キノリンのマウスを用いた経口投与による
13 週 間 毒 性 試 験（混 水 試 験）報 告 書

試験番号：０２９０

# APPENDIX

# APPENDIXES

# APPENDIXES (CONTINUED)

# APPENDIXES (CONTINUED)

# APPENDIX A 1

## CLINICAL OBSERVATION : SUMMARY, MOUSE : FEMALE

## (13 - WEEK STUDY)

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : 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 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| PILOERECTION | Control | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 237 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 355 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 533 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 800 ppm | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 1200 ppm | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 3 | 0 | 0 | 0 | 0 | 0 |

APPENDIX B 1

BODY WEIGHT CHANGES :SUMMARY, MOUSE : MALE

(13 - WEEK STUDY)

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week 0 | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|---|
| Control | 23.1± 0.8 | 24.3± 0.9 | 25.2± 1.1 | 26.5± 1.4 | 27.0± 1.6 | 27.9± 1.8 | 29.1± 2.0 |
| 237 ppm | 23.1± 0.7 | 24.5± 0.9 | 25.3± 1.0 | 26.7± 1.2 | 26.9± 1.3 | 28.2± 1.3 | 29.4± 1.6 |
| 355 ppm | 23.1± 0.8 | 23.8± 0.8 | 24.6± 1.0 | 25.7± 0.9 | 26.0± 1.1 | 26.8± 1.3 | 27.3± 1.4 |
| 533 ppm | 23.1± 0.8 | 23.6± 1.4 | 24.2± 1.7 | 25.1± 1.2* | 25.5± 1.0* | 26.4± 1.1* | 27.1± 0.8 |
| 800 ppm | 23.1± 0.8 | 23.0± 0.6* | 23.9± 0.8 | 24.5± 0.8** | 24.8± 0.6** | 25.5± 0.7** | 25.7± 0.8** |
| 1200 ppm | 23.1± 0.8 | 21.3± 1.0** | 21.8± 1.3** | 22.5± 1.2** | 22.8± 0.9** | 23.3± 0.8** | 24.0± 0.7** |

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

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week 7 | 8 | 9 | 10 | 11 | 12 | 13 |
|---|---|---|---|---|---|---|---|
| Control | 30.0± 2.0 | 31.0± 2.1 | 31.5± 2.1 | 32.9± 2.3 | 33.3± 2.5 | 34.3± 2.5 | 35.1± 2.6 |
| 237 ppm | 30.1± 1.9 | 31.1± 2.0 | 31.8± 2.4 | 33.1± 2.2 | 33.7± 2.7 | 34.3± 2.6 | 35.4± 3.0 |
| 355 ppm | 28.0± 1.5 | 28.7± 1.6 | 29.2± 1.7 | 30.5± 1.8 | 30.6± 1.9 | 31.2± 2.1 | 32.0± 2.2 |
| 533 ppm | 27.3± 0.9 | 28.0± 0.6 | 28.4± 0.9 | 29.2± 0.9 | 29.7± 1.0 | 30.2± 1.0 | 30.8± 1.4 |
| 800 ppm | 25.9± 1.1** | 26.3± 1.0** | 26.4± 1.0** | 27.1± 1.3** | 27.2± 1.2** | 27.4± 1.3** | 27.9± 1.2** |
| 1200 ppm | 23.9± 0.6** | 24.1± 0.5** | 24.3± 0.5** | 24.4± 0.5** | 24.7± 0.7** | 24.6± 0.7** | 24.9± 0.7** |

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

APPENDIX B 2

BODY WEIGHT CHANGES : SUMMARY, MOUSE : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week 0 | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|---|
| Control | 18.9± 0.6 | 19.0± 0.8 | 19.7± 0.9 | 20.7± 0.6 | 21.0± 1.1 | 21.5± 0.7 | 22.1± 1.1 |
| 237 ppm | 18.9± 0.6 | 19.3± 0.5 | 20.1± 0.6 | 21.2± 1.0 | 20.9± 0.6 | 21.5± 0.8 | 22.4± 0.8 |
| 355 ppm | 18.9± 0.6 | 19.2± 0.8 | 20.1± 0.9 | 21.5± 0.9 | 20.7± 0.8 | 21.2± 0.7 | 22.4± 0.8 |
| 533 ppm | 18.9± 0.6 | 19.4± 0.5 | 20.0± 0.9 | 20.8± 0.6 | 20.8± 0.6 | 21.9± 0.7 | 22.2± 0.6 |
| 800 ppm | 18.9± 0.7 | 19.1± 0.6 | 19.9± 0.8 | 20.4± 0.5 | 20.4± 0.8 | 21.0± 0.8 | 22.0± 0.8 |
| 1200 ppm | 18.9± 0.6 | 17.2± 1.1** | 17.8± 1.1** | 19.0± 1.2** | 19.2± 1.4** | 20.0± 1.1** | 20.5± 1.1** |

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

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week 7 | 8 | 9 | 10 | 11 | 12 | 13 |
|---|---|---|---|---|---|---|---|
| Control | 22.1± 0.8 | 22.7± 1.3 | 23.1± 1.1 | 24.2± 1.5 | 23.1± 1.0 | 23.9± 1.1 | 24.7± 1.6 |
| 237 ppm | 23.1± 1.1 | 23.3± 1.1 | 23.5± 0.8 | 23.5± 0.7 | 23.8± 0.9 | 24.7± 1.0 | 24.7± 0.7 |
| 355 ppm | 22.6± 0.9 | 23.0± 0.8 | 23.4± 1.1 | 23.9± 0.9 | 23.3± 1.1 | 23.6± 1.0 | 23.9± 0.9 |
| 533 ppm | 22.6± 0.7 | 22.9± 1.2 | 23.1± 0.7 | 23.4± 0.8 | 23.3± 0.9 | 23.6± 0.8 | 24.1± 1.1 |
| 800 ppm | 21.7± 0.8 | 22.3± 1.0 | 22.5± 0.8 | 23.1± 0.7 | 23.0± 1.3 | 23.1± 0.9 | 23.8± 1.1 |
| 1200 ppm | 21.0± 0.9* | 21.2± 1.0** | 21.6± 0.7** | 22.1± 0.9** | 22.0± 0.7 | 22.3± 0.8** | 22.7± 0.8** |

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

APPENDIX C 1

# WATER CONSUMPTION CHANGES : SUMMARY, MOUSE : MALE

(13 - WEEK STUDY)

STUDY NO. : 0290
ANIMAL : Crj:BDF$_1$ MOUSE
UNIT : g
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

| Group Name | Administration week | | | | | | |
|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| Control | 4.4 | 4.5 | 4.6 | 5.0 | 4.5 | 5.0 | 5.1 |
| 237ppm | 4.2 | 4.3 | 4.2 | 4.7 | 5.0 | 5.3 | 5.7 |
| 355ppm | 3.6 | 3.6 | 3.3 | 3.3 | 3.2 | 3.1 | 3.3 |
| 533ppm | 3.1 | 2.9 | 2.8 | 2.9 | 3.0 | 3.0 | 3.1 |
| 800ppm | 2.3 | 2.1 | 1.9 | 2.0 | 2.1 | 2.3 | 2.2 |
| 1200ppm | 2.0 | 1.5 | 4.7 | 1.6 | 1.7 | 1.7 | 2.5 |

| Group Name | Administration week | | | | | |
|---|---|---|---|---|---|---|
| | 8 | 9 | 10 | 11 | 12 | 13 |
| Control | 5.0 | 5.2 | 5.9 | 5.2 | 5.2 | 5.6 |
| 237ppm | 5.8 | 5.8 | 5.3 | 5.6 | 7.4 | 4.8 |
| 355ppm | 4.1 | 4.2 | 4.4 | 4.0 | 4.0 | 3.8 |
| 533ppm | 3.2 | 3.2 | 3.1 | 2.9 | 3.0 | 2.8 |
| 800ppm | 2.2 | 7.1 | 2.2 | 2.1 | 3.1 | 2.0 |
| 1200ppm | 5.3 | 2.1 | 1.9 | 1.8 | 1.8 | 1.8 |

# APPENDIX C 2

# WATER CONSUMPTION CHANGES : SUMMARY, MOUSE : FEMALE

# (13 - WEEK STUDY)

STUDY NO. : 0290
ANIMAL : Crj:BDF$_1$ MOUSE
UNIT : g
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

| Group Name | Administration week | | | | | | |
|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| Control | 5.0 | 10.8 | 5.2 | 5.2 | 4.7 | 4.3 | 4.2 |
| 237ppm | 4.2 | 4.2 | 4.0 | 4.2 | 4.4 | 4.3 | 4.6 |
| 355ppm | 3.6 | 3.6 | 3.3 | 3.3 | 3.2 | 3.1 | 3.3 |
| 533ppm | 3.0 | 2.6 | 2.4 | 2.5 | 2.4 | 2.3 | 2.5 |
| 800ppm | 8.5 | 5.1 | 3.7 | 2.7 | 1.9 | 1.9 | 1.9 |
| 1200ppm | 1.6 | 1.4 | 1.2 | 1.3 | 1.2 | 1.3 | 1.3 |

| Group Name | Administration week | | | | | |
|---|---|---|---|---|---|---|
| | 8 | 9 | 10 | 11 | 12 | 13 |
| Control | 3.7 | 3.9 | 4.0 | 4.0 | 3.8 | 3.8 |
| 237ppm | 4.0 | 4.3 | 3.8 | 3.7 | 3.5 | 3.5 |
| 355ppm | 3.1 | 3.2 | 3.1 | 3.0 | 2.9 | 2.9 |
| 533ppm | 2.3 | 23.0 | 2.3 | 2.2 | 2.2 | 2.1 |
| 800ppm | 1.8 | 1.8 | 4.8 | 1.8 | 1.7 | 1.7 |
| 1200ppm | 1.3 | 1.3 | 1.3 | 1.3 | 1.2 | 1.2 |

APPENDIX D 1

FOOD CONSUMPTION CHANGES : SUMMARY, MOUSE : MALE

(13 - WEEK STUDY)

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| Control | 3.7± 0.1 | 3.7± 0.3 | 3.8± 0.3 | 3.7± 0.3 | 3.7± 0.3 | 3.8± 0.3 | 3.8± 0.3 |
| 237 ppm | 3.8± 0.2 | 3.7± 0.2 | 3.8± 0.2 | 3.8± 0.2 | 3.9± 0.2 | 3.9± 0.3 | 3.8± 0.2 |
| 355 ppm | 3.6± 0.2 | 3.6± 0.2 | 3.5± 0.2 | 3.6± 0.2 | 3.6± 0.2 | 3.6± 0.2 | 3.5± 0.2 |
| 533 ppm | 3.6± 0.3 | 3.3± 0.4* | 3.4± 0.2** | 3.4± 0.2* | 3.5± 0.2* | 3.5± 0.1** | 3.4± 0.2** |
| 800 ppm | 3.4± 0.2* | 3.3± 0.2** | 3.3± 0.1** | 3.4± 0.1** | 3.4± 0.2** | 3.3± 0.3** | 3.2± 0.3** |
| 1200 ppm | 3.0± 0.3** | 3.2± 0.3** | 3.2± 0.3** | 3.4± 0.2** | 3.3± 0.2** | 3.4± 0.3** | 3.3± 0.3** |

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

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week 8 | 9 | 10 | 11 | 12 | 13 |
|---|---|---|---|---|---|---|
| Control | 3.9± 0.3 | 3.8± 0.2 | 4.0± 0.3 | 3.9± 0.3 | 3.9± 0.3 | 3.8± 0.2 |
| 237 ppm | 4.1± 0.3 | 4.0± 0.4 | 4.0± 0.3 | 4.0± 0.3 | 3.9± 0.3 | 3.9± 0.3 |
| 355 ppm | 3.8± 0.2 | 3.6± 0.3 | 3.7± 0.2 | 3.7± 0.2 | 3.7± 0.3 | 3.7± 0.2 |
| 533 ppm | 3.5± 0.1** | 3.4± 0.1** | 3.6± 0.2** | 3.5± 0.2** | 3.5± 0.2** | 3.4± 0.2** |
| 800 ppm | 3.3± 0.2** | 3.2± 0.2** | 3.4± 0.1** | 3.3± 0.2** | 3.3± 0.2** | 3.2± 0.2** |
| 1200 ppm | 3.3± 0.3** | 3.2± 0.2** | 3.4± 0.3** | 3.3± 0.3** | 3.3± 0.3** | 3.3± 0.3** |

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

APPENDIX D 2

FOOD CONSUMPTION CHANGES : SUMMARY, MOUSE : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| Control | 3.0± 0.2 | 3.2± 0.2 | 3.4± 0.2 | 3.4± 0.2 | 3.6± 0.2 | 3.7± 0.2 | 3.6± 0.2 |
| 237 ppm | 3.1± 0.2 | 3.3± 0.1 | 3.4± 0.2 | 3.4± 0.2 | 3.6± 0.2 | 3.8± 0.1 | 3.8± 0.2 |
| 355 ppm | 3.1± 0.2 | 3.4± 0.2 | 3.4± 0.2 | 3.4± 0.2 | 3.5± 0.2 | 3.7± 0.2 | 3.6± 0.2 |
| 533 ppm | 3.1± 0.2 | 3.1± 0.1 | 3.2± 0.2 | 3.3± 0.2 | 3.5± 0.1 | 3.5± 0.2 | 3.5± 0.2 |
| 800 ppm | 2.9± 0.2 | 3.0± 0.2 | 3.1± 0.2* | 3.1± 0.2** | 3.3± 0.2* | 3.4± 0.2** | 3.3± 0.1** |
| 1200 ppm | 2.6± 0.2** | 2.7± 0.2** | 3.0± 0.3** | 2.9± 0.3** | 3.1± 0.2** | 3.2± 0.3** | 3.2± 0.2** |

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

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS



| Group Name | Administration week 8 | 9 | 10 | 11 | 12 | 13 |
|---|---|---|---|---|---|---|
| Control | 3.7± 0.3 | 3.7± 0.3 | 3.9± 0.3 | 3.6± 0.2 | 3.8± 0.2 | 3.8± 0.3 |
| 237 ppm | 3.7± 0.3 | 3.7± 0.2 | 3.8± 0.2 | 3.8± 0.2* | 3.8± 0.1 | 3.7± 0.2 |
| 355 ppm | 3.7± 0.2 | 3.8± 0.1 | 3.7± 0.2 | 3.6± 0.2 | 3.6± 0.1 | 3.6± 0.2 |
| 533 ppm | 3.5± 0.2 | 3.5± 0.1 | 3.6± 0.1 | 3.6± 0.2 | 3.6± 0.2 | 3.5± 0.2* |
| 800 ppm | 3.3± 0.1** | 3.5± 0.1 | 3.4± 0.1** | 3.5± 0.2 | 3.5± 0.2** | 3.5± 0.3* |
| 1200 ppm | 3.2± 0.2** | 3.3± 0.2** | 3.3± 0.2** | 3.3± 0.2** | 3.3± 0.2** | 3.4± 0.1** |

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

# APPENDIX E 1

## CHEMICAL INTAKE CHANGES : SUMMARY, MOUSE : MALE

## (13 - WEEK STUDY)

STUDY NO. : 0290
ANIMAL : Crj:BDF$_1$ MOUSE
UNIT : mg/kg/day
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

| Group Name | Administration (weeks) | | | | | | |
|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| Control | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 237ppm | 40.5 | 39.3 | 35.9 | 37.0 | 37.1 | 34.4 | 35.9 |
| 355ppm | 53.3 | 52.4 | 45.0 | 44.7 | 42.4 | 40.1 | 42.2 |
| 533ppm | 67.1 | 57.9 | 51.3 | 52.3 | 47.9 | 45.5 | 48.8 |
| 800ppm | 295.2 | 170.2 | 122.2 | 88.5 | 59.2 | 57.8 | 59.6 |
| 1200ppm | 90.1 | 75.5 | 66.3 | 69.2 | 62.5 | 65.7 | 66.7 |

| Group Name | Administration (weeks) | | | | | |
|---|---|---|---|---|---|---|
| | 8 | 9 | 10 | 11 | 12 | 13 |
| Control | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 237ppm | 30.7 | 32.3 | 27.2 | 26.2 | 24.3 | 23.2 |
| 355ppm | 38.7 | 37.7 | 36.2 | 34.8 | 33.5 | 31.9 |
| 533ppm | 44.6 | 44.0 | 42.2 | 39.7 | 39.3 | 35.8 |
| 800ppm | 56.1 | 54.1 | 53.1 | 52.5 | 50.1 | 48.7 |
| 1200ppm | 64.7 | 64.9 | 63.2 | 61.8 | 60.6 | 59.2 |

# APPENDIX E 2

## CHEMICAL INTAKE CHANGES : SUMMARY, MOUSE : FEMALE

## (13 - WEEK STUDY)

STUDY NO. : 0290
ANIMAL : Crj:BDF$_1$ MOUSE
UNIT : mg/kg/day
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

| Group Name | Administration (weeks) 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| Control | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 237ppm | 51.9 | 51.2 | 47.4 | 53.6 | 55.6 | 56.5 | 58.6 |
| 355ppm | 66.8 | 74.9 | 63.5 | 62.7 | 62.9 | 65.0 | 64.4 |
| 533ppm | 86.3 | 78.0 | 70.7 | 75.4 | 73.0 | 72.0 | 73.8 |
| 800ppm | 94.5 | 83.3 | 75.6 | 79.6 | 80.5 | 82.1 | 79.5 |
| 1200ppm | 141.5 | 102.1 | 299.5 | 98.2 | 100.3 | 102.0 | 141.2 |

| Group Name | Administration (weeks) 8 | 9 | 10 | 11 | 12 | 13 |
|---|---|---|---|---|---|---|
| Control | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| 237ppm | 59.1 | 58.2 | 53.7 | 55.6 | 71.1 | 46.2 |
| 355ppm | 63.1 | 64.4 | 65.1 | 61.4 | 59.5 | 56.4 |
| 533ppm | 74.1 | 73.2 | 70.6 | 66.7 | 67.1 | 62.6 |
| 800ppm | 78.9 | 251.4 | 75.2 | 73.0 | 105.9 | 67.2 |
| 1200ppm | 300.8 | 116.7 | 103.2 | 99.0 | 97.6 | 95.9 |

# APPENDIX F 1

## HEMATOLOGY : SUMMARY, MOUSE : MALE

## (13 - WEEK STUDY)

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS ( 14W)



| 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 | 8 | 10.77± 0.19 | 16.1± 0.3 | 49.0± 1.1 | 45.5± 0.5 | 15.0± 0.3 | 32.9± 0.7 | 1385± 75 |
| 237 ppm | 9 | 10.51± 0.45 | 15.9± 0.2 | 48.4± 1.4 | 46.1± 1.0 | 15.1± 0.7 | 32.8± 1.0 | 1391± 128 |
| 355 ppm | 8 | 10.56± 0.48 | 16.0± 0.5 | 48.3± 2.4 | 45.7± 0.4 | 15.2± 0.6 | 33.2± 1.4 | 1453± 60 |
| 533 ppm | 7 | 10.96± 0.29 | 16.1± 0.4 | 49.7± 1.3 | 45.4± 0.7 | 14.7± 0.3 | 32.4± 0.4 | 1516± 79* |
| 800 ppm | 8 | 10.76± 0.28 | 16.1± 0.4 | 49.7± 1.2 | 46.1± 0.5 | 15.0± 0.3 | 32.5± 0.3 | 1436± 87 |
| 1200 ppm | 8 | 10.45± 0.44 | 15.9± 0.5 | 47.7± 2.0 | 45.7± 0.3 | 15.2± 0.5 | 33.3± 1.0 | 1339± 72 |

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

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS ( 14W)



| Group Name | NO. of Animals | WBC $10^3/\mu\ell$ | Differential WBC (%) N-BAND | N-SEG | EOSINO | BASO | MONO | LYMPHO | OTHERS |
|---|---|---|---|---|---|---|---|---|---|
| Control | 8 | 1.48± 0.46 | 0± 0 | 12± 2 | 1± 1 | 0± 0 | 3± 1 | 85± 3 | 0± 0 |
| 237 ppm | 9 | 1.43± 0.47 | 0± 0 | 12± 4 | 1± 1 | 0± 0 | 3± 2 | 85± 6 | 0± 0 |
| 355 ppm | 8 | 1.45± 0.45 | 0± 0 | 13± 4 | 1± 1 | 0± 0 | 3± 2 | 84± 5 | 0± 0 |
| 533 ppm | 7 | 1.15± 0.20 | 0± 0 | 14± 2 | 1± 1 | 0± 0 | 3± 1 | 83± 1 | 0± 0 |
| 800 ppm | 8 | 1.36± 0.66 | 0± 0 | 10± 2 | 1± 1 | 0± 0 | 2± 1 | 88± 3 | 0± 0 |
| 1200 ppm | 8 | 0.79± 0.42* | 0± 0 | 12± 4 | 0± 0 | 0± 0 | 2± 1 | 86± 5 | 0± 0 |

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

(HCL070)

# APPENDIX F 2

## HEMATOLOGY : SUMMARY, MOUSE : FEMALE

## (13 - WEEK STUDY)

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS ( 14W)



| 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 | 8 | 10.70± 0.12 | 16.1± 0.4 | 48.9± 0.7 | 45.7± 0.7 | 15.0± 0.3 | 32.9± 0.6 | 1231± 67 |
| 237 ppm | 10 | 10.52± 0.52 | 16.4± 0.4 | 48.2± 2.5 | 45.9± 0.4 | 15.6± 0.7 | 34.0± 1.6 | 1166± 146 |
| 355 ppm | 8 | 10.53± 0.29 | 16.2± 0.5 | 48.9± 1.3 | 46.5± 0.4 | 15.3± 0.3 | 33.0± 0.7 | 1201± 179 |
| 533 ppm | 10 | 10.45± 0.35 | 16.2± 0.5 | 48.7± 1.7 | 46.6± 0.7** | 15.5± 0.3** | 33.3± 0.5 | 1139± 243 |
| 800 ppm | 7 | 10.47± 0.32 | 16.1± 0.5 | 48.9± 2.0 | 46.7± 0.7** | 15.4± 0.1 | 32.9± 0.7 | 1160± 47 |
| 1200 ppm | 8 | 10.33± 0.28 | 16.0± 0.3 | 47.9± 1.5 | 46.4± 0.5 | 15.5± 0.3* | 33.5± 0.6 | 1228± 52 |

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

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS ( 14W)



| Group Name | NO. of Animals | WBC $10^3/\mu\ell$ | Differential WBC (%) N-BAND | N-SEG | EOSINO | BASO | MONO | LYMPHO | OTHERS |
|---|---|---|---|---|---|---|---|---|---|
| Control | 8 | 1.52± 0.79 | 0± 0 | 13± 5 | 1± 1 | 0± 0 | 3± 1 | 83± 4 | 0± 0 |
| 237 ppm | 10 | 1.47± 0.76 | 0± 0 | 11± 4 | 1± 1 | 0± 0 | 2± 1 | 86± 4 | 0± 0 |
| 355 ppm | 8 | 1.17± 0.86 | 0± 0 | 14± 4 | 1± 1 | 0± 0 | 3± 1 | 83± 4 | 0± 0 |
| 533 ppm | 10 | 1.32± 0.83 | 0± 0 | 12± 3 | 1± 1 | 0± 0 | 2± 1 | 85± 4 | 0± 0 |
| 800 ppm | 7 | 1.31± 0.64 | 0± 0 | 14± 5 | 0± 1 | 0± 0 | 2± 1 | 84± 6 | 0± 0 |
| 1200 ppm | 8 | 0.94± 0.76 | 1± 1 | 15± 5 | 0± 1 | 0± 0 | 2± 1 | 82± 5 | 0± 0 |

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

(HCL070)

APPENDIX G 1

BIOCHEMISTRY : SUMMARY, MOUSE : MALE

(13 - WEEK STUDY)

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS ( 14W)



| 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 | 5.3± | 0.1 | 2.9± | 0.1 | 1.3± | 0.1 | 0.22± | 0.04 | 232± | 42 | 88± | 5 | 48± | 13 |
| 237 ppm | 9 | 5.4± | 0.3 | 3.0± | 0.2 | 1.3± | 0.1 | 0.21± | 0.02 | 221± | 46 | 88± | 8 | 48± | 10 |
| 355 ppm | 9 | 5.4± | 0.3 | 3.0± | 0.1 | 1.3± | 0.1 | 0.21± | 0.02 | 215± | 25 | 87± | 5 | 41± | 8 |
| 533 ppm | 7 | 5.4± | 0.2 | 3.0± | 0.1 | 1.3± | 0.1 | 0.20± | 0.02 | 230± | 33 | 85± | 4 | 37± | 6 |
| 800 ppm | 8 | 5.1± | 0.3 | 2.9± | 0.2 | 1.4± | 0.1 | 0.21± | 0.01 | 218± | 45 | 81± | 8 | 31± | 12** |
| 1200 ppm | 8 | 4.8± | 0.3** | 2.8± | 0.2 | 1.4± | 0.1** | 0.22± | 0.02 | 197± | 34 | 77± | 14* | 20± | 4** |

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

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS ( 14W)



| 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 | 175± 9 | 44± 5 | 17± 2 | 221± 44 | 162± 10 | 2± 1 | 67± 23 |
| 237 ppm | 9 | 181± 21 | 45± 6 | 19± 2 | 219± 27 | 165± 19 | 2± 1 | 77± 35 |
| 355 ppm | 9 | 178± 12 | 44± 4 | 17± 2 | 214± 29 | 176± 12 | 2± 1 | 62± 15 |
| 533 ppm | 7 | 174± 9 | 43± 5 | 17± 3 | 206± 48 | 200± 23** | 1± 1 | 56± 9 |
| 800 ppm | 8 | 169± 18 | 47± 9 | 20± 7 | 244± 76 | 198± 16** | 2± 1 | 113± 86 |
| 1200 ppm | 8 | 149± 29* | 50± 11 | 21± 4 | 227± 62 | 201± 20** | 1± 1 | 105± 67 |

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

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS ( 14W)



| Group Name | NO. of Animals | UREA NITROGEN mg/dℓ | SODIUM mEq/ℓ | POTASSIUM mEq/ℓ | CHLORIDE mEq/ℓ | CALCIUM mg/dℓ | INORGANIC PHOSPHORUS mg/dℓ |
|---|---|---|---|---|---|---|---|
| Control | 9 | 25.0± 2.5 | 154± 2 | 4.7± 0.5 | 123± 2 | 8.9± 0.3 | 6.9± 0.9 |
| 237 ppm | 9 | 23.7± 2.8 | 154± 1 | 4.8± 0.6 | 123± 2 | 9.0± 0.2 | 7.6± 1.3 |
| 355 ppm | 9 | 27.2± 3.9 | 154± 1 | 4.7± 0.4 | 123± 2 | 8.9± 0.2 | 6.4± 0.9 |
| 533 ppm | 7 | 26.3± 4.7 | 154± 1 | 4.6± 0.5 | 123± 3 | 9.0± 0.2 | 6.4± 1.0 |
| 800 ppm | 8 | 23.5± 3.8 | 154± 2 | 4.9± 0.7 | 123± 2 | 8.9± 0.2 | 6.5± 1.2 |
| 1200 ppm | 8 | 25.8± 2.2 | 155± 1 | 4.8± 0.6 | 123± 2 | 8.6± 0.3 | 7.2± 1.0 |

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

APPENDIX G 2

BIOCHEMISTRY : SUMMARY, MOUSE : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS ( 14W)



| 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 | 5.3± | 0.1 | 3.2± | 0.1 | 1.5± | 0.1 | 0.23± | 0.08 | 173± | 26 | 80± | 8 | 23± | 5 |
| 237 ppm | 10 | 5.4± | 0.1 | 3.3± | 0.1 | 1.5± | 0.0 | 0.20± | 0.02 | 179± | 22 | 78± | 11 | 17± | 5 |
| 355 ppm | 10 | 5.4± | 0.1 | 3.2± | 0.1 | 1.6± | 0.1 | 0.22± | 0.04 | 183± | 35 | 76± | 8 | 17± | 6 |
| 533 ppm | 10 | 5.3± | 0.1 | 3.2± | 0.1 | 1.5± | 0.1 | 0.21± | 0.03 | 176± | 15 | 78± | 10 | 18± | 7 |
| 800 ppm | 7 | 5.0± | 0.1** | 3.0± | 0.1* | 1.5± | 0.1 | 0.20± | 0.02 | 189± | 34 | 74± | 9 | 17± | 7 |
| 1200 ppm | 9 | 4.9± | 0.2** | 3.0± | 0.1** | 1.6± | 0.1 | 0.20± | 0.02 | 183± | 20 | 73± | 9 | 13± | 4** |

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

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS ( 14W)



| 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 | 157± 15 | 51± 7 | 20± 5 | 257± 98 | 246± 19 | 1± 1 | 156± 205 |
| 237 ppm | 10 | 148± 24 | 50± 7 | 22± 4 | 229± 47 | 260± 33 | 1± 1 | 83± 36 |
| 355 ppm | 10 | 143± 22 | 60± 9 | 25± 4 | 265± 49 | 276± 24 | 2± 1 | 163± 129 |
| 533 ppm | 10 | 146± 22 | 58± 8 | 25± 3 | 256± 61 | 285± 20 | 1± 1 | 74± 26 |
| 800 ppm | 7 | 132± 24 | 48± 5 | 24± 5 | 213± 31 | 267± 38 | 1± 1 | 71± 27 |
| 1200 ppm | 9 | 123± 26** | 54± 13 | 28± 8** | 232± 56 | 274± 35 | 1± 1 | 107± 47 |

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

(HCL074)

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS ( 14W)



| Group Name | NO. of Animals | UREA NITROGEN mg/dℓ | | SODIUM mEq/ℓ | | POTASSIUM mEq/ℓ | | CHLORIDE mEq/ℓ | | CALCIUM mg/dℓ | | INORGANIC PHOSPHORUS mg/dℓ | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Control | 9 | 21.8± | 1.6 | 152± | 1 | 4.8± | 0.4 | 123± | 1 | 8.8± | 0.2 | 5.9± | 1.0 |
| 237 ppm | 10 | 23.1± | 2.7 | 153± | 2 | 4.8± | 0.3 | 123± | 2 | 8.9± | 0.2 | 5.9± | 0.7 |
| 355 ppm | 10 | 23.5± | 2.7 | 154± | 2 | 5.0± | 0.6 | 125± | 2 | 8.9± | 0.2 | 6.1± | 1.1 |
| 533 ppm | 10 | 22.9± | 2.1 | 153± | 1 | 4.8± | 0.4 | 123± | 2 | 8.9± | 0.1 | 6.0± | 0.6 |
| 800 ppm | 7 | 22.7± | 5.5 | 153± | 1 | 4.4± | 0.3 | 123± | 2 | 8.8± | 0.2 | 5.6± | 0.5 |
| 1200 ppm | 9 | 26.9± | 5.5 | 153± | 2 | 4.5± | 0.4 | 122± | 3 | 8.6± | 0.3 | 6.6± | 0.9 |

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

(HCL074)

# APPENDIX H 1

## URINALYSIS : SUMMARY, MOUSE : MALE

## (13 - WEEK STUDY)

STUDY NO. : 0290 URINALYSIS
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1



| 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 | 0 | 2 | 6 | 2 | | 0 | 0 | 10 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | 0 | | 4 | 3 | 3 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | |
| 237 ppm | 10 | 0 | 0 | 0 | 0 | 1 | 8 | 1 | | 0 | 1 | 9 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | 0 | | 3 | 3 | 4 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | |
| 355 ppm | 10 | 0 | 0 | 0 | 0 | 4 | 6 | 0 | | 0 | 0 | 8 | 2 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | 0 | | 0 | 7 | 2 | 1 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | |
| 533 ppm | 10 | 0 | 0 | 1 | 3 | 2 | 4 | 0 | | 0 | 0 | 3 | 7 | 0 | 0 | ** | 10 | 0 | 0 | 0 | 0 | 0 | | 0 | 4 | 4 | 2 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | |
| 800 ppm | 10 | 0 | 0 | 3 | 6 | 0 | 1 | 0 | ** | 0 | 0 | 1 | 9 | 0 | 0 | ** | 10 | 0 | 0 | 0 | 0 | 0 | | 0 | 2 | 5 | 3 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | |
| 1200 ppm | 9 | 0 | 3 | 4 | 1 | 1 | 0 | 0 | ** | 0 | 0 | 4 | 5 | 0 | 0 | ** | 9 | 0 | 0 | 0 | 0 | 0 | | 0 | 4 | 4 | 1 | 0 | 0 | | 9 | 0 | 0 | 0 | 0 | |

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

STUDY NO. : 0290 URINALYSIS
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1 

| Group Name | NO. of Animals | Urobilinogen ± | + | 2+ | 3+ | 4+ | CHI |
|---|---|---|---|---|---|---|---|
| Control | 10 | 10 | 0 | 0 | 0 | 0 | |
| 237 ppm | 10 | 10 | 0 | 0 | 0 | 0 | |
| 355 ppm | 10 | 10 | 0 | 0 | 0 | 0 | |
| 533 ppm | 10 | 10 | 0 | 0 | 0 | 0 | |
| 800 ppm | 10 | 10 | 0 | 0 | 0 | 0 | |
| 1200 ppm | 9 | 9 | 0 | 0 | 0 | 0 | |

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

# APPENDIX H 2

## URINALYSIS : SUMMARY, MOUSE : FEMALE

## (13 - WEEK STUDY)

STUDY NO. : 0290 URINALYSIS
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1



| 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 | 3 | 0 | 4 | 3 | 0 | | 0 | 0 | 10 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | 0 | | 4 | 6 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | |
| 237 ppm | 10 | 0 | 0 | 2 | 0 | 1 | 7 | 0 | | 0 | 1 | 9 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | 0 | | 3 | 7 | 0 | 0 | 0 | 0 | | 10 | 0 | 0 | 0 | 0 | |
| 355 ppm | 10 | 0 | 0 | 0 | 3 | 4 | 3 | 0 | | 0 | 0 | 3 | 7 | 0 | 0 | ** | 10 | 0 | 0 | 0 | 0 | 0 | | 0 | 8 | 2 | 0 | 0 | 0 | * | 10 | 0 | 0 | 0 | 0 | |
| 533 ppm | 10 | 0 | 1 | 5 | 4 | 0 | 0 | 0 | * | 0 | 0 | 5 | 5 | 0 | 0 | ** | 10 | 0 | 0 | 0 | 0 | 0 | | 0 | 5 | 5 | 0 | 0 | 0 | * | 10 | 0 | 0 | 0 | 0 | |
| 800 ppm | 10 | 0 | 0 | 4 | 2 | 3 | 1 | 0 | | 0 | 1 | 0 | 9 | 0 | 0 | ** | 10 | 0 | 0 | 0 | 0 | 0 | | 0 | 2 | 7 | 1 | 0 | 0 | ** | 10 | 0 | 0 | 0 | 0 | |
| 1200 ppm | 10 | 0 | 1 | 2 | 5 | 1 | 1 | 0 | | 0 | 0 | 1 | 9 | 0 | 0 | ** | 10 | 0 | 0 | 0 | 0 | 0 | | 0 | 4 | 4 | 2 | 0 | 0 | * | 10 | 0 | 0 | 0 | 0 | |

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

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

URINALYSIS



| Group Name | NO. of Animals | Urobilinogen ± | + | 2+ | 3+ | 4+ | CHI |
|---|---|---|---|---|---|---|---|
| Control | 10 | 10 | 0 | 0 | 0 | 0 | |
| 237 ppm | 10 | 10 | 0 | 0 | 0 | 0 | |
| 355 ppm | 10 | 10 | 0 | 0 | 0 | 0 | |
| 533 ppm | 10 | 10 | 0 | 0 | 0 | 0 | |
| 800 ppm | 10 | 10 | 0 | 0 | 0 | 0 | |
| 1200 ppm | 10 | 10 | 0 | 0 | 0 | 0 | |

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

APPENDIX I 1

GROSS FINDINGS : SUMMARY, MOUSE : MALE ALL ANIMALS

(13 - WEEK STUDY)

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

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



| Organ | Findings | Group Name<br>NO. of Animals | Control<br>10 (%) | 237 ppm<br>10 (%) | 355 ppm<br>10 (%) | 533 ppm<br>10 (%) |
|---|---|---|---|---|---|---|
| spleen | black zone | | 0 ( 0) | 2 ( 20) | 0 ( 0) | 1 ( 10) |
| kidney | hydronephrosis | | 0 ( 0) | 0 ( 0) | 0 ( 0) | 1 ( 10) |

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

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



| Organ | Findings | Group Name<br>NO. of Animals | 800 ppm<br>10 (%) | 1200 ppm<br>10 (%) |
|---|---|---|---|---|
| spleen | black zone | | 1 ( 10) | 3 ( 30) |
| kidney | hydronephrosis | | 0 ( 0) | 0 ( 0) |

APPENDIX I 2

GROSS FINDINGS : SUMMARY, MOUSE : FEMALE ALL ANIMALS

(13 - WEEK STUDY)

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

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



| Organ | Findings | Group Name<br>NO. of Animals | Control<br>10 (%) | 237 ppm<br>10 (%) | 355 ppm<br>10 (%) | 533 ppm<br>10 (%) |
|---|---|---|---|---|---|---|
| spleen | black zone | | 1 ( 10) | 1 ( 10) | 2 ( 20) | 1 ( 10) |

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

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



| Organ | Findings | Group Name / NO. of Animals | 800 ppm 10 (%) | 1200 ppm 10 (%) |
|---|---|---|---|---|
| spleen | black zone | | 1 ( 10) | 0 ( 0) |

APPENDIX J 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOUSE : MALE

(13 - WEEK STUDY)

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

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



| Group Name | NO. of Animals | Body Weight | THYMUS | ADRENALS | TESTES | HEART | LUNGS |
|---|---|---|---|---|---|---|---|
| Control | 10 | 31.6± 2.6 | 0.041± 0.008 | 0.009± 0.001 | 0.227± 0.025 | 0.141± 0.013 | 0.163± 0.016 |
| 237 ppm | 10 | 31.7± 2.7 | 0.044± 0.007 | 0.007± 0.001 | 0.236± 0.024 | 0.144± 0.009 | 0.166± 0.022 |
| 355 ppm | 10 | 28.7± 2.1 | 0.035± 0.003 | 0.009± 0.003 | 0.216± 0.021 | 0.133± 0.011 | 0.160± 0.013 |
| 533 ppm | 10 | 27.7± 1.2 | 0.035± 0.008 | 0.008± 0.002 | 0.223± 0.026 | 0.130± 0.005 | 0.167± 0.013 |
| 800 ppm | 10 | 25.2± 1.1** | 0.031± 0.006** | 0.009± 0.001 | 0.234± 0.013 | 0.125± 0.004* | 0.159± 0.017 |
| 1200 ppm | 10 | 23.0± 0.7** | 0.028± 0.004** | 0.007± 0.001 | 0.224± 0.019 | 0.113± 0.005** | 0.153± 0.008 |

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

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

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



| Group Name | NO. of Animals | KIDNEYS | SPLEEN | LIVER | BRAIN |
|---|---|---|---|---|---|
| Control | 10 | 0.427± 0.018 | 0.049± 0.008 | 1.182± 0.080 | 0.448± 0.007 |
| 237 ppm | 10 | 0.431± 0.024 | 0.051± 0.007 | 1.286± 0.111* | 0.452± 0.013 |
| 355 ppm | 10 | 0.419± 0.026 | 0.047± 0.010 | 1.209± 0.107 | 0.442± 0.011 |
| 533 ppm | 10 | 0.507± 0.305 | 0.047± 0.009 | 1.196± 0.065 | 0.442± 0.012 |
| 800 ppm | 10 | 0.407± 0.019 | 0.042± 0.005 | 1.138± 0.060 | 0.446± 0.009 |
| 1200 ppm | 10 | 0.386± 0.015** | 0.038± 0.005* | 1.009± 0.048** | 0.441± 0.017 |

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

# APPENDIX J 2

## ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOUSE : FEMALE

## (13 - WEEK STUDY)

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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



| Group Name | NO. of Animals | Body Weight | THYMUS | ADRENALS | OVARIES | HEART | LUNGS |
|---|---|---|---|---|---|---|---|
| Control | 10 | 21.1± 1.3 | 0.042± 0.004 | 0.011± 0.001 | 0.029± 0.007 | 0.118± 0.005 | 0.160± 0.011 |
| 237 ppm | 10 | 21.2± 0.6 | 0.040± 0.004 | 0.009± 0.003 | 0.026± 0.004 | 0.118± 0.004 | 0.163± 0.013 |
| 355 ppm | 10 | 20.6± 1.0 | 0.040± 0.005 | 0.009± 0.002 | 0.026± 0.006 | 0.118± 0.008 | 0.162± 0.010 |
| 533 ppm | 10 | 20.8± 0.7 | 0.037± 0.006 | 0.009± 0.002 | 0.025± 0.004 | 0.115± 0.005 | 0.161± 0.009 |
| 800 ppm | 10 | 21.3± 1.0 | 0.038± 0.007 | 0.009± 0.002 | 0.022± 0.002* | 0.114± 0.009 | 0.155± 0.010 |
| 1200 ppm | 10 | 20.4± 0.8 | 0.033± 0.005** | 0.008± 0.001 | 0.022± 0.004* | 0.106± 0.010** | 0.145± 0.011* |

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

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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



| Group Name | NO. of Animals | KIDNEYS | SPLEEN | LIVER | BRAIN |
|---|---|---|---|---|---|
| Control | 10 | 0.286± 0.017 | 0.056± 0.008 | 0.929± 0.053 | 0.456± 0.016 |
| 237 ppm | 10 | 0.300± 0.010 | 0.058± 0.007 | 0.962± 0.048 | 0.465± 0.010 |
| 355 ppm | 10 | 0.309± 0.018** | 0.055± 0.006 | 0.950± 0.050 | 0.455± 0.014 |
| 533 ppm | 10 | 0.319± 0.016** | 0.055± 0.008 | 0.952± 0.062 | 0.453± 0.012 |
| 800 ppm | 10 | 0.336± 0.015** | 0.059± 0.012 | 1.014± 0.069* | 0.452± 0.010 |
| 1200 ppm | 10 | 0.331± 0.009** | 0.051± 0.004 | 0.935± 0.079 | 0.446± 0.014 |

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

# APPENDIX K 1

## ORGAN WEIGHT, RELATIVE : SUMMARY, MOUSE : MALE

## (13 - WEEK STUDY)

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

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



| Group Name | NO. of Animals | Body Weight (g) | THYMUS | ADRENALS | TESTES | HEART | LUNGS |
|---|---|---|---|---|---|---|---|
| Control | 10 | 31.6± 2.6 | 0.130± 0.021 | 0.028± 0.004 | 0.721± 0.070 | 0.447± 0.028 | 0.518± 0.063 |
| 237 ppm | 10 | 31.7± 2.7 | 0.137± 0.016 | 0.023± 0.005 | 0.747± 0.070 | 0.456± 0.034 | 0.524± 0.043 |
| 355 ppm | 10 | 28.7± 2.1 | 0.122± 0.015 | 0.031± 0.009 | 0.755± 0.053 | 0.464± 0.031 | 0.562± 0.053 |
| 533 ppm | 10 | 27.7± 1.2 | 0.127± 0.028 | 0.029± 0.007 | 0.808± 0.092* | 0.471± 0.027 | 0.605± 0.038** |
| 800 ppm | 10 | 25.2± 1.1** | 0.125± 0.019 | 0.035± 0.003* | 0.932± 0.045** | 0.498± 0.025** | 0.634± 0.067** |
| 1200 ppm | 10 | 23.0± 0.7** | 0.124± 0.019 | 0.031± 0.006 | 0.975± 0.068** | 0.492± 0.026** | 0.666± 0.028** |

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

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

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



| Group Name | NO. of Animals | KIDNEYS | SPLEEN | LIVER | BRAIN |
|---|---|---|---|---|---|
| Control | 10 | 1.359± 0.085 | 0.155± 0.024 | 3.750± 0.122 | 1.427± 0.114 |
| 237 ppm | 10 | 1.365± 0.083 | 0.162± 0.021 | 4.062± 0.176** | 1.433± 0.117 |
| 355 ppm | 10 | 1.467± 0.074 | 0.164± 0.033 | 4.220± 0.166** | 1.548± 0.112* |
| 533 ppm | 10 | 1.852± 1.180 | 0.169± 0.034 | 4.324± 0.156** | 1.600± 0.063** |
| 800 ppm | 10 | 1.622± 0.085** | 0.166± 0.020 | 4.523± 0.126** | 1.778± 0.104** |
| 1200 ppm | 10 | 1.683± 0.076** | 0.166± 0.019 | 4.392± 0.214** | 1.919± 0.083** |

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

# APPENDIX K 2

## ORGAN WEIGHT, RELATIVE : SUMMARY, MOUSE : FEMALE

## (13 - WEEK STUDY)

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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



| Group Name | NO. of Animals | Body Weight (g) | THYMUS | ADRENALS | OVARIES | HEART | LUNGS |
|---|---|---|---|---|---|---|---|
| Control | 10 | 21.1± 1.3 | 0.199± 0.022 | 0.050± 0.007 | 0.136± 0.032 | 0.560± 0.039 | 0.761± 0.064 |
| 237 ppm | 10 | 21.2± 0.6 | 0.188± 0.016 | 0.044± 0.012 | 0.122± 0.020 | 0.555± 0.026 | 0.768± 0.059 |
| 355 ppm | 10 | 20.6± 1.0 | 0.192± 0.021 | 0.046± 0.008 | 0.124± 0.025 | 0.574± 0.036 | 0.784± 0.032 |
| 533 ppm | 10 | 20.8± 0.7 | 0.179± 0.026 | 0.044± 0.009 | 0.118± 0.017 | 0.555± 0.025 | 0.775± 0.033 |
| 800 ppm | 10 | 21.3± 1.0 | 0.178± 0.033 | 0.044± 0.009 | 0.103± 0.011** | 0.536± 0.034 | 0.729± 0.054 |
| 1200 ppm | 10 | 20.4± 0.8 | 0.163± 0.026** | 0.039± 0.005 | 0.110± 0.020* | 0.523± 0.044 | 0.714± 0.048 |

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

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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



| Group Name | NO. of Animals | KIDNEYS | SPLEEN | LIVER | BRAIN |
|---|---|---|---|---|---|
| Control | 10 | 1.358± 0.091 | 0.263± 0.031 | 4.400± 0.169 | 2.167± 0.152 |
| 237 ppm | 10 | 1.418± 0.084 | 0.273± 0.028 | 4.534± 0.151 | 2.197± 0.101 |
| 355 ppm | 10 | 1.498± 0.085** | 0.264± 0.022 | 4.608± 0.155 | 2.212± 0.090 |
| 533 ppm | 10 | 1.532± 0.061** | 0.266± 0.040 | 4.571± 0.198 | 2.178± 0.094 |
| 800 ppm | 10 | 1.578± 0.079** | 0.277± 0.046 | 4.750± 0.213** | 2.123± 0.117 |
| 1200 ppm | 10 | 1.627± 0.051** | 0.249± 0.019 | 4.588± 0.311 | 2.192± 0.069 |

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

APPENDIX L 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : MALE : ALL ANIMALS

(13 - WEEK STUDY)

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

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



| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 10 1 (%) | Control 10 2 (%) | Control 10 3 (%) | Control 10 4 (%) | 237 ppm 10 1 (%) | 237 ppm 10 2 (%) | 237 ppm 10 3 (%) | 237 ppm 10 4 (%) | 355 ppm 10 1 (%) | 355 ppm 10 2 (%) | 355 ppm 10 3 (%) | 355 ppm 10 4 (%) | 533 ppm 10 1 (%) | 533 ppm 10 2 (%) | 533 ppm 10 3 (%) | 533 ppm 10 4 (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| nasal cavit | | <10> | 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) |
| | respiratory metaplasia:gland | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 10) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| spleen | | <10> | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | < 9> | 0 | 0 | 0 | <10> | 1 | 0 | 0 |
| | deposit of melanin | | ( 0) | ( 0) | ( 0) | ( 0) | ( 20) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 10) | ( 0) | ( 0) | ( 0) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| liver | | <10> | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | <10> | 0 | 0 | 0 | <10> | 0 | 0 | 0 |
| | granulation | | ( 0) | ( 0) | ( 0) | ( 0) | ( 10) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | | <10> | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | <10> | 0 | 0 | 0 | <10> | 0 | 1 | 0 |
| | basophilic change | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 10) | ( 0) |

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

| Organ | Findings | Group Name | 800 ppm | | | | 1200 ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 10 | | | | 10 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Respiratory system] | | | | | | | | | | |
| nasal cavit | | | <10> | | | | <10> | | | |
| | respiratory metaplasia:olfactory epithelium | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 10) | ( 0) | ( 0) | ( 0) |
| | respiratory metaplasia:gland | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| [Hematopoietic system] | | | | | | | | | | |
| spleen | | | <10> | | | | <10> | | | |
| | deposit of melanin | | 1 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| | | | ( 10) | ( 0) | ( 0) | ( 0) | ( 30) | ( 0) | ( 0) | ( 0) |
| [Digestive system] | | | | | | | | | | |
| liver | | | <10> | | | | <10> | | | |
| | granulation | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| [Urinary system] | | | | | | | | | | |
| kidney | | | <10> | | | | <10> | | | |
| | basophilic change | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |

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

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

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



| Organ | Findings | Group Name / No. of Animals on Study / Grade | Control 10 1 (%) | Control 10 2 (%) | Control 10 3 (%) | Control 10 4 (%) | 237 ppm 10 1 (%) | 237 ppm 10 2 (%) | 237 ppm 10 3 (%) | 237 ppm 10 4 (%) | 355 ppm 10 1 (%) | 355 ppm 10 2 (%) | 355 ppm 10 3 (%) | 355 ppm 10 4 (%) | 533 ppm 10 1 (%) | 533 ppm 10 2 (%) | 533 ppm 10 3 (%) | 533 ppm 10 4 (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| [Urinary system] | | | | | | | | | | | | | | | | | | |
| kidney | | | <10> | | | | <10> | | | | <10> | | | | <10> | | | |
| | vacuolization of proximal tubule | | 8 ( 80) | 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) ** |
| | hydronephrosis | | 0 ( 0) | 0 ( 0) | 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) |
| [Endocrine system] | | | | | | | | | | | | | | | | | | |
| adrenal | | | <10> | | | | <10> | | | | <10> | | | | <10> | | | |
| | 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) | 0 ( 0) | 0 ( 0) | 0 ( 0) | 0 ( 0) |

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

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

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



| Organ | Findings | Group Name | 800 ppm | | | | 1200 ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 10 | | | | 10 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Urinary system] | | | | | | | | | | |
| kidney | | | <10> | | | | <10> | | | |
| | vacuolization of proximal tubule | | 0 | 0 | 0 | 0 ** | 0 | 0 | 0 | 0 ** |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | hydronephrosis | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| [Endocrine system] | | | | | | | | | | |
| adrenal | | | <10> | | | | <10> | | | |
| | cyst | | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 10) | ( 0) | ( 0) |

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

APPENDIX L 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : FEMALE: ALL ANIMALS

(13 - WEEK STUDY)

| Organ | Findings | Group Name | Control | | | | 237 ppm | | | | 355 ppm | | | | 533 ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 10 | | | | 10 | | | | 10 | | | | 10 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Respiratory system] | | | | | | | | | | | | | | | | | | |
| nasal cavit | | | <10> | | | | <10> | | | | <10> | | | | <10> | | | |
| | respiratory metaplasia: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) |
| | atrophy:olfactory epithelium | | 0 | 0 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 40) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| [Hematopoietic system] | | | | | | | | | | | | | | | | | | |
| spleen | | | <10> | | | | <10> | | | | <10> | | | | <10> | | | |
| | deposit of melanin | | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | ( 10) | ( 0) | ( 0) | ( 0) | ( 10) | ( 0) | ( 0) | ( 0) | ( 20) | ( 0) | ( 0) | ( 0) | ( 10) | ( 0) | ( 0) | ( 0) |
| [Digestive system] | | | | | | | | | | | | | | | | | | |
| liver | | | <10> | | | | <10> | | | | <10> | | | | <10> | | | |
| | granulation | | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | ( 20) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 10) | ( 0) | ( 0) | ( 0) |
| [Endocrine system] | | | | | | | | | | | | | | | | | | |
| thyroid | | | <10> | | | | <10> | | | | <10> | | | | <10> | | | |
| | ectopic thymic tissue | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 10) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |

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

| Organ | Findings | Group Name | 800 ppm | | | | 1200 ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 10 | | | | 10 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Respiratory system] | | | | | | | | | | |
| nasal cavit | | | <10> | | | | <10> | | | |
| | respiratory metaplasia:gland | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 10) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| | atrophy:olfactory epithelium | | 0 | 3 | 0 | 0 | 1 | 1 | 0 | 0 |
| | | | ( 0) | ( 30) | ( 0) | ( 0) | ( 10) | ( 10) | ( 0) | ( 0) |
| [Hematopoietic system] | | | | | | | | | | |
| spleen | | | <10> | | | | <10> | | | |
| | deposit of melanin | | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 10) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |
| [Digestive system] | | | | | | | | | | |
| liver | | | <10> | | | | <10> | | | |
| | granulation | | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | ( 10) | ( 0) | ( 0) | ( 0) | ( 10) | ( 0) | ( 0) | ( 0) |
| [Endocrine system] | | | | | | | | | | |
| thyroid | | | <10> | | | | <10> | | | |
| | ectopic thymic tissue | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |

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

| Organ | Findings | Group Name | Control | | | | 237 ppm | | | | 355 ppm | | | | 533 ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 10 | | | | 10 | | | | 10 | | | | 10 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Endocrine system] | | | | | | | | | | | | | | | | | | |
| adrenal | | | <10> | | | | <10> | | | | <10> | | | | <10> | | | |
| | 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) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) | ( 0) |

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

STUDY NO. : 0290
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

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



| Organ | Findings | Group Name | 800 ppm | | | | 1200 ppm | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | No. of Animals on Study | 10 | | | | 10 | | | |
| | | Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| | | | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| [Endocrine system] | | | | | | | | | | |
| adrenal | | | <10> | | | | <10> | | | |
| | cyst | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| | | | ( 0) | ( 0) | ( 0) | ( 0) | ( 10) | ( 0) | ( 0) | ( 0) |

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

# APPENDIX M 1

# IDENTITY AND IMPURITY OF QUINOLINE IN THE 13 - WEEK DRINKING WATER STUDY

IDENTITY AND IMPURITY OF QUINOLINE IN THE 13-WEEK DRINKING WATER STUDY

Test Substance : Quinoline (Tokyo Kasei Kogyo Co., Ltd.)

Lot No. : FHD03

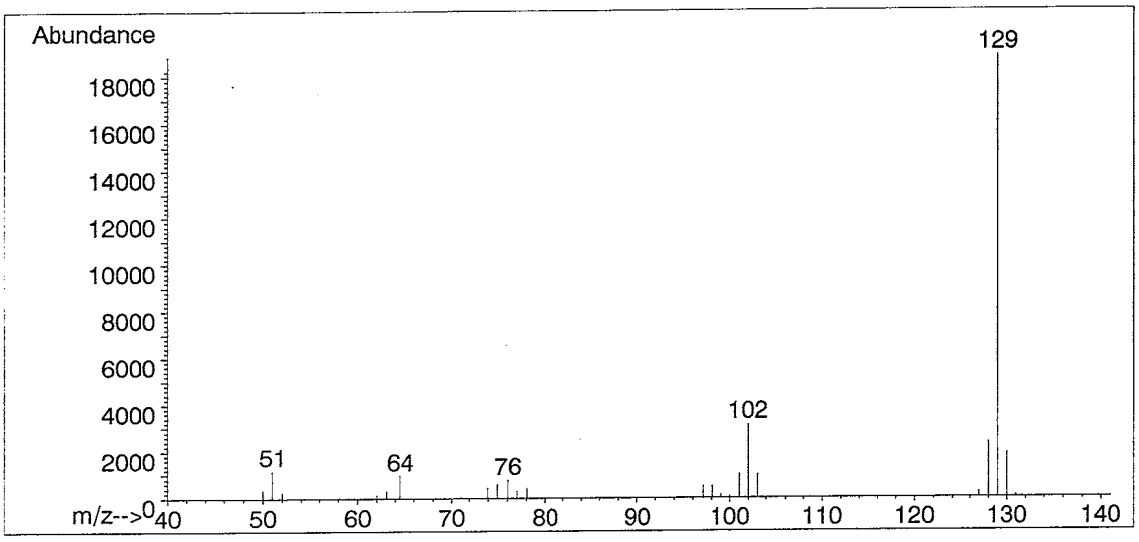
1. Spectral Data

Mass Spectrometry

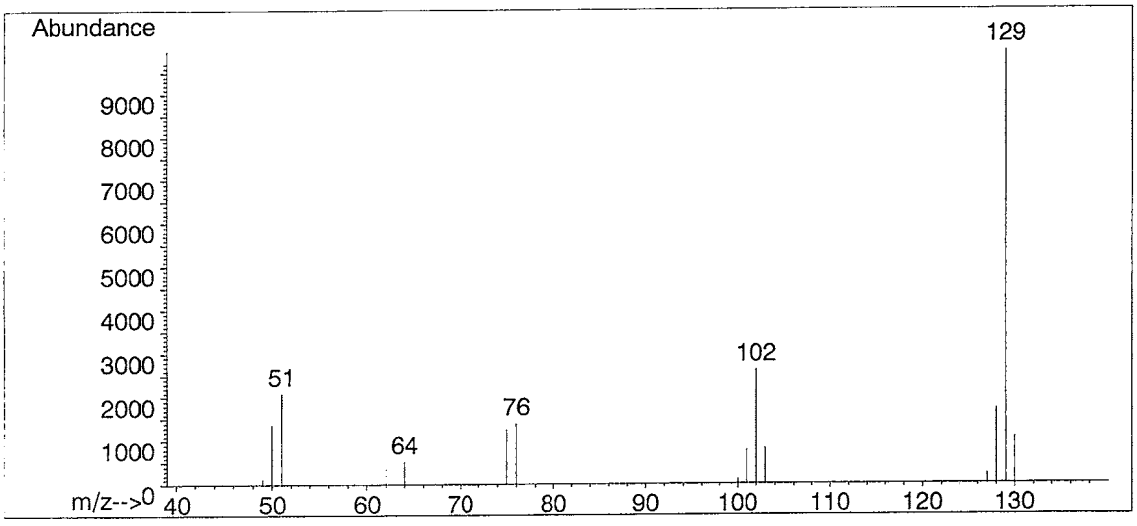
Instrument : Hewlett Packard 5989B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV




Mass Spectrum of Test Substance




Mass Spectrum of Literature Data*

Results: The mass spectrum was consistent with literature spectrum.

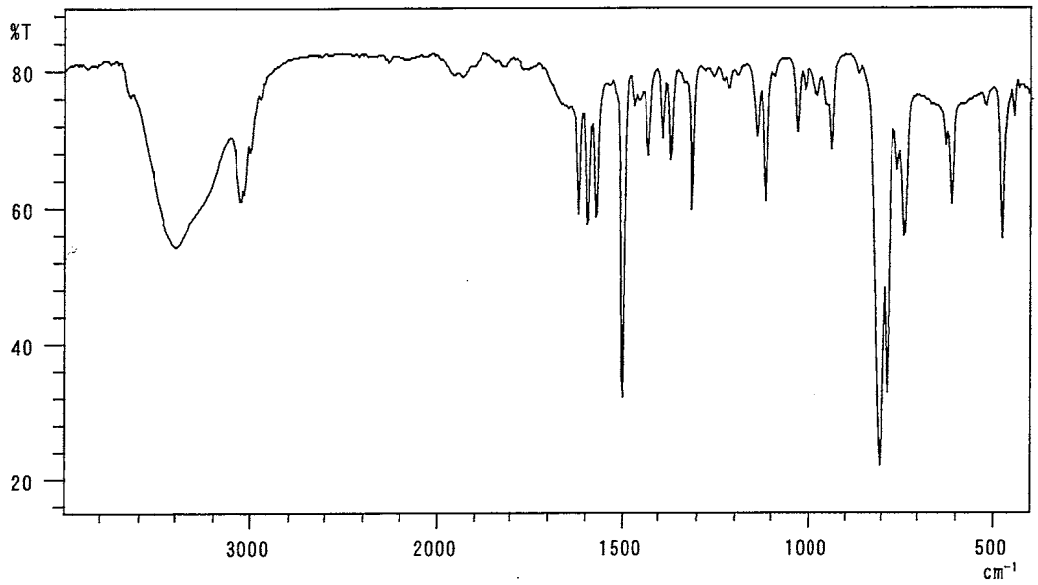
(*Fred W. McLafferty (1994) Wiley Registry of Mass Spectral Data, 6th edition. John Wiley and Sons, Inc. (U.S.), Entry Number 6221)

Infrared Spectrometry

Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 4 $cm^{-1}$




Infrared Spectrum of Test Substance

| Determined Values | Literature Values* |
|---|---|
| Wave Number ($cm^{-1}$) | Wave Number ($cm^{-1}$) |
| 440～ 460 | 440～ 460 |
| 460～ 500 | 460～ 500 |
| 600～ 640 | 600～ 640 |
| 720～ 760 | 720～ 760 |
| 760～ 800 | 760～ 800 |
| 800～ 840 | 800～ 840 |
| 920～ 960 | 920～ 960 |
| 1020～1040 | 1020～1040 |
| 1100～1130 | 1100～1130 |
| 1130～1160 | 1130～1160 |
| 1300～1320 | 1300～1320 |
| 1340～1380 | 1340～1380 |
| 1380～1400 | 1380～1400 |
| 1400～1440 | 1400～1440 |
| 1480～1520 | 1480～1520 |
| 1560～1580 | 1560～1580 |
| 1580～1600 | 1580～1600 |
| 1600～1640 | 1600～1640 |
| 2890～3120 | |
| 3120～3720 | 3120～3720 |

Results: The infrared spectrum was consistent with literature spectrum.
(*William W. Simons (1978) The Sadtler Handbook of Infrared Spectra. Sadtler Research Laboratories, Inc. (U.K.), pp.218)

2. Impurity

| | |
|---|---|
| Instrument | : Hewlett Packard 5890A Gas Chromatograph |
| Column | : INNOWAX (0.2 mm$\phi$ $\times$50 m) |
| Column Temperature | : 190° C |
| Flow Rate | : 1 mL/min |
| Detector | : FID (Flame Ionization Detector) |
| Injection Volume | : 1 μL |

| Sample Name | Peak No. | Area (%) | Peak Name |
|---|---|---|---|
| Test Substance | 1 | 0.166 | 2-Methyl Naphthalene |
| | 2 | 99.685 | Quinoline |
| | 3 | 0.149 | Isoquinoline |

Results: Gas chromatography indicated one major peak (peak No.2) and two impurities. It was identified only by comparing its gas chromatograph with that of 2-methyl naphthalene (peak No.1) and isoquinoline (peak No.3) in the quinoline, the amount in the test substance were 0.166%, and 0.149%.

3. Conclusions: The test substance was identified as quinoline by the mass spectrum and the infrared spectrum. Gas chromatography indicated one major peak (peak No.2) and two impurities. It was identified only by comparing its gas chromatograph with that of 2-methyl naphthalene and isoquinoline, the amount in the test substance were 0.166% and 0.149%.

# APPENDIX M 2

# STABILITY OF QUINOLINE IN THE 13 - WEEK DRINKING WATER STUDY

STABILITY OF QUINOLINE IN THE 13-WEEK DRINKING WATER STUDY

Test Substance : Quinoline (Tokyo Kasei Kogyo Co., Ltd.)

Lot No. : FHD03

1. Sample Storage : This lot was used from 1995.6.21 to 1995.9.22. Test substance was stored in a dark place at room temperature.

2. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : INNOWAX (0.2 mm$\phi$ × 50 m)

Column Temperature : 190° C

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μL

| Date (date analyzed) | Peak No. | Retention Time (min) | Area (%) |
|---|---|---|---|
| 1995.05.30 | 1 | 5.397 | 0.166 |
| | 2 | 6.354 | 99.685 |
| | 3 | 6.779 | 0.149 |
| 1995.09.29 | 1 | 5.398 | 0.166 |
| | 2 | 6.353 | 99.686 |
| | 3 | 6.777 | 0.148 |

Results: Gas chromatography indicated one major peak (peak No.2) and two impurities (peaks No.1 and No.3 < 0.4% of total area) analyzed on 1995.5.30 and one major peak (peak No.2) and two impurities (peaks No.1 and No.3 < 0.4% of total area) analyzed on 1995.9.29. No new trace impurity peak in the test substance analyzed on 1995.9.29 was detected.

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

APPENDIX M 3

CONCENTMOUSEION OF QUINOLINE IN FORMULATED WATER IN THE

13 - WEEK DRINKING WATER STUDY

CONCENTRATION OF QUINOLINE IN FORMULATED WATER IN THE 13-WEEK DRINKING WATER STUDY

| | Target Concentration | | | | |
|---|---|---|---|---|---|
| Date Analyzed | 237[a] | 355 | 533 | 800 | 1200 |
| 1995.06.20 | 233.3( 98.4)[b] | 351.8( 99.1) | 530.5( 99.5) | 797.5( 99.7) | 1194.4( 99.5) |

[a] ppm
[b] %

Analytical Method : The samples were analyzed by high performance liquid chromatography.

Instrument : Hewlett Packard 1090 High Performance Liquid Chromatograph
Column : TSK GEL ODS 80TM (4.6 mm$\phi$ $\times$150 mm)
Column Temperature : 50℃
Flow Rate : 1 mL/min
Mobile Phase : Methanol : Distilled water = 3 : 2
Detector : UV (280 nm)
Injection Volume : 10 μL

# APPENDIX M 4

# STABILITY OF QUINOLINE IN FORMULATED WATER

# IN THE 13 - WEEK DRINKING WATER STUDY

STABILITY OF QUINOLINE IN FORMULATED WATER IN THE 13-WEEK DRINKING WATER STUDY

| | | Target Concentration | |
|---|---|---|---|
| Date Prepare | Date Analyzed | 237[a] | 1200 |
| 1995.06.20 | 1995.06.20 | 233.3(100)[b] | 1194.4(100) |
| | 1995.06.28[c] | 232.6( 99.7) | 1189.7( 99.6) |

[a] ppm
[b] %(Percentage was based on the concentration on date of preparation.)
[c] animal room samples

Analytical Method : The samples were analyzed by high performance liquid chromatography.

Instrument : Hewlett Packard 1090 High Performance Liquid Chromatograph
Column : TSK GEL ODS 80TM (4.6 mm$\phi$ $\times$150 mm)
Column Temperature : 50℃
Flow Rate : 1 mL/min
Mobile Phase : Methanol : Distilled water = 3 : 2
Detector : UV (280 nm)
Injection Volume : 10 μL

# APPENDIX N 1

# METHODS FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13 - WEEK DRINKING WATER STUDY OF QUINOLINE

# METHODS FOR HEMATOLOGY,BIOCHEMISTRY AND URINALYSIS IN THE 13-WEEK DRINKING WATER STUDY OF QUINOLINE

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

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

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

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

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

# APPENDIX O 1

## UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13 - WEEK DRINKING WATER STUDY OF QUINOLINE

# UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK DRINKING WATER STUDY OF QUINOLINE

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