p-ニトロアニソールのラットを用いた経口投与による
2 週 間 毒 性 試 験 (混 餌 試 験)報 告 書

試験番号:0360

APPENDIX

APPENDIXES

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|--------------|---|
| | STUDY) |

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APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, RAT : MALE

STUDY NO. : 0360 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 2

SEX : MALE

PAGE: 1

| Group Name | | stration We | | | |
|------------|--|--|---|---|---|
| | 1-1 | 1-3 | 1-7 | 2-3 | 2-7 |
| | 1 | 1 | 1 | 1 | 1 |
| | | | | | |
| Control | 0 | 0 | 0 | 0 | 0 |
| | 0 | 0 | 0 | 0 | 0 |
| | 0 | 0 | 0 | 0 | 0 |
| | | õ | Õ | 5 | 5 |
| | | õ | - | | 5 |
| | | õ | - | | Ő |
| Traine bhu | v | Ū | v | Ŭ | Ū |
| Control | 0 | 0 | 0 | 0 | 0 |
| 1250 ppm | 0 | 0 | 0 | 0 | 0 |
| 2500 ppm | 0 | 0 | 0 | 0 | 0 |
| 5000 ppm | 0 | 0 | 0 | 0 | 0 |
| | 0 | 0 | 0 | 0 | 0 |
| 20000 ppm | 0 | 0 | 5 | 5 | 5 |
| | | | | | • |
| | | 0 | | | 0 |
| | | 0 | • | | 0 |
| 2500 ppm | | 0 | • | | 0 |
| | - | 0 | • | - | 0 |
| | 0 | | | | 0 |
| 20000 ppm | 0 | 0 | 3 | 3 | 3 |
| Control | ٥ | ٥ | 0 | ٥ | 0 |
| | | | | | 0 |
| | - | - | - | | 5 |
| | - | • | • | | 5 |
| | - | | - | | 5 |
| | | | | | 5 |
| | v | U | J | U | U |
| Control | 0 | 0 | 0 | 0 | 0 |
| | 0 | 0 | 0 | 0 | 0 |
| | 0 | 0 | 0 | 0 | 0 |
| | | 0 | 0 | 0 | 0 |
| | | | 5 | 0 | 0 |
| | | 5 | | | 5 |
| | Control 1250 ppm 2500 ppm 5000 ppm 10000 ppm 20000 ppm Control 1250 ppm 2500 ppm 5000 ppm | Control 0 1250 ppm 0 2500 ppm 0 5000 ppm 0 10000 ppm 0 20000 ppm 0 20000 ppm 0 2500 ppm 0 2500 ppm 0 2500 ppm 0 5000 ppm 0 20000 ppm </td <td>Central 0 0 1250 ppm 0 0 2500 ppm 0 0 5000 ppm 0 0 10000 ppm 0 0 20000 ppm 0 0 20000 ppm 0 0 20000 ppm 0 0 2500 ppm 0 0 2500 ppm 0 0 5000 ppm 0 0 20000 ppm 0 0 20000 ppm 0 0 20000 ppm 0 0 20000 ppm 0 0 2500 ppm 0 0 2500 ppm 0 0 2500 ppm 0 0 20000 ppm 0 0 2500 ppm 0 0 2500 ppm 0 0 2500 ppm 0 0 20000 ppm 0 0 20000 ppm 0 0 20000 ppm</td> <td>Control 0 0 0 1250 ppm 0 0 0 2500 ppm 0 0 0 5000 ppm 0 0 0 10000 ppm 0 0 0 20000 ppm 0 0 0 20000 ppm 0 0 0 20000 ppm 0 0 0 2500 ppm 0 0 0 2500 ppm 0 0 0 5000 ppm 0 0 0 10000 ppm 0 0 0 20000 ppm 0 0 0</td> <td>Control 0 0 0 0 1250 ppm 0 0 0 0 0 2500 ppm 0 0 0 0 0 0 5000 ppm 0 0 0 0 5 10000 ppm 0 0 0 5 10000 ppm 0 0 0 0 0 0 0 Control 0 0 0 0 0 0 0 20000 ppm 0 0 0 0 0 0 0 2500 ppm 0 0 0 0 0 0 0 20000 ppm 0</td> | Central 0 0 1250 ppm 0 0 2500 ppm 0 0 5000 ppm 0 0 10000 ppm 0 0 20000 ppm 0 0 20000 ppm 0 0 20000 ppm 0 0 2500 ppm 0 0 2500 ppm 0 0 5000 ppm 0 0 20000 ppm 0 0 20000 ppm 0 0 20000 ppm 0 0 20000 ppm 0 0 2500 ppm 0 0 2500 ppm 0 0 2500 ppm 0 0 20000 ppm 0 0 2500 ppm 0 0 2500 ppm 0 0 2500 ppm 0 0 20000 ppm 0 0 20000 ppm 0 0 20000 ppm | Control 0 0 0 1250 ppm 0 0 0 2500 ppm 0 0 0 5000 ppm 0 0 0 10000 ppm 0 0 0 20000 ppm 0 0 0 20000 ppm 0 0 0 20000 ppm 0 0 0 2500 ppm 0 0 0 2500 ppm 0 0 0 5000 ppm 0 0 0 10000 ppm 0 0 0 20000 ppm 0 0 0 | Control 0 0 0 0 1250 ppm 0 0 0 0 0 2500 ppm 0 0 0 0 0 0 5000 ppm 0 0 0 0 5 10000 ppm 0 0 0 5 10000 ppm 0 0 0 0 0 0 0 Control 0 0 0 0 0 0 0 20000 ppm 0 0 0 0 0 0 0 2500 ppm 0 0 0 0 0 0 0 20000 ppm 0 |

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ALL ANIMALS

CLINICAL OBSERVATION (SUMMARY)

APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, RAT : FEMALE

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

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STUDY NO. : 0360 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 2

SEX : FEMALE

PAGE: 2

| Clinical sign | Group Name | Admini | stration We | ek-day | | | | | | | |
|-----------------------|----------------------|--------|-------------|--------|-----|--------|------|------|-------------|------|--|
| | | 1-1 | 1-3 | 1-7 | 2-3 | 2-7 | | | | | |
| | | 1 | 1 | 1 | 1 | 1 | | | <u></u> | | |
| | | | | | | | | | | | |
| DEATH | Control | 0 | 0 | 0 | 0 | 0 | | | | | |
| | 1250 ppm | 0 | 0 | 0 | 0 | 0 | | | | | |
| | 2500 ppm | 0 | 0 | 0 | 0 | 0 | | | | | |
| | 5000 ppm | 0 | 0 | 0 | 0 | 0 | | | | | |
| | 10000 ppm | 0 | 0 | 0 | 0 | 0 | | | | | |
| | 20000 ppm | 0 | 0 · | Ő | 1 | 5 | | | | | |
| HUNCHBACK POSITION | Control | 0 | 0 | 0 | 0 | 0 | | | | | |
| | 1250 ppm | õ | Ő | Ō | Ō | Ō | | | | | |
| | 2500 ppm | 0 | 0 | õ | 0 | 0 0 | | | | | |
| | 2000 ppm 5000 ppm | 0 | 0 | 0 | 0 | 0 | | | | | |
| | | - | - | 0 | | | | | | | |
| | 10000 ppm | 0 | 0 | | 0 | 0 | | | | | |
| | 20000 ppm | 0 | 0 | 1 | 1 | 0 | | | | | |
| WASTING | Contral | 0 | 0 | 0 | 0 | 0 | | | | | |
| | 1250 ppm | 0 | 0 | 0 | 0 | 0 | | | | | |
| | 2500 ppm | 0 | 0 | 0 | . 0 | 0 | | | | | |
| | 5000 ppm | 0 | 0 | 0 | 0 | 0 | | | | | |
| | 10000 ppm | 0 | 0 | 0 | 0 | 0 | | | | | |
| | 20000 ppm | 0 | 0 | 0 | 4 | 0 | | | | | |
| COLORED | Control | 0 | 0 | 0 | 0 | 0 | | | | | |
| | 1250 ppm | 0 | 0 | 0 | 0 | 4 | | | | | |
| | 2500 ppm | Õ | 0 | 0 | 2 | 5 | | | | | |
| | 5000 ppm | Ö | Ő | Ő | 5 | 5 | | | | | |
| | 10000 ppm | õ | 5 | 5 | 5 | 5 | | | | | |
| | 20000 ppm | õ | 5 | 5 | 4 | 0 | | | | | |
| PILOERECTION | Control | 0 | 0 | 0 | 0 | 0 | | | | | |
| F HOCACOI ION | | 0 | 0 | 0 | 0 | 0 | | | | | |
| | 1250 ppm | • | - | 0 | | | | | | | |
| | 2500 ppm | 0 | 0 | - | 0 | 0 | | | | | |
| | 5000 ppm | 0 | 0 | 0 | 0 | 0 | | | | | |
| | 10000 ppm | 0 | 0 | 0 | 0 | 0 | | | | | |
| | 20000 ppm | 0 | 0 | 5 | 4 | 0 | | | | | |
| SOILED PERI GENITALIA | Control | 0 | 0 | 0 | 0 | 0 | | | | | |
| | 1250 ppm | 0 | 0 | 0 | 0 | 0 | | | | | |
| | 2500 ppm | 0 | 0 | 0 | 0 | 0 | | | | | |
| | 5000 ppm | 0 | 0 | 0 | 0 | 0 | | | | | |
| | 10000 ppm | Ō | Ō | 0 | 0 | 0 | | | | | |
| | 20000 ppm | Ő | Ö | 5 | 4 | 0 | | | | | |

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STUDY NO. : 0360 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 2 CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : FEMALE

PAGE: 3

| Clinical sign | Group Name | Admini | stration W | eek-day |     |     |      |  |
|---------------|------------|--------|------------|---------|-----|-----|------|--|
|               |            | 1-1    | 1-3        | 1-7     | 2-3 | 2-7 |      |  |
|               |            | 1      | 1          | 1       | 1   | 1   | <br> |  |
| YELLOW URINE  | Control    | 0      | 0          | 0       | 0   | 0   |      |  |
| IELLOW UNINE  | 1250 ppm   | 0      | 0          | 0       | 1   | 5   |      |  |
|               | 2500 ppm   | Ő      | · õ        | õ       | 5   | 5   |      |  |
|               | 5000 ppm   | 0      | 0          | 0       | 5   | 5   |      |  |
|               | 10000 ppm  | 0      | 0          | 1       | 5   | 5   |      |  |
|               | 20000 ppm  | 0      | 5          | 5       | 4   | 0   |      |  |
| OLIGO-STOOL   | Control    | 0      | 0          | 0       | 0   | 0   |      |  |
|               | 1250 ppm   | 0      | 0          | 0       | 0   | 0   |      |  |
|               | 2500 ppm   | 0      | 0          | 0       | 0   | 0   |      |  |
|               | 5000 ppm   | 0      | 0          | 0       | 0   | 0   |      |  |
|               | 10000 ppm  | 5      | 5          | 5       | 0   | 0   |      |  |
|               | 20000 ppm  | 5      | 5          | 5       | 4   | 0   |      |  |

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APPENDIX B 1

BODY WEIGHT CHANGES : SUMMARY, RAT : MALE

| up Name               | Admin    | stration | week-day     |     |          |     |            |     |      |     |          |      | <br> |
|-----------------------|----------|----------|--------------|-----|----------|-----|------------|-----|------|-----|----------|------|------|
|                       | 0-0      |          | 1-1          |     | 1-3      |     | 1-7        |     | 2-3  |     | 2-7      |      |      |
| Control               | 130±     | 4        | 136±         | 3   | 144±     | 4   | 161±       | 4   | 178± | 5   | 192±     | 4    |      |
| 1250 ppm              | 129±     | 4        | 133±         | 5   | $142\pm$ | 6   | 160±       | 5   | 176± | 6   | 190±     | 5    |      |
| 2500 ppm              | 130±     | 4        | $131\pm$     | 3   | 141土     | 4   | 159±       | 4   | 174± | 6   | 190±     | 6    |      |
| 5000 ppm              | 129±     | 5        | 125±         | 3** | 134±     | 3** | 153±       | 4   | 168± | 5   | 184±     | 5    |      |
| 10000 ppm             | 129±     | 4        | 120±         | 4** | 120±     | 4** | $135\pm$   | 5** | 145± | 4** | $157\pm$ | 3**  |      |
| 20000 mag             | $129\pm$ | 4        | 116±         | 3** | 108±     | 3** | 102±       | 6** | 99±  | 9** | 87±      | 10** |      |
| Significant differenc |          | ), 05    | ** : P ≦ 0.0 | 01  |          |     | Test of Du |     |      |     |          |      | <br> |

(SUMMARY)

STUDY NO. : 0360

UNIT : g REPORT TYPE : A1 2

ANIMAL : RAT F344/DuCrj

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BODY WEIGHT CHANGES

ALL ANIMALS

APPENDIX B 2

BODY WEIGHT CHANGES : SUMMARY, RAT : FEMALE

| oup Name  | Admini | stration | week-day |     |                                       |     |                   |          |      |     |          |     |         |
|-----------|--------|----------|----------|-----|---------------------------------------|-----|-------------------|----------|------|-----|----------|-----|---------|
| ·····     | 0-0    |          | 1-1      |     | 1-3                                   |     | 1-7               |          | 2-3  |     | 2-7      |     | <u></u> |
| Control   | 98±    | 3        | 99±      | 4   | 103±                                  | 6   | 111±              | 5        | 119± | 5   | 126±     | 6   |         |
| 1250 ppm  | 98±    | 3        | 100±     | 5   | 103±                                  | 4   | 111±              | 4        | 118± | 5   | $123\pm$ | 7   |         |
| 2500 ppm  | 98±    | 3        | 97±      | 4   | 102±                                  | 4   | 109±              | 5        | 112± | 7   | 120±     | 8   |         |
| 5000 ppm  | 98±    | 3        | 93±      | 3*  | 97±                                   | 4   | 105±              | 5        | 112± | 5   | 118±     | 5   |         |
| 10000 ppm | 98±    | 2        | 90±      | 2** | 88±                                   | 2** | 95 <del>1</del> : | 2**      | 98±  | 4** | 107±     | 6** |         |
| 20000 maa | 98±    | 4        | 88土      | 5** | 79±                                   | 5** | 69±               | 5**      | 61±  | 6** | -        |     |         |
|           |        |          |          |     | · · · · · · · · · · · · · · · · · · · |     |                   | <u> </u> |      |     |          |     |         |

(SUMMARY)

STUDY NO. : 0360

ANIMAL : RAT F344/DuCrj

BODY WEIGHT CHANGES

ALL ANIMALS

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# APPENDIX C 1

# FOOD CONSUMPTION CHANGES : SUMMARY, RAT : MALE

STUDY NO. : 0360 ANIMAL : RAT F344/DuCrj UNIT : g REPORT TYPE : A1 2 SEX : MALE FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

PAGE: 1

| up Name                  | Administration | n week-day(effective) |             |                 | <br> |
|--------------------------|----------------|-----------------------|-------------|-----------------|------|
|                          | 1-3(3)         | 1-7(4)                | 2-3(3)      | 2-7(4)          | <br> |
| Control                  | 13.8± 0.2      | 14.0± 0.6             | 14.7± 0.4   | 13.9± 0.2       |      |
| 1250 ppm                 | 12.9± 0.5      | 13.4± 0.7             | 14.2± 0.8   | 14.1± 0.7       |      |
| 2500 ppm                 | 11.8± 0.6**    | 13.0± 0.5*            | 14.1± 0.8   | 14.2± 0.6       |      |
| 5000 maa                 | 8.8± 0.6**     | 12.0± 0.4**           | 13.6± 0.4   | 14.1± 0.9       |      |
| 10000 ppm                | 6.3± 0.6**     | 9.7± 0.6**            | 10.5± 0.5** | 11.5± 0.6       |      |
| mqq 00002                | 5.5± 1.3**     | 6.3± 0.8**            | 6.9± 1.4**  | 7.8± 1.9*       |      |
|                          |                |                       |             |                 |      |
| Significant difference ; | *:P≦ 0.05      | ** : P ≦ 0.01         |             | Test of Dunnett |      |
| N260)                    |                |                       |             |                 | <br> |

APPENDIX C 2

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

STUDY NO. : 0360 ANIMAL : RAT F344/DuCrj UNIT : g REPORT TYPE : A1 2 SEX : FEMALE FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS -

PAGE: 2

| Group Name | Administration<br>1–3(3) | week-day(effective)<br>1-7(4) | 2-3(3)     | 2-7(4)     |
|------------|--------------------------|-------------------------------|------------|------------|
| Control    | 9.7± 0.6                 | 10.2± 0.5                     | 10.7± 0.4  | 10.1± 0.4  |
| 1250 ppm   | 9.2± 0.4                 | 9.6± 0.5                      | 9.7± 0.6   | 9.7± 0.6   |
| 2500 ppm   | 8.5± 0.4                 | 9.1± 0.7                      | 8.9± 1.0   | 9.4± 0.9   |
| 5000 ppm   | 7.2± 0.8*                | 8.7± 0.7                      | 9.2± 0.7   | 9.2± 0.6   |
| 10000 mad  | 8.5± 8.7*                | 6.7± 0.4**                    | 6.8± 0.4** | 7.8± 0.4** |
| 20000 maa  | 8.5± 7.1                 | 6.2± 1.8**                    | 9.6± 1.8   | -          |
|            |                          |                               |            |            |

Test of Dunnett

(HAN260)

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

APPENDIX D 1

CHEMICAL INTAKE CHANGES : SUMMARY, RAT : MALE

| STUDY NO.: 0360<br>ANIMAL : RAT F344/DuCrj<br>UNIT : mg/kg/day<br>REPORT TYPE : A1 2 |                        |                        | CHEMICAL INTAKE CHANGES<br>ALL ANIMALS | (SUMMARY) |           |          |
|--------------------------------------------------------------------------------------|------------------------|------------------------|----------------------------------------|-----------|-----------|----------|
| SEX : MALE                                                                           |                        |                        |                                        |           |           | PAGE : 1 |
| Group Name                                                                           | Administration<br>1    | (weeks)2               |                                        |           | <br>····· |          |
| Control                                                                              | 0.000± 0.000           | 0.000± 0.000           |                                        |           |           |          |
| 1250 ppm                                                                             | 104.619± 3.495         | 92.523± 3.307          |                                        |           |           |          |
| 2500 ppm                                                                             | 204.014± 6.034         | 186.475± 5.544         |                                        |           |           |          |
| 5000 mag                                                                             | 393.469± 7.635         | 383.459± 17.661        |                                        |           |           |          |
| 10000 ppm                                                                            | 714.559± 19.160        | 729.282± 42.825        |                                        |           |           |          |
| 20000 mag                                                                            | $1245.493 \pm 211.429$ | $1838.292 \pm 634.463$ | i                                      |           |           |          |

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APPENDIX D 2

CHEMICAL INTAKE CHANGES : SUMMARY, RAT : FEMALE

| STUDY NO. : 0360<br>ANIMAL : RAT F344/DuCrj<br>UNIT : mg/kg/day<br>REPORT TYPE : A1 2<br>CPV : FEMALE |                     |                 | CHEMICAL INTAKE CHANGES<br>ALL ANIMALS | (SUMMARY) |      | PAGE : 2                              |
|-------------------------------------------------------------------------------------------------------|---------------------|-----------------|----------------------------------------|-----------|------|---------------------------------------|
| SEX : FEMALE                                                                                          |                     |                 |                                        |           | <br> |                                       |
| Group Name                                                                                            | Administration<br>1 | (weeks)<br>2    |                                        |           | <br> | · · · · · · · · · · · · · · · · · · · |
| Control                                                                                               | 0.000± 0.000        | 0.000± 0.000    |                                        |           |      |                                       |
| 1250 ppm                                                                                              | 108.059± 2.452      | 98.423± 2.684   |                                        |           |      |                                       |
| 2500 ppm                                                                                              | 209.425± 7.183      | 196.728± 9.246  |                                        |           |      |                                       |
| 5000 maa                                                                                              | 415.143± 18.409     | 391.529± 16.011 |                                        |           |      |                                       |
| 10000 ppm                                                                                             | 708.988± 58.196     | 730.714± 27.128 |                                        |           |      |                                       |
| 20000 ppm                                                                                             | 1781.984±416.691    | -               |                                        |           |      |                                       |

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APPENDIX E 1

HEMATOLOGY : SUMMARY, RAT : MALE

|                               | F344/DuCrj        |           |                |                 |       | EMATOLOGY (SU<br>LL ANIMALS ( |       |             |      |           |       |               |       |                                |          |
|-------------------------------|-------------------|-----------|----------------|-----------------|-------|-------------------------------|-------|-------------|------|-----------|-------|---------------|-------|--------------------------------|----------|
| MEASURE. TIME :<br>SEX : MALE |                   | ΓΥΡΕ : A1 |                |                 |       |                               |       |             |      |           |       |               |       |                                | PAGE: 1  |
| Group Name                    | NO. of<br>Animals | RED BL    | DOD CELL<br>µl | HEMOGLO<br>g∕dl | BIN   | HEMATOC<br>%                  | CRIT  | MCV<br>f Q  |      | MCH<br>Pg |       | MCHC<br>g ⁄dl |       | PLATELE<br>1 0 <sup>3</sup> /µ |          |
| Control                       | 5                 | 7.82±     | 0.14           | 14.4±           | 0.2   | 43.6±                         | 0.9   | 55.8±       | 0.4  | 18.4±     | 0.2   | 33.0±         | 0.2   | 875±                           | 32       |
| 1250 ppm                      | 5                 | 7.88±     | 0.28           | 14.3±           | 0.4   | 43.5±                         | 1.6   | 55.2±       | 0.2  | 18.1±     | 0.2   | 32.8±         | 0.5   | 866±                           | 73       |
| 2500 ppm                      | 5                 | 7.45±     | 0.28           | 13.6±           | 0.5   | 41.7±                         | 1.5   | 56.0±       | 0.3  | 18.3±     | 0.2   | 32.6±         | 0.3   | 986±                           | 25**     |
| 5000 ppm                      | 5                 | 6.32±     | 0.25**         | 12.1±           | 0.4** | 38.2±                         | 1.2** | 60.5±       | 1.0  | 19.2±     | 0.4** | 31.6±         | 0.8** | 1098±                          | 43**     |
| 10000 ppm                     | 4                 | $5.79\pm$ | 0.26**         | 11.6±           | 0.5** | 36.3±                         | 1.0** | 62.8±       | 1.3* | 20.0±     | 0.5** | 31.9±         | 0.4*  | 1056±                          | 55**     |
| 20000 ppm                     | 5                 | 5.66±     | 0.33**         | 11.3±           | 0.7** | 31.8±                         | 2.7** | 56.0±       | 1.5  | 20.0±     | 0.3** | 35.8±         | 0.8** | 619±                           | 33**     |
| Significant                   | difference ;      | *:Р≦      | 0.05 *         | ** : P ≦ 0.0    | )1    |                               |       | Test of Dur | mett |           |       |               |       |                                | <u> </u> |

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(HCL070)

|                             | F344/DuCrj        |              |       |              |        | HEMATOLOGY (SU<br>ALL ANIMALS ( |            |             |                                       |                                       |        |
|-----------------------------|-------------------|--------------|-------|--------------|--------|---------------------------------|------------|-------------|---------------------------------------|---------------------------------------|--------|
| EASURE. TIME :<br>EX : MALE |                   | TYPE : A1    |       |              |        |                                 |            |             |                                       |                                       | PAGE : |
| roup Name                   | NO. of<br>Animals | RETICUL<br>% | OCYTE | METHEMO<br>% | GLOBIN | PROTHRC<br>sec                  | OMBIN TIME | APTT<br>sec | · · · · · · · · · · · · · · · · · · · | · · · · · · · · · · · · · · · · · · · | ,      |
| Control                     | 5                 | 26±          | 6     | 0.3±         | 0.1    | 14.0±                           | 0.2        | 18.4±       | 2.8                                   |                                       |        |
| 1250 ppm                    | 5                 | 31±          | 6     | 0.3±         | 0.1    | 14.1±                           | 0.2        | 15.9±       | 2.9                                   |                                       |        |
| 2500 ppm                    | 5                 | 38±          | 5     | 0.4±         | 0.1    | 14.1±                           | 0.5        | 16.8±       | 2.4                                   |                                       |        |
| 5000 ppm                    | 5                 | 107±         | 12    | 0.5±         | 0.5    | 13.5±                           | 0.2        | 14.3±       | 2.7                                   |                                       |        |
| 10000 ppm                   | 4                 | 194±         | 25**  | 0.7±         | 0.5    | 14.1±                           | 0.3        | 11.9±       | 1.1*                                  |                                       |        |
| 20000 ppm                   | 5                 | 238±         | 92**  | $1.4\pm$     | 1.0    | 16.0±                           | 0.5**      | 21.9±       | 5.8                                   |                                       |        |
| Significant                 | difference ;      | *:P≦0        | .05 * | *:P≦0.(      | )1     |                                 |            | Test of Dur | Nett                                  |                                       |        |
| HCL070)                     |                   |              |       |              |        |                                 |            |             |                                       |                                       | BAIS   |

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(HCL070)

| oup Name  | NO. of<br>Animals | ₩BC<br>1 O <sup>3</sup> / |       | Dit<br>N-BAND | ferentia | L WBC (9<br>N-SEG | 6)   | EOSINO |   | BASO |   | MONO |   | LYMPHO  |      | OTHER |   |
|-----------|-------------------|---------------------------|-------|---------------|----------|-------------------|------|--------|---|------|---|------|---|---------|------|-------|---|
| Control   | 5                 | 3.01±                     | 0.52  | 0±            | 0        | 10±               | 4    | 1±     | 1 | 0±   | 0 | 1±   | 0 | 87±     | 4    | 0±    |   |
| 1250 ppm  | 5                 | $3.47\pm$                 | 1.31  | 0±            | 1        | 13±               | 1    | 0±     | 1 | 0±   | 0 | 1±   | 1 | $85\pm$ | 1    | 0±    |   |
| 2500 ppm  | 5                 | 4.47±                     | 0.97  | 0±            | 0        | 11±               | 3    | 1±     | 1 | 0±   | 0 | 2±   | 3 | 87±     | 4    | 0±    |   |
| 5000 ppm  | 5                 | 4.23±                     | 0.38  | 1±            | 1        | $16\pm$           | 4    | 1±     | 1 | 0±   | 0 | 2±   | 1 | 81±     | 3    | 0±    | ţ |
| 10000 ppm | 4                 | 5.96±                     | 1.90* | . 0±          | 1        | 21±               | 7    | 0±     | 0 | 0±   | 0 | 4土   | 4 | 75±     | 9    | 0±    | ( |
| 20000 ppm | 5                 | 2.92±                     | 0.59  | 1±            | 1        | 40±               | 18** | 0±     | 0 | 0±   | 0 | 1±   | 1 | 57±     | 18** | 0±    |   |

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APPENDIX E 2

HEMATOLOGY : SUMMARY, RAT : FEMALE

| : FEMALE  | NO. of  | RED BU    | OOD CELL | HEMOGLO | DRIN  | НЕМАТОС | 281T  | MCV       |      | MCH   |       | MCHC   |       | PLATELE             | PAGE |
|-----------|---------|-----------|----------|---------|-------|---------|-------|-----------|------|-------|-------|--------|-------|---------------------|------|
|           | Animals | 1 06/1    |          | g / dl  |       | %       |       | fl        |      | Pg    |       | g / dl |       | 1 0 <sup>3</sup> /μ |      |
| Control   | 5       | $8.21\pm$ | 0.26     | 15.2±   | 0.5   | 44.4±   | 1.2   | 54.1±     | 0.4  | 18.5± | 0.2   | 34.2±  | 0.3   | 871±                | 49   |
| 1250 ppm  | 5       | 8.02±     | 0.11     | 14.8±   | 0.3   | 43.3±   | 0.4   | 53.9±     | 0.3  | 18.5± | 0.2   | 34.3±  | 0.4   | 815±                | 75   |
| 2500 ppm  | 5       | 7.52±     | 0.29**   | 13.6±   | 0.7** | 40.6±   | 1.6   | 53.9±     | 0.4  | 18.1± | 0.2   | 33.6±  | 0.4   | 852±                | 63   |
| 5000 ppm  | 5       | 6.15±     | 0.23**   | 11.5±   | 0.5** | 36.0±   | 1.4** | $58.6\pm$ | 0.4  | 18.8± | 0.2   | 32.0±  | 0.6** | 894±                | 48   |
| 10000 ppm | 5       | 5.75±     | 0,28**   | 11.1±   | 0.7** | 34.9±   | 2.6** | 60.6±     | 1.6* | 19.3± | 0.3** | 31.8±  | 0.6** | 971±                | 56*  |
| 20000 ppm | 0       | -         |          | -       |       | -       |       | -         |      | -     |       | -      |       | -                   |      |

| -oup Name | NO. of<br>Animals | RETICUL<br>% | OCYTE | METHEMO<br>% | GLOBIN | PROTHRC<br>sec | MBIN TIME | APTT<br>sec |     |  |
|-----------|-------------------|--------------|-------|--------------|--------|----------------|-----------|-------------|-----|--|
| Control   | 5                 | 22±          | 9     | 0.2±         | 0.1    | 15.1±          | 0.2       | 20.7±       | 5.5 |  |
| 1250 ppm  | 5                 | 22±          | 7     | 0.2±         | 0.1    | 14.7±          | 0.1       | 15.4±       | 2.9 |  |
| 2500 ppm  | 5                 | 32±          | 13    | 0.3±         | 0.1    | 14.7±          | 0.4       | 16.6±       | 4.1 |  |
| 5000 ppm  | 5                 | $111\pm$     | 18*   | 0.7±         | 0.4    | 14.4±          | 0.5*      | 16.8±       | 2.9 |  |
| 10000 ppm | 5                 | 199土         | 41**  | 0.8±         | 0.4    | 15.2±          | 0.2       | 29.0±       | 8.7 |  |
| 20000 ppm | 0                 | -            |       | -            |        | -              |           | -           |     |  |

HEMATOLOGY (SUMMARY)

ALL ANIMALS ( 2W)

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(HCL070)

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STUDY NO. : 0360

ANIMAL : RAT F344/DuCrj

| oup Name  | NO. of<br>Animals | ₩BC<br>1 0³/ |      | Dif<br>N-BAND | ferentia | L WBC (%<br>N-SEG | .) | EOSINO |   | BASO |   | MONO |   | LYMPHO |   | OTHER |  |
|-----------|-------------------|--------------|------|---------------|----------|-------------------|----|--------|---|------|---|------|---|--------|---|-------|--|
| Control   | 5                 | 4.08±        | 0.86 | 0±            | 0        | 14±               | 2  | 0±     | 1 | 0±   | 0 | 2±   | 2 | 83±    | 3 | 0±    |  |
| 1250 ppm  | 5                 | $3.68\pm$    | 0.93 | 0±            | 0        | 9±                | 5  | 2±     | 1 | 0±   | 0 | 2±   | 0 | 87±    | 6 | 0±    |  |
| 2500 ppm  | 5                 | 5.07±        | 3.14 | 0±            | 1        | 15±               | 5  | 1±     | 1 | 0±   | 0 | 1±   | 1 | 83±    | 6 | 0±    |  |
| 5000 ppm  | 5                 | $4.57\pm$    | 1.20 | 1±            | 1        | 15±               | 4  | 1±     | 1 | 0±   | 0 | 1±   | 0 | 81±    | 3 | 0±    |  |
| 10000 ppm | 5                 | 4.05±        | 1.00 | 1±            | 1        | 13±               | 2  | 0±     | 1 | 0±   | 0 | 1±   | 1 | 84±    | 3 | 0±    |  |
| 20000 ppm | 0                 | _            |      | -             |          | -                 |    | -      |   | -    |   | -    |   | -      |   | -     |  |

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#### APPENDIX F 1

# BIOCHEMISTRY : SUMMARY, RAT : MALE

| up Name   | NO. of<br>Animals | TOTAL F<br>g⁄dl | ROTEIN | ALBUMIN<br>g⁄dl |       | A/G RAT | 10    | T-BILI<br>mg∕dl |        | GLUCOSE<br>mg∕dl |     | T-CHOLE<br>mg∕dl | STEROL | PHOSPHOI<br>mg/dl | LIPID |
|-----------|-------------------|-----------------|--------|-----------------|-------|---------|-------|-----------------|--------|------------------|-----|------------------|--------|-------------------|-------|
| Control   | 5                 | 5.6±            | 0.1    | 3.6±            | 0.1   | 1.9±    | 0.0   | 0.12±           | 0.01   | 178±             | 11  | 64±              | 3      | 123±              | 5     |
| 1250 ppm  | 5                 | $5.6\pm$        | 0.2    | 3.7±            | 0.1   | 1.9±    | 0.1   | 0.12±           | 0.02   | 202±             | 16  | 63±              | 4      | 120±              | 6     |
| 2500 ppm  | 5                 | $5.9\pm$        | 0.1    | 3.8±            | 0.1   | 1.8±    | 0.1   | 0.13±           | 0.01   | 183±             | 12  | 74±              | 3      | 142±              | 5     |
| 5000 ppm  | 5                 | 6.3±            | 0.3**  | 4.0±            | 0.2*  | 1.8±    | 0.0   | 0.15±           | 0.02*  | 179±             | 10  | 98±              | 8      | 180±              | 14    |
| 10000 ppm | 4                 | 6.6±            | 0.4**  | 4.2±            | 0.3*  | 1.8±    | 0.1   | 0.22±           | 0.02** | $152\pm$         | 2   | 141±             | 13**   | $255\pm$          | 24**  |
| 20000 ppm | 5                 | 6.8±            | 0.2**  | 4.6±            | 0.2** | 2.1±    | 0.1** | 0.24±           | 0.02** | 97±              | 22* | $143\pm$         | 23**   | 249±              | 43**  |

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BIOCHEMISTRY (SUMMARY) ALL ANIMALS ( 2W)

(HCL074)

STUDY NO. : 0360

ANIMAL : RAT F344/DuCrj

|                               | F344/DuCrj        |             |     |              |     | IOCHEMISTRY (<br>LL ANIMALS ( |     |               |      |               |     |                 |       |                  |        |
|-------------------------------|-------------------|-------------|-----|--------------|-----|-------------------------------|-----|---------------|------|---------------|-----|-----------------|-------|------------------|--------|
| HEASURE. TIME :<br>SEX : MALE |                   | YPE: A1     |     |              |     |                               |     |               |      |               |     |                 |       |                  | PAGE : |
| Foup Name                     | NO. of<br>Animals | GOT<br>IU/J | 2   | GPT<br>IU/Q  | ļ   | LDH<br>IU/                    | Q   | G-GTP<br>IU∕Ω | )    | CPK<br>IU/1   | 2   | UREA N<br>mg⁄dl |       | CREATIN<br>mg/dl | INE    |
| Control                       | 5                 | 55±         | 2   | 29±          | 1   | 207±                          | 77  | 2±            | 1    | 176±          | 59  | 14.8±           | 1.7   | 0.4±             | 0.0    |
| 1250 ppm                      | 5                 | 57±         | 3   | 28±          | 2   | 185±                          | 70  | 2±            | 1    | 190±          | 87  | 16.5±           | 1.9   | 0.4±             | 0.1    |
| 2500 ppm                      | 5                 | 52土         | 3   | 29±          | 2   | 175±                          | 66  | 2土            | 1    | 160±          | 41  | 15.6±           | 2.4   | 0.4±             | 0.1    |
| 5000 maa                      | 5                 | 51±         | 1   | 29±          | 2   | 153±                          | 33  | 2±            | 0    | 128±          | 14  | 16.5±           | 2.2   | 0.4±             | 0.0    |
| 10000 ppm                     | 4                 | 43±         | 3*  | 28±          | 5   | 168±                          | 40  | 7±            | 1    | 1 <b>23</b> ± | 11  | 17.9±           | 1.0   | 0.4±             | 0.0    |
| 20000 ppm                     | 5                 | 90±         | 56  | 104±         | 79* | 304±                          | 137 | 53±           | 28   | 112±          | 55* | 37.2±           | 9.2** | 0.4±             | 0.0    |
| Significant                   | difference ;      | *:P≦0       | .05 | ** : P ≦ 0.0 | 1   | <u>. ,, </u>                  |     | Test of Dun   | nett | -             |     |                 |       |                  |        |
| IICL074)                      |                   |             |     |              |     |                               |     |               |      |               |     |                 |       |                  | BAIS   |

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|                               | F344/DuCrj        |                 |       |                 |       | OCHEMISTRY (S<br>L ANIMALS ( |     |                 |       |                  |                |          |
|-------------------------------|-------------------|-----------------|-------|-----------------|-------|------------------------------|-----|-----------------|-------|------------------|----------------|----------|
| MEASURE. TIME :<br>SEX : MALE |                   | CYPE : A1       |       |                 |       |                              |     |                 |       |                  |                | PAGE : 3 |
| Group Name                    | NO. of<br>Animals | SODIUM<br>mEq⁄Q |       | POTASSI<br>mEq⁄ |       | CHLORIDE<br>mEq⁄2            |     | CALCIU<br>mg⁄d£ |       | INORGAI<br>mg/d& | NIC PHOSPHORUS |          |
| Control                       | 5                 | 140±            | 1     | 4.1±            | 0.3   | 105±                         | 1   | 10.9±           | 0.1   | 7.7±             | 1.2            |          |
| 1250 ppm                      | 5                 | 140±            | 1     | 4.0±            | 0.2   | 104±                         | 1   | 10.9±           | 0.2   | 7.8±             | 1.2            |          |
| 2500 ppm                      | 5                 | $139\pm$        | 1     | 4.3±            | 0.3   | 104±                         | 0   | 11.0±           | 0.1   | 8.6±             | 1.2            |          |
| 5000 mag                      | 5                 | 140±            | 1     | 4.5±            | 0.2   | 102±                         | 1*  | 11.3±           | 0.1*  | 9.7±             | 1.6*           |          |
| 10000 ppm                     | 4                 | 138±            | 2     | 5.3±            | 0.3** | 101±                         | 1** | 11.4±           | 0.2** | 9.5±             | 0.8            |          |
| 20000 maja                    | 5                 | 143±            | 1**   | 4.8±            | 0.7*  | 105±                         | 2   | 10.8±           | 0.3   | 6.8±             | 0.5            |          |
| Significant                   | difference ;      | *:P≦0.          | .05 * |                 |       |                              |     | Test of Dur     | nnett |                  | <u></u>        |          |
| (HCL074)                      |                   |                 |       |                 |       |                              |     |                 |       |                  |                | BAIS 3   |

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# APPENDIX F 2

# BIOCHEMISTRY : SUMMARY, RAT : FEMALE

| up Name     | NO. of<br>Animals | TOTAL F<br>g⁄dl | ROTEIN | ALBUMIN<br>g⁄dl | Į<br> | A/G RAT | 017 | T-BILI<br>mg∕dl |        | GLUCOSE<br>mg∕dl |     | T-CHOLES<br>mg∕dl | TEROL | PHOSPHO<br>mg/dl | LIPID |
|-------------|-------------------|-----------------|--------|-----------------|-------|---------|-----|-----------------|--------|------------------|-----|-------------------|-------|------------------|-------|
| Control     | 5                 | 5.4±            | 0.1    | 3.6±            | 0.1   | 1.9±    | 0.1 | 0.12±           | 0.00   | 173±             | 12  | 69±               | 2     | 125±             | 6     |
| 1250 ppm    | 5                 | 5.4±            | 0.2    | 3.5±            | 0.1   | 1.9±    | 0.1 | 0.13±           | 0.01   | 177±             | 14  | 68±               | 4     | 124±             | 10    |
| 2500 ppm    | 5                 | 5.4±            | 0.1    | $3.5\pm$        | 0.1   | 1.9±    | 0.1 | 0.14±           | 0.01   | 174±             | 12  | 73±               | 6     | 133±             | 11    |
| 5000 ppm    | 5                 | 5.8±            | 0.2**  | 3.8±            | 0.2   | 1.9±    | 0.1 | 0.18±           | 0.02** | 160±             | 13  | 105±              | 7**   | 177±             | 8**   |
| 10000 ppm · | 5                 | 6.4±            | 0.1**  | 4.2±            | 0.1** | 1.9±    | 0.1 | 0.22±           | 0.04** | $145\pm$         | 4** | $141\pm$          | 2**   | $235\pm$         | 6**   |
| 20000 ppm   | 0                 | -               |        | -               |       | -       |     |                 |        | -                |     | -                 |       | -                |       |

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| up Name   | NO. of<br>Animals | GOT<br>IU∕₽ | ······ | GPT<br>IU/& |   | LDH<br>IU/J | 2   | G-GTP<br>IU∕& |     | CPK<br>IU/Q |    | UREA NI<br>mg∕dl |     | CREATIN<br>mg∕dl | INE |
|-----------|-------------------|-------------|--------|-------------|---|-------------|-----|---------------|-----|-------------|----|------------------|-----|------------------|-----|
| Control   | 5                 | 59±         | 4      | 28±         | 1 | 246±        | 54  | 2± -          | 1   | 153±        | 29 | 16.9±            | 3.4 | 0.4±             | 0.1 |
| 1250 ppm  | 5                 | 63±         | 5      | 30±         | 3 | 358±        | 198 | 3±            | 1   | 183±        | 66 | 17.4±            | 2.8 | 0.4±             | 0.1 |
| 2500 ppm  | 5                 | 64±         | 6      | 29±         | 3 | 346±        | 94  | 3±            | 1   | 183±        | 45 | 18.8±            | 3.5 | 0.4±             | 0.1 |
| 5000 ppm  | 5                 | $58\pm$     | 4      | 28±         | 3 | 333±        | 141 | 3±            | 1   | 161土        | 43 | 20.4±            | 1.5 | 0.4±             | 0.0 |
| 10000 ppm | 5                 | $59\pm$     | 4      | $31\pm$     | 5 | 498±        | 230 | 13±           | 1** | 192±        | 52 | 20.4±            | 2.7 | 0.4±             | 0.0 |
| 20000 ppm | 0                 | -           |        |             |   | -           |     | -             |     | -           |    | ***              |     | -                |     |

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| X : FEMALE | REPORT T          | YPE : A1        |   |                  |      |                   |   |                  |       |                  |               | PAGE : |
|------------|-------------------|-----------------|---|------------------|------|-------------------|---|------------------|-------|------------------|---------------|--------|
| DUP Name   | NO. of<br>Animals | SODIUM<br>mEq⁄Q |   | POTASSI<br>mEq/1 |      | CHLORIDE<br>mEq/l |   | CALCIUM<br>mg/dl |       | INORGAN<br>mg∕dl | IC PHOSPHORUS |        |
| Control    | 5                 | 139±            | 1 | 4.1±             | 0.4  | 106±              | 1 | 10.5±            | 0.1   | 7.0±             | 1.1           |        |
| 1250 ppm   | 5                 | 139±            | 1 | 4.3±             | 0.6  | 106±              | 2 | 10.5±            | 0.1   | 7.1±             | 1.5           |        |
| 2500 ppm   | 5                 | $139\pm$        | 1 | 4.0±             | 0.4  | 107±              | 3 | 10.4±            | 0.1   | 6.3±             | 1.6           |        |
| 5000 ppm   | 5                 | 138±            | 1 | 4.7±             | 0.4  | 105±              | 2 | 10.8±            | 0.2*  | 7.9±             | 1.9           |        |
| 10000 ppm  | 5                 | 139±            | 1 | 5.1±             | 0.7* | 105±              | 2 | 11.0±            | 0.1** | 7.9±             | 0.9           |        |
| 20000 ppm  | 0                 | -               |   | -                |      | -                 |   | -                |       | -                |               |        |

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## APPENDIX G 1

# GROSS FINDINGS : SUMMARY, RAT : MALE ALL ANIMALS (2-WEEK STUDY)

| ANIMAL<br>REPORT TYPE | : 0360<br>: RAT F344/DuCrj<br>: A1<br>: MALE | GROSS FINDINGS (SUMMARY)<br>ALL ANIMALS (O- 2W) |                  |                   | PAGE : 1          |                   |
|-----------------------|----------------------------------------------|-------------------------------------------------|------------------|-------------------|-------------------|-------------------|
| 0rgan                 | Findings                                     | Group Name<br>NO. of Animals                    | Control<br>5 (%) | 1250 ppm<br>5 (%) | 2500 ppm<br>5 (%) | 5000 ppm<br>5 (%) |
|                       | aturah ia                                    |                                                 | 0 ( 0)           | 0 ( 0)            | 0 ( 0)            | 0 ( 0)            |
| thymus                | atrophic                                     |                                                 | 0 ( 0)           | 0 ( 0)            | 0 ( 0)            | 0 ( 0)            |
| spleen                | dark                                         |                                                 | 0 ( 0)           | 0 ( 0)            | 0 ( 0)            | 5 (100)           |
| liver                 | dark                                         |                                                 | 0 ( 0)           | 0 ( 0)            | 0 ( 0)            | 0 ( 0)            |
|                       | herniation                                   |                                                 | 0 ( 0)           | 1 (20)            | 0 ( 0)            | 0 ( 0)            |
|                       |                                              |                                                 |                  |                   |                   |                   |

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| ANIMAL<br>REPORT TYPE | : 0360<br>: RAT F344/DuCrj<br>: A1<br>: MALE | GROSS FINDINGS (SUMMARY)<br>ALL ANIMALS (O- 2W) |                    |                    |  |  |  |  |
|-----------------------|----------------------------------------------|-------------------------------------------------|--------------------|--------------------|--|--|--|--|
| Organ                 | Findings                                     | Group Name<br>NO. of Animals                    | 10000 ppm<br>5 (%) | 20000 ppm<br>5 (%) |  |  |  |  |
| thymus                | atrophic                                     |                                                 | 0 ( 0)             | 5 (100)            |  |  |  |  |
| spleen                | dark                                         |                                                 | 4 (80)             | 5 (100)            |  |  |  |  |
| liver                 | dark                                         |                                                 | 0 ( 0)             | 5 (100)            |  |  |  |  |
|                       | herniation                                   |                                                 | 0 ( 0)             | 0 ( 0)             |  |  |  |  |

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## APPENDIX G 2

# GROSS FINDINGS : SUMMARY, RAT : FEMALE ALL ANIMALS (2-WEEK STUDY)

| ANIMAL<br>REPORT TYPE | : 0360<br>: RAT F344/DuGrj<br>: A1<br>: FEMALE | GROSS FINDINGS (SUMMARY)<br>ALL ANIMALS (0- 2W)<br>PACE : |                  |                   |                   |                   |  |  |  |
|-----------------------|------------------------------------------------|-----------------------------------------------------------|------------------|-------------------|-------------------|-------------------|--|--|--|
| 0rgan                 | Findings                                       | Group Name<br>NO. of Animals                              | Contral<br>5 (%) | 1250 ppm<br>5 (%) | 2500 ppm<br>5 (%) | 5000 ppm<br>5 (%) |  |  |  |
| thymus                | atrophic                                       |                                                           | 0 ( 0)           | 0 ( 0)            | 0 ( 0)            | 0 ( 0)            |  |  |  |
| spleen                | dark                                           |                                                           | 0 ( 0)           | 0 ( 0)            | 0 ( 0)            | 5 (100)           |  |  |  |
| liver                 | herniation                                     |                                                           | 0 ( 0)           | 2 (40)            | 0 ( 0)            | 0 ( 0)            |  |  |  |
|                       |                                                |                                                           |                  |                   |                   |                   |  |  |  |

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| ANIMAL<br>REPORT TYPE | : 0360<br>: RAT F344/DuCrj<br>: A1<br>: FEMALE | GROSS FINDINGS (SUMMARY)<br>ALL ANIMALS (O- 2W) | GROSS FINDINGS (SUMMARY)<br>ALL ANIMALS (0- 29) |                    |  |  |  |  |
|-----------------------|------------------------------------------------|-------------------------------------------------|-------------------------------------------------|--------------------|--|--|--|--|
| 0rgan                 | Findings                                       | Group Name<br>NO. of Animals                    | 10000 ppm<br>5 (%)                              | 20000 ppm<br>5 (%) |  |  |  |  |
| thymus                | atrophic                                       |                                                 | 0 ( 0)                                          | 5 (100)            |  |  |  |  |
| spleen                | · dark                                         |                                                 | 4 (80)                                          | 0 ( 0)             |  |  |  |  |
| liver                 | herniation                                     |                                                 | 0 ( 0)                                          | 0 ( 0)             |  |  |  |  |
|                       |                                                |                                                 |                                                 |                    |  |  |  |  |

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APPENDIX G 3

# GROSS FINDINGS : SUMMARY, RAT : FEMALE : DEAD AND MORIBUND ANIMALS (2-WEEK STUDY)

| STUDY NO. : 0360<br>ANIMAL : RAT F344/DuCrj<br>REPORT TYPE : A1<br>SEX : FEMALE | GROSS FINDINGS (SUMMARY)<br>DEAD AND MORIBUND ANIMALS (0- 2W)<br>PAGE : |               |                   |                   |                   |  |  |  |
|---------------------------------------------------------------------------------|-------------------------------------------------------------------------|---------------|-------------------|-------------------|-------------------|--|--|--|
| Organ Findings                                                                  | Group Name Co<br>NO. of Animals 0                                       | ontrol<br>(%) | 1250 ppm<br>0 (%) | 2500 ppm<br>0 (%) | 5000 ppm<br>0 (%) |  |  |  |
| thymus atrophic                                                                 |                                                                         | ( -)          | - ( -)            | - ( -)            | - ( -)            |  |  |  |
|                                                                                 |                                                                         |               |                   |                   | D1100             |  |  |  |

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(HPT080)

| STUDY NO. : 0360<br>ANIMAL : RAT F344/DuCrj<br>REPORT TYPE : A1<br>SEX : FEMALE | GROSS FINDINGS (SUMMARY)<br>DEAD AND MORIBUND ANIMALS (0- 2W) | PAGE : 2 |
|---------------------------------------------------------------------------------|---------------------------------------------------------------|----------|
| Organ Findings                                                                  | Group Name 10000 ppm 20000 ppm<br>NO. of Animals 0 (%) 5 (%)  |          |
| thymus atrophic                                                                 | - ( -) 5 (100)                                                |          |
| (HPT080)                                                                        |                                                               | BAIS 3   |

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### APPENDIX G 4

# GROSS FINDINGS : SUMMARY, RAT : MALE : SACRIFICED ANIMALS (2-WEEK STUDY)

| ANIMAL<br>REPORT TYPE | : 0360<br>: RAT F344/DuCrj<br>: A1<br>: MALE | GROSS FINDINGS (SUMMARY)<br>SACRIFICED ANIMALS ( 2W)<br>PAGE : |                  |                   |                   |                   |  |  |  |  |
|-----------------------|----------------------------------------------|----------------------------------------------------------------|------------------|-------------------|-------------------|-------------------|--|--|--|--|
| Organ                 | Findings                                     | Group Name<br>NO, of Animals                                   | Control<br>5 (%) | 1250 ppm<br>5 (%) | 2500 ppm<br>5 (%) | 5000 ppm<br>5 (%) |  |  |  |  |
| thymus                | atrophic                                     |                                                                | 0 ( 0)           | 0 ( 0)            | 0 ( 0)            | 0 ( 0)            |  |  |  |  |
| spleen                | dark                                         |                                                                | 0 ( 0)           | 0 ( 0)            | 0 ( 0)            | 5 (100)           |  |  |  |  |
| liver                 | dark                                         |                                                                | 0 ( 0)           | 0 ( 0)            | 0 ( 0)            | 0 ( 0)            |  |  |  |  |
|                       | herniation                                   |                                                                | 0 ( 0)           | 1 (20)            | 0 ( 0)            | 0 ( 0)            |  |  |  |  |
|                       |                                              |                                                                |                  |                   |                   |                   |  |  |  |  |

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(HPT080)

| ANIMAL<br>REPORT TYPE | : 0360<br>: RAT F344/DuCrj<br>: A1<br>: MALE | GROSS FINDINGS (SUMMARY)<br>SACRIFICED ANIMALS ( 2W) | PAGE : 2           |                    |  |
|-----------------------|----------------------------------------------|------------------------------------------------------|--------------------|--------------------|--|
| 0rgan                 | Findings                                     | Group Name<br>NO. of Animals                         | 10000 ppm<br>5 (%) | 20000 ppm<br>5 (%) |  |
| thymus                | atrophic                                     |                                                      | 0 ( 0)             | 5 (100)            |  |
| spleen                | dark                                         |                                                      | 4 (80)             | 5 (100)            |  |
| liver                 | dark                                         |                                                      | 0 ( 0)             | 5 (100)            |  |
|                       | herniation                                   |                                                      | 0 ( 0)             | 0 ( 0)             |  |
|                       |                                              |                                                      |                    |                    |  |

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## APPENDIX G 5

# GROSS FINDINGS : SUMMARY, RAT : FEMALE : SACRIFICED ANIMALS (2-WEEK STUDY)

| STUDY NO.<br>ANIMAL<br>REPORT TYPE<br>SEX | : 0360<br>: RAT F344/DuCrj<br>: A1<br>: FEMALE | GROSS FINDINGS (SUMMARY)<br>SACRIFICED ANIMALS ( 2W) | PAGE : 3         |                   |                   |                   |
|-------------------------------------------|------------------------------------------------|------------------------------------------------------|------------------|-------------------|-------------------|-------------------|
| Organ                                     | Findings                                       | Group Name<br>NO. of Animals                         | Control<br>5 (%) | 1250 ppm<br>5 (%) | 2500 ppm<br>5 (%) | 5000 ppm<br>5 (%) |
| spleen                                    | dark                                           |                                                      | 0 ( 0)           | 0 ( 0)            | 0 ( 0)            | 5 (100)           |
| liver                                     | herniation                                     |                                                      | 0 ( 0)           | 2 (40)            | 0 ( 0)            | 0 ( 0)            |
| (HPT080)                                  |                                                |                                                      |                  |                   |                   | BAIS 3            |

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| ANIMAL<br>REPORT TYPE | : 0360<br>: RAT F344/DuCrj<br>: A1<br>: FEMALE | GROSS FINDINGS (SUMMARY)<br>SACRIFICED ANIMALS ( 2W) |                    |                    | PAGE: 4 |
|-----------------------|------------------------------------------------|------------------------------------------------------|--------------------|--------------------|---------|
| Organ                 | Findings                                       | Group Name<br>NO. of Animals                         | 10000 ppm<br>5 (%) | 20000 ppm<br>0 (%) |         |
| spleen                | dark                                           |                                                      | 4 (80)             | - ( -)             |         |
| liver                 | herniation                                     |                                                      | 0 ( 0)             | - ( -)             |         |
| (HPT080)              |                                                |                                                      |                    |                    | BAIS3   |

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APPENDIX H 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : MALE

(2-WEEK STUDY)

| STUDY NO. : 036<br>ANIMAL : RAT<br>REPORT TYPE : 1<br>SEX : MALE | ſ F344/DuCrj      |          | ORGAN WEIGHT:ABSOLUTE (SUMMARY)<br>SURVIVAL ANIMALS ( 2W) |               |         |        |       |               |       |        |         |        |         |          |
|------------------------------------------------------------------|-------------------|----------|-----------------------------------------------------------|---------------|---------|--------|-------|---------------|-------|--------|---------|--------|---------|----------|
| UNIT: g<br>Group Name                                            | NO. of<br>Animals | Body     | Weight                                                    | ТНҮМ          | US      | ADRE   | NALS  | TESTI         | ES    | HEAR   | Γ       | LUNG   | S       | PAGE : 1 |
| Control                                                          | 5                 | 192±     | 4                                                         | 0.361±        | 0.019   | 0.045± | 0.003 | 2.469±        | 0.110 | 0.662± | 0.046   | 0.839± | 0.020   |          |
| 1250 ppm                                                         | 5                 | 190±     | 5                                                         | 0.354±        | 0.031   | 0.044± | 0.004 | $2.465 \pm$   | 0.078 | 0.692± | 0.028   | 0.818± | 0.046   |          |
| 2500 ppm                                                         | 5                 | 190±     | 6                                                         | 0.360±        | 0.030   | 0.043± | 0.004 | $2.482\pm$    | 0.124 | 0.697± | 0.042   | 0.825± | 0.033   |          |
| 5000 ppm                                                         | 5                 | 184±     | 5                                                         | 0.349±        | 0,032   | 0.046± | 0.004 | $2.567\pm$    | 0.134 | 0.691± | 0.062   | 0.819± | 0.023   |          |
| 10000 ppm                                                        | 5                 | $157\pm$ | 3**                                                       | 0.282±        | 0.018** | 0.046± | 0.004 | 2.472±        | 0.111 | 04562± | 0.020** | 0.767± | 0.098   |          |
| 20000 ppm                                                        | 5                 | 87±      | 10**                                                      | 0.039±        | 0.016** | 0.043± | 0.003 | 1.545±        | 0.387 | 0.369± | 0.049** | 0.540± | 0.031** |          |
| Significan                                                       | t difference ;    | *:P≦0.   | 05                                                        | ** : P ≦ 0.01 |         |        | Te    | st of Dunnett |       |        |         |        |         |          |
| (UCL040)                                                         |                   |          |                                                           |               |         |        |       |               |       |        |         |        |         | DALCO    |

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(HCL040)

| NIT: g<br>roup Name | NO. of  | KID    | NEYS    | SPL    | EEN     | LIV        | ER      | BRA        |        | PAGE : |
|---------------------|---------|--------|---------|--------|---------|------------|---------|------------|--------|--------|
|                     | Animals |        |         |        |         |            |         | <u> </u>   |        |        |
| Control             | 5       | 1.473± | 0.059   | 0.483± | 0.028   | $7.582\pm$ | 0.408   | 1.716±     | 0.042  |        |
| 1250 ppm            | 5       | 1.459± | 0.025   | 0.472± | 0.018   | 7.648±     | 0.380   | 1.726±     | 0.029  |        |
| 2500 ppm            | 5       | 1.575± | 0.102   | 0.539± | 0.040   | 8.612±     | 0.378   | 1.759±     | 0.062  |        |
| 5000 ppm            | 5       | 1.725± | 0.079** | 0.820± | 0.065** | 9.830±     | 0.353*  | $1.752\pm$ | 0.061  |        |
| 10000 ppm           | 5       | 1.577± | 0.105   | 0.858± | 0.078** | 10.952±    | 1.061** | 1.678±     | 0.054  |        |
| 20000 mag           | 5       | 1.204± | 0.106** | 0.381± | 0.041*  | 6.960±     | 1.232   | 1.616±     | 0.022* |        |
| 20000 maa           |         | 1.204± | 0.106** |        |         |            | 1.232   |            | 0.022* |        |

STUDY NO. : 0360

ORGAN WEIGHT: ABSOLUTE (SUMMARY)

APPENDIX H 2

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

| REPORT TYPE : 1         | ſ F344/DuCrj      |         |        |              |                                       | WEIGHT:ABSOLU<br>VAL ANIMALS ( |       | RY)           |         |        |         |        |        |          |
|-------------------------|-------------------|---------|--------|--------------|---------------------------------------|--------------------------------|-------|---------------|---------|--------|---------|--------|--------|----------|
| SEX : FEMALE<br>UNIT: g |                   |         |        |              |                                       |                                |       |               |         |        |         |        |        | PAGE : 3 |
| Group Name              | NO. of<br>Animals | Body 🖡  | leight | ТНУМ         | US                                    | ADREI                          | NALS  | OVAR          | IES     | HEAR   | ſ       | LUNG   | S      |          |
| Control                 | 5                 | 126±    | 6      | 0.286±       | 0.020                                 | 0.050±                         | 0.005 | 0.105±        | 0.015   | 0.499± | 0.020   | 0.646± | 0.046  |          |
| 1250 ppm                | 5 ·               | 123±    | 7      | 0.293±       | 0.014                                 | 0.052±                         | 0.008 | 0.098±        | 0.007   | 0.484± | 0.030   | 0.647± | 0.036  |          |
| 2500 ppm                | 5                 | 120±    | 8      | 0.280±       | 0.026                                 | 0.049±                         | 0.006 | 0.097±        | 0.015   | 0.480± | 0.046   | 0.615± | 0.031  |          |
| 5000 ppm                | 5                 | 118±    | 5      | 0.271±       | 0.022                                 | 0.044±                         | 0.006 | 0.095±        | 0.020   | 0.491± | 0.027   | 0.628± | 0.043  |          |
| 10000 ppm               | 5                 | 107±    | 6**    | 0.248±       | 0.021*                                | 0.042±                         | 0.004 | 0.064±        | 0.009** | 0.424± | 0.026** | 0.573± | 0.022* |          |
| 20000 ppm .             | 0                 | _       |        | -            |                                       | -                              |       | -             |         | -      |         |        |        |          |
| Significan              | t difference ;    | *:P≦0.0 | )5 *   | * : P ≤ 0.01 |                                       |                                | Te    | st of Dunnett |         |        |         |        |        |          |
| (HCL040)                |                   |         |        |              | · · · · · · · · · · · · · · · · · · · |                                |       |               | u       |        |         |        |        | BAIS 3   |

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(HCL040)

| STUDY NO. : 036<br>ANIMAL : RA<br>REPORT TYPE : A<br>SEX : FEMALE<br>UNIT: g | T F344/DuCrj      |        | ORGAN WEIGHT:ABSOLUTE (SUMMARY)<br>SURVIVAL ANIMALS ( 2W) |                                        |         |        |         |              |       |      |                                       | PAGE: 4    |
|------------------------------------------------------------------------------|-------------------|--------|-----------------------------------------------------------|----------------------------------------|---------|--------|---------|--------------|-------|------|---------------------------------------|------------|
| Group Name                                                                   | NO. of<br>Animals | KID    | NEYS                                                      | SPL                                    | EEN     | LIV    | ER      | BRA          | IN    | <br> |                                       |            |
| Control                                                                      | 5                 | 1.006± | 0.040                                                     | 0.330±                                 | 0.026   | 4.462± | 0.381   | 1.611±       | 0.039 |      |                                       |            |
| 1250 ppm                                                                     | 5                 | 1.021± | 0.079                                                     | $0.340\pm$                             | 0.024   | 4.485± | 0.233   | 1.619±       | 0.024 |      |                                       |            |
| 2500 ppm                                                                     | 5                 | 1.026± | 0.059                                                     | 0.354±                                 | 0.027   | 4.767± | 0.496   | $1.637\pm$   | 0.024 |      |                                       |            |
| 5000 ppm                                                                     | 5                 | 1.076± | 0.089                                                     | 0.606±                                 | 0.054** | 6.022± | 0.363** | $1.618 \pm$  | 0.070 |      |                                       |            |
| mqq 00001                                                                    | 5                 | 1.045± | 0.066                                                     | 0.580±                                 | 0.028** | 7.019± | 0.509** | 1.606±       | 0.025 |      |                                       |            |
| 20000 ppm                                                                    | 0                 | -      |                                                           | -                                      |         | -      |         | -            |       |      |                                       |            |
| Significan                                                                   | t difference ;    | *:P≦0. | 05 **                                                     | : P ≦ 0.01                             |         |        | Te      | st of Dunnet | t     | <br> |                                       | <br>       |
| (HCL040)                                                                     |                   |        |                                                           | ······································ |         |        |         |              |       | <br> | · · · · · · · · · · · · · · · · · · · | <br>BAIS 3 |

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APPENDIX I 1

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : MALE

(2-WEEK STUDY)

| STUDY NO. : 036<br>ANIMAL : RAT<br>REPORT TYPE : A | F344/DuCrj        |        | ORGAN WEIGHT:RELATIVE (SUMMARY)<br>SURVIVAL ANIMALS ( 2W) |                |                |               |                |               |          |  |  |
|----------------------------------------------------|-------------------|--------|-----------------------------------------------------------|----------------|----------------|---------------|----------------|---------------|----------|--|--|
| SEX : MALE<br>UNIT: %                              |                   |        |                                                           |                |                |               |                |               | PAGE : 1 |  |  |
| Group Name                                         | NO. of<br>Animals |        | Weight<br>(g)                                             | THYMUS         | ADRENALS       | TESTES        | HEART          | LUNGS         |          |  |  |
| Control                                            | 5                 | 192±   | 4                                                         | 0.188± 0.007   | 0.023± 0.002   | 1.287± 0.032  | 0.345± 0.019   | 0.438± 0.015  |          |  |  |
| 1250 ppm                                           | 5                 | 190±   | 5                                                         | 0.186± 0.011   | 0.023± 0.001   | 1.296± 0.029  | 0.364± 0.007   | 0.430± 0.016  |          |  |  |
| 2500 ppm                                           | 5                 | 190±   | 6                                                         | 0.189± 0.015   | 0.023± 0.003   | 1.304± 0.054  | 0.366± 0.016   | 0.433± 0.007  |          |  |  |
| 5000 ppm                                           | 5                 | 184±   | 5                                                         | 0.190± 0.017   | 0.025± 0.002   | 1.396± 0.059  | 0.376± 0.025   | 0.446± 0.009  |          |  |  |
| 10000 ppm                                          | 5                 | 157±   | 3**                                                       | 0.179± 0.014   | 0.029± 0.002   | 1.572± 0.051* | 0.358± 0.019   | 0.487± 0.055  |          |  |  |
| 20000 ppm                                          | 5                 | 87±    | 10**                                                      | 0.043± 0.013** | 0.050± 0.008** | 1.755± 0.298* | 0.422± 0.024** | 0.624± 0.059* |          |  |  |
| Significant                                        | t difference ;    | *:P≦0. | 05 **                                                     | : P ≤ 0.01     | Test           | t of Dunnett  |                |               |          |  |  |

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(IICL042)

| oup Name  | NO. of<br>Animals | KIDNEYS        | SPLEEN         | LIVER          | BRAIN          |  |
|-----------|-------------------|----------------|----------------|----------------|----------------|--|
| Control   | 5                 | 0.769± 0.034   | 0.252± 0.015   | 3.954± 0.207   | 0.895± 0.029   |  |
| 1250 ppm  | 5                 | 0.767± 0.017   | 0.248± 0.011   | 4.021± 0.158   | 0.908± 0.024   |  |
| 2500 ppm  | 5                 | 0.827± 0.035   | 0.283± 0.015   | 4.524± 0.171   | 0.924± 0.025   |  |
| 5000 ppm  | 5                 | 0.938± 0.030** | 0.446± 0.029** | 5.350± 0.210   | 0.953± 0.033   |  |
| 10000 mag | 5                 | 1.003± 0.052** | 0.545± 0.040** | 6.963± 0.607** | 1.067± 0.024*  |  |
| 20000 ppm | 5                 | 1.385± 0.057** | 0.438± 0.040** | 7.943± 0.613** | 1.869± 0.186** |  |

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APPENDIX I 2

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

(2-WEEK STUDY)

| ANIMAL : RAT<br>REPORT TYPE : A | REPORT TYPE : A1<br>SEX : FEMALE |          | ORGAN WEIGHT:RELATIVE (SUMMARY)<br>SURVIVAL ANIMALS ( 2W) |              |              |                |              |              |          |  |  |
|---------------------------------|----------------------------------|----------|-----------------------------------------------------------|--------------|--------------|----------------|--------------|--------------|----------|--|--|
| UNIT: %                         |                                  |          |                                                           |              |              |                |              |              | PAGE : 3 |  |  |
| Group Name                      | NO. of<br>Animals                |          | leight<br>(g)                                             | THYMUS       | ADRENALS     | OVARIES        | HEART        | LUNGS        |          |  |  |
| Control                         | 5                                | 126±     | 6                                                         | 0.226± 0.013 | 0.040± 0.004 | 0.083± 0.014   | 0.396± 0.021 | 0.512± 0.019 |          |  |  |
| 1250 ppm                        | 5                                | $123\pm$ | 7                                                         | 0.238± 0.019 | 0.042± 0.005 | 0.079± 0.007   | 0.393± 0.025 | 0.525± 0.017 |          |  |  |
| 2500 mag                        | 5                                | 120±     | 8                                                         | 0.234± 0.015 | 0.041± 0.004 | 0.081± 0.008   | 0.400± 0.017 | 0.514± 0.024 |          |  |  |
| 5000 ppm                        | 5                                | 118±     | 5                                                         | 0.230± 0.011 | 0.037± 0.005 | 0.080± 0.014   | 0.416± 0.017 | 0.532± 0.021 |          |  |  |
| 10000 ppm                       | 5                                | 107±     | 6**                                                       | 0.232± 0.011 | 0.040± 0.004 | 0.060± 0.006** | 0.398± 0.022 | 0.538± 0.020 |          |  |  |
| 20000 ppm                       | 0                                | -        |                                                           | -            | -            | -              | -            | -            |          |  |  |
| Significant                     | difference;                      | *:P≦0.   | 05 **                                                     | : P ≦ 0.01   | Te           | st of Dunnett  |              |              |          |  |  |

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(HCL042)

| REPORT TYPE : /         | NIMAL : RAT F344/DuC-j<br>EPORT TYPE : A1<br>EX : FEMALE |                |                | VEIGHT:RELATIVE (SUMMARY<br>NL ANIMALS ( 2W) | )              |          |
|-------------------------|----------------------------------------------------------|----------------|----------------|----------------------------------------------|----------------|----------|
| SEX : FEMALE<br>UNIT: % |                                                          |                |                |                                              |                | PAGE : 4 |
| Group Name              | NO. of<br>Animals                                        | KIDNEYS        | SPLEEN         | LIVER                                        | BRAIN          |          |
| Control                 | 5                                                        | 0.798± 0.030   | 0.262± 0.016   | 3.532± 0.177                                 | 1.278± 0.051   |          |
| 1250 ppm                | 5                                                        | 0.828± 0.031   | 0.276± 0.010   | 3.644± 0.160                                 | 1.317± 0.057   |          |
| 2500 ppm                | 5                                                        | 0.857± 0.025*  | 0.296± 0.020   | 3.973± 0.194**                               | 1.372± 0.097   |          |
| 5000 ppm                | 5                                                        | 0.911± 0.047** | 0.514± 0.046** | 5.103± 0.189**                               | 1.372± 0.046   |          |
| 10000 ppm               | 5                                                        | 0.979± 0.032** | 0.543± 0.026** | 6.568± 0.190**                               | 1.506± 0.058** |          |
| 20000 ppm               | 0                                                        |                | _              |                                              | _              |          |
| Significan              | t difference ;                                           | *:P≦0.05 **:   | P ≤ 0.01       | Test                                         | of Dunnett     |          |
| (IICL042)               |                                                          |                |                |                                              |                | BAIS 3   |

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APPENDIX J 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : ALL ANIMALS

(2-WEEK STUDY)

#### STUDY NO. : 0360 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- 2W)

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|               |                              |                                                                                            |                                                            |                                                                                                                  | · · · · · · · · · · · · · · · · · · ·                                                                   |
|---------------|------------------------------|--------------------------------------------------------------------------------------------|------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------|
| 0rgan         | Findings                     | Group Name Control<br>No. of Animals on Study 5<br>Grade <u>1 2 3 4</u><br>(%) (%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$      | $\begin{array}{c} 2500 \text{ ppm} \\ 5 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{c} 5000 \text{ ppm} \\ 5 \\ 1 & 2 & 3 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array} $ |
| [Respiratory  | system]                      |                                                                                            |                                                            |                                                                                                                  |                                                                                                         |
| nasal cavit   | respiratory metaplasia:gland | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                     | <pre> &lt; 5&gt;<br/>0 0 0 0<br/>( 0) ( 0) ( 0) ( 0)</pre> | <pre> &lt; 5&gt;<br/>1 0 0 0<br/>( 20) ( 0) ( 0) ( 0)</pre>                                                      | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                  |
|               | engargement of erythrocyte   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                             | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                             | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                          |
| [Hematopoieti | c system]                    |                                                                                            |                                                            |                                                                                                                  |                                                                                                         |
| bone marrow   | congestion                   | <pre>&lt; 5&gt; 0 0 0 0 ( 0) ( 0) ( 0) </pre>                                              | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                           | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                  |
| thymus        | atrophy                      | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                     | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                           | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                  |
| spleen        | deposit of hemosiderin       | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                     | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                           | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                  |
|               | extramedullary hematopoiesis | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                             | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                             | 4 0 0 0<br>(80)(0)(0)(0)                                                                                         | 5 0 0 0<br>(100) ( 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

(HPT150)

BAIS3

PAGE: 1

STUDY NO. : 0360 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- 2W)

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| )rgan         | Findinss                     | Group Name 10000 ppm<br>No. of Animals on Study 5<br>Grade <u>1 2 3 4</u><br>(%) (%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |  |
|---------------|------------------------------|----------------------------------------------------------------------------------------------|-------------------------------------------------------|--|
| Respiratory   | system]                      |                                                                                              |                                                       |  |
| nasal ca∪it   | respiratory metaplasia:gland | <pre> &lt;5&gt; 1 0 0 0 (20) (0) (0) (0) </pre>                                              | < 5><br>1 0 0 0<br>( 20) ( 0) ( 0) ( 0)               |  |
|               | engargement of erythrocyte   | 0 1 0 0<br>( 0) ( 20) ( 0) ( 0)                                                              | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        |  |
| [Hematopoieti | c system]                    |                                                                                              |                                                       |  |
| oone marrow   | congestion                   | <pre> &lt; 5&gt;<br/>0 0 0 0<br/>( 0) ( 0) ( 0) ( 0)</pre>                                   | <pre>&lt; 5&gt; 2 1 0 0 ( 40) ( 20) ( 0) ( 0)</pre>   |  |
| thymus        | atrophy                      | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                       | < 5><br>0 0 5 0<br>( 0) ( 0) (100) ( 0)               |  |
| spleen        | deposit of hemosiderin       | < 5><br>2 0 0 0<br>( 40) ( 0) ( 0) ( 0)                                                      | < 5><br>5 0 0 0<br>(100) ( 0) ( 0) ( 0)               |  |
|               | extramedullary hematopoiesis | 5 0 0 0<br>(100) ( 0) ( 0) ( 0)                                                              | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        |  |

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

b b: Number of animals with lesion

(c) c:b/a\*100

(HPT150)

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PAGE : 2

| STUDY NO.<br>ANIMAL<br>REPORT TYPE | : RAT F344/DuCrj                                                                                                       | HISTOLOGICAL FINDINGS :NON-NI<br>ALL ANIMALS (0- 20)                                                                     | EOPLASTIC LESIONS (SUMMARY)                           |                                                                                                                  |                                                       |
|------------------------------------|------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|
| SEX                                | : MALE                                                                                                                 |                                                                                                                          |                                                       | • · · · ·                                                                                                        | PAGE: 3                                               |
| Organ                              | No                                                                                                                     | Oup Name         Control           . of Animals on Study         5           ade         1         2         3         4 | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | $\begin{array}{c} 2500 \text{ ppm} \\ 5 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |
| [Hematopoie                        | tic system]                                                                                                            |                                                                                                                          |                                                       |                                                                                                                  | Ň                                                     |
| spleen                             | engargement of erythracyte                                                                                             | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                   | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | < 5><br>4 0 0 0<br>(80) (0) (0) (0)                                                                              | < 5><br>5 0 0 0<br>(100) ( 0) ( 0) ( 0)               |
| [Digestive                         | system]                                                                                                                |                                                                                                                          |                                                       |                                                                                                                  |                                                       |
| liver                              | herniation                                                                                                             | <pre>&lt; 5&gt; 0 0 0 0 ( 0) ( 0) ( 0) ( 0)</pre>                                                                        | < 5><br>1 0 0 0<br>( 20) ( 0) ( 0) ( 0)               | <.5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                           | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |
|                                    | necrosis:focal                                                                                                         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        |
|                                    | hepatocellular hypertrophy:central                                                                                     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                   | 3 0 0 0<br>(60)(0)(0)(0)                              |
| [Urinary sy                        | stem]                                                                                                                  |                                                                                                                          |                                                       |                                                                                                                  |                                                       |
| kidney                             | basophilic change                                                                                                      | < 5><br>1 0 0 0<br>( 20) ( 0) ( 0) ( 0)                                                                                  | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                           | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |
| Grade<br>< a ><br>b<br>( c )       | 1: Slight 2: Moderate 3:<br>a: Number of animals examined at the site<br>b: Number of animals with lesion<br>c:b/a*100 | Marked 4 : Severe                                                                                                        | W. <u>L. W</u>                                        |                                                                                                                  |                                                       |

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| A1<br>MALE                         | ALL ANIMALS (O- 2W)                                                           | XOPLASTIC LESIONS (SUMMARY)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | PAGE : 4                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|------------------------------------|-------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ······                             | Group Name 10000 ppm<br>No. of Animals on Study 5<br>Grade <u>1 2 3 4</u>     | 20000 ppm<br>5<br>1 2 3 4                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| Findings                           | (%) (%) (%) (%)                                                               | (%) (%) (%) (%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| system]                            |                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| ensorgement of erythrocyte         | $\begin{array}{cccc} < 5 \\ 5 & 0 & 0 \\ (100) & ( & 0) & ( & 0) \end{array}$ | < 5><br>5 0 0 0<br>(100) ( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| stem]                              |                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| herniation                         | <pre> &lt; 5&gt;<br/>0 0 0 0<br/>( 0) ( 0) ( 0) ( 0)</pre>                    | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| necrosis:focal                     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                | 0 3 0 0<br>( 0) ( 60) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| hepatocellular hypertrophy:central | 5 0 0 0<br>(100) ( 0) ( 0) ( 0)                                               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| [m                                 |                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| basophilic change                  | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                        | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|                                    | Findings                                                                      | Group Name<br>No. of Animals on Study         10000 ppm<br>5           Findings $\frac{1}{(x)}$ $\frac{2}{(x)}$ $\frac{3}{(x)}$ $\frac{4}{(x)}$ system]         engorgement of erythrocyte $5$ $0$ $0$ $0$ tem]         herniation $0$ $0$ $0$ $0$ $0$ herniation $0$ $0$ $0$ $0$ $0$ $0$ necrosis:focal $0$ $0$ $0$ $0$ $0$ $0$ hepatocellular hypertrophy:central $5$ $0$ $0$ $0$ $0$ m] $(100)$ $0$ $0$ $0$ $0$ $0$ hepatocellular hypertrophy:central $5$ $0$ $0$ $0$ $0$ m] $(0)$ $0$ $0$ $0$ $0$ $0$ $0$ | Indings       2000 ppm         Findings       2000 ppm       2000 ppm         Findings       1       2       3       4         Grade       1       2       3       4       1       2       3       4         System] $(x)$ encorgement of erythrocyte $5$ $6$ $0$ $5$ $6$ $0$ $(100)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $(0)$ $($ |

 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

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(c) c:b/a\*100

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STUDY NO. : 0360 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- 2W)

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| Organ         |                                        | Group Name<br>No. of Animals on Study<br>Grade <u>1</u><br>(%) | Control<br>5<br><u>2 3</u><br>(%) (%) | $\frac{4}{(\%)}$ $\frac{1}{(\%)}$ | 1250<br>5<br>2<br>(%) | ppm<br><u>3 4</u><br>(%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$        | 5000 ppm<br>5<br><u>1 2 3</u><br>(%) (%) (%)          | <u>4</u><br>(%) |
|---------------|----------------------------------------|----------------------------------------------------------------|---------------------------------------|-----------------------------------|-----------------------|------------------------------|--------------------------------------------------------------|-------------------------------------------------------|-----------------|
| [Urinary syst | tem]                                   |                                                                |                                       |                                   |                       |                              |                                                              |                                                       |                 |
| kidney        | eosinophilic body                      | 4                                                              | < 5><br>0 0<br>( 0) ( 0) (            | 0 5<br>0) (100)                   | < 5><br>0<br>( 0) (   | 0 0<br>0) ( 0)               | < 5><br>0 5 0 0<br>( 0) (100) ( 0) ( 0)                      | <pre></pre>                                           | 0<br>0)         |
|               | mineralization:cortico-medullary junct | tion 1<br>(20)                                                 | 0 0<br>(0)(0)(                        | 0 0<br>0) ( 0)                    | 0<br>( 0) (           | 0 0<br>0) ( 0)               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                               | 0 0 0<br>( 0) ( 0) ( 0) (                             | 0<br>0)         |
| [Endocrine sy | ystem]                                 |                                                                |                                       |                                   |                       |                              |                                                              |                                                       |                 |
| pituitary     | Rathke pouch                           | 2<br>( 40)                                                     | < 5><br>0 0<br>( 0) ( 0) (            | 0 0<br>0) ( 0)                    | < 5><br>0<br>( 0) (   | 0 0<br>0) ( 0)               | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       | <pre> &lt; 5&gt;<br/>0 0 0<br/>( 0) ( 0) ( 0) (</pre> | 0<br>0)         |
| [Reproductiv  | e system]                              |                                                                |                                       |                                   |                       |                              |                                                              |                                                       |                 |
| testis        | germ cell necrosis                     | 0<br>( 0)                                                      | < 5><br>0 0<br>( 0) ( 0) (            | 0 0<br>0) ( 0)                    | < 5><br>0<br>( 0) (   | 0 0<br>0) ( 0)               | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       | < 5><br>0 0 0<br>( 0) ( 0) ( 0) (                     | 0<br>0)         |
| epididymis    | debris of spermatic elements           | 0<br>( 0)                                                      | < 5><br>0 0<br>( 0) ( 0) (            | 0 0<br>0) ( 0)                    | < 52<br>0<br>( 0) (   | ,<br>0 0<br>0) ( 0)          | <pre> &lt; 5&gt;<br/>0 0 0 0 0<br/>( 0) ( 0) ( 0) ( 0)</pre> | < 5><br>0 0 0<br>( 0) ( 0) ( 0) (                     | 0<br>0)         |

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

b b: Number of animals with lesion

(c) c:b/a\*100

(HPT150)

BAIS3

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STUDY NO. : 0360 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- 2W)

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| 0rgan                        |                                                                                                                                | Do Name 10000 ppm<br>Dof Animals on Study 5<br>De <u>1 2 3 4</u><br>(%) (%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$       |  |
|------------------------------|--------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|-------------------------------------------------------------|--|
| [Urinary syst                | tem]                                                                                                                           |                                                                                     |                                                             |  |
| kidney                       | easinaphilic bady                                                                                                              | < 5><br>0 2 3 0<br>( 0) ( 40) ( 60) ( 0)                                            | < 5><br>3 0 0 0<br>(60) (0) (0) (0)                         |  |
|                              | mineralization:cortico-medullary junction                                                                                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                              |  |
| [Endocrine sy                | vstem]                                                                                                                         |                                                                                     |                                                             |  |
| pituitary                    | Rathke pouch                                                                                                                   | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                              | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      |  |
| [Reproductive                | e system]                                                                                                                      |                                                                                     |                                                             |  |
| testis                       | germ cell necrosis                                                                                                             | <pre> &lt; 5&gt;<br/>0 0 0 0<br/>( 0) ( 0) ( 0) ( 0)</pre>                          | < 5><br>2 0 0 0<br>( 40) ( 0) ( 0) ( 0)                     |  |
| epididymis                   | debris of spermatic elements                                                                                                   | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                              | <pre> &lt; 5&gt;<br/>3 0 0 0<br/>( 60) ( 0) ( 0) ( 0)</pre> |  |
| Grade<br>< a ><br>b<br>( c ) | 1: Slight 2: Moderate 3: Ma<br>a: Number of animals examined at the site<br>b: Number of animals with lesion<br>c: b / a * 100 | rked 4 : Severe                                                                     |                                                             |  |

(HPT150)

#### STUDY NO. : 0360 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 SEX : MALE

## HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- 2W)

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| Organ         | Findings                 | Group Name<br>No. of Animals on Study<br>Grade <u>1</u><br>(%) | Co<br>2<br>(%) | ontrol<br>5<br><u>3</u><br>(%) | 4           | <u>1</u><br>(%) | 1:<br>2<br>(%) |      | m<br>3<br>(%) | 4       | 7 | 1<br>%)   | 2500<br>E<br>2<br>(%) | ) ppm<br>5<br>3<br>(%) | <u>4</u><br>(%) | <br>(%    | <u> </u>  |         | 0 ppm<br>5<br><u>3</u><br>(%) |   | 4(%)    |
|---------------|--------------------------|----------------------------------------------------------------|----------------|--------------------------------|-------------|-----------------|----------------|------|---------------|---------|---|-----------|-----------------------|------------------------|-----------------|-----------|-----------|---------|-------------------------------|---|---------|
| 0rgan         | 1 manes                  | (N)                                                            | (107           | (%)                            |             |                 | <b>.</b>       |      |               | (M)     |   | ~         |                       | (///                   |                 | ()        |           | (M)     |                               |   |         |
| [Special sens | e organs/appendage]      |                                                                |                |                                |             |                 |                |      |               |         |   |           |                       |                        |                 |           |           |         |                               |   |         |
| Harder sl     |                          |                                                                | <              | 5>                             |             |                 |                | < 5> |               |         |   |           | < 8                   |                        |                 |           |           | <       | 5>                            |   |         |
|               | degeneration             | 0<br>( 0)                                                      | 0<br>( 0)      | 0<br>( 0)                      | 0<br>) ( 0) | 0<br>( 0)       | 0<br>( 0)      |      | 0<br>0) (     | 0<br>0) |   | 0<br>0) ( | 0<br>0) (             | 0<br>( 0)              | 0<br>( 0)       | 5<br>(100 |           | 0<br>0) | 0<br>( 0)                     | ( | 0<br>0) |
|               | lymphocytic infiltration | 0<br>( 0)                                                      | 0<br>( 0)      | 0<br>( 0)                      |             | 0<br>( 0)       | 0<br>( 0       |      | 0<br>0) (     | 0<br>0) |   | 0<br>0) ( | 0<br>0)               | 0<br>( 0)              | 0<br>( 0)       | 1<br>(20  | l<br>)) ( | 0<br>0) | 0<br>( 0)                     |   | 0<br>0) |

b : Number of animals with lesion c : b / a \* 100 ь (с)

(HPT150)

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#### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- 2W)

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| Organ                    | Findings                                                                                                            | Group Name         10000 ppm           No. of Animals on Study         5           Grade         1         2         3         4           (%)         (%)         (%)         (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |  |
|--------------------------|---------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|--|
| Special sens             | se organs/appendage]                                                                                                |                                                                                                                                                                                    |                                                       |  |
| larder gl                | degeneration                                                                                                        | < 5><br>4 1 0 0<br>( 80) ( 20) ( 0) ( 0)                                                                                                                                           | < 5><br>0 5 0 0<br>( 0) (100) ( 0) ( 0)               |  |
|                          | lymphocytic infiltration                                                                                            | $\begin{array}{cccccccccccccccccccccccccccccccccccc$                                                                                                                               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        |  |
| Grade<br>(a)<br>b<br>(c) | 1: Slight 2: Moderate<br>a: Number of animals examined at the<br>b: Number of animals with lesion<br>c: b / a * 100 | 3: Marked 4: Severe<br>site                                                                                                                                                        |                                                       |  |

(HPT150)

APPENDIX J 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : ALL ANIMALS

(2-WEEK STUDY)

#### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- 2W)

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| 0rgan          | Findings                     | Group Name         Control           No. of Animals on Study         5           Grade         1         2         3         4            (%)         (%)         (%)         (%)         (%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | $ \begin{array}{c}     1250 \text{ ppm} \\     5 \\     \frac{1}{6} \\     \hline                               $ | $\begin{array}{cccc} 2500 \text{ ppm} \\ 5 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \\ \hline \end{array}$ | 5000 ppm<br>5<br><u>1 2 3 4</u><br>(%) (%) (%) (%)         |
|----------------|------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------|
| [Respiratory s | system]                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                   |                                                                                                                               |                                                            |
| nasal cauit    | respiratory metaplasia:gland | <pre>&lt; 5&gt; 0 0 0 ( 0 0) ( 0) ( 0) ( 0) ( 0) ( 0) (</pre>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | < 5><br>0 0 0 0 0<br>0) ( 0) ( 0) ( 0) ( 0)                                                                       | . < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                      | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     |
| [Hematopoietic | system]                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                   |                                                                                                                               |                                                            |
| bone marrow    | congestion                   | <br>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | <pre> &lt; 5&gt;<br/>0 0 0 0 0<br/>0) ( 0) ( 0) ( 0) ( 0)</pre>                                                   | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                        | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     |
| thymus         | atrophy                      | <pre> <pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre> | <pre></pre>                                                                                                       | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                        | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     |
| spleen         | atrophy                      | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | <pre></pre>                                                                                                       | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                        | <pre> &lt; 5&gt;<br/>0 0 0 0<br/>( 0) ( 0) ( 0) ( 0)</pre> |
|                | deposit of hemosiderin       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                             |
|                | extramedullary hematopoiesis | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                   | 1 0 0 0<br>(20)(0)(0)(0)                                                                                                      | 5 0 0 0<br>(100) ( 0) ( 0) ( 0)                            |

(c) c:b/a\*100

(HPT150)

#### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- 2W)

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| Organ          | Findings                     | Group Name<br>No. of Animals on Study<br>Grade <u>1</u> (%) | 10000 ppm<br>5<br><u>2 3 4</u><br>(%) (%) (%) | $ \begin{array}{c} 20000 \text{ ppm} \\ 5 \\ \frac{1}{(\%)} (\%) (\%) (\%) (\%) \end{array} $ |  |
|----------------|------------------------------|-------------------------------------------------------------|-----------------------------------------------|-----------------------------------------------------------------------------------------------|--|
| [Respiratory s | system]                      |                                                             |                                               |                                                                                               |  |
| nasal cavit    | respiratory metaplasia:gland | 0<br>( 0)                                                   | < 5><br>1 0 0<br>( 20) ( 0) ( 0)              | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                        |  |
| [Hematopoietic | c system]                    |                                                             |                                               |                                                                                               |  |
| bone marrow    | congestion                   | 0<br>( 0)                                                   | < 5><br>0 0 0<br>( 0) ( 0) ( 0)               | < 5><br>0 5 0 0<br>( 0) (100) ( 0) ( 0)                                                       |  |
| thymus         | atrophy                      | 0<br>( 0)                                                   | < 5><br>0 0 0<br>( 0) ( 0) ( 0)               | < 5><br>0 0 5 0<br>( 0) ( 0) (100) ( 0)                                                       |  |
| spleen         | atrophy                      | 0<br>( 0)                                                   | < 5><br>0 0 0<br>( 0) ( 0) ( 0)               | < 5><br>0 5 0 0<br>( 0) (100) ( 0) ( 0)                                                       |  |
|                | deposit of hemosiderin       | 0<br>( 0)                                                   | 0 0 0<br>( 0) ( 0) ( 0)                       | 2 0 0 0<br>(40)(0)(0)(0)                                                                      |  |
|                | extramedullary hematopoiesis |                                                             | 0 0 0<br>( 0) ( 0) ( 0)                       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                |  |

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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

(HPT150)

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| )rgan         | i                                  | Group Name Control<br>No. of Animals on Study 5<br>Grade <u>1 2 3 4</u><br>(%) (%) (%) (%) | $\begin{array}{ccc} 1250 & \text{ppm} \\ 5 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $\begin{array}{ccc} 2500 \text{ ppm} \\ 5 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$                        |
|---------------|------------------------------------|--------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|
| Hematopoieti  | c system]                          |                                                                                            |                                                                                                                     |                                                                                                                    |                                                                              |
| spleen        | engorgement of erythrocyte         | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                     | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                              | <pre> &lt; 5&gt;     5     0     0     0 (100) ( 0) ( 0) ( 0) ( 0)</pre>                                           | <pre> &lt; 5&gt;     5     0     0     0     (100) ( 0) ( 0) ( 0) ( 0)</pre> |
| Digestive sy  | rstem]                             |                                                                                            |                                                                                                                     |                                                                                                                    |                                                                              |
| Liver         | herniation                         | <pre></pre>                                                                                | <pre> &lt; 5&gt;     2 0 0 0     ( 40) ( 0) ( 0) ( 0)     ( 0) ( 0)</pre>                                           | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                             | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                       |
|               | hepatocellular hypertrophy:central | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                             | 0 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                     | 2 0 0 0<br>(40)(0)(0)(0)(0)                                                  |
| [Urinary syst | cem]                               |                                                                                            |                                                                                                                     |                                                                                                                    |                                                                              |
| kidney        | basophilic change                  | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                     | <pre> &lt; 5&gt;     1 0 0 0     ( 20) ( 0) ( 0) ( 0) ( 0)</pre>                                                    | <pre> &lt; 5&gt;<br/>0 0 0 0<br/>( 0) ( 0) ( 0) ( 0)</pre>                                                         | < 5><br>1 0 0 0<br>( 20) ( 0) ( 0) ( 0)                                      |
|               | tubular necrosis                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                             | 0 0 0 0<br>(0)(0)(0)(0)(0)                                                                                          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                               |

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

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(HPT150)

STUDY NO. : 0360

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## HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- 2W)

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| 0rgan                        |                                                                                                                                     | up Name 10000 ppm<br>of Animals on Study 5<br>de <u>1 2 3 4</u><br>(%) (%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |     |
|------------------------------|-------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------|-------------------------------------------------------|-----|
| [Hematopoie                  | ptic system]                                                                                                                        |                                                                                    |                                                       |     |
| spleen                       | ensorgement of erythrocyte                                                                                                          | < 5><br>5 0 0 0<br>(100) ( 0) ( 0) ( 0)                                            |                                                       |     |
| [Digestive                   | system]                                                                                                                             |                                                                                    |                                                       |     |
| liver                        | herniation                                                                                                                          | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                             | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |     |
|                              | hepatocellular hypertrophy:central                                                                                                  | 4 0 0 0<br>(80) (0) (0) (0)                                                        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        |     |
| [Urinary sy                  | vstem]                                                                                                                              |                                                                                    |                                                       |     |
| kidney                       | basophilic change                                                                                                                   | <pre> &lt; 5&gt;     1 0 0 0     ( 20) ( 0) ( 0) ( 0)</pre>                        | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |     |
|                              | tubular necrosis                                                                                                                    | 0 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                   | 0 2 2 0<br>( 0) ( 40) ( 40) ( 0) .                    |     |
| Grade<br>< a ><br>b<br>( c ) | 1 : Slight 2 : Moderate 3 : M<br>a : Number of animals examined at the site<br>b : Number of animals with lesion<br>c : b / a * 100 | arked 4 : Severe                                                                   |                                                       |     |
| (HPT150)                     |                                                                                                                                     |                                                                                    | ······                                                | BAI |

#### STUDY NO. : 0360 HISTOLOC ANIMAL : RAT F344/DuCrj ALL ANIM REPORT TYPE : A1 SEX : FEMALE Group Name No. of Animals on Study Grade 1 (%)

| idney       |                                           | < 5>                                                        | < 5>                                                       | < 5>                                   | < 5>                                    |
|-------------|-------------------------------------------|-------------------------------------------------------------|------------------------------------------------------------|----------------------------------------|-----------------------------------------|
|             | mineralization:cortico-medullary junction | $\begin{array}{cccccccccccccccccccccccccccccccccccc$        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                             | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)          |
|             | mineralization:papilla                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                              | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                             | 1 0 0 0<br>(20)(0)(0)(0)               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)          |
|             | mineralization:cortex                     | 1 0 0 0<br>(20) (0) (0) (0)                                 | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                             | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)          |
| Endocrine s | vstem]                                    |                                                             |                                                            |                                        |                                         |
| ituitary    | Rathke pouch                              | <pre> &lt; 5&gt;<br/>1 0 0 0<br/>( 20) ( 0) ( 0) ( 0)</pre> | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
| thyroid     | ultimibranchial body remanet              | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
| Special sen | se organs/appendage]                      |                                                             |                                                            |                                        |                                         |
| Harder gl   | degeneration                              | <pre></pre>                                                 | <pre> &lt; 5&gt;<br/>0 0 0 0<br/>( 0) ( 0) ( 0) ( 0)</pre> | <pre></pre>                            | < 5><br>1 0 0 0<br>( 20) ( 0) ( 0) ( 0) |

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

(c) c:b/a\*100

1250 ppm

3

(%)

4

(%)

5

2

(%)

1

(%)

2500 ppm

5

2

1

(%)

<u>3</u>

(%) (%) (%)

4

Control

3

(%)

4

(%)

5

2

(%)

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5000 ppm

5

2 3 (%) (%)

1

(%)

4

(%)

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HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

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ALL ANIMALS (0- 2W)

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| 0rgan          | Findings                             | Group Name<br>No. of Animals on Stud<br>Grade | y<br><u>1</u><br>(%) | 10000<br>E<br>2<br>(%) |                | <u>4</u><br>(%) | - | 1<br>(%)  | 20000<br>2<br>(%) |                 |   | <u>4</u><br>(%)                         |
|----------------|--------------------------------------|-----------------------------------------------|----------------------|------------------------|----------------|-----------------|---|-----------|-------------------|-----------------|---|-----------------------------------------|
| [Urinary syste | em]                                  |                                               |                      |                        |                |                 |   |           |                   |                 |   |                                         |
| kidney         | mineralization:cortico-medullary jur | nction (                                      | 0<br>0) (            | < 8<br>0<br>( 0) 1     | 5><br>0<br>(0) | 0<br>(0)        | ( | 0<br>0) ( | < 4<br>0<br>0)    | 5><br>0<br>(0)  | ( | 0<br>0)                                 |
|                | mineralization:papilla               | (                                             | 0<br>0) (            | 0<br>( 0) 1            | 0<br>( 0)      | 0<br>( 0)       | ( | 0<br>0) ( | 0<br>0)           | 0<br>(0)        | ( | 0 · · · · · · · · · · · · · · · · · · · |
|                | mineralization:cortex                | (                                             | 0<br>0) (            | 0<br>( 0)              | 0<br>(0)       | 0<br>( 0)       | ( | 0<br>0) ( | 0<br>0)           | 0<br>( 0)       | ( | 0<br>0)                                 |
| [Endacrine sys | stem]                                |                                               |                      |                        |                |                 |   |           |                   |                 |   |                                         |
| pituitary      | Rathke pouch                         | (                                             | 0<br>0) (            | ( 0)                   | 5><br>0<br>(0) | 0<br>( 0)       | ( | 0<br>0) ( | く<br>0<br>0)      | 5><br>0<br>( 0) | ( | 0<br>0)                                 |
| thyroid        | ultimibranchial body remanet         |                                               | 1<br>20)             | ()<br>()               | 0              | 0<br>( 0)       | ( | 0<br>0) ( | <<br>0<br>0)      | 5><br>0<br>( 0) | ( | 0)                                      |
| [Special sense | e organs/appendage]                  |                                               |                      |                        |                |                 |   |           |                   |                 |   |                                         |
| Harder gl      | degeneration                         | (                                             | 2<br>40)             | ( 0)                   | 0              | 0<br>( 0)       | ( | 0<br>0) ( |                   | 5><br>0<br>(0)  |   | 0<br>0)                                 |

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

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

b : Number of animals with lesion b

(c) c:b/a\*100 PAGE: 14

| rgan       | Findings                 | Group Name<br>No. of Animals on Study<br>Grade <u>1</u><br>(%) | Control<br>5<br>2 3 4<br>(%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | 2500 ppm<br>5<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 5000 ppm<br>5<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|------------|--------------------------|----------------------------------------------------------------|--------------------------------------|-------------------------------------------------------|----------------------------------------------------|----------------------------------------------------|
|            |                          |                                                                |                                      |                                                       |                                                    |                                                    |
| pecial sen | se organs/appendage]     |                                                                |                                      |                                                       |                                                    |                                                    |
| rder gl    | lymphocytic infiltration | 0<br>( 0)                                                      | < 5><br>0 0 0<br>( 0) ( 0) ( 0)      | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <pre></pre>                                        | < 5><br>2 2 0 0<br>( 40) ( 40) ( 0) ( 0)           |

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

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(HPT150)

STUDY NO. : 0360

#### HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- 2W)

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| Organ                      | Findings                                                                                                                 | Group Name<br>No. of Animals on Study<br>Grade <u>1</u><br>(%) | 10000 ppm<br>5<br><u>2 3 4</u><br>(%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | <br> |
|----------------------------|--------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------|-----------------------------------------------|-------------------------------------------------------|------|
| [Special ser               | nse organs/appendage]                                                                                                    |                                                                |                                               |                                                       |      |
| Harder gl                  | lymphocytic infiltration                                                                                                 | 5<br>(100)                                                     | < 5><br>0 0 0<br>( 0) ( 0) ( 0)               | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |      |
| Grade<br>< a ><br>b<br>(c) | 1 : Slight 2 : Moderate<br>a : Number of animals examined at the<br>b : Number of animals with lesion<br>c : b / a * 100 | 3 : Marked 4 : Severe<br>site                                  |                                               |                                                       | <br> |

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(HPT150)

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APPENDIX J 3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

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

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PAGE: 1

| )rgan        | Findings                   | Group Name Control<br>No. of Animals on Study 0<br>Grade <u>1 2 3 4</u><br>(%) (%) (%) (%) | 1250 ppm<br>0<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 2500 ppm<br>0<br>1 2 3 4<br>(%) (%) (%) (%) | 5000 ppm<br>0<br>1 2 3 4<br>(%) (%) (%) (%) |
|--------------|----------------------------|--------------------------------------------------------------------------------------------|----------------------------------------------------|---------------------------------------------|---------------------------------------------|
| Hematopoieti | c system]                  |                                                                                            |                                                    |                                             |                                             |
| one marrow   |                            | < 0>                                                                                       | < 0>                                               | < 0>                                        | < 0>                                        |
|              | consection                 | < 0><br>( -) ( -) ( -) ( -)                                                                | < 0><br><br>( -) ( -) ( -) ( -)                    | < 0><br><br>( -) ( -) ( -) ( -)             | ( -) ( -) ( -) ( -)                         |
| nymus        |                            | < 0>                                                                                       | < 0>                                               | < 0>                                        | < 0>                                        |
|              | atrophy                    | ( -) ( -) ( -) ( -)                                                                        |                                                    |                                             | ( -) ( -) ( -) ( -)                         |
| pleen        |                            | < 0>                                                                                       | < 0>                                               | < 0>                                        | < 0>                                        |
|              | atrophy                    | ( -) ( -) ( -) ( -)                                                                        | ( -) ( -) ( -) ( -)                                | ( -) ( -) ( -) ( -)                         | ( -) ( -) ( -) ( -)                         |
|              | deposit of hemosiderin     | ( -) ( -) ( -) ( -)                                                                        | ( -) ( -) ( -) ( -)                                | ( -) ( -) ( -) ( -)                         |                                             |
|              | engorgement of erythrocyte | ·                                                                                          | ( -) ( -) ( -) ( -)                                | ( -) ( -) ( -) ( -)                         | ( -) ( -) ( -) ( -)                         |
| Urinary syst | em]                        |                                                                                            |                                                    |                                             |                                             |
| idney        |                            | < 0>                                                                                       | < 0>                                               | < 0>                                        | < 0>                                        |
|              | tubular necrosis           | ( -) ( -) ( -) ( -)                                                                        | < 0><br>( -) ( -) ( -) ( -)                        |                                             | (-) (-) (-) (-)                             |

(c) c:b/a\*100

(HPT150)

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## HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 2W)

20000 ppm

5

| 0rgan         | Findings                   | No. of Animals on Study 0<br>Grade <u>1 2 3 4</u><br>(%) (%) (%) (%) | $\frac{1}{(\%)} \frac{2}{(\%)} \frac{3}{(\%)} \frac{4}{(\%)}$ |  |
|---------------|----------------------------|----------------------------------------------------------------------|---------------------------------------------------------------|--|
| [Hematopoieti | c system]                  |                                                                      |                                                               |  |
| bone marrow   | congestian                 | < 0><br>                                                             | <pre> &lt; 5&gt; 0 5 0 0   ( 0) (100) ( 0) ( 0)</pre>         |  |
| thymus        | atrophy                    | < 0><br><br>( -) ( -) ( -) ( -)                                      | < 5><br>0 0 5 0<br>( 0) ( 0) (100) ( 0)                       |  |
| spleen        | atrophy                    | < 0><br><br>( -) ( -) ( -) ( -)                                      | <pre> &lt; 5&gt;<br/>0 5 0 0<br/>( 0) (100) ( 0) ( 0)</pre>   |  |
|               | deposit of hemosiderin     | ( -) ( -) ( -) ( -)                                                  | 2 0 0 0<br>(40) (0) (0) (0)                                   |  |
|               | ensarsement of erythracyte | ( -) ( -) ( -) ( -)                                                  | 3 0 0 0<br>(60) (0) (0) (0)                                   |  |
| [Urinary syst | em]                        |                                                                      |                                                               |  |
| kidney        | tubular necrosis           | < 0><br>                                                             | < 5><br>0 2 2 0<br>( 0) ( 40) ( 40) ( 0)                      |  |

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

b b : Number of animals with lesion

(c) c:b/a\*100

(HPT150)

PAGE : 2

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Group Name 10000 ppm No. of Animals on Study 0

 $\sim$ 

| rgan                    | Findings                             | Group Name<br>No. of Animals c<br>Grade | Control<br>on Study 0<br>$\frac{1 - 2 - 3 - 4}{(\%) - (\%) - (\%) - (\%)}$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | 2500 ppm<br>0<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 5000 ppm<br>0<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|-------------------------|--------------------------------------|-----------------------------------------|----------------------------------------------------------------------------|-------------------------------------------------------|----------------------------------------------------|----------------------------------------------------|
|                         |                                      |                                         |                                                                            |                                                       |                                                    |                                                    |
|                         |                                      |                                         |                                                                            |                                                       |                                                    |                                                    |
| pecial sens<br>Inder gl | se organs/appendage]<br>degeneration |                                         |                                                                            | < 0><br>                                              | < 0>                                               | < 0>                                               |

(c) c:b/a\*100

(HPT150)

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

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STUDY NO. : 0360 ANIMAL : RAT F344/DuCrj

BAIS3

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

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PAGE: 4

| Organ                      | Findings                                                                                                          | Group Name<br>No. of Animals on Study<br>Grade <u>1</u><br>(%) | 10000 ppm<br>0<br><u>2 3 4</u><br>(%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |  |
|----------------------------|-------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------|-----------------------------------------------|-------------------------------------------------------|--|
| [Special ser<br>Harder gl  | nse organs/appendage]<br>degeneration                                                                             | _<br>( _)                                                      | < 0><br><br>( _) ( _) ( _)                    | < 5><br>0 3 0 0<br>( 0) ( 60) ( 0) ( 0)               |  |
| Grade<br>< a ><br>b<br>(c) | 1: Slight 2: Moderate<br>a: Number of animals examined at the<br>b: Number of animals with lesion<br>c: b/a * 100 | 3:Marked 4:Severe<br>site                                      | )                                             |                                                       |  |

(HPT150)

APPENDIX J 4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : SACRIFICED ANIMALS

(2-WEEK STUDY)

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

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| 0rgan         | Findings                     | Group Name<br>No. of Animals on Study<br>Grade <u>1</u> (%) | Control<br>5<br>2 3 4<br>(%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | $\begin{array}{c} 2500 \text{ ppm} \\ 5 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$  |
|---------------|------------------------------|-------------------------------------------------------------|--------------------------------------|-------------------------------------------------------|------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------|
| [Respiratory  | system]                      |                                                             |                                      |                                                       |                                                                                                                  |                                                        |
| nasal cavit   | respiratory metaplasia:gland | 0<br>( 0) (                                                 | < 5><br>0 0 0<br>0) ( 0) ( 0)        | < 5><br>0 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | $\langle 5 \rangle$<br>1 0 0 0<br>( 20) ( 0) ( 0) ( 0)                                                           | <pre> &lt; 5&gt; 0 0 0 0<br/>( 0) ( 0) ( 0) ( 0)</pre> |
|               | engorgement of erythrocyte   | 0<br>( 0) (                                                 | 0 0 0<br>0)(0)(0)                    | 0 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                         |
| [Hematopoieti | c system]                    |                                                             |                                      |                                                       |                                                                                                                  |                                                        |
| bone marrow   | congestion                   | 0<br>( 0) (                                                 | < 5><br>0 0 0<br>0) ( 0) ( 0)        | < 5><br>0 0 0 0<br>0 0) ( 0) ( 0) ( 0)                | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                           | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                 |
| thymus        | atrophy                      | 0<br>( 0) (                                                 | < 5><br>0 0 0<br>0) ( 0) ( 0)        | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                           | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                 |
| spleen        | deposit of hemosiderin       | 0<br>( 0) (                                                 | < 5><br>0 0 0<br>0) ( 0) ( 0)        | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                           | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                 |
|               | extramedullary hematopoiesis | 0<br>( 0) (                                                 | 0 0 0<br>0)(0)(0)                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 4 0 0 0<br>(80)(0)(0)(0)                                                                                         | 5 0 0 0<br>(100) ( 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

(HPT150)

PAGE: 1

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

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PAGE: 2

| 0rgan | Findines | Group Name 10000 ppm No. of Animals on Study 5 Grade 1 2 3 4 (%) (%) (%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | |
|---------------|------------------------------|--|---|--|
| [Respiratory | system] | | | |
| nasal cavit | respiratory metaplasia:gland | < 5> 1 0 0 0 (20) (0) (0) (0) | < 5> 1 0 0 0 (20) (0) (0) (0) | |
| | engargement of erythracyte | $\begin{pmatrix} 0 & 1 & 0 & 0 \\ (& 0) & (& 20) & (& 0) & (& 0) \end{pmatrix}$ | 0 0 0 0 (0) (0) (0) (0) | |
| [Hematopoieti | c system] | | | |
| bone marrow | congestion | <pre> < 5> 0 0 0 0 (0) (0) (0) </pre> | <pre></pre> | |
| thymus | atrophy | < 5> 0 0 0 0 (0) (0) (0) (0) | <pre> < 5> 0 0 5 0 (0) (0) (100) (0)</pre> | |
| spleen | deposit of hemosiderin | < 5> 2 0 0 0 (40) (0) (0) (0) | < 5> 5 0 0 0 (100) (0) (0) (0) | |
| | extramedullary hematopoiesis | 5 0 0 0 (100) (0) (0) (0) | 0 0 0 0 (0) (0) (0) (0) | |

b : Number of animals with lesion c : b / a * 100 b (c)

(HPT150)

| REPORT TYPE SEX | : AI : MALE | | | | PAGE : |
|----------------------------|---|---|---|---|---|
| Organ | No | Control Control of Animals on Study 5 ade 1 2 3 4 (%) (%) (%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | 5000 ppm 5 1 2 3 4 (%) (%) (%) (%) |
| [Hematopoie | tic system] | | | | |
| spleen | engorgement of erythrocyte | < 5> 0 0 0 0 (0) (0) (0) (0) | < 5> 0 0 0 0 (0) (0) (0) (0) | < 5> 4 0 0 0 (80) (0) (0) (0) | < 5> 5 0 0 0 (100) (0) (0) (0) |
| [Digestive | system] | | | | |
| Liver | herniation | < 5> 0 0 0 0 (0) (0) (0) (0) | < 5> 1 0 0 0 (20) (0) (0) (0) | < 5> 0 0 0 0 (0) (0) (0) (0) | < 5> 0 0 0 0 (0) (0) (0) (0) |
| | necrosis:focal | 0 0 0 0 (0) (0) (0) (0) | 0 0 0 0 (0) (0) (0) (0) | 0 0 0 0 (0) (0) (0) (0) | 0 0 0 0 (0) (0) (0) (0) |
| | hepatocellular hypertrophy:central | 0 0 0 0 (0) (0) (0) (0) | 0 0 0 0 (0) (0) (0) (0) | 0 0 0 0 (0) (0) (0) (0) | 3 0 0 0 (60)(0)(0)(0) |
| [Urinary sy | rstem] | | | | |
| kidney | basophilic change | < 5> 1 0 0 0 (20) (0) (0) (0) | < 5> 0 0 0 0 (0) (0) (0) (0) | < 5> 0 0 0 0 (0) (0) (0) (0) | < 5> 0 0 0 0 (0) (0) (0) (0) |
| Grade < a > b (c) | 1: Slight 2: Moderate 3: a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 | Marked 4 : Severe | | | |

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(HPT150)

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

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PAGE: 4

| 0rgan                        | Nc                                                                                                                          | Cup Name         10000 ppm           0. of Animals on Study         5           rade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |     |
|------------------------------|-----------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------|-----|
| [Hematopoie                  | etic system]                                                                                                                |                                                                                                                                                                                            |                                                       |     |
| spleen                       | engorgement of erythrocyte                                                                                                  | <pre></pre>                                                                                                                                                                                | <pre> &lt; 5&gt;     5</pre>                          |     |
| (Digestive                   | system]                                                                                                                     |                                                                                                                                                                                            |                                                       |     |
| liver                        | herniation                                                                                                                  | <pre> &lt; 5&gt;<br/>0 0 0 0<br/>( 0) ( 0) ( 0) ( 0)</pre>                                                                                                                                 | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |     |
|                              | necrosis:focal                                                                                                              | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                             | 0 3 0 0<br>( 0) ( 60) ( 0) ( 0)                       |     |
|                              | hepatocellular hypertrophy:central                                                                                          | 5 0 0 0<br>(100) ( 0) ( 0) ( 0)                                                                                                                                                            | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        |     |
| [Urinary sy                  | vstem]                                                                                                                      |                                                                                                                                                                                            |                                                       |     |
| kidney                       | basophilic change                                                                                                           | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                                     | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |     |
| Grade<br>〈 a 〉<br>b<br>( c ) | 1: Slight 2: Moderate 3:<br>a: Number of animals examined at the site<br>b: Number of animals with lesion<br>c: b / a * 100 | Marked 4 : Severe                                                                                                                                                                          |                                                       |     |
| (HPT150)                     |                                                                                                                             | · · · · · · · · · · · · · · · · · · ·                                                                                                                                                      |                                                       | BAI |

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

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| 0rgan                      |                                                                                                                          | Group Name<br>No. of Animals on Study<br>Grade <u>1</u><br>(%) | Control<br>5<br><u>2 3 4</u><br>(%) (%) (%) | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |
|----------------------------|--------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------|---------------------------------------------|------------------------------------------------------|------------------------------------------------------|-------------------------------------------------------|
| [Urinary syst              | rem]                                                                                                                     |                                                                |                                             |                                                      |                                                      |                                                       |
| kidney                     | easinophilic bady                                                                                                        | 4<br>( 80)                                                     | < 5><br>0 0 0<br>( 0) ( 0) ( 0)             | < 5><br>5 0 0 0<br>(100) ( 0) ( 0) ( 0)              | < 5><br>0 5 0 0<br>( 0) (100) ( 0) ( 0)              | < 5><br>0 2 3 0<br>( 0) ( 40) ( 60) ( 0)              |
|                            | mineralization:cortico-medullary junct                                                                                   | ion 1<br>(20)                                                  | 0 0 0<br>( 0) ( 0) ( 0)                     | 0 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        |
| [Endocrine sy              | /stem]                                                                                                                   |                                                                |                                             |                                                      |                                                      |                                                       |
| bituitary                  | Rathke pouch                                                                                                             | 2<br>( 40)                                                     | < 5><br>0 0 0<br>( 0) ( 0) ( 0)             | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               | < 5><br>0 0 0 0<br>0) ( 0) ( 0) ( 0)                 | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |
| Reproductive               | e system]                                                                                                                |                                                                |                                             |                                                      |                                                      |                                                       |
| estis                      | germ cell necrosis                                                                                                       | 0<br>( 0)                                                      | <pre>&lt; 5&gt; 0 0 0 ( 0) ( 0) ( 0)</pre>  | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |
| epididymis                 | debris of spermatic elements                                                                                             | 0<br>( 0)                                                      | < 5><br>0 0 0<br>( 0) ( 0) ( 0)             | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |
| Grade<br>< a ><br>b<br>(c) | 1: Slight 2: Moderate 3<br>a: Number of animals examined at the si<br>b: Number of animals with lesion<br>c: b / a * 100 | : Marked 4 : Sever<br>te                                       | 9                                           |                                                      |                                                      |                                                       |

(HPT150)

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

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| Organ         | Findings                              | Group Name<br>No. of Animals on Study<br>Grade <u>1</u><br>(%) | 10000<br>5<br><u>2</u><br>(%) | 3         | $\frac{4}{(\%)}$ | <u>1</u><br>(%) | 20000<br>2<br>(%) | 0 ppm<br>5<br>3<br>(%) |     | $\frac{4}{5}$ |
|---------------|---------------------------------------|----------------------------------------------------------------|-------------------------------|-----------|------------------|-----------------|-------------------|------------------------|-----|---------------|
|               |                                       |                                                                |                               |           |                  |                 |                   |                        |     |               |
| [Urinary sys1 | tem]                                  |                                                                |                               |           |                  |                 |                   |                        |     |               |
| kidney        | easinaphilic bady                     | 0<br>( 0)                                                      | < 5><br>2<br>( 40) (          | 3         | 0<br>0)          | 3<br>(60)       | ( 0)              | 0                      | (   | 0<br>0)       |
|               | mineralization:cortico-medullary junc | otion 0<br>( 0)                                                | 0<br>( 0) (                   | 0<br>0) ( | 0<br>0)          | 0<br>( 0)       | 0<br>( 0)         | 0<br>( 0)              | (   | 0<br>0)       |
| [Endocrine s) | vstem]                                |                                                                |                               |           |                  |                 |                   |                        |     |               |
| pituitary     | Rathke pouch                          | 0<br>( 0)                                                      | < 5)<br>0<br>( 0) (           | )<br>0)(  | 0<br>0)          | 0<br>( 0)       | ()<br>()          | 5><br>0<br>( 0)        | ) ( | 0<br>0)       |
| [Reproductive | e system]                             |                                                                |                               |           |                  |                 |                   |                        |     |               |
| testis        | germ cell necrosis                    | 0<br>( 0)                                                      | < 52<br>0<br>( 0) (           | 0         | 0<br>0)          | 2<br>(40)       | ( 0)              | 0                      | ) ( | 0<br>0)       |
| epididymis    | debris of spermatic elements          | 0<br>( 0)                                                      | < 52<br>0<br>( 0) (           | 0         | 0<br>0)          | 3<br>(60)       | < !<br>0<br>( 0)  | 0                      |     | 0<br>0)       |

(c) c:b/a\*100

(HPT150)

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

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|                     |                                                                                                                                          | nimals on Study 5                                               | 1250 ppm<br>5                                                    | 2500 ppm<br>5                                                    | 5000 ppm<br>5                                                                    |
|---------------------|------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------|------------------------------------------------------------------|------------------------------------------------------------------|----------------------------------------------------------------------------------|
| )rgan               | Grade                                                                                                                                    | $\underbrace{\begin{array}{ccccccccccccccccccccccccccccccccccc$ | $\frac{1}{(\%)}  \frac{2}{(\%)}  \frac{3}{(\%)}  \frac{4}{(\%)}$ | $\frac{1}{(\%)}  \frac{2}{(\%)}  \frac{3}{(\%)}  \frac{4}{(\%)}$ | $\frac{1}{(\%)}  \frac{2}{(\%)}  \frac{3}{(\%)}  \frac{4}{(\%)}  \frac{4}{(\%)}$ |
| Special sens        | se organs/appendage]                                                                                                                     |                                                                 |                                                                  |                                                                  |                                                                                  |
| arder gl            | degeneration                                                                                                                             | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                          | <pre> &lt; 5&gt;<br/>0 0 0 0 0<br/>. ( 0) ( 0) ( 0) ( 0)</pre>   | < 5><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                           | < 5><br>5 0 0 0<br>(100) ( 0) ( 0) ( 0)                                          |
|                     | lymphocytic infiltration                                                                                                                 | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                   | 1 0 0 0<br>(20) (0) (0) (0)                                                      |
| Grade<br>(a)<br>(c) | 1 : Slight 2 : Moderate 3 : Marked<br>a : Number of animals examined at the site<br>b : Number of animals with lesion<br>c : b / a * 100 | 4 : Severe                                                      |                                                                  |                                                                  |                                                                                  |

(HPT150)

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

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PAGE: 8

| 0rgan | Findings | Group Name 10000 ppm No. of Animals on Study 5 Grade 1 2 3 4 (%) (%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | |
|------------------------------|--|--|---|--|
| [Special sen | se organs/appendage] | | | |
| Harder gl | degeneration | $\begin{array}{c} < 5 > \\ 4 & 1 & 0 & 0 \\ (80) & (20) & (0) & (0) \end{array}$ | < 5> 0 5 0 0 (0) (100) (0) (0) | |
| | lymphocytic infiltration | 1 0 0 0 (20) (0) (0) (0) | 0 0 0 0 (0) (0) (0) (0) | |
| Grade < a > b (c) | 1 : Slight 2 : Moderate 3 a : Number of animals examined at the s b : Number of animals with lesion c : b / a * 100 | : Marked 4 : Severe te | | |

(HPT150)

APPENDIX J 5

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : SACRIFICED ANIMALS

(2-WEEK STUDY)

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

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| Findings | Group Name Control No. of Animals on Study 5 Grade 1 2 3 4 (%) (%) (%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | 5000 ppm 5 <u>1 2 3 4</u> (%) (%) (%) (%) |
|------------------------------------|--|---|---|--|
| vstem] | | | | |
| respiratory metaplasia:gland | < 5> 0 0 0 0 (0) (0) (0) (0) | <pre> < 5> 0 0 0 0 (0) (0) (0) (0)</pre> | < 5> 0 0 0 0 (0) (0) (0) (0) | < 5> 0 0 0 0 (0) (0) (0) (0) |
| system] | | | | |
| extramedullary hematopoiesis | <pre>< 5> 0 0 0 0 (0) (0) (0) (0)</pre> | < 5> 0 0 0 0 (0) (0) (0) (0) | < 5> 1 0 0 0 (20) (0) (0) (0) | < 5> 5 0 0 0 (100) (0) (0) (0) |
| engargement of erythrocyte | 0 0 0 0 (0) (0) (0) (0) | 0 0 0 0 (0) (0) (0) (0) | 5 0 0 0 (100) (0) (0) (0) | 5 0 0 0 (100) (0) (0) (0) |
| tem] | | | | |
| herniation | | <pre></pre> | < 5> 0 0 0 0 (0) (0) (0) (0) | <pre> < 5> 0 0 0 0 (0) (0) (0) (0)</pre> |
| hepatocellular hypertrophy:central | 0 0 0 0 (0) (0) (0) (0) | 0 0 0 0 (0) (0) (0) (0) | 0 0 0 0 (0) (0) (0) (0) | 2 0 0 0 (40)(0)(0)(0) |
| | ystem] respiratory metaplasia:gland system] extramedullary hematopoiesis engorgement of erythrocyte :tem] herniation | No. of Animals on Study 5 Grade 1 2 3 4 Findines (%) (%) (%) (%) (%) ystem] 5 0 0 0 0 0 respiratory metaplasia:gland 55 0 | No. of Animals on Study 5 5 Grade 1 2 3 4 Findines 1 2 3 4 (%) (%) (%) (%) (%) (%) ystem] (%) (%) 0 | No. of Animals on Study 5 5 5 5 5 5 5 5 5 5 5 6 0 </td |

(HPT150)

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

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| 0rgan | Findings | Group Name 10000 ppm No. of Animals on Study 5 Grade 1 2 3 4 (%) (%) (%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | |
|--------------|------------------------------------|--|---|--|
| [Respiratory | system] | | | |
| nasal cavit | respiratory metaplasia:gland | $\begin{pmatrix} < 5 \\ 0 & 1 & 0 & 0 \\ (& 0) & (& 20) & (& 0) & (& 0) \\ \end{pmatrix}$ | < 0> (-) (-) (-) (-) | |
| [Hematopoiet | ic system] | | | |
| spleen | extramedullary hematopoiesis | <pre>< 5> 5 0 0 0 (100) (0) (0) (0)</pre> | < 0> (-) (-) (-) (-) | |
| | ensorgement of erythrocyte | 5 0 0 0 (100) (0) (0) (0) | (-) (-) (-) (-) | |
| [Digestive s | vstem] | | | |
| iver | herniation | <pre></pre> | < 0> | |
| | hepatocellular hypertrophy:central | 4 0 0 0 (80) (0) (0) (0) | (-) (-) (-) (-) | |

(HPT150)

BAIS3

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

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| Drgan | | Name Control of Animals on Study 5 0 1 2 3 4 (%) (%) (%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | $\begin{array}{c} 2500 \text{ ppm} \\ 5 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | 5000 ppm 5 <u>1 2 3 4</u> (%) (%) (%) (%) |
|------------------------------|---|--|--|--|--|
| [Urinary sys | tem] | | | | |
| ki dhey | basophilic change | < 5> 0 0 0 0 (0) (0) (0) (0) | < 5> 1 0 0 0 (20) (0) (0) (0) | < 5> 0 0 0 0 (0) (0) (0) (0) | < 5> 1 0 0 0 (20) (0) (0) (0) |
| | mineralization:cortico-medullary junction | 1 0 0 0 (20)(0)(0)(0) | 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:papilla | 0 0 0 0 (0) (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) |
| | mineralization:cortex | 1 0 0 0 (20) (0) (0) (0) | 0 0 0 0 (0) (0) (0) (0) | 0 0 0 0 (0) (0) (0) (0) | 0 0 0 0 (0) (0) (0) (0) |
| Endocrine s | vstem] | | | | |
| pituitary | Rathke pouch | $\begin{array}{cccc} & < 5 \\ 1 & 0 & 0 & 0 \\ (20) & (0) & (0) & (0) \end{array}$ | <pre> < 5> 0 0 0 0 (0) (0) (0) (0)</pre> | <pre> < 5> 0 0 0 0 (0) (0) (0) (0)</pre> | < 5> 0 0 0 0 (0) (0) (0) (0) |
| thyroid | ultimibranchial body remanet | < 5> 0 0 0 0 (0) (0) (0) (0) | < 5> 0 0 0 0 (0) (0) (0) (0) | < 5> 0 0 0 0 (0) (0) (0) (0) | < 5> 0 0 0 0 (0) (0) (0) (0) |
| Grade < a > b (c) | 1: Slight 2: Moderate 3: Mar a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100 | rked 4 : Severe | | | · · · · · · · · · · · · · · · · · · · |

(HPT150)

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

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PAGE: 12

| Organ | Group Name No. of Anima Grade Findings | $\begin{array}{cccc} 10000 \text{ ppm} \\ \text{als an Study} & 5 \\ & \underline{1 & 2 & 3 & 4} \\ & \underline{1 & (\%) & (\%) & (\%)} \\ \end{array}$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | |
|--|--|--|---|--|
| [Urinary sys | tem] | | | |
| <idney< td=""><td>basophilic change</td><td>< 5> 1 0 0 0 (20) (0) (0) (0)</td><td>< 0> </td><td></td></idney<> | basophilic change | < 5> 1 0 0 0 (20) (0) (0) (0) | < 0> | |
| | mineralization:cortico-medullary junction | 0 0 0 0 0 (0) (0) (0) (0) | (-) (-) (-) (-) | |
| | mineralization:papilla | 0 0 0 0 (0) (0) (0) (0) | (-) (-) (-) (-) | |
| | mineralization:cortex | 0 0 0 0 (0) (0) (0) (0) | (-) (-) (-) (-) | |
| [Endocrine s | system] | | | |
| pituitary | Rathke pouch | < 5> 0 0 0 0 (0) (0) (0) (0) | < 0> | |
| thyroid | ultimibranchial body remanet | < 5> 1 0 0 0 (20) (0) (0) (0) | < 0> (-) (-) (-) (-) | |
| Grade < a > b (c) | 1 : Slight 2 : Moderate 3 : Marked a : Number of animals examined at the site b : Number of animals with lesion c : b / a * 100 | 4 : Severe | | |

(HPT150)

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

PAGE : 13

| | (%) | (%) (%) | (%) | 1 2 (%) (%) | | <u>4</u> (%) (9 | L 2 6) (% | | <u>4</u> (%) | 1 (%) | 2 (%) | 3 (%) | 4(%) |
|------------------------|--|---|--|---|--|--|--------------------------------|--------------------------------|--|--------------------------------|---|--------------------------------|--------------------------------|
| ans/appendage] | | | | | | | | | | | | | |
| generation | 0 (0) | < 5> 0 0 (0) (0) | 0 (0) (| 0 0 0) (0) | < 5> 0) (0) (| 0 (0) ((| | < 5> 0 0 0) (0) | 0 (0) | 1 (20) | 0 | 0 | 0 0) |
| mphocytic infiltration | 0 (0) | 0 0 (0)(0) | 0 (0) (| 0 0 0) (0) | 0) (0) (| 0 (0) ((|) ())((|) 0))(0) | 0 (0) | 2 (40) (| 2 (40) (| 0 0) (| 0 0) |
| | | Э | | | | | | | | | <u></u> | <u></u> | 2 |
| | generation mohocytic infiltration Slight 2 : Moderate 3 Number of animals examined at the si Number of animals with lesion | generation 0 (0) mohocytic infiltration 0 (0) Slight 2: Moderate 3: Marked 4: Severa Number of animals examined at the site Number of animals with lesion | generation $\begin{pmatrix} \langle 5 \rangle \\ 0 & 0 & 0 \\ (0) & (0) & (0) \end{pmatrix}$ mohocytic infiltration $\begin{pmatrix} 0 & 0 & 0 \\ (0) & (0) & (0) \end{pmatrix}$ Slight 2: Moderate 3: Marked 4: Severe Number of animals examined at the site Number of animals with lesion | generation $\begin{pmatrix} < 5 \\ 0 & 0 & 0 & 0 \\ (& 0) & (&$ | generation 0 | generation < 5> < 5> 0 | generation | generation | generation < 5> < 5> < 5> < 5> 0 </td <td>generation </td> <td>generation $\begin{pmatrix} < 5 \rangle & < 5 \rangle & < 5 \rangle & < 5 \rangle & \\ 0 & 0 &$</td> <td>generation </td> <td>generation </td> | generation | generation $\begin{pmatrix} < 5 \rangle & < 5 \rangle & < 5 \rangle & < 5 \rangle & \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 &$ | generation | generation |

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

PAGE: 14

| rgan | Ν | roup Name 10000 ppm o. of Animals on Study 5 rade 1 2 3 4 | $\begin{array}{c} 20000 \text{ ppm} \\ 0 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | |
|-------------------------|--|---|---|---|
| Special sens | se organs/appendage] | | | • |
| arder gl | degeneration | <pre></pre> | < 0> () () () () | |
| | lymphocytic infiltration | 5 0 0 0 (100) (0) (0) (0) | (-) (-) (-) (-) | |
| rade a > b c) | 1: Slight 2: Moderate 3: a: Number of animals examined at the sit b: Number of animals with lesion c: b / a * 100 | Marked 4 : Severe te | | |

(HPT150)

APPENDIX K 1

IDENTITY AND IMPURITY OF p-NITROANISOLE

IN THE 2-WEEK FEED STUDY

IDENTITY AND IMPURITY OF p-NITROANISOLE IN THE 2-WEEK FEED STUDY

| Test Substance | : p-Nitroanisole (Kanto Chemical Co., Inc.) |
|----------------|---|
| Lot No. | : 704S4061 |

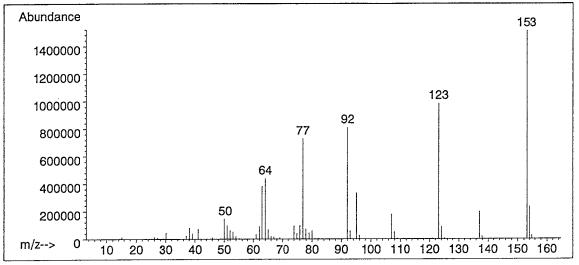
1. Spectral data

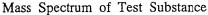
Mass Spectrometry

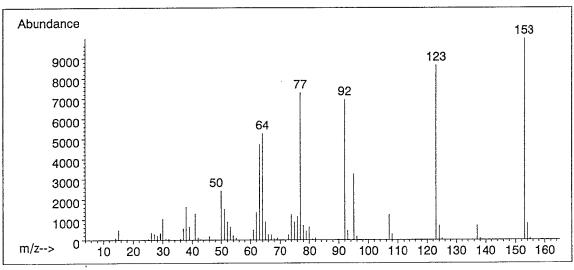
| Instrument | : Hewlett Packard 5989B Mass Spectrometer | |
|------------|---|--|
| | | |

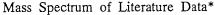
Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



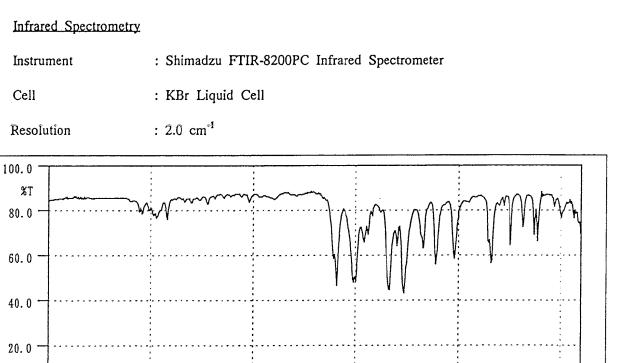


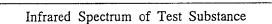




Results: The mass spectrum was consistent with literature spectrum.

(*Fred W. McLafferty (1994) Wiley Registry of Mass Spectral Data, 6th edition. John Wiley and Sons, Inc. (U.S.), Entry Number 38330)





1500.0

1000.0

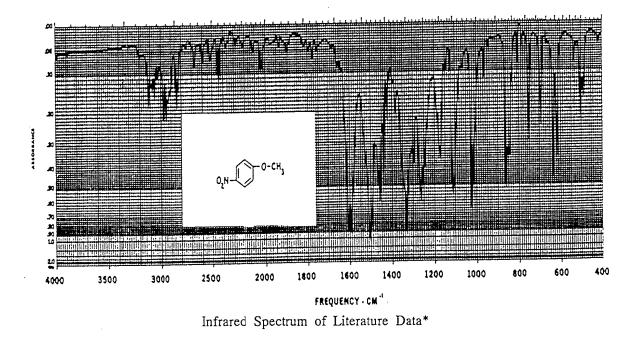
500.0 cm⁻

2000.0

40.0

0.0 -+ 4000.0

3000.0



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.443)

(Study No. 0360)

2. Impurity

| Instrument | : Hewlett Packard 5890A Gas Chromatograph |
|--------------------|---|
| Column | : INNOWAX (0.2 mm ϕ \times 50 m) |
| Column Temperature | : 80 $^{\circ}C \rightarrow (15 ^{\circ}C/min) \rightarrow 280 ^{\circ}C (5 min)$ |
| Flow Rate | : 1 mL/min |
| Detector | : FID (Flame Ionization Detector) |
| Injection Volume | : 1 μL |

| Sample Name | Peak No. | Area (%) | Peak Name |
|----------------|----------|-------------|----------------------|
| Test Substance | 1 | 0.14 | m-Chloronitrobenzene |
| | 2 | 0.11 | p-Chloronitrobenzene |
| | 3 | 0.01 | o-Chloronitrobenzene |
| | 4 | 99.74 | p-Nitroanisole |

- Results: Gas chromatography indicated one major peak (peak No.4) and three impurities. It was identified only by comparing its gas chromatograph with that of m-chloronitrobenzene (peak No.1), p-chloronitrobenzene (peak No.2) and o-chloronitrobenzene (peak No.3) in the p-nitroanisole, the amount in the test substance were 0.14%, 0.11% and 0.01%.
- 3. Conclusions: The test substance was identified as p-nitroanisole, by the mass spectrum and the infrared spectrum. Gas chromatography indicated one major peak (peak No.4) and three impurities. It was identified only by comparing its gas chromatograph with that of m-chloronitrobenzene, p-chloronitrobenzene and o-chloronitrobenzene, the amount in the test substance were 0.14%, 0.11% and 0.01%.

APPENDIX K 2

STABILITY OF p-NITROANISOLE IN FEEDING OF RATS

IN THE 2-WEEK FEED STUDY

STABILITY OF p-NITROANISOLE IN THE 2-WEEK FEED STUDY

Test Substance : p-Nitroanisole (Kanto Chemical Co., Inc.)

Lot No. : 704S4061

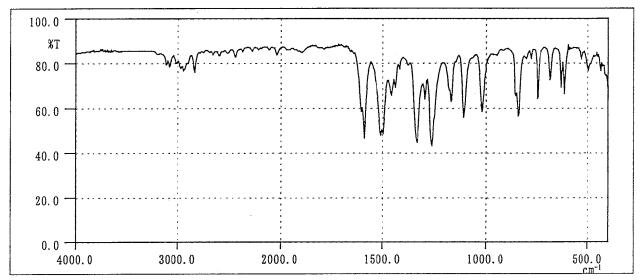
- 1. Sample : This lot was used from 1998.6.26 to 1998.7.10. Test substance was stored in a dark place at room temperature.
- 2. Infrared Spectrometry

ŀ

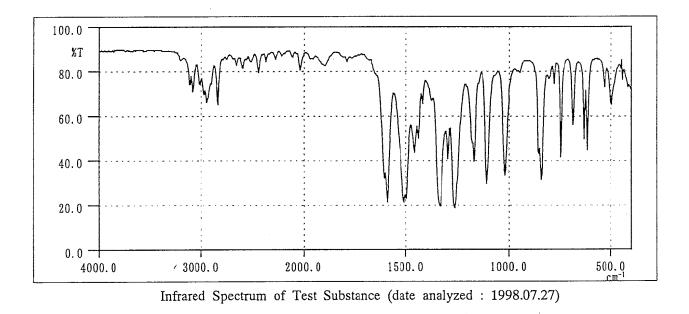
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 2.0 cm^{-1}



Infrared Spectrum of Test Substance (date analyzed : 1998.06.08)



Results: The results of infrared spectrum did not change before and after the study.

3. Gas Chromatography

_____);

| Instrument | : Hewlett Packard 5890A Gas Chromatograph |
|--------------------|--|
| Column | : INNOWAX (0.2 mm ϕ $	imes$ 50 m) |
| Column Temperature | : 80 °C \rightarrow (15 °C/min) \rightarrow 280 °C (5 min) |
| Flow Rate | : 1 mL/min |
| Detector | : FID (Flame Ionization Detector) |
| Injection Volume | : 1 µL |

| Date (date analyzed) | Peak No. | Retention Time (min) | Area (%) |
|-------------------------|----------|-------------------------|---------------|
| 1998.06.08 | 1 | 10.230 | 0.14 |
| | 2 | 10.518 | 0.11 |
| | 3 | 10.983 | 0.01 |
| | 4 | 13.106 | 99.7 4 |
| 1998.07.28 | 1 | 10.235 | 0.15 |
| | 2 | 10.521 | 0.12 |
| | 3 | 10.982 | 0.01 |
| | 4 | 13.127 | 99.72 |

- Results: Gas chromatography indicated one major peak (peak No.4) and three impurities (peak No. 1, 2, 3 < 0.3% of total area) analyzed at 1998.6.8 and one major peak (peak No.4) and three impurities (peak No.1, 2, 3 < 0.3% of total area) analyzed at 1998.7.28. No new trace impurity peak in the test substance analyzed at 1998.7.28 was detected.
- 4. Conclusions: The test substance was stable for about 2 months in a dark place at room temperature.

APPENDIX K 3

CONCENTRATION OF p-NITROANISOLE IN FORMULATED

DIETS IN THE 2-WEEK FEED STUDY

CONCENTRATION OF p-NITROANISOLE IN FORMULATED DIETS IN THE 2-WEEK FEED STUDY

| | Target Concentration | | | | | | | |
|------------------------------------|-------------------------|---------------------|-------------------|--------------------|---------------|--|--|--|
| Date Analyzed | 1250ª | 2500 | 5000 | 10000 | 20000 | | | |
| 1998.06.25 | 1270 (102) ^b | 2470 (98.8) | 4930 (98.6) | 9860 (98.6) | 19500 (97.5) | | | |
| ^a ppm ^b % | | | | | <u> </u> | | | |
| % nalytical method | : The samples were an | alyzed by the high | performance liqu | id chromatography. | | | | |
| Instrument | : Hewlett Packard 1090 | High Performance | e Liquid Chromato | ograph | | | | |
| Column | : TSK GEL ODS-80TN | - | - | 8 | | | | |
| Column Temperature | : Room Temperature | | , | | | | | |
| Flow Rate | : 1 mL/min | | | | | | | |
| Mobile Phase | : Distilled Water : Ace | tonitrile = $1 : 1$ | | | | | | |
| Detector | : UV (295 nm) | | | | | | | |
| Injection Volume | : 10 µL | | | | | | | |

APPENDIX K 4

STABILITY OF p-NITROANISOLE IN FORMULATED DIETS

IN THE 2-WEEK FEED STUDY

| STABILITY OF | ⁷ p-NITROANISOLE | IN | FORMULATED | DIETS IN | THE | 2-WEEK | FEED | STUDY |
|--------------|-----------------------------|----|------------|----------|-----|--------|------|-------|
|--------------|-----------------------------|----|------------|----------|-----|--------|------|-------|

| | | Target Concentration | | |
|---------------|-------------------------|-------------------------|---------------|--|
| Date Prepared | Date Analyzed | 1250 ^a | 20000 | |
| 1998.05.28 | 1998.05.28 | 1250 (100) ^b | 19200 (100) | |
| | 1998.06.05° | 1040 (83.2) | 17900 (93.2) | |
| | 1998.06.05 ^d | 1260 (101) | 19400 (101) | |

.

^a ppm
 ^b % (Percentage was based on the concentration on date of preparation.)
 ^c Animal room samples
 ^d Cold storage samples

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

| Instrument | : Hewlett Packard 1090 High Performance Liquid Chromatograph | | | |
|---------------------------------------|--|--|--|--|
| Column | : TSK GEL ODS-80TM (4.6 mm ϕ $	imes$ 15 cm) | | | |
| Column Temperature : Room Temperature | | | | |
| Flow Rate | : 1 mL/min | | | |
| Mobile Phase | : Distilled Water : Acetonitrile = 1 : 1 | | | |
| Detector | : UV (295 nm) | | | |
| Injection Volume | : 10 μL | | | |

APPENDIX L 1

METHODS FOR HEMATOLOGY, BIOCHEMISTRY IN THE 2-WEEK FEED STUDY OF p-NITROANISOLE

METHODS FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK FEED STUDY OF p-NITROANISOLE

| Item | Method | |
|--|---|--|
| Hematology | | |
| Red blood cell (RBC) | Light scattering method ¹⁾ | |
| Hemoglobin (Hgb) | Cyanmethemoglobin method ¹⁾ | |
| Methemoglobin | Multiple-wavelength Spectrophotometric | |
| | method " | |
| Hematocrit (Hct) | Calculated as RBC \times MCV/10 ¹⁾ | |
| Mean corpuscular volume (MCV) | Light scattering method ¹⁾ | |
| Mean corpuscular hemoglobin (MCH) | Calculated as Hgb/RBC $\times 10^{1}$ | |
| Mean corpuscular hemoglobin concentration (MCHC) | Calculated as Hgb/Hct $\times 100^{11}$ | |
| Platelet | Light scattering method ¹⁾ | |
| Reticulocyte | Pattern recognition method ³⁾ | |
| | (New methyleneblue staining) | |
| Prothrombin time | Quick one stage method ²⁾ | |
| Activated partial thromboplastin time (APTT) | Ellagic acid activaterd method ²⁾ | |
| White blood cell (WBC) | Light scattering method ¹⁾ | |
| Differential WBC | Pattern recognition method ³⁾ | |
| | (Wright staining) | |
| Biochemistry | | |
| Total protein (TP) | Biuret method ⁴⁾ | |
| Albumin (Alb) | BCG method ⁴⁾ | |
| A/G ratio | Calculated as $Alb/(TP - Alb)^{4}$ | |
| T-bilirubin | Alkaline azobilirubin method ⁴⁾ | |
| Glucose | GlcK·G-6-PDH method 4) | |
| T-cholesterol | CE·COD·POD method ⁴⁾ | |
| Phospholipid | PLD · ChOD · POD method 4) | |
| Glutamic oxaloacetic transaminase (GOT) | JSCC method ⁴⁾ | |
| Glutamic pyruvic transaminase (GPT) | JSCC method ⁴⁾ | |
| Lactate dehydrogenase (LDH) | SFBC method ⁴⁾ | |
| γ -Glutamyl transpeptidase (γ -GTP) | L- γ -Glutamyl-p-nitroanilide method ⁴⁾ | |
| Creatine phosphokinase (CPK) | JSCC method ⁴⁾ | |
| Urea nitrogen | Urease • GLDH method 4) | |
| Creatinine | Jaffe method 4) | |
| Sodium | Ion selective electrode method 4) | |
| Potassium | Ion selective electrode method 4) | |
| Chloride | Ion selective electrode method 4) | |
| Calcium | OCPC method ⁴⁾ | |
| Inorganic phosphorus | PNP·XOD·POD method 4) | |

1) Automatic blood cell analyzer (Technicon H·1: Bayer Corporation)

2) Automatic coagulometer (Sysmex CA-5000 : Sysmex Corporation)

3) Automatic blood cell differential analyzer (MICROX HEG-120NA : OMRON Corporation,)

4) Automatic analyzer (Hitachi 7070 : Hitachi,Ltd.)

1

5) CO-oximeter (CIBA · CORNING 270 : Bayer Corporation)

APPENDIX M 1

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK FEED STUDY OF p-NITROANISOLE

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK FEED STUDY OF p-NITROANISOLE

| Item | Unit | Decimal Place |
|--|-----------------------|------------------|
| Hematology | | |
| Red blood cell (RBC) | $\times 10^{6}/\mu$ L | 2 |
| Hemoglobin | g/dL | 1 |
| Methemoglobin | % | 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 |
| Reticulocyte | % | 0 |
| Prothrombin time | sec | 1 |
| Activated partial thromboplastin time (APTT) | sec | 1 |
| 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 |
| Phospholipid | mg/dL | 0 |
| Glutamic oxaloacetic transminase (GOT) | IU/L | 0 |
| Glutamic pyruvic transaminase (GPT) | IU/L | 0 |
| Lactate dehydrogenase (LDH) | IU/L | 0 |
| γ -Glutamyl transpeptidase (γ -GTP) | IU/L | 0 |
| Creatine phosphokinase (CPK) | IU/L | 0 |
| Urea nitrogen | mg/dL | 1 |
| Creatinine | mg/dL | 1 |
| Sodium | mEq/L | 0 |
| Potassium | mEq/L | . 1 |
| Chloride | mEq/L | 0 |
| Calcium | mg/dL | 1 |
| Inorganic phosphorus | mg/dL | 1 |