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | TOTAL PROTEIN g/dl | ALBUMIN g/dl | A/G RATIO | T-BILIRUBIN mg/dl | GLUCOSE mg/dl | T-CHOLESTEROL mg/dl | TRIGLYCERIDE mg/dl |
|---|---|---|---|---|---|---|---|---|
| Control | 10 | 6.8± 0.2 | 3.8± 0.1 | 1.2± 0.1 | 0.21± 0.03 | 199± 11 | 60± 3 | 76± 26 |
| 2500 ppm | 10 | 6.8± 0.3 | 3.8± 0.1 | 1.2± 0.1 | 0.22± 0.03 | 197± 17 | 61± 5 | 93± 29 |
| 5000 ppm | 10 | 6.7± 0.2 | 3.7± 0.1 | 1.2± 0.1 | 0.21± 0.04 | 195± 22 | 60± 6 | 85± 35 |
| 10000 ppm | 10 | 6.7± 0.2 | 3.7± 0.1 | 1.2± 0.1 | 0.22± 0.03 | 191± 19 | 58± 6 | 81± 31 |
| 20000 ppm | 10 | 6.6± 0.3* | 3.6± 0.1 | 1.3± 0.1 | 0.21± 0.05 | 201± 21 | 59± 3 | 72± 22 |
| 40000 ppm | 10 | 6.5± 0.2** | 3.7± 0.1 | 1.3± 0.0 | 0.21± 0.04 | 204± 13 | 61± 4 | 88± 20 |

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

STUDY NO. : 0201
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | PHOSPHOLIPID mg/dl | GOT IU/l | GPT IU/l | LDH IU/l | ALP IU/l | G-GTP IU/l | CPK IU/l |
|---|---|---|---|---|---|---|---|---|
| Control | 10 | 106± 6 | 75± 12 | 25± 2 | 159± 37 | 288± 22 | 1± 1 | 84± 7 |
| 2500 ppm | 10 | 113± 11 | 72± 11 | 24± 4 | 163± 26 | 294± 22 | 1± 1 | 89± 13 |
| 5000 ppm | 10 | 108± 10 | 79± 15 | 26± 5 | 162± 35 | 307± 26 | 1± 1 | 80± 5 |
| 10000 ppm | 10 | 106± 14 | 67± 10 | 23± 4 | 152± 18 | 297± 26 | 1± 1 | 82± 5 |
| 20000 ppm | 10 | 109± 9 | 73± 16 | 26± 5 | 161± 42 | 291± 27 | 1± 1 | 84± 11 |
| 40000 ppm | 10 | 115± 7 | 78± 18 | 25± 4 | 164± 43 | 287± 31 | 1± 1 | 83± 12 |

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

STUDY NO. : 0201
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | UREA NITROGEN mg/dℓ | CREATININE mg/dℓ | SODIUM mEq/ℓ | POTASSIUM mEq/ℓ | CHLORIDE mEq/ℓ | CALCIUM mg/dℓ | INORGANIC PHOSPHORUS mg/dℓ |
|---|---|---|---|---|---|---|---|---|
| Control | 10 | 17.6± 0.9 | 0.5± 0.1 | 143± 1 | 3.1± 0.1 | 106± 1 | 10.4± 0.2 | 5.1± 0.7 |
| 2500 ppm | 10 | 17.8± 1.2 | 0.5± 0.1 | 143± 1 | 3.1± 0.2 | 106± 1 | 10.4± 0.3 | 5.4± 0.9 |
| 5000 ppm | 10 | 16.9± 1.2 | 0.5± 0.1 | 143± 1 | 3.1± 0.2 | 106± 1 | 10.4± 0.2 | 5.1± 0.8 |
| 10000 ppm | 10 | 17.5± 0.8 | 0.5± 0.1 | 143± 2 | 3.2± 0.2 | 106± 2 | 10.3± 0.2 | 5.0± 0.7 |
| 20000 ppm | 10 | 18.0± 1.3 | 0.5± 0.1 | 142± 1 | 3.2± 0.2 | 105± 2 | 10.2± 0.4 | 5.1± 0.6 |
| 40000 ppm | 10 | 20.7± 1.6** | 0.5± 0.1 | 141± 1** | 3.2± 0.1 | 104± 1* | 10.2± 0.2 | 4.9± 0.7 |

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

APPENDIX B 7-2

BIOCHEMISTRY(THIRTEEN−WEEK STUDY: SUMMARY)

RAT : FEMALE

STUDY NO. : 0201
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | TOTAL PROTEIN g/dl | | ALBUMIN g/dl | | A/G RATIO | | T-BILIRUBIN mg/dl | | GLUCOSE mg/dl | | T-CHOLESTEROL mg/dl | | TRIGLYCERIDE mg/dl | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Control | 9 | 6.6± | 0.1 | 3.7± | 0.1 | 1.2± | 0.1 | 0.23± | 0.02 | 150± | 15 | 82± | 7 | 34± | 4 |
| 2500 ppm | 10 | 6.6± | 0.2 | 3.6± | 0.1 | 1.2± | 0.1 | 0.24± | 0.03 | 150± | 17 | 79± | 5 | 35± | 5 |
| 5000 ppm | 10 | 6.5± | 0.3 | 3.6± | 0.2 | 1.3± | 0.1 | 0.26± | 0.04 | 152± | 28 | 78± | 7 | 35± | 6 |
| 10000 ppm | 10 | 6.4± | 0.3 | 3.6± | 0.1 | 1.3± | 0.1 | 0.25± | 0.03 | 151± | 18 | 76± | 9 | 32± | 4 |
| 20000 ppm | 10 | 6.5± | 0.2 | 3.6± | 0.1 | 1.2± | 0.1 | 0.28± | 0.08 | 138± | 19 | 78± | 9 | 32± | 3 |
| 40000 ppm | 10 | 6.0± | 0.2** | 3.4± | 0.1** | 1.3± | 0.1 | 0.26± | 0.05 | 147± | 17 | 70± | 4** | 28± | 3* |

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

STUDY NO. : 0201
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | PHOSPHOLIPID mg/dℓ | GOT IU/ℓ | GPT IU/ℓ | LDH IU/ℓ | ALP IU/ℓ | G-GTP IU/ℓ | CPK IU/ℓ |
|---|---|---|---|---|---|---|---|---|
| Control | 9 | 143± 9 | 66± 10 | 21± 5 | 201± 46 | 195± 21 | 2± 1 | 100± 13 |
| 2500 ppm | 10 | 138± 8 | 78± 29 | 25± 11 | 222± 62 | 199± 25 | 1± 1 | 99± 16 |
| 5000 ppm | 10 | 134± 12 | 71± 16 | 23± 8 | 217± 64 | 207± 27 | 2± 1 | 98± 17 |
| 10000 ppm | 10 | 130± 14 | 78± 14 | 24± 5 | 245± 56 | 205± 23 | 2± 1 | 104± 16 |
| 20000 ppm | 10 | 133± 13 | 75± 16 | 22± 7 | 222± 78 | 224± 32 | 2± 1 | 103± 28 |
| 40000 ppm | 10 | 119± 7** | 66± 6 | 18± 4 | 216± 62 | 200± 19 | 2± 1 | 97± 17 |

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

STUDY NO. : 0201
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | UREA NITROGEN mg/dl | CREATININE mg/dl | SODIUM mEq/l | POTASSIUM mEq/l | CHLORIDE mEq/l | CALCIUM mg/dl | INORGANIC PHOSPHORUS mg/dl |
|---|---|---|---|---|---|---|---|---|
| Control | 9 | 19.6± 1.7 | 0.5± 0.1 | 143± 1 | 3.0± 0.2 | 108± 2 | 10.0± 0.4 | 4.9± 0.9 |
| 2500 ppm | 10 | 19.6± 2.8 | 0.5± 0.1 | 142± 2 | 3.1± 0.2 | 107± 2 | 10.1± 0.2 | 4.7± 1.1 |
| 5000 ppm | 10 | 19.9± 1.4 | 0.5± 0.1 | 142± 1 | 3.0± 0.2 | 108± 1 | 10.0± 0.3 | 4.7± 1.1 |
| 10000 ppm | 10 | 20.8± 1.6 | 0.5± 0.1 | 143± 2 | 3.1± 0.2 | 108± 2 | 9.9± 0.3 | 4.6± 1.2 |
| 20000 ppm | 10 | 20.3± 1.8 | 0.5± 0.1 | 142± 2 | 3.2± 0.3 | 108± 2 | 9.9± 0.3 | 5.0± 1.1 |
| 40000 ppm | 10 | 22.3± 2.4* | 0.5± 0.1 | 141± 2 | 3.3± 0.2 | 108± 1 | 9.6± 0.2** | 4.8± 1.3 |

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

APPENDIX B 7-3

BIOCHEMISTRY (THIRTEEN－WEEK　STUDY: SUMMARY)

MOSUE : MALE

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | TOTAL PROTEIN g/dℓ | ALBUMIN g/dℓ | A/G RATIO | T-BILIRUBIN mg/dℓ | GLUCOSE mg/dℓ | T-CHOLESTEROL mg/dℓ | TRIGLYCERIDE mg/dℓ |
|---|---|---|---|---|---|---|---|---|
| Control | 10 | 5.3± 0.1 | 2.8± 0.1 | 1.2± 0.1 | 0.32± 0.08 | 227± 50 | 89± 5 | 79± 14 |
| 5000ppm | 10 | 5.3± 0.4 | 2.8± 0.2 | 1.1± 0.0 | 0.34± 0.11 | 233± 41 | 90± 9 | 81± 8 |
| 10000ppm | 10 | 5.3± 0.2 | 2.8± 0.1 | 1.1± 0.1 | 0.32± 0.10 | 241± 29 | 91± 6 | 75± 15 |
| 20000ppm | 10 | 5.3± 0.2 | 2.8± 0.1 | 1.1± 0.1 | 0.34± 0.20 | 229± 53 | 88± 9 | 75± 17 |
| 40000ppm | 10 | 5.2± 0.2 | 2.7± 0.1 | 1.1± 0.0 | 0.28± 0.12 | 240± 31 | 84± 5 | 73± 20 |
| 80000ppm | 9 | 5.0± 0.2 | 2.7± 0.1* | 1.1± 0.1 | 0.38± 0.20 | 242± 34 | 88± 4 | 72± 12 |

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

(HCL074)

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | GOT IU/ℓ | | GPT IU/ℓ | | LDH IU/ℓ | | ALP IU/ℓ | | CPK IU/ℓ | | UREA NITROGEN mg/dℓ | | SODIUM mEq/ℓ | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Control | 10 | 46± | 6 | 11± | 2 | 231± | 35 | 180± | 20 | 55± | 19 | 25.4± | 1.9 | 154± | 2 |
| 5000ppm | 10 | 43± | 5 | 13± | 2 | 237± | 56 | 176± | 19 | 63± | 25 | 25.0± | 1.4 | 154± | 2 |
| 10000ppm | 10 | 40± | 8 | 14± | 5 | 242± | 79 | 177± | 8 | 67± | 54 | 24.6± | 4.1 | 154± | 2 |
| 20000ppm | 10 | 42± | 5 | 14± | 3 | 227± | 46 | 168± | 16 | 55± | 21 | 25.4± | 2.2 | 154± | 2 |
| 40000ppm | 10 | 39± | 5 | 12± | 3 | 229± | 49 | 169± | 16 | 55± | 17 | 26.1± | 1.5 | 154± | 1 |
| 80000ppm | 9 | 40± | 6 | 13± | 4 | 279± | 154 | 158± | 40 | 59± | 19 | 25.5± | 2.7 | 153± | 2 |

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

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | POTASSIUM mEq／ℓ | | CHLORIDE mEq／ℓ | | CALCIUM mg／dℓ | | INORGANIC PHOSPHORUS mg／dℓ | |
|---|---|---|---|---|---|---|---|---|---|
| Control | 10 | 3.9± | 0.4 | 122± | 2 | 8.7± | 0.3 | 7.2± | 0.8 |
| 5000ppm | 10 | 4.3± | 0.5 | 122± | 3 | 8.8± | 0.5 | 8.3± | 1.7 |
| 10000ppm | 10 | 4.2± | 0.4 | 121± | 2 | 8.6± | 0.2 | 7.1± | 1.3 |
| 20000ppm | 10 | 4.1± | 0.4 | 121± | 2 | 8.8± | 0.3 | 7.8± | 1.9 |
| 40000ppm | 10 | 4.0± | 0.3 | 122± | 2 | 8.7± | 0.2 | 7.5± | 1.0 |
| 80000ppm | 9 | 3.9± | 0.4 | 120± | 2 | 8.6± | 0.3 | 7.6± | 1.1 |

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

APPENDIX B 7-4

BIOCHEMISTRY (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : FEMALE

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | TOTAL PROTEIN g/dℓ | ALBUMIN g/dℓ | A/G RATIO | T-BILIRUBIN mg/dℓ | GLUCOSE mg/dℓ | T-CHOLESTEROL mg/dℓ | TRIGLYCERIDE mg/dℓ |
|---|---|---|---|---|---|---|---|---|
| Control | 10 | 5.5± 0.2 | 3.1± 0.1 | 1.3± 0.0 | 0.39± 0.09 | 189± 22 | 76± 4 | 49± 10 |
| 5000ppm | 10 | 5.4± 0.3 | 3.1± 0.1 | 1.3± 0.1 | 0.37± 0.07 | 167± 23 | 74± 10 | 49± 18 |
| 10000ppm | 10 | 5.3± 0.3 | 3.0± 0.2 | 1.3± 0.0 | 0.39± 0.12 | 178± 28 | 74± 7 | 44± 9 |
| 20000ppm | 9 | 5.3± 0.2 | 3.1± 0.1 | 1.4± 0.1 | 0.34± 0.05 | 178± 20 | 78± 9 | 51± 15 |
| 40000ppm | 10 | 5.3± 0.3 | 3.0± 0.1 | 1.3± 0.1 | 0.42± 0.09 | 183± 22 | 72± 11 | 43± 13 |
| 80000ppm | 9 | 5.0± 0.2** | 2.9± 0.1** | 1.4± 0.1 | 0.39± 0.17 | 185± 25 | 73± 7 | 44± 9 |

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

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | GOT IU/ℓ | | GPT IU/ℓ | | LDH IU/ℓ | | ALP IU/ℓ | | CPK IU/ℓ | | UREA NITROGEN mg/dℓ | | SODIUM mEq/ℓ | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Control | 10 | 60± | 14 | 14± | 3 | 274± | 67 | 281± | 38 | 73± | 30 | 21.8± | 1.9 | 154± | 3 |
| 5000ppm | 10 | 64± | 15 | 14± | 4 | 290± | 75 | 298± | 31 | 82± | 25 | 22.8± | 2.0 | 153± | 2 |
| 10000ppm | 10 | 53± | 9 | 13± | 2 | 252± | 40 | 277± | 30 | 76± | 14 | 23.3± | 2.6 | 154± | 2 |
| 20000ppm | 9 | 52± | 7 | 14± | 5 | 246± | 42 | 272± | 24 | 74± | 23 | 22.4± | 1.9 | 154± | 3 |
| 40000ppm | 10 | 58± | 12 | 16± | 4 | 368± | 145 | 292± | 33 | 134± | 127 | 24.0± | 2.5 | 154± | 3 |
| 80000ppm | 9 | 53± | 14 | 13± | 5 | 319± | 92 | 304± | 29 | 113± | 102 | 22.5± | 2.4 | 155± | 3 |

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

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | POTASSIUM mEq/ℓ | | CHLORIDE mEq/ℓ | | CALCIUM mg/dℓ | | INORGANIC PHOSPHORUS mg/dℓ | |
|---|---|---|---|---|---|---|---|---|---|
| Control | 10 | 3.9± | 0.6 | 121± | 3 | 8.8± | 0.2 | 6.8± | 0.9 |
| 5000ppm | 10 | 3.5± | 0.4 | 123± | 3 | 8.7± | 0.3 | 6.5± | 1.0 |
| 10000ppm | 10 | 3.7± | 0.4 | 124± | 3 | 8.6± | 0.4 | 6.6± | 1.7 |
| 20000ppm | 9 | 3.8± | 0.4 | 120± | 2 | 8.6± | 0.3 | 6.3± | 1.4 |
| 40000ppm | 10 | 3.7± | 0.4 | 122± | 3 | 8.6± | 0.4 | 6.4± | 1.1 |
| 80000ppm | 9 | 3.6± | 0.4 | 121± | 3 | 8.5± | 0.4 | 7.1± | 1.1 |

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

APPENDIX B 8-1

URINALYSIS (THIRTEEN−WEEK STUDY: SUMMARY)

RAT : MALE

STUDY NO. : 0201
ANIMAL : RAT F344
SAMPLING DATE : 013-4
SEX : MALE REPORT TYPE : A1

URINALYSIS



| Group Name | NO. of Animals | pH 5.0 | 6.0 | 6.5 | 7.0 | 7.5 | 8.0 | 8.5 | CHI | Protein − | ± | + | 2+ | 3+ | 4+ | CHI | Glucose − | ± | + | 2+ | 3+ | 4+ | CHI | Ketone body − | ± | + | 2+ | 3+ | 4+ | CHI | Bilirubin − | + | 2+ | 3+ | CHI |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Control | 10 | 0 | 0 | 0 | 0 | 3 | 7 | 0 | | 0 | 0 | 7 | 3 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | 0 | | 0 | 10 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | |
| 2500 ppm | 10 | 0 | 0 | 0 | 1 | 2 | 7 | 0 | | 0 | 0 | 5 | 5 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | 0 | | 1 | 9 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | |
| 5000 ppm | 10 | 0 | 0 | 0 | 0 | 5 | 5 | 0 | | 0 | 0 | 3 | 7 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | 0 | | 2 | 7 | 1 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | |
| 10000 ppm | 10 | 0 | 0 | 0 | 0 | 8 | 2 | 0 | * | 0 | 0 | 2 | 5 | 3 | 0 | * | 10 | 0 | 0 | 0 | 0 | 0 | | 7 | 3 | 0 | 0 | 0 | 0 | ** | 10 | 0 | 0 | 0 | |
| 20000 ppm | 10 | 0 | 0 | 0 | 0 | 7 | 3 | 0 | | 0 | 0 | 0 | 5 | 5 | 0 | ** | 10 | 0 | 0 | 0 | 0 | 0 | | 9 | 1 | 0 | 0 | 0 | 0 | ** | 10 | 0 | 0 | 0 | |
| 40000 ppm | 10 | 0 | 0 | 1 | 6 | 3 | 0 | 0 | ** | 0 | 0 | 0 | 0 | 2 | 8 | ** | 10 | 0 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | 0 | ** | 10 | 0 | 0 | 0 | |

Significent difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

STUDY NO. : 0201
ANIMAL : RAT F344
SAMPLING DATE : 013-4
SEX : MALE REPORT TYPE : A1

URINALYSIS



| Group Name | NO. of Animals | Occult blood − | ± | + | 2+ | 3+ | CHI | Urobilinogen ± | + | 2+ | 3+ | 4+ | CHI |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Control | 10 | 10 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | |
| 2500 ppm | 10 | 9 | 1 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | |
| 5000 ppm | 10 | 10 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | |
| 10000 ppm | 10 | 10 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | |
| 20000 ppm | 10 | 10 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | |
| 40000 ppm | 10 | 10 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | |

Significent difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

APPENDIX B 8-2

URINALYSIS (THIRTEEN−WEEK STUDY: SUMMARY)

RAT : FEMALE

STUDY NO. : 0201
ANIMAL : RAT F344
SAMPLING DATE : 013-4
SEX : FEMALE REPORT TYPE : A1

URINALYSIS



| Group Name | NO. of Animals | pH 5.0 | 6.0 | 6.5 | 7.0 | 7.5 | 8.0 | 8.5 | CHI | Protein − | ± | + | 2+ | 3+ | 4+ | CHI | Glucose − | ± | + | 2+ | 3+ | 4+ | CHI | Ketone body − | ± | + | 2+ | 3+ | 4+ | CHI | Bilirubin − | + | 2+ | 3+ | CHI |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Control | 10 | 0 | 0 | 0 | 1 | 1 | 7 | 1 | | 0 | 0 | 9 | 1 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | 0 | | 9 | 1 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | |
| 2500 ppm | 10 | 0 | 0 | 0 | 0 | 1 | 8 | 1 | | 0 | 0 | 9 | 1 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | |
| 5000 ppm | 10 | 0 | 0 | 0 | 0 | 0 | 9 | 1 | | 0 | 0 | 8 | 2 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | |
| 10000 ppm | 10 | 0 | 0 | 1 | 0 | 2 | 6 | 1 | | 0 | 0 | 7 | 3 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | |
| 20000 ppm | 10 | 0 | 0 | 0 | 1 | 2 | 6 | 1 | | 0 | 0 | 0 | 8 | 2 | 0 | ** | 10 | 0 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | |
| 40000 ppm | 10 | 0 | 0 | 0 | 1 | 8 | 1 | 0 | * | 0 | 0 | 0 | 0 | 5 | 5 | ** | 10 | 0 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | |

Significent difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

STUDY NO. : 0201
ANIMAL : RAT F344
SAMPLING DATE : 013-4
SEX : FEMALE REPORT TYPE : A1

URINALYSIS



| Group Name | NO. of Animals | Occult blood − | ± | + | 2+ | 3+ | CHI | Urobilinogen ± | + | 2+ | 3+ | 4+ | CHI |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Control | 10 | 10 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | |
| 2500 ppm | 10 | 10 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | |
| 5000 ppm | 10 | 10 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | |
| 10000 ppm | 10 | 10 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | |
| 20000 ppm | 10 | 10 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | |
| 40000 ppm | 10 | 10 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | |

Significent difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

APPENDIX B 8-3

URINALYSIS (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : MALE

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
SAMPLING DATE : 013-4
SEX : MALE REPORT TYPE : A1

URINALYSIS



| Group Name | NO. of Animals | pH 5.0 | 6.0 | 6.5 | 7.0 | 7.5 | 8.0 | 8.5 | CHI | Protein − | ± | + | 2+ | 3+ | 4+ | CHI | Glucose − | ± | + | 2+ | 3+ | 4+ | CHI | Ketone body − | ± | + | 2+ | 3+ | 4+ | CHI | Occult blood − | ± | + | 2+ | 3+ | CHI |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Control | 10 | 0 | 0 | 0 | 1 | 3 | 6 | 0 | | 0 | 0 | 7 | 3 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | 0 | | 1 | 6 | 3 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | |
| 5000ppm | 10 | 0 | 0 | 0 | 0 | 5 | 5 | 0 | | 0 | 0 | 5 | 5 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | 0 | | 1 | 9 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | |
| 10000ppm | 10 | 0 | 0 | 0 | 0 | 6 | 3 | 1 | | 0 | 0 | 2 | 7 | 1 | 0 | | 10 | 0 | 0 | 0 | 0 | 0 | | 7 | 3 | 0 | 0 | 0 | 0 | * | 10 | 0 | 0 | 0 | 0 | |
| 20000ppm | 10 | 0 | 0 | 0 | 0 | 4 | 6 | 0 | | 0 | 0 | 0 | 5 | 4 | 1 | ** | 10 | 0 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | 0 | ** | 10 | 0 | 0 | 0 | 0 | |
| 40000ppm | 10 | 0 | 0 | 0 | 0 | 7 | 3 | 0 | | 0 | 0 | 0 | 3 | 2 | 5 | ** | 10 | 0 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | 0 | ** | 10 | 0 | 0 | 0 | 0 | |
| 80000ppm | 9 | 0 | 0 | 0 | 3 | 6 | 0 | 0 | * | 0 | 0 | 0 | 0 | 0 | 9 | ** | 9 | 0 | 0 | 0 | 0 | 0 | | 9 | 0 | 0 | 0 | 0 | 0 | ** | 9 | 0 | 0 | 0 | 0 | |

Significent difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
SAMPLING DATE : 013-4
SEX : MALE REPORT TYPE : A1

URINALYSIS



| Group Name | NO. of Animals | Urobilinogen ± | + | 2+ | 3+ | 4+ | CHI |
|---|---|---|---|---|---|---|---|
| Control | 10 | 10 | 0 | 0 | 0 | 0 | |
| 5000ppm | 10 | 10 | 0 | 0 | 0 | 0 | |
| 10000ppm | 10 | 10 | 0 | 0 | 0 | 0 | |
| 20000ppm | 10 | 10 | 0 | 0 | 0 | 0 | |
| 40000ppm | 10 | 10 | 0 | 0 | 0 | 0 | |
| 80000ppm | 9 | 9 | 0 | 0 | 0 | 0 | |

Significent difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

APPENDIX B 8-4

URINALYSIS (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : FEMALE

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
SAMPLING DATE : 013-4
SEX : FEMALE REPORT TYPE : A1

URINALYSIS



| Group Name | NO. of Animals | pH 5.0 | 6.0 | 6.5 | 7.0 | 7.5 | 8.0 | 8.5 | CHI | Protein − | ± | + | 2+ | 3+ | 4+ | CHI | Glucose − | ± | + | 2+ | 3+ | 4+ | CHI | Ketone body − | ± | + | 2+ | 3+ | 4+ | CHI | Occult blood − | ± | + | 2+ | 3+ | CHI |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Control | 10 | 0 | 1 | 0 | 1 | 4 | 4 | 0 | | 0 | 1 | 8 | 1 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | 0 | | 5 | 5 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | |
| 5000ppm | 10 | 0 | 0 | 2 | 1 | 6 | 1 | 0 | | 0 | 0 | 8 | 2 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | 0 | | 6 | 3 | 1 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | |
| 10000ppm | 10 | 0 | 0 | 0 | 1 | 2 | 7 | 0 | | 0 | 0 | 4 | 5 | 0 | 1 | | 10 | 0 | 0 | 0 | 0 | 0 | | 8 | 2 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | |
| 20000ppm | 10 | 0 | 0 | 0 | 0 | 8 | 2 | 0 | | 0 | 0 | 4 | 3 | 3 | 0 | | 10 | 0 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | 0 | ** | 10 | 0 | 0 | 0 | 0 | |
| 40000ppm | 10 | 0 | 0 | 0 | 2 | 7 | 1 | 0 | | 0 | 0 | 0 | 0 | 4 | 6 | ** | 10 | 0 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | 0 | ** | 10 | 0 | 0 | 0 | 0 | |
| 80000ppm | 9 | 0 | 0 | 0 | 5 | 4 | 0 | 0 | | 0 | 0 | 0 | 0 | 2 | 7 | ** | 9 | 0 | 0 | 0 | 0 | 0 | | 9 | 0 | 0 | 0 | 0 | 0 | * | 9 | 0 | 0 | 0 | 0 | |

Significent difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
SAMPLING DATE : 013-4
SEX : FEMALE REPORT TYPE : A1

URINALYSIS



| Group Name | NO. of Animals | Urobilinogen ± | + | 2+ | 3+ | 4+ | CHI |
|---|---|---|---|---|---|---|---|
| Control | 10 | 10 | 0 | 0 | 0 | 0 | |
| 5000ppm | 10 | 10 | 0 | 0 | 0 | 0 | |
| 10000ppm | 10 | 10 | 0 | 0 | 0 | 0 | |
| 20000ppm | 10 | 10 | 0 | 0 | 0 | 0 | |
| 40000ppm | 10 | 10 | 0 | 0 | 0 | 0 | |
| 80000ppm | 9 | 9 | 0 | 0 | 0 | 0 | |

Significent difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

APPENDIX B 9-1

GROSS FINDINGS (THIRTEEN−WEEK STUDY: SUMMARY)

RAT : MALE :SACRIFICED ANIMALS

STUDY NO. : 0201
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
ALL ANIMALS (0- 14W)



| Organ | Findings | Group Name<br>NO. of Animals | Control<br>10 (%) | 2500 ppm<br>10 (%) | 5000 ppm<br>10 (%) | 10000 ppm<br>10 (%) |
|---|---|---|---|---|---|---|
| other | hair:colored | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

| Organ | Findings | Group Name<br>NO. of Animals | 20000 ppm<br>10 (%) | 40000 ppm<br>10 (%) |
|---|---|---|---|---|
| other | hair:colored | | 6 ( 60) | 10 (100) |

APPENDIX B 9-2

GROSS FINDINGS (THIRTEEN−WEEK STUDY: SUMMARY)

RAT : FEMALE :SACRIFICED ANIMALS

STUDY NO. : 0201
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
ALL ANIMALS (0- 14W)



| Organ | Findings | Group Name<br>NO. of Animals | Control<br>10 (%) | 2500 ppm<br>10 (%) | 5000 ppm<br>10 (%) | 10000 ppm<br>10 (%) |
|---|---|---|---|---|---|---|
| liver | herniation | | 0 ( 0) | 0 ( 0) | 1 ( 10) | 1 ( 10) |
| other | hair:colored | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

| Organ | Findings | Group Name<br>NO. of Animals | 20000 ppm<br>10 (%) | 40000 ppm<br>10 (%) |
|---|---|---|---|---|
| liver | herniation | | 0 ( 0) | 0 ( 0) |
| other | hair:colored | | 7 ( 70) | 10 (100) |

APPENDIX B 9-3

GROSS FINDINGS (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : MALE DEAD AND MORIBUND ANIMALS

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 14W)



| Organ | Findings | Group Name | Control | 5000ppm | 10000ppm | 20000ppm |
|---|---|---|---|---|---|---|
| | | NO. of Animals | 0 (%) | 0 (%) | 0 (%) | 0 (%) |
| thymus | atrophic | | - ( -) | - ( -) | - ( -) | - ( -) |

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 14W)



| Organ | Findings | Group Name | 40000ppm | 80000ppm |
|---|---|---|---|---|
| | | NO. of Animals | 0 (%) | 1 (%) |
| thymus | atrophic | | - ( -) | 1 (100) |

APPENDIX B 9-4

GROSS FINDINGS (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : FEMALE DEAD AND MORIBUND ANIMALS

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 14W)



| Organ | Findings | Group Name / NO. of Animals | Control 0 (%) | 5000ppm 0 (%) | 10000ppm 0 (%) | 20000ppm 0 (%) |
|---|---|---|---|---|---|---|
| whole body | wasting | | - ( -) | - ( -) | - ( -) | - ( -) |

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 14W)



| Organ | Findings | Group Name | 40000ppm | | 80000ppm | |
|---|---|---|---|---|---|---|
| | | NO. of Animals | 0 | (%) | 1 | (%) |
| whole body | wasting | | - | ( -) | 1 | (100) |

APPENDIX B 9-5

GROSS FINDINGS (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : MALE :SACRIFICED ANIMALS

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS ( 14W)



| Organ | Findings | Group Name / NO. of Animals | Control 10 (%) | 5000ppm 10 (%) | 10000ppm 10 (%) | 20000ppm 10 (%) |
|---|---|---|---|---|---|---|
| spleen | black zone | | 0 ( 0) | 1 ( 10) | 0 ( 0) | 1 ( 10) |
| kidney | white zone | | 0 ( 0) | 2 ( 20) | 0 ( 0) | 0 ( 0) |

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS ( 14W)



| Organ | Findings | Group Name | 40000ppm | 80000ppm |
|---|---|---|---|---|
| | | NO. of Animals | 10 (%) | 9 (%) |
| spleen | black zone | | 0 ( 0) | 0 ( 0) |
| kidney | white zone | | 0 ( 0) | 0 ( 0) |

APPENDIX B 9-6

GROSS FINDINGS (THIRTEEN−WEEK STUDY: SUMMARY)

MOSUE : FEMALE :SACRIFICED ANIMALS

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS ( 14W)



| Organ | Findings | Group Name | Control | 5000ppm | 10000ppm | 20000ppm |
|---|---|---|---|---|---|---|
| | | NO. of Animals | 10 (%) | 10 (%) | 10 (%) | 10 (%) |
| spleen | black zone | | 1 ( 10) | 2 ( 20) | 0 ( 0) | 0 ( 0) |

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS ( 14W)



| Organ | Findings | Group Name | 40000ppm | | 80000ppm | |
|---|---|---|---|---|---|---|
| | | NO. of Animals | 10 | (%) | 9 | (%) |
| spleen | black zone | | 0 | ( 0) | 0 | ( 0) |

APPENDIX B 10-1

ORGAN WEIGHT (THIRTEEN−WEEK STUDY: SUMMARY),ABSOLUTE

RAT : MALE

STUDY NO. : 0201
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | Body Weight | THYMUS | ADRENALS | TESTES | HEART | LUNGS |
|---|---|---|---|---|---|---|---|
| Control | 10 | 321± 14 | 0.255± 0.026 | 0.048± 0.007 | 2.876± 0.129 | 0.923± 0.038 | 1.009± 0.059 |
| 2500 ppm | 10 | 303± 21 | 0.225± 0.019* | 0.049± 0.012 | 2.806± 0.127 | 0.885± 0.036 | 0.993± 0.057 |
| 5000 ppm | 10 | 304± 22 | 0.230± 0.031 | 0.047± 0.005 | 2.737± 0.131 | 0.876± 0.047 | 0.976± 0.059 |
| 10000 ppm | 10 | 299± 22 | 0.238± 0.025 | 0.047± 0.008 | 2.852± 0.096 | 0.886± 0.051 | 0.959± 0.042 |
| 20000 ppm | 10 | 299± 19 | 0.225± 0.017* | 0.046± 0.008 | 2.847± 0.127 | 0.916± 0.054 | 0.985± 0.040 |
| 40000 ppm | 10 | 284± 22** | 0.207± 0.021** | 0.045± 0.004 | 2.827± 0.120 | 0.865± 0.047* | 0.964± 0.077 |

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

STUDY NO. : 0201
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | KIDNEYS | SPLEEN | LIVER | BRAIN |
|---|---|---|---|---|---|
| Control | 10 | 1.913± 0.091 | 0.551± 0.031 | 8.008± 0.454 | 1.901± 0.034 |
| 2500 ppm | 10 | 1.814± 0.102 | 0.517± 0.029 | 7.545± 0.390 | 1.865± 0.032 |
| 5000 ppm | 10 | 1.812± 0.148 | 0.493± 0.035** | 7.492± 0.773 | 1.864± 0.047 |
| 10000 ppm | 10 | 1.839± 0.108 | 0.517± 0.042 | 7.486± 0.579 | 1.874± 0.040 |
| 20000 ppm | 10 | 1.890± 0.112 | 0.516± 0.033 | 7.574± 0.552 | 1.866± 0.066 |
| 40000 ppm | 10 | 1.895± 0.099 | 0.497± 0.032** | 7.530± 0.769 | 1.869± 0.036 |

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

APPENDIX B 10-2

ORGAN WEIGHT (THIRTEEN−WEEK STUDY: SUMMARY),ABSOLUTE

RAT : FEMALE

STUDY NO. : 0201
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | Body Weight | THYMUS | ADRENALS | OVARIES | HEART | LUNGS |
|---|---|---|---|---|---|---|---|
| Control | 10 | 182± 12 | 0.196± 0.020 | 0.053± 0.004 | 0.103± 0.016 | 0.613± 0.042 | 0.734± 0.057 |
| 2500 ppm | 10 | 178± 9 | 0.185± 0.016 | 0.054± 0.005 | 0.095± 0.017 | 0.603± 0.023 | 0.731± 0.032 |
| 5000 ppm | 10 | 179± 7 | 0.198± 0.024 | 0.050± 0.004 | 0.098± 0.018 | 0.608± 0.021 | 0.741± 0.032 |
| 10000 ppm | 10 | 170± 11* | 0.191± 0.012 | 0.054± 0.007 | 0.090± 0.017 | 0.587± 0.031 | 0.726± 0.055 |
| 20000 ppm | 10 | 172± 10 | 0.196± 0.019 | 0.055± 0.006 | 0.088± 0.018 | 0.607± 0.043 | 0.744± 0.041 |
| 40000 ppm | 10 | 166± 8** | 0.174± 0.015* | 0.053± 0.008 | 0.082± 0.020 | 0.578± 0.037 | 0.718± 0.033 |

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

STUDY NO. : 0201
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | KIDNEYS | SPLEEN | LIVER | BRAIN |
|---|---|---|---|---|---|
| Control | 10 | 1.220± 0.116 | 0.371± 0.044 | 4.377± 0.500 | 1.732± 0.033 |
| 2500 ppm | 10 | 1.179± 0.038 | 0.359± 0.036 | 4.170± 0.289 | 1.729± 0.032 |
| 5000 ppm | 10 | 1.180± 0.054 | 0.356± 0.032 | 4.179± 0.188 | 1.716± 0.055 |
| 10000 ppm | 10 | 1.162± 0.059 | 0.351± 0.029 | 3.977± 0.291 | 1.699± 0.052 |
| 20000 ppm | 10 | 1.201± 0.057 | 0.357± 0.019 | 4.038± 0.365 | 1.738± 0.025 |
| 40000 ppm | 10 | 1.267± 0.057 | 0.363± 0.031 | 3.974± 0.225 | 1.681± 0.056 |

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

APPENDIX B 10-3

ORGAN WEIGHT (THIRTEEN−WEEK STUDY: SUMMARY),ABSOLUTE

MOUSE: MALE

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | Body Weight | THYMUS | ADRENALS | TESTES | HEART | LUNGS |
|---|---|---|---|---|---|---|---|
| Control | 10 | 32.5± 2.0 | 0.046± 0.009 | 0.009± 0.002 | 0.197± 0.025 | 0.145± 0.007 | 0.144± 0.004 |
| 5000ppm | 10 | 33.7± 2.5 | 0.044± 0.008 | 0.009± 0.002 | 0.208± 0.030 | 0.149± 0.011 | 0.150± 0.013 |
| 10000ppm | 10 | 33.2± 2.6 | 0.048± 0.012 | 0.010± 0.002 | 0.206± 0.022 | 0.147± 0.010 | 0.148± 0.008 |
| 20000ppm | 10 | 32.2± 1.9 | 0.045± 0.007 | 0.010± 0.002 | 0.223± 0.030 | 0.148± 0.009 | 0.153± 0.010 |
| 40000ppm | 10 | 31.9± 2.7 | 0.047± 0.009 | 0.010± 0.002 | 0.211± 0.019 | 0.149± 0.009 | 0.145± 0.010 |
| 80000ppm | 9 | 29.6± 1.2* | 0.038± 0.004 | 0.010± 0.002 | 0.227± 0.021 | 0.146± 0.011 | 0.147± 0.010 |

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

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | KIDNEYS | SPLEEN | LIVER | BRAIN |
|---|---|---|---|---|---|
| Control | 10 | 0.433± 0.015 | 0.045± 0.005 | 1.144± 0.061 | 0.447± 0.010 |
| 5000ppm | 10 | 0.440± 0.033 | 0.048± 0.005 | 1.165± 0.057 | 0.444± 0.011 |
| 10000ppm | 10 | 0.445± 0.023 | 0.049± 0.007 | 1.152± 0.052 | 0.445± 0.010 |
| 20000ppm | 10 | 0.445± 0.032 | 0.052± 0.008 | 1.164± 0.049 | 0.442± 0.009 |
| 40000ppm | 10 | 0.455± 0.015 | 0.047± 0.006 | 1.162± 0.042 | 0.446± 0.008 |
| 80000ppm | 9 | 0.468± 0.029 | 0.047± 0.003 | 1.127± 0.052 | 0.436± 0.016 |

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

APPENDIX B 10-4

ORGAN WEIGHT (THIRTEEN−WEEK STUDY: SUMMARY),ABSOLUTE

MOUSE: FEMALE

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | Body Weight | THYMUS | ADRENALS | OVARIES | HEART | LUNGS |
|---|---|---|---|---|---|---|---|
| Control | 10 | 21.7± 1.0 | 0.045± 0.006 | 0.012± 0.002 | 0.028± 0.006 | 0.119± 0.006 | 0.143± 0.013 |
| 5000ppm | 10 | 20.9± 1.2 | 0.043± 0.007 | 0.011± 0.002 | 0.032± 0.008 | 0.118± 0.007 | 0.143± 0.009 |
| 10000ppm | 10 | 20.9± 1.2 | 0.041± 0.005 | 0.010± 0.001 | 0.028± 0.007 | 0.121± 0.009 | 0.140± 0.010 |
| 20000ppm | 10 | 21.3± 1.0 | 0.043± 0.005 | 0.011± 0.002 | 0.030± 0.006 | 0.117± 0.006 | 0.145± 0.010 |
| 40000ppm | 10 | 20.4± 0.8* | 0.039± 0.004 | 0.010± 0.002 | 0.027± 0.004 | 0.117± 0.007 | 0.142± 0.016 |
| 80000ppm | 9 | 20.4± 0.9* | 0.038± 0.006* | 0.010± 0.002 | 0.027± 0.005 | 0.114± 0.005 | 0.137± 0.011 |

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

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | KIDNEYS | SPLEEN | LIVER | BRAIN |
|---|---|---|---|---|---|
| Control | 10 | 0.292± 0.012 | 0.054± 0.007 | 0.907± 0.069 | 0.458± 0.021 |
| 5000ppm | 10 | 0.298± 0.014 | 0.049± 0.007 | 0.857± 0.062 | 0.457± 0.018 |
| 10000ppm | 10 | 0.285± 0.018 | 0.051± 0.007 | 0.860± 0.042 | 0.450± 0.017 |
| 20000ppm | 10 | 0.294± 0.021 | 0.051± 0.009 | 0.897± 0.045 | 0.450± 0.019 |
| 40000ppm | 10 | 0.292± 0.015 | 0.043± 0.005** | 0.847± 0.040 | 0.455± 0.013 |
| 80000ppm | 9 | 0.306± 0.022 | 0.042± 0.004** | 0.844± 0.045* | 0.440± 0.013 |

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

APPENDIX B 11-1

ORGAN WEIGHT (THIRTEEN−WEEK STUDY: SUMMARY), RELATIVE

RAT : MALE

STUDY NO. : 0201
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | Body Weight (g) | THYMUS | ADRENALS | TESTES | HEART | LUNGS |
|---|---|---|---|---|---|---|---|
| Control | 10 | 321± 14 | 0.079± 0.007 | 0.015± 0.002 | 0.896± 0.045 | 0.287± 0.014 | 0.314± 0.016 |
| 2500 ppm | 10 | 303± 21 | 0.074± 0.004 | 0.016± 0.003 | 0.928± 0.049 | 0.293± 0.017 | 0.328± 0.010 |
| 5000 ppm | 10 | 304± 22 | 0.076± 0.008 | 0.016± 0.001 | 0.905± 0.075 | 0.289± 0.012 | 0.323± 0.025 |
| 10000 ppm | 10 | 299± 22 | 0.079± 0.005 | 0.016± 0.003 | 0.957± 0.062 | 0.297± 0.012 | 0.321± 0.013 |
| 20000 ppm | 10 | 299± 19 | 0.075± 0.005 | 0.016± 0.003 | 0.956± 0.077 | 0.306± 0.010* | 0.330± 0.020 |
| 40000 ppm | 10 | 284± 22** | 0.073± 0.008 | 0.016± 0.002 | 1.000± 0.056** | 0.306± 0.021* | 0.340± 0.013** |

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

STUDY NO. : 0201
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | KIDNEYS | SPLEEN | LIVER | BRAIN |
|---|---|---|---|---|---|
| Control | 10 | 0.595± 0.016 | 0.171± 0.007 | 2.491± 0.073 | 0.592± 0.027 |
| 2500 ppm | 10 | 0.599± 0.015 | 0.171± 0.009 | 2.491± 0.065 | 0.618± 0.048 |
| 5000 ppm | 10 | 0.596± 0.021 | 0.163± 0.009 | 2.461± 0.122 | 0.616± 0.041 |
| 10000 ppm | 10 | 0.615± 0.023 | 0.173± 0.007 | 2.502± 0.069 | 0.629± 0.044 |
| 20000 ppm | 10 | 0.632± 0.016** | 0.173± 0.008 | 2.532± 0.079 | 0.625± 0.032 |
| 40000 ppm | 10 | 0.670± 0.025** | 0.176± 0.010 | 2.652± 0.096** | 0.663± 0.050** |

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

APPENDIX B 11-2

ORGAN WEIGHT (THIRTEEN−WEEK STUDY: SUMMARY), RELATIVE

RAT : FEMALE

STUDY NO. : 0201
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | Body Weight (g) | THYMUS | ADRENALS | OVARIES | HEART | LUNGS |
|---|---|---|---|---|---|---|---|
| Control | 10 | 182± 12 | 0.107± 0.007 | 0.029± 0.003 | 0.057± 0.008 | 0.337± 0.022 | 0.403± 0.015 |
| 2500 ppm | 10 | 178± 9 | 0.104± 0.009 | 0.030± 0.003 | 0.054± 0.010 | 0.339± 0.020 | 0.411± 0.023 |
| 5000 ppm | 10 | 179± 7 | 0.111± 0.011 | 0.028± 0.002 | 0.055± 0.010 | 0.340± 0.014 | 0.414± 0.012 |
| 10000 ppm | 10 | 170± 11* | 0.113± 0.006 | 0.032± 0.004 | 0.054± 0.011 | 0.347± 0.017 | 0.428± 0.017* |
| 20000 ppm | 10 | 172± 10 | 0.115± 0.012 | 0.032± 0.003 | 0.052± 0.010 | 0.354± 0.018 | 0.434± 0.021** |
| 40000 ppm | 10 | 166± 8** | 0.105± 0.011 | 0.032± 0.004 | 0.049± 0.012 | 0.349± 0.018 | 0.434± 0.020** |

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

STUDY NO. : 0201
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | KIDNEYS | SPLEEN | LIVER | BRAIN |
|---|---|---|---|---|---|
| Control | 10 | 0.669± 0.041 | 0.203± 0.016 | 2.400± 0.190 | 0.954± 0.063 |
| 2500 ppm | 10 | 0.663± 0.034 | 0.201± 0.014 | 2.340± 0.102 | 0.973± 0.056 |
| 5000 ppm | 10 | 0.660± 0.022 | 0.199± 0.013 | 2.337± 0.066 | 0.960± 0.036 |
| 10000 ppm | 10 | 0.687± 0.032 | 0.207± 0.007 | 2.347± 0.073 | 1.007± 0.081 |
| 20000 ppm | 10 | 0.700± 0.021 | 0.208± 0.008 | 2.350± 0.094 | 1.016± 0.059 |
| 40000 ppm | 10 | 0.764± 0.022** | 0.219± 0.018* | 2.398± 0.109 | 1.015± 0.036 |

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

APPENDIX B 11-3

ORGAN WEIGHT (THIRTEEN−WEEK STUDY: SUMMARY), RELATIVE

MOUSE: MALE

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | Body Weight (g) | THYMUS | ADRENALS | TESTES | HEART | LUNGS |
|---|---|---|---|---|---|---|---|
| Control | 10 | 32.5± 2.0 | 0.141± 0.026 | 0.028± 0.007 | 0.608± 0.091 | 0.448± 0.029 | 0.444± 0.027 |
| 5000ppm | 10 | 33.7± 2.5 | 0.131± 0.018 | 0.026± 0.006 | 0.619± 0.096 | 0.444± 0.041 | 0.446± 0.036 |
| 10000ppm | 10 | 33.2± 2.6 | 0.145± 0.030 | 0.031± 0.008 | 0.624± 0.095 | 0.443± 0.032 | 0.447± 0.024 |
| 20000ppm | 10 | 32.2± 1.9 | 0.139± 0.016 | 0.031± 0.008 | 0.691± 0.079 | 0.462± 0.046 | 0.476± 0.027 |
| 40000ppm | 10 | 31.9± 2.7 | 0.148± 0.022 | 0.030± 0.004 | 0.665± 0.083 | 0.470± 0.035 | 0.457± 0.054 |
| 80000ppm | 9 | 29.6± 1.2* | 0.129± 0.008 | 0.032± 0.007 | 0.766± 0.064** | 0.495± 0.031* | 0.498± 0.039** |

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

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | KIDNEYS | SPLEEN | LIVER | BRAIN |
|---|---|---|---|---|---|
| Control | 10 | 1.338± 0.094 | 0.137± 0.010 | 3.526± 0.189 | 1.379± 0.087 |
| 5000ppm | 10 | 1.311± 0.113 | 0.143± 0.020 | 3.468± 0.188 | 1.326± 0.130 |
| 10000ppm | 10 | 1.342± 0.082 | 0.147± 0.020 | 3.480± 0.225 | 1.347± 0.109 |
| 20000ppm | 10 | 1.385± 0.086 | 0.161± 0.025 | 3.625± 0.210 | 1.376± 0.075 |
| 40000ppm | 10 | 1.433± 0.115 | 0.148± 0.023 | 3.657± 0.218 | 1.406± 0.123 |
| 80000ppm | 9 | 1.580± 0.070** | 0.160± 0.011 | 3.808± 0.132* | 1.473± 0.033 |

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

APPENDIX B 11-4

ORGAN WEIGHT (THIRTEEN−WEEK STUDY: SUMMARY), RELATIVE

MOUSE: FEMALE

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | Body Weight (g) | THYMUS | ADRENALS | OVARIES | HEART | LUNGS |
|---|---|---|---|---|---|---|---|
| Control | 10 | 21.7± 1.0 | 0.206± 0.024 | 0.055± 0.009 | 0.131± 0.025 | 0.548± 0.030 | 0.658± 0.063 |
| 5000ppm | 10 | 20.9± 1.2 | 0.206± 0.025 | 0.053± 0.011 | 0.151± 0.034 | 0.566± 0.023 | 0.685± 0.033 |
| 10000ppm | 10 | 20.9± 1.2 | 0.198± 0.017 | 0.048± 0.006 | 0.133± 0.034 | 0.581± 0.030 | 0.673± 0.041 |
| 20000ppm | 10 | 21.3± 1.0 | 0.203± 0.022 | 0.052± 0.006 | 0.141± 0.026 | 0.548± 0.024 | 0.681± 0.051 |
| 40000ppm | 10 | 20.4± 0.8* | 0.190± 0.018 | 0.051± 0.011 | 0.131± 0.021 | 0.577± 0.045 | 0.698± 0.079 |
| 80000ppm | 9 | 20.4± 0.9* | 0.185± 0.027 | 0.050± 0.008 | 0.132± 0.025 | 0.559± 0.033 | 0.674± 0.040 |

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

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS ( 14)



| Group Name | NO. of Animals | KIDNEYS | SPLEEN | LIVER | BRAIN |
|---|---|---|---|---|---|
| Control | 10 | 1.346± 0.075 | 0.249± 0.025 | 4.172± 0.201 | 2.113± 0.157 |
| 5000ppm | 10 | 1.425± 0.073 | 0.235± 0.024 | 4.094± 0.149 | 2.187± 0.087 |
| 10000ppm | 10 | 1.369± 0.077 | 0.244± 0.027 | 4.127± 0.169 | 2.161± 0.075 |
| 20000ppm | 10 | 1.379± 0.083 | 0.236± 0.033 | 4.214± 0.106 | 2.118± 0.111 |
| 40000ppm | 10 | 1.437± 0.095 | 0.209± 0.020** | 4.167± 0.184 | 2.237± 0.122 |
| 80000ppm | 9 | 1.504± 0.106** | 0.207± 0.017** | 4.148± 0.150 | 2.164± 0.097 |

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

APPENDIX B 12-1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN−WEEK STUDY: SUMMARY)

RAT : MALE : SACRIFICED ANIMALS

STUDY NO. : 0201
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
ALL ANIMALS (0- 14W)



| Organ | Findings | Group Name | Control | | | | 2500 ppm | | | | 5000 ppm | | | | 10000 ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals | 10 | | | | 10 | | | | 10 | | | | 10 | | | |
| | | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| larynx | inflammation | | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| lung | 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) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | osseous metaplasia | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| spleen | deposit of hemosiderin | | 0 ( 0) | 10 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 10 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 10 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 10 (100) | 0 ( 0) | 0 ( 0) |
| [Circulatory system] | | | | | | | | | | | | | | | | | | |
| heart | granulation | | 3 ( 30) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 20) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 30) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 40) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| stomach | erosion:glandular stomach | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | increase in superficial layer of fundus | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| liver | 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) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | cyst | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

| Organ | Findings | Group Name | 20000 ppm | | | | 40000 ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals | 10 | | | | 10 | | | |
| | | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |
| [Respiratory system] | | | | | | | | | | |
| larynx | inflammation | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| lung | granulation | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | osseous metaplasia | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Hematopoietic system] | | | | | | | | | | |
| spleen | deposit of hemosiderin | | 0 ( 0) | 10 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 10 (100) | 0 ( 0) | 0 ( 0) |
| [Circulatory system] | | | | | | | | | | |
| heart | granulation | | 3 ( 30) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 20) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Digestive system] | | | | | | | | | | |
| stomach | erosion:glandular stomach | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) |
| | increase in superficial layer of fundus | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 40) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| liver | necrosis:focal | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Urinary system] | | | | | | | | | | |
| kidney | cyst | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

STUDY NO. : 0201
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
ALL ANIMALS (0- 14W)



| Organ | Findings | Group Name | Control | | | | 2500 ppm | | | | 5000 ppm | | | | 10000 ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals | 10 | | | | 10 | | | | 10 | | | | 10 | | | |
| | | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | basophilic change | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | eosinophilic body | | 1 ( 10) | 9 ( 90) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 10 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 10 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 10 (100) | 0 ( 0) | 0 ( 0) |
| [Endocrine system] | | | | | | | | | | | | | | | | | | |
| pituitary | cyst | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | Rathke pouch | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| thyroid | ultimibranchial body remanet | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 20) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Reproductive system] | | | | | | | | | | | | | | | | | | |
| prostate | inflammation | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Special sense organs/appandage] | | | | | | | | | | | | | | | | | | |
| Harder gl | inflammation | | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

| Organ | Findings | Group Name | 20000 ppm | | | | 40000 ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals | 10 | | | | 10 | | | |
| | | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |
| [Urinary system] | | | | | | | | | | |
| kidney | basophilic change | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | eosinophilic body | | 0 ( 0) | 10 (100) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 9 ( 90) | 0 ( 0) | 0 ( 0) |
| [Endocrine system] | | | | | | | | | | |
| pituitary | cyst | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | Rathke pouch | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| thyroid | ultimibranchial body remanet | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Reproductive system] | | | | | | | | | | |
| prostate | inflammation | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Special sense organs/appandage] | | | | | | | | | | |
| Harder gl | inflammation | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

APPENDIX B 12-2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN−WEEK STUDY: SUMMARY)

RAT : FEMALE : SACRIFICED ANIMALS

| Organ | Findings | Group Name | Control | | | | 2500 ppm | | | | 5000 ppm | | | | 10000 ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals | 10 | | | | 10 | | | | 10 | | | | 10 | | | |
| | | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| nasal cavit | inflammation:squamous epithelium | | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 20) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| bone marrow | granulation | | 3 ( 30) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 20) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 30) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 30) | 1 ( 10) | 0 ( 0) | 0 ( 0) |
| lymph node | granulation | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 1 ( 10) | 0 ( 0) | 0 ( 0) |
| spleen | deposit of hemosiderin | | 0 ( 0) | 10 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 10 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 10 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 10 (100) | 0 ( 0) | 0 ( 0) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| tongue | inflammation | | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| stomach | erosion:glandular stomach | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | decrease in middle layer of fundus | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| liver | herniation | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | vacuolic change | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | granulation | | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 20) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

| Organ | Findings | Group Name | 20000 ppm | | | | 40000 ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals | 10 | | | | 10 | | | |
| | | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |
| [Respiratory system] | | | | | | | | | | |
| nasal cavit | inflammation:squamous epithelium | | 2 ( 20) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Hematopoietic system] | | | | | | | | | | |
| bone marrow | granulation | | 4 ( 40) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 30) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| lymph node | granulation | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| spleen | deposit of hemosiderin | | 0 ( 0) | 10 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 10 (100) | 0 ( 0) | 0 ( 0) |
| [Digestive system] | | | | | | | | | | |
| tongue | inflammation | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| stomach | erosion:glandular stomach | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | decrease in middle layer of fundus | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| liver | herniation | | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | vacuolic change | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | granulation | | 2 ( 20) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

| Organ | Findings | Group Name / No. of Animals | Control 10 | | | | 2500 ppm 10 | | | | 5000 ppm 10 | | | | 10000 ppm 10 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| pancreas | atrophy | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 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) |
| | mineralization:cortico-medullary junction | | 10 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 10 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 10 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 10 (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 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| thyroid | ultimibranchial body remanet | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Special sense organs/appandage] | | | | | | | | | | | | | | | | | | |
| Harder gl | inflammation | | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 20) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 30) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

| Organ | Findings | Group Name | 20000 ppm | | | | 40000 ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals | 10 | | | | 10 | | | |
| | | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |
| [Digestive system] | | | | | | | | | | |
| pancreas | atrophy | | 1 ( 10) | 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) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | mineralization:cortico-medullary junction | | 10 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 9 ( 90) | 1 ( 10) | 0 ( 0) | 0 ( 0) |
| [Endocrine system] | | | | | | | | | | |
| pituitary | Rathke pouch | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| thyroid | ultimibranchial body remanet | | 2 ( 20) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 20) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Special sense organs/appandage] | | | | | | | | | | |
| Harder gl | inflammation | | 2 ( 20) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

APPENDIX B 12-3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN−WEEK STUDY: SUMMARY)

MOUSE: MALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 14W)



| Organ | Findings | Group Name | Control | | | | 5000ppm | | | | 10000ppm | | | | 20000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 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 | | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) |
| | deposit of hemosiderin | | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| liver | necrosis:single cell | | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | vacuolization of proximal tubule | | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) |
| [Reproductive system] | | | | | | | | | | | | | | | | | | |
| testis | degeneration:seminiferous epithelium | | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) |

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

| Organ | Findings | Group Name | 40000ppm | | | | 80000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals | 0 | | | | 1 | | | |
| | | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |
| [Hematopoietic system] | | | | | | | | | | |
| thymus | atrophy | | - ( -) | - ( -) | - ( -) | - ( -) | 0 ( 0) | 0 ( 0) | 1 (100) | 0 ( 0) |
| spleen | atrophy | | - ( -) | - ( -) | - ( -) | - ( -) | 0 ( 0) | 1 (100) | 0 ( 0) | 0 ( 0) |
| | deposit of hemosiderin | | - ( -) | - ( -) | - ( -) | - ( -) | 1 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Digestive system] | | | | | | | | | | |
| liver | necrosis:single cell | | - ( -) | - ( -) | - ( -) | - ( -) | 0 ( 0) | 1 (100) | 0 ( 0) | 0 ( 0) |
| [Urinary system] | | | | | | | | | | |
| kidney | vacuolization of proximal tubule | | - ( -) | - ( -) | - ( -) | - ( -) | 1 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Reproductive system] | | | | | | | | | | |
| testis | degeneration:seminiferous epithelium | | - ( -) | - ( -) | - ( -) | - ( -) | 1 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

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

APPENDIX B 12-4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN−WEEK STUDY: SUMMARY)

MOUSE: FEMALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 14W)



| Organ | Findings | Group Name | Control | | | | 5000ppm | | | | 10000ppm | | | | 20000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 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 | | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) |
| [Circulatory system] | | | | | | | | | | | | | | | | | | |
| heart | necrosis | | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) | - ( -) |

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

| Organ | Findings | Group Name | 40000ppm | | | | 80000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals | 0 | | | | 1 | | | |
| | | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |
| [Hematopoietic system] | | | | | | | | | | |
| thymus | atrophy | | - ( -) | - ( -) | - ( -) | - ( -) | 0 ( 0) | 0 ( 0) | 1 (100) | 0 ( 0) |
| spleen | atrophy | | - ( -) | - ( -) | - ( -) | - ( -) | 1 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Circulatory system] | | | | | | | | | | |
| heart | necrosis | | - ( -) | - ( -) | - ( -) | - ( -) | 1 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

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

APPENDIX B 12-3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN−WEEK STUDY: SUMMARY)

MOUSE: MALE : SACRIFICED ANIMALS

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS ( 14W)



| Organ | Findings | Group Name | Control | | | | 5000ppm | | | | 10000ppm | | | | 20000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals | 10 | | | | 10 | | | | 10 | | | | 10 | | | |
| | | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| nasal cavit | eosinophilic change:olfactory epithelium | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 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 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | duct ectasia:olfactory gland | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| spleen | deposit of hemosiderin | | 5 ( 50) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 40) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 7 ( 70) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 5 ( 50) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | deposit of melanin | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Circulatory system] | | | | | | | | | | | | | | | | | | |
| heart | arthritis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 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 | increase in superficial layer of fundus | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | decrease in middle layer of fundus | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | decrease in deep layer of fundus | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

| Organ | Findings | Group Name | 40000ppm | | | | 80000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals | 10 | | | | 9 | | | |
| | | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |
| [Respiratory system] | | | | | | | | | | |
| nasal cavit | eosinophilic change:olfactory epithelium | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 11) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | duct ectasia:olfactory gland | | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 6 ( 67) | 0 ( 0) | 0 ( 0) | 0 ** ( 0) |
| [Hematopoietic system] | | | | | | | | | | |
| spleen | deposit of hemosiderin | | 5 ( 50) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 44) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | deposit of melanin | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Circulatory system] | | | | | | | | | | |
| heart | arthritis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Digestive system] | | | | | | | | | | |
| stomach | increase in superficial layer of fundus | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 8 ( 89) | 0 ( 0) | 0 ( 0) | 0 ** ( 0) |
| | decrease in middle layer of fundus | | 5 ( 50) | 0 ( 0) | 0 ( 0) | 0 * ( 0) | 5 ( 56) | 0 ( 0) | 0 ( 0) | 0 * ( 0) |
| | decrease in deep layer of fundus | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 6 ( 67) | 0 ( 0) | 0 ( 0) | 0 ** ( 0) |

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS ( 14W)



| Organ | Findings | Group Name | Control | | | | 5000ppm | | | | 10000ppm | | | | 20000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals | 10 | | | | 10 | | | | 10 | | | | 10 | | | |
| | | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| liver | granulation | | 4 ( 40) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 30) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 3 ( 30) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 40) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | basophilic change | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 20) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | vacuolization of proximal tubule | | 8 ( 80) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 7 ( 70) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 9 ( 90) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 10 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Endocrine system] | | | | | | | | | | | | | | | | | | |
| adrenal | accesory cortical nodule | | 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 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS ( 14W)



| Organ | Findings | Group Name | 40000ppm | | | | 80000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals | 10 | | | | 9 | | | |
| | | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |
| [Digestive system] | | | | | | | | | | |
| liver | granulation | | 3 ( 30) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 22) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Urinary system] | | | | | | | | | | |
| kidney | basophilic change | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 11) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | vacuolization of proximal tubule | | 9 ( 90) | 0. ( 0) | 0 ( 0) | 0 ( 0) | 8 ( 89) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Endocrine system] | | | | | | | | | | |
| adrenal | accesory cortical nodule | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

APPENDIX B 12-4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(THIRTEEN−WEEK STUDY: SUMMARY)

MOUSE: FEMALE : SACRIFICED ANIMALS

| Organ | Findings | Group Name | Control | | | | 5000ppm | | | | 10000ppm | | | | 20000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals | 10 | | | | 10 | | | | 10 | | | | 10 | | | |
| | | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| nasal cavit | eosinophilic change:olfactory epithelium | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | eosinophilic change:respiratory epithelium | | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | respiratory metaplasia:olfactory epithelium | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | duct ectasia:olfactory gland | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| spleen | deposit of hemosiderin | | 10 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 10 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 10 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 10 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | deposit of melanin | | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 20) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | extramedullary hematopoiesis | | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| stomach | increase in superficial layer of fundus | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| liver | granulation | | 4 ( 40) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 20) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 4 ( 40) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 6 ( 60) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Endocrine system] | | | | | | | | | | | | | | | | | | |
| adrenal | accesory cortical nodule | | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

| Organ | Findings | Group Name | 40000ppm | | | | 80000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals | 10 | | | | 9 | | | |
| | | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |
| [Respiratory system] | | | | | | | | | | |
| nasal cavit | eosinophilic change:olfactory epithelium | | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 11) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | eosinophilic change:respiratory epithelium | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 22) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | respiratory metaplasia:olfactory epithelium | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 11) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | duct ectasia:olfactory gland | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 9 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) ** |
| [Hematopoietic system] | | | | | | | | | | |
| spleen | deposit of hemosiderin | | 10 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 9 (100) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| | deposit of melanin | | 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) |
| [Digestive system] | | | | | | | | | | |
| stomach | increase in superficial layer of fundus | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 11) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| liver | granulation | | 3 ( 30) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 2 ( 22) | 0 ( 0) | 0 ( 0) | 0 ( 0) |
| [Endocrine system] | | | | | | | | | | |
| adrenal | accesory cortical nodule | | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 11) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS ( 14W)



| Organ | Findings | Group Name | Control | | | | 5000ppm | | | | 10000ppm | | | | 20000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals | 10 | | | | 10 | | | | 10 | | | | 10 | | | |
| | | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |
| [Special sense organs/appandage] | | | | | | | | | | | | | | | | | | |
| Harder gl | inflammation | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

STUDY NO. : 0202
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS ( 14W)



| Organ | Findings | Group Name | 40000ppm | | | | 80000ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals | 10 | | | | 9 | | | |
| | | | <1> (%) | <2> (%) | <3> (%) | <4> (%) | <1> (%) | <2> (%) | <3> (%) | <4> (%) |
| [Special sense organs/appandage] | | | | | | | | | | |
| Harder gl | inflammation | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

APPENDIX B 13-1

# IDENTITY AND PURITY OF BIPHENYL

# PERFORMED AT THE JAPAN BIOASSAY LABORATORY

# (THIRTEEN−WEEK STUDY)

IDENTITY OF 1,3,5,7-TETRAAZATRICYCLO[3.3.1.1$^{3,7}$]DECANE PERFORMED AT THE JAPAN BIOASSAY LABORATORY (THIRTEEN-WEEK STUDIES)

Lot no. TWQ4880

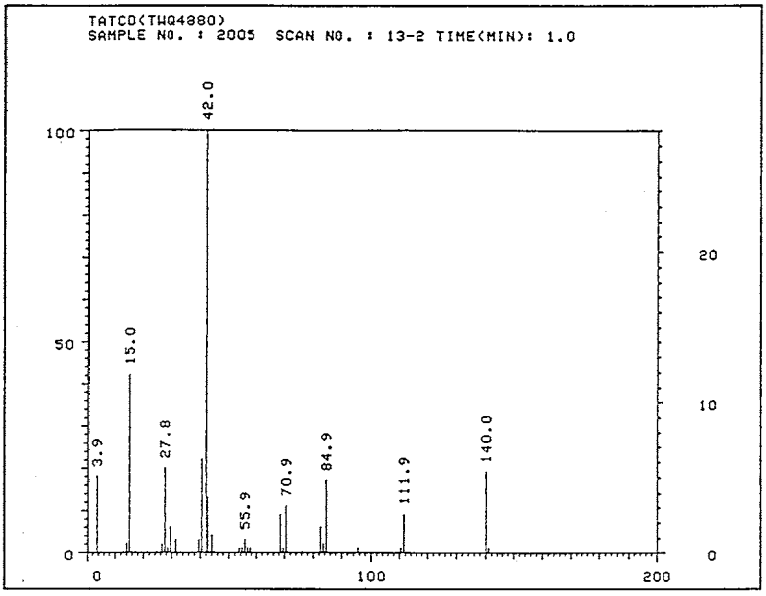
1. Spectral data

Mass Spectrometry

Instrument : Hitachi M-80B

Ionization : EI(Electron Ionization)

Ionization Voltage : 70eV




Mass Spectrum of 1,3,5,7-Tetraazatricyclo[3.3.1.1$^{3,7}$]decane

Result:

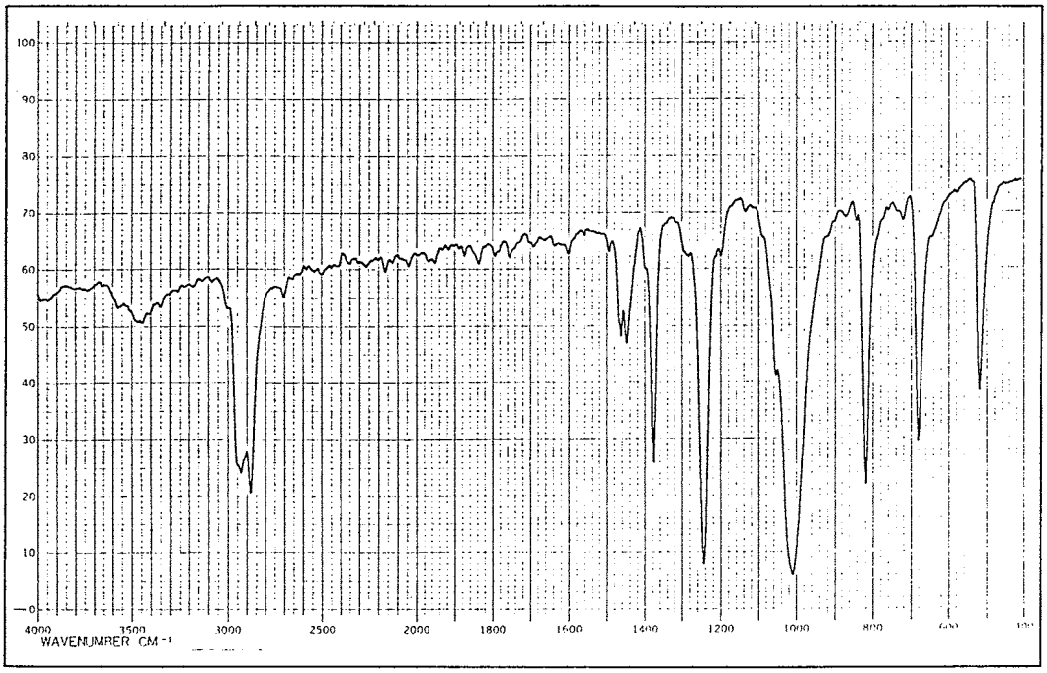
| | Molecular Weight |
|---|---|
| Theoretical Value | 140.1(Calculated) |
| Determined | 140.0 |

Infrared Spectrum

Instrument : Hitachi 270-30

Cell : KBr

Slit : Medium




Infrared Spectrum of 1,3,5,7-Tetraazatricyclo[3.3.1.1$^{3,7}$]decane

Results:

Wave Number($CM^{-1}$)

| Determined | Literature Value |
|---|---|
| 480～ 530 | 480～ 530 |
| 640～ 700 | 640～ 700 |
| 780～ 830 | 780～ 830 |
| 910～1100 | 910～1100 |
| 1200～1270 | 1200～1270 |
| 1350～1420 | 1350～1420 |
| 1420～1490 | 1420～1490 |
| 2800～3000 | 2800～3000 |

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

2. Conclusions: The result of the mass spectrum agreed with the theoretical value and the infrared spectrum agreed with the literature value.

APPENDIX B 13-2

# STABILITY OF BIPHENYL AT THE JAPAN BIOASSAY LABORATORY

## (THIRTEEN−WEEK STUDY)

STABILITY OF 1,3,5,7-TETRAAZATRICYCLO[3.3.1.1$^{3,7}$]DECANE AT THE JAPAN BIOASSAY LABORATORY (THIRTEEN-WEEK STUDIES)

Lot no. TWQ4880

1. Sample storage: 1,3,5,7-Tetraazatricyclo[3.3.1.1$^{3,7}$]decane was stored for about 15 weeks at 5°C.

2. Infrared Spectrum

Instrument : Hitachi 270-30

Cell : KBr

Slit : Medium

Results:

Wave Number ($CM^{-1}$)

| 03/06/92 | 06/17/92 |
|---|---|
| 480～ 530 | 480～ 530 |
| 640～ 700 | 640～ 700 |
| 780～ 830 | 780～ 830 |
| 910～1100 | 910～1100 |
| 1200～1270 | 1200～1270 |
| 1350～1420 | 1350～1420 |
| 1420～1490 | 1420～1490 |
| 2800～3000 | 2800～3000 |

3. Conclusions: No notable differrence was observed between infrared spectrums of pre- and post-examination of the study.
Consequently, 1,3,5,7-tetraazatricyclo[3.3.1.1$^{3,7}$]decane was stable as the chemical when stored for about 15 weeks at 5°C.

APPENDIX B 13-3-1

# ANALYSIS OF TATCD CONCENTRATION IN DRINKING WATER OF THE THIRTEEN −WEEK STUDIES

ANALYSIS OF 1,3,5,7-TETRAAZATRICYCLO[3.3.1.1$^{3,7}$]DECANE CONCENTRATION IN DRINKING WATER OF THE THIRTEEN-WEEK STUDIES

(Rat)

| Concentration of 1,3,5,7-Tetraazatricyclo[3.3.1.1$^{3,7}$]decane in Drinking Water for Target Concentration(ppm) | | | | |
|---|---|---|---|---|
| 2500 ( a ) | 5000 ( a ) | 10000 ( a ) | 20000 ( a ) | 40000 ( a ) |
| 2687.2(107.5) | 5352.0(107.0) | 10585.9(105.9) | 20804.6(104.0) | 40204.5(100.5) |

(Mouse)

| Concentration of 1,3,5,7-Tetraazatricyclo[3.3.1.1$^{3,7}$]decane in Drinking Water for Target Concentration(ppm) | | | | |
|---|---|---|---|---|
| 5000 ( a ) | 10000 ( a ) | 20000 ( a ) | 40000 ( a ) | 80000 ( a ) |
| 5352.0(107.0) | 10585.9(105.9) | 20804.6(104.0) | 40204.5(100.5) | 80738.5(100.9) |

(a) Percent of target concentration

Analytical method : The sample were analyzed by the Gas Chromatography.

Instrument : Hewlett Packard 5890A
Column : 4% Carbowax 20M / 0.8% KOH / 60/80 Carbopack B (2mm$\phi$ × 2m)
Column Temperature: 215℃
Flow Rate : 34.5ml/min
Detector : FID(Hydrogen Flame Ionization)
Injection Volume : 1$\mu$l

APPENDIX B 31-3-2

# STABILITY OF TATCD CONCENTRATION IN DRINKING WATER OF THE THIRTEEN - WEEK STUDIES

STABILITY OF 1,3,5,7-TETRAAZATRICYCLO[3.3.1.1$^{3,7}$]DECANE IN DRINKING WATER OF THE THIRTEEN-WEEK STUDIES

(Rat)

| | Concentration of 1,3,5,7-Tetraazatricyclo[3.3.1.1$^{3,7}$]decane in Drinking Water for Target Concentration(ppm) | |
|---|---|---|
| Date | 2500 ( b ) | 40000 ( b ) |
| 03/19/92(a) | 2687.2(100) | 40204.5(100) |
| 03/23/92 | 2666.1( 99.2) | 40131.5( 99.8) |

(Mouse)

| | Concentration of 1,3,5,7-Tetraazatricyclo[3.3.1.1$^{3,7}$]decane in Drinking Water for Target Concentration(ppm) | |
|---|---|---|
| Date | 5000 ( b ) | 80000 ( b ) |
| 03/19/92(a) | 5352.0(100) | 80738.5(100) |
| 03/23/92 | 5357.6(100.1) | 80487.0( 99.7) |

(a) Date of preparation
(b) Percent of concentration on preparation day

Analytical method : The sample were analyzed by the Gas Chromatography.

Instrument : Hewlett Packard 5890A
Column : 4% Carbowax 20M / 0.8% KOH / 60/80 Carbopack B (2mm$\phi$ × 2m)
Column Temperature: 215℃
Flow Rate : 34.5ml/min
Detector : FID(Hydrogen Flame Ionization)
Injection Volume : 1$\mu$l

# APPENDIX C 1

# METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALSYS

# METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS

| Item | Method | Unit |
|---|---|---|
| **Hematology** | | |
| Red blood cell (RBC) | Light scattering method [1] | $\times 10^6/\mu l$ |
| Hemoglobin (Hgb) | Cyanmethemoglobin method [1] | g/dl |
| Hematocrit (Hct) | Calculated as RBC×MCV/10 [1] | % |
| Mean corpuscular volume (MCV) | Light scattering method [1] | fl |
| Mean corpuscular hemoglobin (MCH) | Calculated as Hgb/RBC×10 [1] | pg |
| Mean corpuscular hemoglobin concentration (MCHC) | Calculated as Hgb/Hct×100 [1] | g/dl |
| Platelet | Light scattering method [1] | $\times 10^3/\mu l$ |
| White blood cell (WBC) | Light scattering method [1] | $\times 10^3/\mu l$ |
| Differential WBC | Pattern recognition method [2] (May-Grunwald-Giemsa staining) | % |
| **Biochemistry** | | |
| Total protein (TP) | Biuret method [3] | g/dl |
| Albumin (Alb) | BCG method [3] | g/dl |
| A/G ratio | Calculated as Alb/ (TP−Alb) [3] | |
| T-bilirubin | Michaelson method [3] | mg/dl |
| Glucose | Enzymatic method (HK•G-6-PDH) [3] | mg/dl |
| T-cholesterol | Enzymatic method (CEH•COD•POD) [3] | mg/dl |
| Triglyceride | Enzymatic method (GK•GPO•POD) [3] | mg/dl |
| Phospholipid | Enzymatic method (PLD•COD•POD) [3] | mg/dl |
| Glutamic oxaloacetic transaminase (GOT) | Karmen method [3] | IU/l |
| Glutamic pyruvic transaminase (GPT) | Karmen method [3] | IU/l |
| Lactate dehydrogenase (LDH) | Wroblewski-LaDue method [3] | IU/l |
| Alkaline phosphatase (ALP) | GSCC method [3] | IU/l |
| $\gamma$-Glutamyl transpeptidase (G-GTP) | L-$\gamma$-Glutamyl-p-nitroanilide substrate method [3] | IU/l |
| Creatine phosphokinase (CPK) | GSCC method [3] | IU/l |
| Urea nitrogen | Enzymatic method (Urease•GLDH) [3] | mg/dl |
| Creatinine | Jaffe method [3] | mg/dl |
| Sodium | Flame photometry [4] | mEq/l |
| Potassium | Flame photometry [4] | mEq/l |
| Chloride | Coulometric titration [4] | mEq/l |
| Calcium | OCPC method [3] | mg/dl |
| Inorganic phosphorus | Enzymatic method (SPL•PGM•G-6-PDH) [3] | mg/dl |
| **Urinalysis** | | |
| pH, Protein, Glucose, Ketone body, Bilirubin, Occult blood, Urobilinogen | Urinalysis reagent paper method [5] | |

1) Automatic blood cell analyzer (Technicon H•1 : Technicon Instruments Corporation,USA)
2) Automatic blood cell differential analyzer (Hitachi 8200 : Hitachi,Ltd.,Japan)
3) Automatic analyzer (Hitachi 705 : Hitachi,Ltd.,Japan)
4) Flame photometer (Hitachi 750 : Hitachi,Ltd.,Japan)
5) Ames reagent strips for urinalysis (Multistix, Uro-Labstix : Miles Sankyo Co.,Ltd.,Japan)

# APPENDIX C 2

# UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

# UNITS AND DECIMNAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

| | TEST ITEM | DECIMAL PLACE | UNIT |
|---|---|---|---|
| HEMATOLOGY | Red blood cell | 2 | $\times 10^6/\mu l$ |
| | Hemoglobin | 1 | g/dl |
| | Hematocrit | 1 | % |
| | MCV | 1 | fl |
| | MCH | 1 | pg |
| | MCHC | 1 | g/dl |
| | Platelet | 0 | $\times 10^3/\mu l$ |
| | White blood cell | 2 | $\times 10^3/\mu l$ |
| | Differntial WBC | 0 | % |
| BIOCHEMISTRY | Total protein | 1 | g/dl |
| | Albumin | 1 | g/dl |
| | A/G ratio | 1 | |
| | T-bilirubin | 2 | mg/dl |
| | Glucose | 0 | mg/dl |
| | T-cholesterol | 0 | mg/dl |
| | Triglyceride | 0 | mg/dl |
| | Phospholipid | 0 | mg/dl |
| | GOT | 0 | IU/l |
| | GPT | 0 | IU/l |
| | LDH | 0 | IU/l |
| | ALP | 0 | IU/l |
| | $\gamma$ -GTP | 0 | IU/l |
| | CPK | 0 | IU/l |
| | Urea nitrogen | 1 | mg/dl |
| | Creatinine | 1 | mg/dl |
| | Sodium | 0 | mEq/l |
| | Potassium | 1 | mEq/l |
| | Chloride | 0 | mEq/l |
| | Calcium | 1 | mg/dl |
| | Inorganic phosphorus | 1 | mg/dl |