

# アクロレインのラットを用いた吸入によるがん原性試験報告書

試験番号：0816

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TABLE A

CONCENTRATIONS OF ACROLEIN  
IN THE INHALATION CHAMBER  
OF THE 2-YEAR INHALATION STUDY

CONCENTRATIONS OF ACROLEIN IN THE INHALATION  
CHAMBER OF THE 2-YEAR INHALATION STUDY

| Group Name | Concentration(ppm) |
|------------|--------------------|
|            | Mean $\pm$ S.D.    |
| Control    | 0.00 $\pm$ 0.00    |
| 0.1 ppm    | 0.10 $\pm$ 0.00    |
| 0.5 ppm    | 0.50 $\pm$ 0.00    |
| 2 ppm      | 2.01 $\pm$ 0.02    |

TABLE B1

SURVIVAL ANIMAL NUMBERS : MALE

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCrIj[F344/DuCrj]  
REPORT TYPE : A1 104  
SEX : MALE

SURVIVAL ANIMAL NUMBERS

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| Group                                           | Name    | Animals<br>At start | Administration (Weeks) |       |       |       |       |       |       |       |       |       |       |       |       |       |
|-------------------------------------------------|---------|---------------------|------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
|                                                 |         |                     | 0                      | 1     | 2     | 3     | 4     | 5     | 6     | 7     | 8     | 9     | 10    | 11    | 12    | 13    |
|                                                 | Control | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 |
|                                                 |         |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |
|                                                 | 0.1ppm  | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 |
|                                                 |         |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |
|                                                 | 0.5ppm  | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 |
|                                                 |         |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |
|                                                 | 2ppm    | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 |
|                                                 |         |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |
| Number of survival/ Number of effective animals |         |                     | Survival rate(%)       |       |       |       |       |       |       |       |       |       |       |       |       |       |

| SURVIVAL |    | ANIMAL NUMBERS |     |
|----------|----|----------------|-----|
| 1        | 2  | 3              | 4   |
| 5        | 6  | 7              | 8   |
| 9        | 10 | 11             | 12  |
| 13       | 14 | 15             | 16  |
| 17       | 18 | 19             | 20  |
| 21       | 22 | 23             | 24  |
| 25       | 26 | 27             | 28  |
| 29       | 30 | 31             | 32  |
| 33       | 34 | 35             | 36  |
| 37       | 38 | 39             | 40  |
| 41       | 42 | 43             | 44  |
| 45       | 46 | 47             | 48  |
| 49       | 50 | 51             | 52  |
| 53       | 54 | 55             | 56  |
| 57       | 58 | 59             | 60  |
| 61       | 62 | 63             | 64  |
| 65       | 66 | 67             | 68  |
| 69       | 70 | 71             | 72  |
| 73       | 74 | 75             | 76  |
| 77       | 78 | 79             | 80  |
| 81       | 82 | 83             | 84  |
| 85       | 86 | 87             | 88  |
| 89       | 90 | 91             | 92  |
| 93       | 94 | 95             | 96  |
| 97       | 98 | 99             | 100 |

REPORT TYPE : A1 104

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| Group                                                               | Name    | Animals<br>At start | Administration (Weeks) |                |                |                |                |                |                |                |                |                |                |                |                |
|---------------------------------------------------------------------|---------|---------------------|------------------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                                                                     |         |                     | 14                     | 15             | 16             | 17             | 18             | 19             | 20             | 21             | 22             | 23             | 24             | 25             | 26             |
|                                                                     | Control | 50                  | 50/50<br>100.0         | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 |
|                                                                     | 0.1ppm  | 50                  | 50/50<br>100.0         | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 |
|                                                                     | 0.5ppm  | 50                  | 50/50<br>100.0         | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 |
|                                                                     | 2ppm    | 50                  | 50/50<br>100.0         | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 | 50/50<br>100.0 |
| Number of survival/ Number of effective animals<br>Survival rate(%) |         |                     |                        |                |                |                |                |                |                |                |                |                |                |                |                |

BAIS5

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCrI CrIj[F344/DuCrj]  
REPORT TYPE : A1 104  
SEX : MALE

SURVIVAL ANIMAL NUMBERS

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| Group Name                                      | Animals<br>At start | Administration (Weeks) |       |       |       |       |       |       |       |       |       |       |       |       |       |
|-------------------------------------------------|---------------------|------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
|                                                 |                     | 28                     | 29    | 30    | 31    | 32    | 33    | 34    | 35    | 36    | 37    | 38    | 39    | 40    | 41    |
| Control                                         | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 |
|                                                 |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |
| 0.1ppm                                          | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 |
|                                                 |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |
| 0.5ppm                                          | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 |
|                                                 |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |
| 2ppm                                            | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 |
|                                                 |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |
| Number of survival/ Number of effective animals |                     |                        |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Survival rate(%)                                |                     |                        |       |       |       |       |       |       |       |       |       |       |       |       |       |

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1 104  
SEX : MALE

SURVIVAL ANIMAL NUMBERS

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| Group                                           | Name    | Animals<br>At start | Administration (Weeks) |       |       |       |       |       |       |       |       |       |       |       |       |       |
|-------------------------------------------------|---------|---------------------|------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
|                                                 |         |                     | 42                     | 43    | 44    | 45    | 46    | 47    | 48    | 49    | 50    | 51    | 52    | 53    | 54    | 55    |
|                                                 | Control | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 |
|                                                 |         |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 98.0  | 98.0  | 98.0  | 98.0  |
|                                                 | 0.1ppm  | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 |
|                                                 |         |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |
|                                                 | 0.5ppm  | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 |
|                                                 |         |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |
|                                                 | 2ppm    | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 |
|                                                 |         |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |
| Number of survival/ Number of effective animals |         |                     |                        |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Survival rate(%)                                |         |                     |                        |       |       |       |       |       |       |       |       |       |       |       |       |       |

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1 104  
SEX : MALE

SURVIVAL ANIMAL NUMBERS

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| Group                                           | Name    | Animals<br>At start | Administration (Weeks) |       |       |       |       |       |       |       |       |       |       |       |       |       |
|-------------------------------------------------|---------|---------------------|------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
|                                                 |         |                     | 56                     | 57    | 58    | 59    | 60    | 61    | 62    | 63    | 64    | 65    | 66    | 67    | 68    | 69    |
|                                                 | Control | 50                  | 49/50                  | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 |
|                                                 |         |                     | 98.0                   | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  |
|                                                 | 0.1ppm  | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 |
|                                                 |         |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  |
|                                                 | 0.5ppm  | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 49/50 | 49/50 | 49/50 |
|                                                 |         |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 98.0  | 98.0  |
|                                                 | 2ppm    | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 |
|                                                 |         |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |
| Number of survival/ Number of effective animals |         |                     |                        |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Survival rate(%)                                |         |                     |                        |       |       |       |       |       |       |       |       |       |       |       |       |       |

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1 104  
SEX : MALE

SURVIVAL ANIMAL NUMBERS

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| Group                                                               | Name    | Animals<br>At start | Administration (Weeks) |       |       |       |       |       |       |       |       |       |       |       |       |       |
|---------------------------------------------------------------------|---------|---------------------|------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
|                                                                     |         |                     | 70                     | 71    | 72    | 73    | 74    | 75    | 76    | 77    | 78    | 79    | 80    | 81    | 82    | 83    |
|                                                                     | Control | 50                  | 49/50                  | 48/50 | 48/50 | 48/50 | 47/50 | 47/50 | 47/50 | 47/50 | 47/50 | 47/50 | 46/50 | 46/50 | 46/50 | 46/50 |
|                                                                     |         |                     | 98.0                   | 96.0  | 96.0  | 96.0  | 94.0  | 94.0  | 94.0  | 94.0  | 94.0  | 94.0  | 94.0  | 92.0  | 92.0  | 92.0  |
|                                                                     | 0.1ppm  | 50                  | 49/50                  | 49/50 | 48/50 | 48/50 | 47/50 | 47/50 | 47/50 | 47/50 | 46/50 | 46/50 | 46/50 | 46/50 | 46/50 | 46/50 |
|                                                                     |         |                     | 98.0                   | 98.0  | 96.0  | 96.0  | 94.0  | 94.0  | 94.0  | 94.0  | 94.0  | 92.0  | 92.0  | 92.0  | 92.0  | 92.0  |
|                                                                     | 0.5ppm  | 50                  | 49/50                  | 49/50 | 49/50 | 49/50 | 48/50 | 48/50 | 48/50 | 48/50 | 48/50 | 48/50 | 48/50 | 48/50 | 48/50 | 48/50 |
|                                                                     |         |                     | 98.0                   | 98.0  | 98.0  | 98.0  | 96.0  | 96.0  | 96.0  | 96.0  | 96.0  | 96.0  | 96.0  | 96.0  | 96.0  | 96.0  |
|                                                                     | 2ppm    | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 49/50 | 48/50 | 48/50 |
|                                                                     |         |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 98.0  | 96.0  |
| Number of survival/ Number of effective animals<br>Survival rate(%) |         |                     |                        |       |       |       |       |       |       |       |       |       |       |       |       |       |

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1 104  
 SEX : MALE

SURVIVAL ANIMAL NUMBERS

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| Group                                           | Name    | Animals<br>At start | Administration (Weeks) |       |       |       |       |       |       |       |       |       |       |       |       |       |
|-------------------------------------------------|---------|---------------------|------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
|                                                 |         |                     | 84                     | 85    | 86    | 87    | 88    | 89    | 90    | 91    | 92    | 93    | 94    | 95    | 96    | 97    |
|                                                 | Control | 50                  | 46/50                  | 46/50 | 46/50 | 45/50 | 45/50 | 45/50 | 45/50 | 44/50 | 44/50 | 44/50 | 44/50 | 44/50 | 44/50 | 44/50 |
|                                                 |         |                     | 92.0                   | 92.0  | 92.0  | 90.0  | 90.0  | 90.0  | 90.0  | 88.0  | 88.0  | 88.0  | 88.0  | 88.0  | 88.0  | 88.0  |
|                                                 | 0.1ppm  | 50                  | 46/50                  | 45/50 | 45/50 | 44/50 | 43/50 | 43/50 | 43/50 | 43/50 | 43/50 | 43/50 | 43/50 | 43/50 | 42/50 | 42/50 |
|                                                 |         |                     | 92.0                   | 90.0  | 90.0  | 88.0  | 86.0  | 86.0  | 86.0  | 86.0  | 86.0  | 86.0  | 86.0  | 86.0  | 84.0  | 84.0  |
|                                                 | 0.5ppm  | 50                  | 48/50                  | 48/50 | 47/50 | 46/50 | 46/50 | 45/50 | 43/50 | 43/50 | 43/50 | 42/50 | 42/50 | 42/50 | 42/50 | 41/50 |
|                                                 |         |                     | 96.0                   | 96.0  | 94.0  | 92.0  | 92.0  | 90.0  | 86.0  | 86.0  | 86.0  | 84.0  | 84.0  | 84.0  | 84.0  | 82.0  |
|                                                 | 2ppm    | 50                  | 48/50                  | 48/50 | 48/50 | 48/50 | 48/50 | 48/50 | 48/50 | 48/50 | 48/50 | 48/50 | 48/50 | 48/50 | 48/50 | 48/50 |
|                                                 |         |                     | 96.0                   | 96.0  | 96.0  | 96.0  | 96.0  | 96.0  | 96.0  | 96.0  | 96.0  | 96.0  | 96.0  | 96.0  | 96.0  | 96.0  |
| Number of survival/ Number of effective animals |         |                     |                        |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Survival rate(%)                                |         |                     |                        |       |       |       |       |       |       |       |       |       |       |       |       |       |

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCrI CrIj [F344/DuCrj]  
REPORT TYPE : A1 104  
SEX : MALE

SURVIVAL ANIMAL NUMBERS

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| Group Name                                      | Animals<br>At start | Administration (Weeks) |       |       |       |       |       |       |
|-------------------------------------------------|---------------------|------------------------|-------|-------|-------|-------|-------|-------|
|                                                 |                     | 98                     | 99    | 100   | 101   | 102   | 103   | 104   |
| Control                                         | 50                  | 44/50                  | 43/50 | 42/50 | 42/50 | 42/50 | 42/50 | 41/50 |
|                                                 |                     | 88.0                   | 86.0  | 84.0  | 84.0  | 84.0  | 84.0  | 82.0  |
| 0.1ppm                                          | 50                  | 42/50                  | 41/50 | 41/50 | 41/50 | 41/50 | 41/50 | 40/50 |
|                                                 |                     | 84.0                   | 82.0  | 82.0  | 82.0  | 82.0  | 82.0  | 80.0  |
| 0.5ppm                                          | 50                  | 39/50                  | 39/50 | 39/50 | 39/50 | 38/50 | 38/50 | 37/50 |
|                                                 |                     | 78.0                   | 78.0  | 78.0  | 78.0  | 76.0  | 76.0  | 74.0  |
| 2ppm                                            | 50                  | 48/50                  | 48/50 | 47/50 | 44/50 | 42/50 | 42/50 | 42/50 |
|                                                 |                     | 96.0                   | 96.0  | 94.0  | 88.0  | 84.0  | 84.0  | 84.0  |
| Number of survival/ Number of effective animals |                     |                        |       |       |       |       |       |       |
| Survival rate(%)                                |                     |                        |       |       |       |       |       |       |

**TABLE B2**

**SURVIVAL ANIMAL NUMBERS : FEMALE**

STUDY NO. : 0816

ANIMAL : RAT F344/DuCrI CrIj[F344/DuCrj]

REPORT TYPE : A1 104

SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

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| Group                                           | Name    | Animals<br>At start | Administration (Weeks) |       |       |       |       |       |       |       |       |       |       |       |       |       |
|-------------------------------------------------|---------|---------------------|------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
|                                                 |         |                     | 0                      | 1     | 2     | 3     | 4     | 5     | 6     | 7     | 8     | 9     | 10    | 11    | 12    | 13    |
|                                                 | Control | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 |
|                                                 |         |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |
|                                                 | 0.1ppm  | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 |
|                                                 |         |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |
|                                                 | 0.5ppm  | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 |
|                                                 |         |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |
|                                                 | 2ppm    | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 |
|                                                 |         |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |
| Number of survival/ Number of effective animals |         |                     | Survival rate(%)       |       |       |       |       |       |       |       |       |       |       |       |       |       |

(HAN360)

BA1S5

STUDY NO. : 0816

ANIMAL : RAT F344/DuCrI CrIj[F344/DuCrJ]

REPORT TYPE : A1 104

SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

PAGE : 10

| Group                                           | Name    | Animals<br>At start | Administration (Weeks) |       |       |       |       |       |       |       |       |       |       |       |       |       |
|-------------------------------------------------|---------|---------------------|------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
|                                                 |         |                     | 14                     | 15    | 16    | 17    | 18    | 19    | 20    | 21    | 22    | 23    | 24    | 25    | 26    | 27    |
|                                                 | Control | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 |
|                                                 |         |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |
|                                                 | 0.1ppm  | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 |
|                                                 |         |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |
|                                                 | 0.5ppm  | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 |
|                                                 |         |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |
|                                                 | 2ppm    | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 |
|                                                 |         |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |
| Number of survival/ Number of effective animals |         |                     |                        |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Survival rate(%)                                |         |                     |                        |       |       |       |       |       |       |       |       |       |       |       |       |       |

(HAN360)

BAIS5

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1 104  
SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

PAGE : 11

| Group Name                                                          | Animals<br>At start | Administration (Weeks) |       |       |       |       |       |       |       |       |       |       |       |       |       |
|---------------------------------------------------------------------|---------------------|------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
|                                                                     |                     | 28                     | 29    | 30    | 31    | 32    | 33    | 34    | 35    | 36    | 37    | 38    | 39    | 40    | 41    |
| Control                                                             | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 |
|                                                                     |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |
| 0.1ppm                                                              | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 |
|                                                                     |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |
| 0.5ppm                                                              | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 |
|                                                                     |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |
| 2ppm                                                                | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 |
|                                                                     |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |
| Number of survival/ Number of effective animals<br>Survival rate(%) |                     |                        |       |       |       |       |       |       |       |       |       |       |       |       |       |

STUDY NO. : 0816

ANIMAL : RAT F344/DuCrI CrIj[F344/DuCrj]

REPORT TYPE : A1 104

SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

PAGE : 12

| Group                                           | Name    | Animals<br>At start | Administration (Weeks) |       |       |       |       |       |       |       |       |       |       |       |       |       |
|-------------------------------------------------|---------|---------------------|------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
|                                                 |         |                     | 42                     | 43    | 44    | 45    | 46    | 47    | 48    | 49    | 50    | 51    | 52    | 53    | 54    | 55    |
|                                                 | Control | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 |
|                                                 |         |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |
|                                                 | 0.1ppm  | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 |
|                                                 |         |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |
|                                                 | 0.5ppm  | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 |
|                                                 |         |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |
|                                                 | 2ppm    | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 |
|                                                 |         |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 98.0  | 98.0  | 98.0  | 98.0  |
| Number of survival/ Number of effective animals |         |                     |                        |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Survival rate(%)                                |         |                     |                        |       |       |       |       |       |       |       |       |       |       |       |       |       |

(HAN360)

BAIS5

STUDY NO. : 0816

ANIMAL : RAT F344/DuCrI CrIj[F344/DuCrj]

REPORT TYPE : A1 104

SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

PAGE : 13

| Group Name                                      | Animals<br>At start | Administration (Weeks) |       |       |       |       |       |       |       |       |       |       |       |       |       |
|-------------------------------------------------|---------------------|------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
|                                                 |                     | 56                     | 57    | 58    | 59    | 60    | 61    | 62    | 63    | 64    | 65    | 66    | 67    | 68    | 69    |
| Control                                         | 50                  | 50/50                  | 50/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 |
|                                                 |                     | 100.0                  | 100.0 | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  |
| 0.1ppm                                          | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 49/50 | 49/50 | 49/50 |
|                                                 |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 98.0  | 98.0  |
| 0.5ppm                                          | 50                  | 50/50                  | 50/50 | 50/50 | 50/50 | 50/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 48/50 | 48/50 | 48/50 |
|                                                 |                     | 100.0                  | 100.0 | 100.0 | 100.0 | 100.0 | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 96.0  | 96.0  | 96.0  |
| 2ppm                                            | 50                  | 49/50                  | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 48/50 | 48/50 |
|                                                 |                     | 98.0                   | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 96.0  | 96.0  |
| Number of survival/ Number of effective animals |                     |                        |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Survival rate(%)                                |                     |                        |       |       |       |       |       |       |       |       |       |       |       |       |       |

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STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1J[F344/DuCrJ]  
REPORT TYPE : A1 104  
SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

PAGE : 14

| Group Name                                      | Animals<br>At start | Administration (Weeks) |       |       |       |       |       |       |       |       |       |       |       |       |       |
|-------------------------------------------------|---------------------|------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
|                                                 |                     | 70                     | 71    | 72    | 73    | 74    | 75    | 76    | 77    | 78    | 79    | 80    | 81    | 82    | 83    |
| Control                                         | 50                  | 49/50                  | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 48/50 | 48/50 | 48/50 | 48/50 | 48/50 | 48/50 | 48/50 | 48/50 |
|                                                 |                     | 98.0                   | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 96.0  | 96.0  | 96.0  | 96.0  | 96.0  | 96.0  | 96.0  | 96.0  |
| 0.1ppm                                          | 50                  | 48/50                  | 48/50 | 48/50 | 48/50 | 48/50 | 48/50 | 48/50 | 48/50 | 48/50 | 48/50 | 48/50 | 48/50 | 48/50 | 48/50 |
|                                                 |                     | 96.0                   | 96.0  | 96.0  | 96.0  | 96.0  | 96.0  | 96.0  | 96.0  | 96.0  | 96.0  | 96.0  | 96.0  | 96.0  | 96.0  |
| 0.5ppm                                          | 50                  | 48/50                  | 48/50 | 47/50 | 47/50 | 47/50 | 47/50 | 47/50 | 47/50 | 47/50 | 47/50 | 47/50 | 47/50 | 46/50 | 46/50 |
|                                                 |                     | 96.0                   | 96.0  | 94.0  | 94.0  | 94.0  | 94.0  | 94.0  | 94.0  | 94.0  | 94.0  | 94.0  | 94.0  | 92.0  | 92.0  |
| 2ppm                                            | 50                  | 48/50                  | 48/50 | 47/50 | 47/50 | 47/50 | 47/50 | 47/50 | 47/50 | 47/50 | 47/50 | 47/50 | 47/50 | 46/50 | 46/50 |
|                                                 |                     | 96.0                   | 96.0  | 94.0  | 94.0  | 94.0  | 94.0  | 94.0  | 94.0  | 94.0  | 94.0  | 94.0  | 94.0  | 92.0  | 92.0  |
| Number of survival/ Number of effective animals |                     |                        |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Survival rate(%)                                |                     |                        |       |       |       |       |       |       |       |       |       |       |       |       |       |

STUDY NO. : 0816

ANIMAL : RAT F344/DuCrIj[F344/DuCrj]

REPORT TYPE : A1 104

SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

PAGE : 15

| Group                                           | Name    | Animals<br>At start | Administration (Weeks) |       |       |       |       |       |       |       |       |       |       |       |       |       |
|-------------------------------------------------|---------|---------------------|------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
|                                                 |         |                     | 84                     | 85    | 86    | 87    | 88    | 89    | 90    | 91    | 92    | 93    | 94    | 95    | 96    | 97    |
|                                                 | Control | 50                  | 48/50                  | 47/50 | 47/50 | 47/50 | 47/50 | 47/50 | 47/50 | 47/50 | 47/50 | 47/50 | 47/50 | 47/50 | 46/50 | 46/50 |
|                                                 |         |                     | 96.0                   | 94.0  | 94.0  | 94.0  | 94.0  | 94.0  | 94.0  | 94.0  | 94.0  | 94.0  | 94.0  | 94.0  | 92.0  | 92.0  |
|                                                 | 0.1ppm  | 50                  | 48/50                  | 47/50 | 47/50 | 47/50 | 46/50 | 46/50 | 46/50 | 46/50 | 46/50 | 46/50 | 46/50 | 46/50 | 46/50 | 46/50 |
|                                                 |         |                     | 96.0                   | 94.0  | 94.0  | 94.0  | 92.0  | 92.0  | 92.0  | 92.0  | 92.0  | 92.0  | 92.0  | 92.0  | 92.0  | 92.0  |
|                                                 | 0.5ppm  | 50                  | 46/50                  | 46/50 | 46/50 | 46/50 | 46/50 | 44/50 | 43/50 | 43/50 | 41/50 | 41/50 | 41/50 | 41/50 | 41/50 | 41/50 |
|                                                 |         |                     | 92.0                   | 92.0  | 92.0  | 92.0  | 92.0  | 88.0  | 86.0  | 86.0  | 82.0  | 82.0  | 82.0  | 82.0  | 82.0  | 82.0  |
|                                                 | 2ppm    | 50                  | 46/50                  | 45/50 | 45/50 | 44/50 | 44/50 | 44/50 | 44/50 | 44/50 | 44/50 | 43/50 | 43/50 | 43/50 | 41/50 | 41/50 |
|                                                 |         |                     | 92.0                   | 90.0  | 90.0  | 88.0  | 88.0  | 88.0  | 88.0  | 88.0  | 88.0  | 88.0  | 86.0  | 86.0  | 86.0  | 82.0  |
| Number of survival/ Number of effective animals |         |                     |                        |       |       |       |       |       |       |       |       |       |       |       |       |       |
| Survival rate(%)                                |         |                     |                        |       |       |       |       |       |       |       |       |       |       |       |       |       |

(HAN360)

BAIS5

STUDY NO. : 0816

ANIMAL : RAT F344/DuCrI CrIj[F344/DuCrj]

REPORT TYPE : A1 104

SEX : FEMALE

SURVIVAL ANIMAL NUMBERS

PAGE : 16

| Group Name                                                          | Animals<br>At start | Administration (Weeks) |       |       |       |       |       |       |
|---------------------------------------------------------------------|---------------------|------------------------|-------|-------|-------|-------|-------|-------|
|                                                                     |                     | 98                     | 99    | 100   | 101   | 102   | 103   | 104   |
| Control                                                             | 50                  | 45/50                  | 45/50 | 44/50 | 44/50 | 44/50 | 44/50 | 43/50 |
|                                                                     |                     | 90.0                   | 90.0  | 88.0  | 88.0  | 88.0  | 88.0  | 86.0  |
| 0.1ppm                                                              | 50                  | 46/50                  | 46/50 | 45/50 | 45/50 | 44/50 | 43/50 | 42/50 |
|                                                                     |                     | 92.0                   | 92.0  | 90.0  | 90.0  | 88.0  | 86.0  | 84.0  |
| 0.5ppm                                                              | 50                  | 41/50                  | 41/50 | 41/50 | 41/50 | 41/50 | 41/50 | 41/50 |
|                                                                     |                     | 82.0                   | 82.0  | 82.0  | 82.0  | 82.0  | 82.0  | 82.0  |
| 2ppm                                                                | 50                  | 41/50                  | 40/50 | 38/50 | 37/50 | 35/50 | 34/50 | 34/50 |
|                                                                     |                     | 82.0                   | 80.0  | 76.0  | 74.0  | 70.0  | 68.0  | 68.0  |
| Number of survival/ Number of effective animals<br>Survival rate(%) |                     |                        |       |       |       |       |       |       |

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BA1S5

TABLE C1

CLINICAL OBSERVATION : MALE

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrI CrIj [F344/DuCrI]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : MALE

PAGE : 1

| Clinical sign           | Group Name | Administration Week-day |     |     |     |     |     |     |     |     |      |      |      |      |      |
|-------------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|------|
|                         |            | 1-7                     | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 | 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 | 14-7 |
| DEATH                   | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| MORIBUND SACRIFICE      | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| PARALYTIC GAIT          | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| EXCITEMENT              | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| SOILED                  | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| FROG BELLY              | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| SOILED PERI-GENITALIA   | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| CATARACT                | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 1    | 1    | 1    | 1    |
|                         | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 1    | 1    | 1    | 1    | 1    |
|                         | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCrI CrIj [F344/DuCrIj]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : MALE

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| Clinical sign           | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 15-7                    | 16-7 | 17-7 | 18-7 | 19-7 | 20-7 | 21-7 | 22-7 | 23-7 | 24-7 | 25-7 | 26-7 | 27-7 | 28-7 |
| DEATH                   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| MORIBUND SACRIFICE      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PARALYTIC GAIT          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXCITEMENT              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED                  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| FROG BELLY              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED PERI-GENITALIA   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CATARACT                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 2    | 2    | 2    | 2    | 2    |
|                         | 0.5ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    |

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrIj [F344/DuCrj]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : MALE

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| Clinical sign           | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 29-7                    | 30-7 | 31-7 | 32-7 | 33-7 | 34-7 | 35-7 | 36-7 | 37-7 | 38-7 | 39-7 | 40-7 | 41-7 | 42-7 |
| DEATH                   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| MORIBUND SACRIFICE      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PARALYTIC GAIT          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXCITEMENT              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED                  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
| FROG BELLY              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED PERI-GENITALIA   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CATARACT                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                         | 0.5ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                         | 2ppm       | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrIj [F344/DuCrj]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : MALE

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| Clinical sign           | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 43-7                    | 44-7 | 45-7 | 46-7 | 47-7 | 48-7 | 49-7 | 50-7 | 51-7 | 52-7 | 53-7 | 54-7 | 55-7 | 56-7 |
| DEATH                   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| MORIBUND SACRIFICE      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PARALYTIC GAIT          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| EXCITEMENT              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED                  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| FROG BELLY              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED PERI-GENITALIA   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
| CATARACT                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 3    | 3    | 3    | 3    | 3    | 3    | 3    |
|                         | 0.5ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                         | 2ppm       | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrIj [F344/DuCrIj]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

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| Clinical sign           | Group Name | Administration Week-day |      |      | 60-7 | 61-7 | 62-7 | 63-7 | 64-7 | 65-7 | 66-7 | 67-7 | 68-7 | 69-7 | 70-7 |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 57-7                    | 58-7 | 59-7 |      |      |      |      |      |      |      |      |      |      |      |
| DEATH                   | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| MORIBUND SACRIFICE      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PARALYTIC GAIT          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| EXCITEMENT              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED                  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 1                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| FROG BELLY              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED PERI-GENITALIA   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 1                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CATARACT                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 3                       | 3    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    |
|                         | 0.5ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                         | 2ppm       | 1                       | 1    | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |

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| Clinical sign           | Group Name | Administration Week-day |      |      |  | 74-7 | 75-7 | 76-7 | 77-7 | 78-7 | 79-7 | 80-7 | 81-7 | 82-7 | 83-7 | 84-7 |
|-------------------------|------------|-------------------------|------|------|--|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 71-7                    | 72-7 | 73-7 |  |      |      |      |      |      |      |      |      |      |      |      |
| DEATH                   | Control    | 2                       | 2    | 2    |  | 2    | 2    | 2    | 2    | 2    | 2    | 3    | 3    | 3    | 3    | 3    |
|                         | 0.1ppm     | 0                       | 1    | 1    |  | 1    | 1    | 1    | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                         | 0.5ppm     | 0                       | 0    | 0    |  | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                         | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    |
| MORIBUND SACRIFICE      | Control    | 0                       | 0    | 0    |  | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                         | 0.1ppm     | 1                       | 1    | 1    |  | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                         | 0.5ppm     | 1                       | 1    | 1    |  | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                         | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PARALYTIC GAIT          | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 1                       | 1    | 1    |  | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| EXCITEMENT              | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED                  | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                         | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    |
| FROG BELLY              | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    |
|                         | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED PERI-GENITALIA   | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                         | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 1    |  | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| CATARACT                | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 4                       | 4    | 4    |  | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    |
|                         | 0.5ppm     | 1                       | 1    | 1    |  | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 2    | 2    |
|                         | 2ppm       | 2                       | 2    | 2    |  | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |

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| Clinical sign           | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 85-7                    | 86-7 | 87-7 | 88-7 | 89-7 | 90-7 | 91-7 | 92-7 | 93-7 | 94-7 | 95-7 | 96-7 | 97-7 | 98-7 |
| DEATH                   | Control    | 3                       | 3    | 3    | 3    | 3    | 3    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    |
|                         | 0.1ppm     | 2                       | 2    | 3    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    |
|                         | 0.5ppm     | 1                       | 2    | 3    | 3    | 4    | 6    | 6    | 6    | 7    | 7    | 7    | 7    | 7    | 7    |
|                         | 2ppm       | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| MORIBUND SACRIFICE      | Control    | 1                       | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                         | 0.1ppm     | 3                       | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 4    | 4    | 4    | 4    |
|                         | 0.5ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 4    | 4    |
|                         | 2ppm       | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PARALYTIC GAIT          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 0    |
|                         | 2ppm       | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| EXCITEMENT              | Control    | 0                       | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED                  | Control    | 0                       | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 1                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| FROG BELLY              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 1                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
| SOILED PERI-GENITALIA   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 0    | 0    | 0    | 1    | 0    | 0    |
|                         | 2ppm       | 1                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CATARACT                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                         | 0.1ppm     | 4                       | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    |
|                         | 0.5ppm     | 2                       | 2    | 2    | 2    | 3    | 3    | 3    | 4    | 3    | 3    | 3    | 3    | 3    | 3    |
|                         | 2ppm       | 2                       | 2    | 2    | 2    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    |

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|-------------------------|------------|-------------------------|-------|-------|-------|-------|-------|
|                         |            | 99-7                    | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| DEATH                   | Control    | 5                       | 5     | 5     | 5     | 5     | 6     |
|                         | 0.1ppm     | 5                       | 5     | 5     | 5     | 5     | 6     |
|                         | 0.5ppm     | 7                       | 7     | 7     | 8     | 8     | 8     |
|                         | 2ppm       | 1                       | 2     | 4     | 5     | 5     | 5     |
| MORIBUND SACRIFICE      | Control    | 2                       | 3     | 3     | 3     | 3     | 3     |
|                         | 0.1ppm     | 4                       | 4     | 4     | 4     | 4     | 4     |
|                         | 0.5ppm     | 4                       | 4     | 4     | 4     | 4     | 5     |
|                         | 2ppm       | 1                       | 1     | 2     | 3     | 3     | 3     |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
| PARALYTIC GAIT          | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.1ppm     | 0                       | 0     | 1     | 1     | 1     | 1     |
|                         | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 2ppm       | 1                       | 2     | 2     | 2     | 2     | 2     |
| EXCITEMENT              | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
| SOILED                  | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 2ppm       | 0                       | 0     | 1     | 1     | 1     | 1     |
| FROG BELLY              | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 2ppm       | 1                       | 1     | 0     | 0     | 0     | 0     |
| SOILED PERI-GENITALIA   | Control    | 1                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 2ppm       | 0                       | 0     | 1     | 1     | 1     | 1     |
| CATARACT                | Control    | 2                       | 2     | 2     | 2     | 2     | 2     |
|                         | 0.1ppm     | 4                       | 4     | 4     | 4     | 4     | 4     |
|                         | 0.5ppm     | 3                       | 4     | 4     | 3     | 3     | 2     |
|                         | 2ppm       | 3                       | 3     | 3     | 3     | 3     | 3     |

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|---------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|------|
|                     |            | 1-7                     | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 | 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 | 14-7 |
| EXTERNAL MASS       | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| INTERNAL MASS       | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. NOSE             | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. EAR              | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. PERI EAR         | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. NECK             | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. BREAST           | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. ABDOMEN          | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. ANTERIOR. DORSUM | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrI CrIj [F344/DuCrIj]  
 REPORT TYPE : A1 104

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SEX : MALE

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| Clinical sign      | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|--------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                    |            | 15-7                    | 16-7 | 17-7 | 18-7 | 19-7 | 20-7 | 21-7 | 22-7 | 23-7 | 24-7 | 25-7 | 26-7 | 27-7 | 28-7 |
| EXTERNAL MASS      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| INTERNAL MASS      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NOSE            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. EAR             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI EAR        | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NECK            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. BREAST          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ABDOMEN         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ANTERIOR DORSUM | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCrI CrIj [F344/DuCrIj]  
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| Clinical sign       | Group Name | Administration Week-day |      |      |   | 32-7 | 33-7 | 34-7 | 35-7 | 36-7 | 37-7 | 38-7 | 39-7 | 40-7 | 41-7 | 42-7 |
|---------------------|------------|-------------------------|------|------|---|------|------|------|------|------|------|------|------|------|------|------|
|                     |            | 29-7                    | 30-7 | 31-7 |   |      |      |      |      |      |      |      |      |      |      |      |
| EXTERNAL MASS       | Control    | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| INTERNAL MASS       | Control    | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NOSE             | Control    | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. EAR              | Control    | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI EAR         | Control    | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NECK             | Control    | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. BREAST           | Control    | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ABDOMEN          | Control    | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ANTERIOR. DORSUM | Control    | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrI CrIj [F344/DuCrIj]  
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| Clinical sign       | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                     |            | 43-7                    | 44-7 | 45-7 | 46-7 | 47-7 | 48-7 | 49-7 | 50-7 | 51-7 | 52-7 | 53-7 | 54-7 | 55-7 | 56-7 |
| EXTERNAL MASS       | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| INTERNAL MASS       | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NOSE             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. EAR              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI EAR         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NECK             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. BREAST           | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ABDOMEN          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ANTERIOR. DORSUM | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrI CrIj [F344/DuCrI]  
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| Clinical sign      | Group Name | Administration Week-day |      |      | 60-7 | 61-7 | 62-7 | 63-7 | 64-7 | 65-7 | 66-7 | 67-7 | 68-7 | 69-7 | 70-7 |
|--------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                    |            | 57-7                    | 58-7 | 59-7 |      |      |      |      |      |      |      |      |      |      |      |
| EXTERNAL MASS      | Control    | 0                       | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 2    | 2    | 2    | 2    | 2    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 1    | 1    | 1    | 2    | 2    | 2    | 2    | 2    | 3    | 4    | 4    |
|                    | 0.5ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
| INTERNAL MASS      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NOSE            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. EAR             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI EAR        | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                    | 0.5ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NECK            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. BREAST          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ABDOMEN         | Control    | 0                       | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
| M. ANTERIOR DORSUM | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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| Clinical sign       | Group Name | Administration Week-day |      |      |  | 74-7 | 75-7 | 76-7 | 77-7 | 78-7 | 79-7 | 80-7 | 81-7 | 82-7 | 83-7 | 84-7 |
|---------------------|------------|-------------------------|------|------|--|------|------|------|------|------|------|------|------|------|------|------|
|                     |            | 71-7                    | 72-7 | 73-7 |  |      |      |      |      |      |      |      |      |      |      |      |
| EXTERNAL MASS       | Control    | 2                       | 3    | 3    |  | 3    | 3    | 3    | 3    | 4    | 4    | 4    | 4    | 4    | 5    | 5    |
|                     | 0.1ppm     | 4                       | 4    | 4    |  | 3    | 5    | 5    | 5    | 5    | 5    | 5    | 4    | 4    | 4    | 4    |
|                     | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 1    | 1    | 2    | 3    | 3    | 1    | 1    | 1    | 1    | 1    |
|                     | 2ppm       | 1                       | 2    | 2    |  | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 1    | 1    | 1    | 1    |
| INTERNAL MASS       | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NOSE             | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 1                       | 1    | 1    |  | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. EAR              | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI EAR         | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 1                       | 1    | 1    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 1    | 1    |  | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| M. NECK             | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. BREAST           | Control    | 1                       | 1    | 1    |  | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ABDOMEN          | Control    | 1                       | 1    | 1    |  | 1    | 1    | 1    | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                     | 0.1ppm     | 1                       | 1    | 1    |  | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                     | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 1    | 1    | 1    | 2    | 2    | 1    | 1    | 1    | 1    | 1    |
|                     | 2ppm       | 1                       | 1    | 1    |  | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    |
| M. ANTERIOR. DORSUM | Control    | 0                       | 1    | 1    |  | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 2    |
|                     | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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| Clinical sign      | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|--------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                    |            | 85-7                    | 86-7 | 87-7 | 88-7 | 89-7 | 90-7 | 91-7 | 92-7 | 93-7 | 94-7 | 95-7 | 96-7 | 97-7 | 98-7 |
| EXTERNAL MASS      | Control    | 5                       | 5    | 4    | 4    | 4    | 4    | 6    | 6    | 6    | 6    | 6    | 6    | 6    | 6    |
|                    | 0.1ppm     | 4                       | 4    | 4    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 4    | 4    |
|                    | 0.5ppm     | 2                       | 5    | 5    | 6    | 5    | 4    | 4    | 4    | 3    | 2    | 4    | 4    | 5    | 5    |
|                    | 2ppm       | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 2    | 2    |
| INTERNAL MASS      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NOSE            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. EAR             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI EAR        | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| M. NECK            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. BREAST          | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ABDOMEN         | Control    | 2                       | 2    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                    | 0.1ppm     | 2                       | 2    | 2    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                    | 0.5ppm     | 2                       | 2    | 2    | 3    | 3    | 2    | 2    | 2    | 2    | 1    | 1    | 1    | 1    | 1    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ANTERIOR DORSUM | Control    | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                    | 0.1ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                    | 0.5ppm     | 0                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    |

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| Clinical sign       | Group Name | Administration Week-day |       |       |       |       |       |
|---------------------|------------|-------------------------|-------|-------|-------|-------|-------|
|                     |            | 99-7                    | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| EXTERNAL MASS       | Control    | 6                       | 6     | 8     | 9     | 9     | 10    |
|                     | 0.1ppm     | 5                       | 5     | 5     | 7     | 7     | 5     |
|                     | 0.5ppm     | 6                       | 6     | 6     | 6     | 6     | 8     |
|                     | 2ppm       | 2                       | 2     | 1     | 1     | 3     | 4     |
| INTERNAL MASS       | Control    | 0                       | 0     | 0     | 1     | 1     | 0     |
|                     | 0.1ppm     | 0                       | 0     | 0     | 1     | 1     | 1     |
|                     | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. NOSE             | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 0.1ppm     | 0                       | 0     | 0     | 1     | 1     | 0     |
|                     | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. EAR              | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 2ppm       | 0                       | 0     | 0     | 0     | 1     | 1     |
| M. PERI EAR         | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 0.1ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
|                     | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 1     |
|                     | 2ppm       | 1                       | 1     | 0     | 0     | 0     | 0     |
| M. NECK             | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 0.5ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
|                     | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. BREAST           | Control    | 3                       | 3     | 3     | 4     | 4     | 4     |
|                     | 0.1ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
|                     | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 1     |
|                     | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 1     |
| M. ABDOMEN          | Control    | 1                       | 1     | 1     | 1     | 1     | 2     |
|                     | 0.1ppm     | 1                       | 1     | 1     | 2     | 2     | 0     |
|                     | 0.5ppm     | 2                       | 2     | 2     | 2     | 2     | 2     |
|                     | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. ANTERIOR. DORSUM | Control    | 2                       | 2     | 2     | 2     | 2     | 3     |
|                     | 0.1ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
|                     | 0.5ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
|                     | 2ppm       | 1                       | 1     | 1     | 1     | 1     | 1     |

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|---------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|------|
|                     |            | 1-7                     | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 | 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 | 14-7 |
| M. POSTERIOR DORSUM | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. HINDLIMB         | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. GENITALIA        | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. SCROTUM          | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. TAIL             | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| ANEMIA              | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| EROSION             | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| CRUSTA              | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| HEMORRHAGE          | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrIj [F344/DuCrj]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : MALE

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| Clinical sign       | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                     |            | 15-7                    | 16-7 | 17-7 | 18-7 | 19-7 | 20-7 | 21-7 | 22-7 | 23-7 | 24-7 | 25-7 | 26-7 | 27-7 | 28-7 |
| M. POSTERIOR DORSUM | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. HINDLIMB         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. GENITALIA        | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. SCROTUM          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. TAIL             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ANEMIA              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EROSION             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CRUSTA              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HEMORRHAGE          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrIj [F344/DuCrj]  
 REPORT TYPE : A1 104

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SEX : MALE

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| Clinical sign       | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                     |            | 29-7                    | 30-7 | 31-7 | 32-7 | 33-7 | 34-7 | 35-7 | 36-7 | 37-7 | 38-7 | 39-7 | 40-7 | 41-7 | 42-7 |
| M. POSTERIOR DORSUM | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. HINDLIMB         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. GENITALIA        | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. SCROTUM          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. TAIL             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ANEMIA              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EROSION             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CRUSTA              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HEMORRHAGE          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrIj [F344/DuCrj]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : MALE

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| Clinical sign       | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                     |            | 43-7                    | 44-7 | 45-7 | 46-7 | 47-7 | 48-7 | 49-7 | 50-7 | 51-7 | 52-7 | 53-7 | 54-7 | 55-7 | 56-7 |
| M. POSTERIOR DORSUM | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. HINDLIMB         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. GENITALIA        | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. SCROTUM          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. TAIL             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ANEMIA              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EROSION             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CRUSTA              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HEMORRHAGE          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrIj [F344/DuCrj]  
 REPORT TYPE : A1 104

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SEX : MALE

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| Clinical sign       | Group Name | Administration Week-day |      |      | 60-7 | 61-7 | 62-7 | 63-7 | 64-7 | 65-7 | 66-7 | 67-7 | 68-7 | 69-7 | 70-7 |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                     |            | 57-7                    | 58-7 | 59-7 |      |      |      |      |      |      |      |      |      |      |      |
| M. POSTERIOR DORSUM | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. HINDLIMB         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. GENITALIA        | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. SCROTUM          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. TAIL             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ANEMIA              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 1    | 1    | 2    | 1    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EROSION             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CRUSTA              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HEMORRHAGE          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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| Clinical sign       | Group Name | Administration Week-day |      |      |   | 74-7 | 75-7 | 76-7 | 77-7 | 78-7 | 79-7 | 80-7 | 81-7 | 82-7 | 83-7 | 84-7 |
|---------------------|------------|-------------------------|------|------|---|------|------|------|------|------|------|------|------|------|------|------|
|                     |            | 71-7                    | 72-7 | 73-7 |   |      |      |      |      |      |      |      |      |      |      |      |
| M. POSTERIOR DORSUM | Control    | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. HINDLIMB         | Control    | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. GENITALIA        | Control    | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. SCROTUM          | Control    | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 1                       | 1    | 1    | 1 | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. TAIL             | Control    | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ANEMIA              | Control    | 1                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    |
|                     | 0.5ppm     | 1                       | 1    | 1    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    |
|                     | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 1    | 2    | 1    | 0    | 0    | 0    |
| EROSION             | Control    | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    |
| CRUSTA              | Control    | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HEMORRHAGE          | Control    | 1                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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| Clinical sign       | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                     |            | 85-7                    | 86-7 | 87-7 | 88-7 | 89-7 | 90-7 | 91-7 | 92-7 | 93-7 | 94-7 | 95-7 | 96-7 | 97-7 | 98-7 |
| M. POSTERIOR DORSUM | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. HINDLIMB         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. GENITALIA        | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. SCROTUM          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. TAIL             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ANEMIA              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 1    | 2    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 0.1ppm     | 1                       | 1    | 1    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 1                       | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EROSION             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| CRUSTA              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 1                       | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HEMORRHAGE          | Control    | 0                       | 0    | 0    | 1    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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| Clinical sign       | Group Name | Administration Week-day |       |       |       |       |       |
|---------------------|------------|-------------------------|-------|-------|-------|-------|-------|
|                     |            | 99-7                    | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| M. POSTERIOR DORSUM | Control    | 0                       | 0     | 1     | 1     | 1     | 0     |
|                     | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 0.5ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
|                     | 2ppm       | 0                       | 0     | 0     | 0     | 1     | 1     |
| M. HINDLIMB         | Control    | 0                       | 0     | 0     | 0     | 1     | 1     |
|                     | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 1     |
|                     | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. GENITALIA        | Control    | 0                       | 0     | 1     | 1     | 1     | 1     |
|                     | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 0.5ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
|                     | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. SCROTUM          | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 0.1ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
|                     | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. TAIL             | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
| ANEMIA              | Control    | 2                       | 2     | 4     | 2     | 2     | 1     |
|                     | 0.1ppm     | 0                       | 0     | 2     | 0     | 0     | 1     |
|                     | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 2ppm       | 1                       | 0     | 0     | 0     | 0     | 0     |
| EROSION             | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 2ppm       | 1                       | 1     | 1     | 1     | 1     | 1     |
| CRUSTA              | Control    | 0                       | 0     | 1     | 1     | 1     | 2     |
|                     | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
| HEMORRHAGE          | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                     | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |

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| Clinical sign           | Group Name | Administration Week-day |     |     |     |     |     |     |     |     |      |      |      |      |      |
|-------------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|------|
|                         |            | 1-7                     | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 | 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 | 14-7 |
| TORTICOLLIS             | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| PROLAPSE OF PENIS       | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| IRREGULAR BREATHING     | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 3                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| ABNORMAL RESPIRA. SOUND | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |

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|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 15-7                    | 16-7 | 17-7 | 18-7 | 19-7 | 20-7 | 21-7 | 22-7 | 23-7 | 24-7 | 25-7 | 26-7 | 27-7 | 28-7 |
| TORTICOLLIS             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PROLAPSE OF PENIS       | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| IRREGULAR BREATHING     | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ABNORMAL RESPIRA. SOUND | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

(HAN190)

BAIS 5

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCrIj [F344/DuCrj]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : MALE

PAGE : 27

| Clinical sign           | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 29-7                    | 30-7 | 31-7 | 32-7 | 33-7 | 34-7 | 35-7 | 36-7 | 37-7 | 38-7 | 39-7 | 40-7 | 41-7 | 42-7 |
| TORTICOLLIS             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PROLAPSE OF PENIS       | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| IRREGULAR BREATHING     | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ABNORMAL RESPIRA. SOUND | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCrI CrIj [F344/DuCrIj]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : MALE

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| Clinical sign           | Group Name | Administration Week-day |      |      |  | 46-7 | 47-7 | 48-7 | 49-7 | 50-7 | 51-7 | 52-7 | 53-7 | 54-7 | 55-7 | 56-7 |
|-------------------------|------------|-------------------------|------|------|--|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 43-7                    | 44-7 | 45-7 |  |      |      |      |      |      |      |      |      |      |      |      |
| TORTICOLLIS             | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PROLAPSE OF PENIS       | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| IRREGULAR BREATHING     | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 0    | 0    |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ABNORMAL RESPIRA. SOUND | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

(HAN190)

BAIS5

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrI CrIj [F344/DuCrIj]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : MALE

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| Clinical sign           | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 57-7                    | 58-7 | 59-7 | 60-7 | 61-7 | 62-7 | 63-7 | 64-7 | 65-7 | 66-7 | 67-7 | 68-7 | 69-7 | 70-7 |
| TORTICOLLIS             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PROLAPSE OF PENIS       | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| IRREGULAR BREATHING     | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ABNORMAL RESPIRA. SOUND | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

(HAN190)

BAIS5

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1j [F344/DuCrj]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : MALE

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| Clinical sign           | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 71-7                    | 72-7 | 73-7 | 74-7 | 75-7 | 76-7 | 77-7 | 78-7 | 79-7 | 80-7 | 81-7 | 82-7 | 83-7 | 84-7 |
| TORTICOLLIS             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PROLAPSE OF PENIS       | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| IRREGULAR BREATHING     | Control    | 0                       | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ABNORMAL RESPIRA. SOUND | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

(HAN190)

BAIS 5

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrIj [F344/DuCrj]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : MALE

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| Clinical sign           | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 85-7                    | 86-7 | 87-7 | 88-7 | 89-7 | 90-7 | 91-7 | 92-7 | 93-7 | 94-7 | 95-7 | 96-7 | 97-7 | 98-7 |
| TORTICOLLIS             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PROLAPSE OF PENIS       | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| IRREGULAR BREATHING     | Control    | 0                       | 1    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    |
|                         | 0.5ppm     | 1                       | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 0    | 1    | 1    | 1    | 1    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ABNORMAL RESPIRA. SOUND | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

(HAN190)

BAIS 5

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j [F344/DuCrj]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : MALE

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| Clinical sign           | Group Name | Administration Week-day |       |       |       |       |       |
|-------------------------|------------|-------------------------|-------|-------|-------|-------|-------|
|                         |            | 99-7                    | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| TORTICOLLIS             | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
| PROLAPSE OF PENIS       | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
| IRREGULAR BREATHING     | Control    | 0                       | 0     | 1     | 2     | 2     | 0     |
|                         | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.5ppm     | 0                       | 0     | 1     | 0     | 0     | 0     |
|                         | 2ppm       | 0                       | 0     | 1     | 0     | 0     | 0     |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 2ppm       | 0                       | 0     | 1     | 0     | 0     | 0     |
| ABNORMAL RESPIRA. SOUND | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |

(HAN190)

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**TABLE C2**

**CLINICAL OBSERVATION : FEMALE**

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j [F344/DuCrj]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : FEMALE

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| Clinical sign           | Group Name | Administration Week-day |     |     |     |     |     |     |     |     |      |      |      |      |      |
|-------------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|------|
|                         |            | 1-7                     | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 | 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 | 14-7 |
| DEATH                   | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| MORIBUND SACRIFICE      | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| PARALYTIC GAIT          | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| ABNORMAL GAIT           | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| WASTING                 | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| SOILED                  | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| PILOERECTION            | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| FROG BELLY              | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrIj [F344/DuCrj]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
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| Clinical sign           | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 15-7                    | 16-7 | 17-7 | 18-7 | 19-7 | 20-7 | 21-7 | 22-7 | 23-7 | 24-7 | 25-7 | 26-7 | 27-7 | 28-7 |
| DEATH                   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| MORIBUND SACRIFICE      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PARALYTIC GAIT          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ABNORMAL GAIT           | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| WASTING                 | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED                  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PILOERECTION            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| FROG BELLY              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrI CrIj [F344/DuCrj]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
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| Clinical sign           | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 29-7                    | 30-7 | 31-7 | 32-7 | 33-7 | 34-7 | 35-7 | 36-7 | 37-7 | 38-7 | 39-7 | 40-7 | 41-7 | 42-7 |
| DEATH                   | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| MORIBUND SACRIFICE      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PARALYTIC GAIT          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ABNORMAL GAIT           | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| WASTING                 | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED                  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PILOERECTION            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| FROG BELLY              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCrIj [F344/DuCrj]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
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| Clinical sign           | Group Name | Administration Week-day |      |      |  | 46-7 | 47-7 | 48-7 | 49-7 | 50-7 | 51-7 | 52-7 | 53-7 | 54-7 | 55-7 | 56-7 |
|-------------------------|------------|-------------------------|------|------|--|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 43-7                    | 44-7 | 45-7 |  |      |      |      |      |      |      |      |      |      |      |      |
| DEATH                   | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    |
| MORIBUND SACRIFICE      | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PARALYTIC GAIT          | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ABNORMAL GAIT           | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| WASTING                 | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED                  | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PILOERECTION            | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| FROG BELLY              | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrIj [F344/DuCrj]  
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| Clinical sign           | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 57-7                    | 58-7 | 59-7 | 60-7 | 61-7 | 62-7 | 63-7 | 64-7 | 65-7 | 66-7 | 67-7 | 68-7 | 69-7 | 70-7 |
| DEATH                   | Control    | 0                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 2    | 2    | 2    |
|                         | 2ppm       | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 2    | 2    |
| MORIBUND SACRIFICE      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PARALYTIC GAIT          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ABNORMAL GAIT           | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| WASTING                 | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED                  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PILOERECTION            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| FROG BELLY              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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| Clinical sign           | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 71-7                    | 72-7 | 73-7 | 74-7 | 75-7 | 76-7 | 77-7 | 78-7 | 79-7 | 80-7 | 81-7 | 82-7 | 83-7 | 84-7 |
| DEATH                   | Control    | 1                       | 1    | 1    | 1    | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                         | 0.1ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                         | 0.5ppm     | 2                       | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    |
|                         | 2ppm       | 2                       | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    |
| MORIBUND SACRIFICE      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PARALYTIC GAIT          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ABNORMAL GAIT           | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| WASTING                 | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED                  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PILOERECTION            | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| FROG BELLY              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCrIj [F344/DuCrj]  
REPORT TYPE : A1 104

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| Clinical sign           | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 85-7                    | 86-7 | 87-7 | 88-7 | 89-7 | 90-7 | 91-7 | 92-7 | 93-7 | 94-7 | 95-7 | 96-7 | 97-7 | 98-7 |
| DEATH                   | Control    | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 3    | 3    | 4    |
|                         | 0.1ppm     | 1                       | 1    | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                         | 0.5ppm     | 3                       | 3    | 3    | 3    | 4    | 5    | 5    | 5    | 5    | 5    | 5    | 5    | 5    | 5    |
|                         | 2ppm       | 4                       | 4    | 5    | 5    | 5    | 5    | 5    | 5    | 5    | 5    | 5    | 6    | 6    | 6    |
| MORIBUND SACRIFICE      | Control    | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                         | 0.1ppm     | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                         | 0.5ppm     | 1                       | 1    | 1    | 1    | 2    | 2    | 2    | 4    | 4    | 4    | 4    | 4    | 4    | 4    |
|                         | 2ppm       | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 2    | 2    | 3    | 3    | 3    |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0    | 0    | 0    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 0    | 0    | 0    |
| PARALYTIC GAIT          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 1    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ABNORMAL GAIT           | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    |
| WASTING                 | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
| SOILED                  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| PILORECTION             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    |
| FROG BELLY              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrIj [F344/DuCrj]  
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| Clinical sign           | Group Name | Administration Week-day |       |       |       |       |       |
|-------------------------|------------|-------------------------|-------|-------|-------|-------|-------|
|                         |            | 99-7                    | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| DEATH                   | Control    | 4                       | 5     | 5     | 5     | 5     | 6     |
|                         | 0.1ppm     | 2                       | 2     | 2     | 3     | 4     | 5     |
|                         | 0.5ppm     | 5                       | 5     | 5     | 5     | 5     | 5     |
|                         | 2ppm       | 6                       | 7     | 8     | 10    | 10    | 10    |
| MORIBUND SACRIFICE      | Control    | 1                       | 1     | 1     | 1     | 1     | 1     |
|                         | 0.1ppm     | 2                       | 3     | 3     | 3     | 3     | 3     |
|                         | 0.5ppm     | 4                       | 4     | 4     | 4     | 4     | 4     |
|                         | 2ppm       | 4                       | 5     | 5     | 5     | 6     | 6     |
| LOCOMOTOR MOVEMENT DECR | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
| PARALYTIC GAIT          | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.1ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
|                         | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
| ABNORMAL GAIT           | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
| WASTING                 | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
| SOILED                  | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
| PILORECTION             | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
| FROG BELLY              | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.5ppm     | 0                       | 0     | 1     | 1     | 1     | 1     |
|                         | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1j [F344/DuCrj]  
 REPORT TYPE : A1 104

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| Clinical sign          | Group Name | Administration Week-day |     |     |     |     |     |     |     |     |      |      |      |      |      |
|------------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|------|
|                        |            | 1-7                     | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 | 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 | 14-7 |
| SOILED PERI-GENITALIA  | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| EXOPHTHALMOS           | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| EYE HEMORRHAGIC DISCHA | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| CATARACT               | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 1    |
|                        | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 1    | 1    | 1    | 1    | 1    |
|                        | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| CORNEAL OPACITY        | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| EXTERNAL MASS          | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| INTERNAL MASS          | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. NOSE                | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. PERI-MOUTH          | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrI CrIj [F344/DuCrj]  
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| Clinical sign          | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                        |            | 15-7                    | 16-7 | 17-7 | 18-7 | 19-7 | 20-7 | 21-7 | 22-7 | 23-7 | 24-7 | 25-7 | 26-7 | 27-7 | 28-7 |
| SOILED PERI-GENITALIA  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXOPHTHALMOS           | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EYE HEMORRHAGIC DISCHA | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CATARACT               | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 2    | 2    |
|                        | 0.1ppm     | 1                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 3    | 3    | 3    | 3    | 3    |
|                        | 0.5ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CORNEAL OPACITY        | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXTERNAL MASS          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| INTERNAL MASS          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NOSE                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI-MOUTH          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrI CrIj [F344/DuCrIj]  
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| Clinical sign          | Group Name | Administration Week-day |      |      | 32-7 | 33-7 | 34-7 | 35-7 | 36-7 | 37-7 | 38-7 | 39-7 | 40-7 | 41-7 | 42-7 |
|------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                        |            | 29-7                    | 30-7 | 31-7 |      |      |      |      |      |      |      |      |      |      |      |
| SOILED PERI-GENITALIA  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 1                       | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 3    | 2    | 2    | 2    | 2    | 2    | 2    | 1    | 1    | 1    | 1    | 1    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXOPHTHALMOS           | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EYE HEMORRHAGIC DISCHA | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CATARACT               | Control    | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                        | 0.1ppm     | 3                       | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    |
|                        | 0.5ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CORNEAL OPACITY        | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXTERNAL MASS          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 2    |
| INTERNAL MASS          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NOSE                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI-MOUTH          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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 ANIMAL : RAT F344/DuCrIj [F344/DuCrj]  
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| Clinical sign          | Group Name | Administration Week-day |      |      |  | 46-7 | 47-7 | 48-7 | 49-7 | 50-7 | 51-7 | 52-7 | 53-7 | 54-7 | 55-7 | 56-7 |
|------------------------|------------|-------------------------|------|------|--|------|------|------|------|------|------|------|------|------|------|------|
|                        |            | 43-7                    | 44-7 | 45-7 |  |      |      |      |      |      |      |      |      |      |      |      |
| SOILED PERI-GENITALIA  | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 1                       | 1    | 1    |  | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXOPHTHALMOS           | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EYE HEMORRHAGIC DISCHA | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CATARACT               | Control    | 2                       | 2    | 2    |  | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                        | 0.1ppm     | 3                       | 3    | 3    |  | 4    | 4    | 4    | 4    | 4    | 5    | 5    | 5    | 5    | 5    | 5    |
|                        | 0.5ppm     | 1                       | 1    | 1    |  | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                        | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CORNEAL OPACITY        | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXTERNAL MASS          | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 2                       | 2    | 2    |  | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
| INTERNAL MASS          | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NOSE                | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI-MOUTH          | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrI CrIj [F344/DuCrIj]  
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| Clinical sign          | Group Name | Administration Week-day |      |      |  | 60-7 | 61-7 | 62-7 | 63-7 | 64-7 | 65-7 | 66-7 | 67-7 | 68-7 | 69-7 | 70-7 |
|------------------------|------------|-------------------------|------|------|--|------|------|------|------|------|------|------|------|------|------|------|
|                        |            | 57-7                    | 58-7 | 59-7 |  |      |      |      |      |      |      |      |      |      |      |      |
| SOILED PERI-GENITALIA  | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXOPHTHALMOS           | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    |
|                        | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EYE HEMORRHAGIC DISCHA | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CATARACT               | Control    | 2                       | 2    | 2    |  | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                        | 0.1ppm     | 5                       | 5    | 5    |  | 5    | 5    | 5    | 5    | 5    | 5    | 5    | 5    | 5    | 5    | 5    |
|                        | 0.5ppm     | 1                       | 1    | 1    |  | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                        | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    |
| CORNEAL OPACITY        | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXTERNAL MASS          | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    |  | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                        | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 2                       | 2    | 2    |  | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 1    | 1    | 1    | 1    |
| INTERNAL MASS          | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NOSE                | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI-MOUTH          | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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| Clinical sign          | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                        |            | 71-7                    | 72-7 | 73-7 | 74-7 | 75-7 | 76-7 | 77-7 | 78-7 | 79-7 | 80-7 | 81-7 | 82-7 | 83-7 | 84-7 |
| SOILED PERI-GENITALIA  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXOPHTHALMOS           | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 0    | 0    | 0    |
| EYE HEMORRHAGIC DISCHA | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CATARACT               | Control    | 2                       | 2    | 2    | 2    | 2    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    | 3    |
|                        | 0.1ppm     | 5                       | 5    | 5    | 5    | 5    | 5    | 5    | 5    | 5    | 5    | 5    | 5    | 5    | 5    |
|                        | 0.5ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    |
|                        | 2ppm       | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| CORNEAL OPACITY        | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 0    | 0    | 0    |
| EXTERNAL MASS          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 1                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| INTERNAL MASS          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. NOSE                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI-MOUTH          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 1    | 1    | 1    | 1    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrI CrIj [F344/DuCrIj]  
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| Clinical sign          | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                        |            | 85-7                    | 86-7 | 87-7 | 88-7 | 89-7 | 90-7 | 91-7 | 92-7 | 93-7 | 94-7 | 95-7 | 96-7 | 97-7 | 98-7 |
| SOILED PERI-GENITALIA  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 2    | 2    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                        | 2ppm       | 0                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXOPHTHALMOS           | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 2                       | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EYE HEMORRHAGIC DISCHA | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 0    | 0    | 0    |
| CATARACT               | Control    | 3                       | 3    | 3    | 3    | 3    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    | 4    |
|                        | 0.1ppm     | 6                       | 7    | 7    | 6    | 6    | 6    | 6    | 6    | 6    | 6    | 6    | 6    | 6    | 6    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| CORNEAL OPACITY        | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| EXTERNAL MASS          | Control    | 0                       | 2    | 3    | 3    | 4    | 5    | 5    | 5    | 5    | 5    | 5    | 6    | 6    | 6    |
|                        | 0.1ppm     | 2                       | 2    | 2    | 2    | 3    | 3    | 3    | 4    | 4    | 5    | 6    | 6    | 6    | 7    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 1    | 1    | 2    | 2    | 3    | 3    | 4    | 4    | 4    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 2    | 2    | 2    | 2    | 2    | 3    |
| INTERNAL MASS          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    |
| M. NOSE                | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
| M. PERI-MOUTH          | Control    | 0                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                        | 0.1ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                        | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                        | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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| Clinical sign          | Group Name | Administration Week-day |       |       |       |       |       |
|------------------------|------------|-------------------------|-------|-------|-------|-------|-------|
|                        |            | 99-7                    | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| SOILED PERI-GENITALIA  | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                        | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                        | 0.5ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
|                        | 2ppm       | 0                       | 0     | 1     | 0     | 0     | 0     |
| EXOPHTHALMOS           | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                        | 0.1ppm     | 2                       | 2     | 2     | 2     | 2     | 2     |
|                        | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                        | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
| EYE HEMORRHAGIC DISCHA | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                        | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                        | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                        | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
| CATARACT               | Control    | 5                       | 5     | 5     | 5     | 5     | 5     |
|                        | 0.1ppm     | 6                       | 5     | 5     | 5     | 5     | 5     |
|                        | 0.5ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
|                        | 2ppm       | 1                       | 1     | 1     | 1     | 1     | 1     |
| CORNEAL OPACITY        | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                        | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                        | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                        | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
| EXTERNAL MASS          | Control    | 6                       | 6     | 7     | 7     | 7     | 7     |
|                        | 0.1ppm     | 7                       | 6     | 6     | 7     | 8     | 9     |
|                        | 0.5ppm     | 4                       | 5     | 5     | 5     | 7     | 8     |
|                        | 2ppm       | 3                       | 5     | 4     | 4     | 5     | 5     |
| INTERNAL MASS          | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                        | 0.1ppm     | 0                       | 0     | 0     | 1     | 1     | 1     |
|                        | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                        | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. NOSE                | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                        | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                        | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                        | 2ppm       | 1                       | 1     | 0     | 0     | 0     | 0     |
| M. PERI-MOUTH          | Control    | 1                       | 1     | 1     | 1     | 1     | 1     |
|                        | 0.1ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
|                        | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                        | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrI CrIj [F344/DuCrIj]  
 REPORT TYPE : A1 104

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| Clinical sign       | Group Name | Administration Week-day |     |     |     |     |     |     |     |     |      |      |      |      |      |
|---------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|------|
|                     |            | 1-7                     | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 | 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 | 14-7 |
| M. ORAL CAVITY      | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. PERI EAR         | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. FORELIMB         | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. BREAST           | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. ABDOMEN          | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. ANTERIOR. DORSUM | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| M. GENITALIA        | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| ANEMIA              | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| ULCER               | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrI CrIj [F344/DuCrIj]  
 REPORT TYPE : A1 104

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| Clinical sign      | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|--------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                    |            | 15-7                    | 16-7 | 17-7 | 18-7 | 19-7 | 20-7 | 21-7 | 22-7 | 23-7 | 24-7 | 25-7 | 26-7 | 27-7 | 28-7 |
| M. ORAL CAVITY     | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI EAR        | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. FORELIMB        | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. BREAST          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ABDOMEN         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ANTERIOR DORSUM | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. GENITALIA       | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ANEMIA             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ULCER              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1j [F344/DuCrj]  
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| Clinical sign      | Group Name | Administration Week-day |      |      |   | 32-7 | 33-7 | 34-7 | 35-7 | 36-7 | 37-7 | 38-7 | 39-7 | 40-7 | 41-7 | 42-7 |
|--------------------|------------|-------------------------|------|------|---|------|------|------|------|------|------|------|------|------|------|------|
|                    |            | 29-7                    | 30-7 | 31-7 |   |      |      |      |      |      |      |      |      |      |      |      |
| M. ORAL CAVITY     | Control    | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI EAR        | Control    | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. FORELIMB        | Control    | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. BREAST          | Control    | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    |
| M. ABDOMEN         | Control    | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ANTERIOR DORSUM | Control    | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. GENITALIA       | Control    | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
| ANEMIA             | Control    | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ULCER              | Control    | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrI CrIj [F344/DuCrIj]  
 REPORT TYPE : A1 104

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| Clinical sign      | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|--------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                    |            | 43-7                    | 44-7 | 45-7 | 46-7 | 47-7 | 48-7 | 49-7 | 50-7 | 51-7 | 52-7 | 53-7 | 54-7 | 55-7 | 56-7 |
| M. ORAL CAVITY     | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI EAR        | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. FORELIMB        | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. BREAST          | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| M. ABDOMEN         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ANTERIOR DORSUM | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. GENITALIA       | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| ANEMIA             | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
| ULCER              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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 ANIMAL : RAT F344/DuCrI CrIj [F344/DuCrIj]  
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| Clinical sign      | Group Name | Administration Week-day |      |      |  | 60-7 | 61-7 | 62-7 | 63-7 | 64-7 | 65-7 | 66-7 | 67-7 | 68-7 | 69-7 | 70-7 |
|--------------------|------------|-------------------------|------|------|--|------|------|------|------|------|------|------|------|------|------|------|
|                    |            | 57-7                    | 58-7 | 59-7 |  |      |      |      |      |      |      |      |      |      |      |      |
| M. ORAL CAVITY     | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI EAR        | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. FORELIMB        | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. BREAST          | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    |  | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                    | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 1                       | 1    | 1    |  | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| M. ABDOMEN         | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ANTERIOR DORSUM | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. GENITALIA       | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 1                       | 1    | 1    |  | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    |
| ANEMIA             | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    |
|                    | 2ppm       | 1                       | 1    | 1    |  | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    |
| ULCER              | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    |

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| Clinical sign       | Group Name | Administration Week-day |      |      |  | 74-7 | 75-7 | 76-7 | 77-7 | 78-7 | 79-7 | 80-7 | 81-7 | 82-7 | 83-7 | 84-7 |
|---------------------|------------|-------------------------|------|------|--|------|------|------|------|------|------|------|------|------|------|------|
|                     |            | 71-7                    | 72-7 | 73-7 |  |      |      |      |      |      |      |      |      |      |      |      |
| M. ORAL CAVITY      | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI EAR         | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. FORELIMB         | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. BREAST           | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 1                       | 1    | 1    |  | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 1                       | 1    | 1    |  | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| M. ABDOMEN          | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. ANTERIOR. DORSUM | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. GENITALIA        | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ANEMIA              | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                     | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 1    | 1    | 1    | 1    | 0    | 1    | 0    | 1    | 1    |
|                     | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                     | 2ppm       | 0                       | 0    | 0    |  | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 1    |
| ULCER               | Control    | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    |  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 1                       | 1    | 1    |  | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |

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 ANIMAL : RAT F344/DuCrIj [F344/DuCrj]  
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| Clinical sign       | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|---------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                     |            | 85-7                    | 86-7 | 87-7 | 88-7 | 89-7 | 90-7 | 91-7 | 92-7 | 93-7 | 94-7 | 95-7 | 96-7 | 97-7 | 98-7 |
| M. ORAL CAVITY      | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. PERI EAR         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. FORELIMB         | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. BREAST           | Control    | 0                       | 1    | 1    | 1    | 2    | 3    | 3    | 3    | 3    | 3    | 3    | 4    | 4    | 4    |
|                     | 0.1ppm     | 1                       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 1    | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 2    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
| M. ABDOMEN          | Control    | 0                       | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 2    | 3    | 3    | 3    | 3    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    |
| M. ANTERIOR. DORSUM | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| M. GENITALIA        | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 2    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ANEMIA              | Control    | 0                       | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 1                       | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 1                       | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 1    | 1    | 1    | 2    | 2    | 2    | 2    | 1    | 1    | 1    |
| ULCER               | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                     | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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| Clinical sign      | Group Name | Administration Week-day |       |       |       |       |       |
|--------------------|------------|-------------------------|-------|-------|-------|-------|-------|
|                    |            | 99-7                    | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| M. ORAL CAVITY     | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                    | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                    | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                    | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. PERI EAR        | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                    | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                    | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 1     |
|                    | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. FORELIMB        | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                    | 0.1ppm     | 0                       | 0     | 0     | 0     | 1     | 0     |
|                    | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                    | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. BREAST          | Control    | 4                       | 4     | 4     | 4     | 4     | 4     |
|                    | 0.1ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
|                    | 0.5ppm     | 2                       | 2     | 2     | 2     | 2     | 2     |
|                    | 2ppm       | 1                       | 1     | 1     | 1     | 1     | 1     |
| M. ABDOMEN         | Control    | 1                       | 1     | 1     | 1     | 1     | 1     |
|                    | 0.1ppm     | 3                       | 3     | 3     | 4     | 4     | 5     |
|                    | 0.5ppm     | 1                       | 1     | 1     | 1     | 2     | 2     |
|                    | 2ppm       | 1                       | 1     | 1     | 1     | 1     | 1     |
| M. ANTERIOR DORSUM | Control    | 1                       | 1     | 1     | 1     | 1     | 0     |
|                    | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                    | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                    | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
| M. GENITALIA       | Control    | 0                       | 0     | 1     | 1     | 1     | 1     |
|                    | 0.1ppm     | 2                       | 1     | 1     | 1     | 1     | 2     |
|                    | 0.5ppm     | 1                       | 2     | 2     | 2     | 3     | 3     |
|                    | 2ppm       | 0                       | 2     | 2     | 2     | 3     | 3     |
| ANEMIA             | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                    | 0.1ppm     | 1                       | 1     | 1     | 1     | 1     | 1     |
|                    | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                    | 2ppm       | 1                       | 1     | 1     | 1     | 1     | 1     |
| ULCER              | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                    | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                    | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                    | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrI CrIj [F344/DuCrj]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : FEMALE

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| Clinical sign           | Group Name | Administration Week-day |     |     |     |     |     |     |     |     |      |      |      |      |      |
|-------------------------|------------|-------------------------|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|------|
|                         |            | 1-7                     | 2-7 | 3-7 | 4-7 | 5-7 | 6-7 | 7-7 | 8-7 | 9-7 | 10-7 | 11-7 | 12-7 | 13-7 | 14-7 |
| CRUSTA                  | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| HEMORRHAGE              | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| IRREGULAR BREATHING     | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| SALIVATION              | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |

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STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrIj [F344/DuCrj]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : FEMALE

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| Clinical sign           | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 15-7                    | 16-7 | 17-7 | 18-7 | 19-7 | 20-7 | 21-7 | 22-7 | 23-7 | 24-7 | 25-7 | 26-7 | 27-7 | 28-7 |
| CRUSTA                  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HEMORRHAGE              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| IRREGULAR BREATHING     | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SALIVATION              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrI CrIj [F344/DuCrj]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : FEMALE

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| Clinical sign           | Group Name | Administration Week-day |      |      | 32-7 | 33-7 | 34-7 | 35-7 | 36-7 | 37-7 | 38-7 | 39-7 | 40-7 | 41-7 | 42-7 |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 29-7                    | 30-7 | 31-7 |      |      |      |      |      |      |      |      |      |      |      |
| CRUSTA                  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HEMORRHAGE              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| IRREGULAR BREATHING     | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SALIVATION              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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STUDY NO. : 0816  
ANIMAL : RAT F344/DuCrI CrIj [F344/DuCrI]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : FEMALE

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| Clinical sign           | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 43-7                    | 44-7 | 45-7 | 46-7 | 47-7 | 48-7 | 49-7 | 50-7 | 51-7 | 52-7 | 53-7 | 54-7 | 55-7 | 56-7 |
| CRUSTA                  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HEMORRHAGE              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 1    |
| IRREGULAR BREATHING     | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SALIVATION              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrIj [F344/DuCrj]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : FEMALE

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| Clinical sign           | Group Name | Administration Week-day |      |      | 60-7 | 61-7 | 62-7 | 63-7 | 64-7 | 65-7 | 66-7 | 67-7 | 68-7 | 69-7 | 70-7 |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 57-7                    | 58-7 | 59-7 |      |      |      |      |      |      |      |      |      |      |      |
| CRUSTA                  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HEMORRHAGE              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| IRREGULAR BREATHING     | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SALIVATION              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

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STUDY NO. : 0816  
ANIMAL : RAT F344/DuCrIj [F344/DuCrIj]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : FEMALE

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| Clinical sign           | Group Name | Administration Week-day |      |      |   | 74-7 | 75-7 | 76-7 | 77-7 | 78-7 | 79-7 | 80-7 | 81-7 | 82-7 | 83-7 | 84-7 |
|-------------------------|------------|-------------------------|------|------|---|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 71-7                    | 72-7 | 73-7 |   |      |      |      |      |      |      |      |      |      |      |      |
| CRUSTA                  | Control    | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 1                       | 1    | 1    | 1 | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                         | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HEMORRHAGE              | Control    | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| IRREGULAR BREATHING     | Control    | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 1                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 1    | 1    | 1    |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SALIVATION              | Control    | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0 | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    | 0    | 1    |

(HAN190)

BAIS 5

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrI CrIj [F344/DuCrI]  
 REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
 ALL ANIMALS

SEX : FEMALE

PAGE : 63

| Clinical sign           | Group Name | Administration Week-day |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-------------------------|------------|-------------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|
|                         |            | 85-7                    | 86-7 | 87-7 | 88-7 | 89-7 | 90-7 | 91-7 | 92-7 | 93-7 | 94-7 | 95-7 | 96-7 | 97-7 | 98-7 |
| CRUSTA                  | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 1                       | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| HEMORRHAGE              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 1                       | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| IRREGULAR BREATHING     | Control    | 0                       | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 2    | 2    | 1    | 1    | 1    |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SALIVATION              | Control    | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.1ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 0.5ppm     | 0                       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2ppm       | 1                       | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

(HAN190)

BAIS5

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCrI CrIj [F344/DuCrI]  
REPORT TYPE : A1 104

CLINICAL OBSERVATION (SUMMARY)  
ALL ANIMALS

SEX : FEMALE

PAGE : 64

| Clinical sign           | Group Name | Administration Week-day |       |       |       |       |       |
|-------------------------|------------|-------------------------|-------|-------|-------|-------|-------|
|                         |            | 99-7                    | 100-7 | 101-7 | 102-7 | 103-7 | 104-7 |
| CRUSTA                  | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 1     |
|                         | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         |            |                         |       |       |       |       |       |
| HEMORRHAGE              | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         |            |                         |       |       |       |       |       |
| IRREGULAR BREATHING     | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.1ppm     | 0                       | 0     | 0     | 1     | 1     | 0     |
|                         | 0.5ppm     | 1                       | 1     | 1     | 2     | 2     | 2     |
|                         | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         |            |                         |       |       |       |       |       |
| RESPIRATORY SOUND ABNOR | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 1     |
|                         | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         |            |                         |       |       |       |       |       |
| SALIVATION              | Control    | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.1ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 0.5ppm     | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         | 2ppm       | 0                       | 0     | 0     | 0     | 0     | 0     |
|                         |            |                         |       |       |       |       |       |

(HAN190)

BAIS 5

TABLE D1

BODY WEIGHT CHANGES AND SURVIVAL ANIMAL  
NUMBERS : MALE

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
UNIT : g  
REPORT TYPE : A1 104  
SEX : MALE

MEAN BODY WEIGHTS AND SURVIVAL

PAGE : 1

| Week<br>on Study                                          | Control  |                           |          | 0.1ppm                |                   | 0.5ppm   |                       |                   | 2ppm     |                       |                   |
|-----------------------------------------------------------|----------|---------------------------|----------|-----------------------|-------------------|----------|-----------------------|-------------------|----------|-----------------------|-------------------|
|                                                           | Av. Wt.  | No. of<br>Surviv.<br><50> | Av. Wt.  | % of<br>cont.<br><50> | No. of<br>Surviv. | Av. Wt.  | % of<br>cont.<br><50> | No. of<br>Surviv. | Av. Wt.  | % of<br>cont.<br><50> | No. of<br>Surviv. |
| 0                                                         | 119 (50) | 50/50                     | 119 (50) | 100                   | 50/50             | 119 (50) | 100                   | 50/50             | 119 (50) | 100                   | 50/50             |
| 1                                                         | 151 (50) | 50/50                     | 149 (50) | 99                    | 50/50             | 151 (50) | 100                   | 50/50             | 129 (50) | 85                    | 50/50             |
| 2                                                         | 185 (50) | 50/50                     | 183 (50) | 99                    | 50/50             | 186 (50) | 101                   | 50/50             | 159 (50) | 86                    | 50/50             |
| 3                                                         | 212 (50) | 50/50                     | 209 (50) | 99                    | 50/50             | 213 (50) | 100                   | 50/50             | 180 (50) | 85                    | 50/50             |
| 4                                                         | 235 (50) | 50/50                     | 231 (50) | 98                    | 50/50             | 235 (50) | 100                   | 50/50             | 198 (50) | 84                    | 50/50             |
| 5                                                         | 252 (50) | 50/50                     | 247 (50) | 98                    | 50/50             | 253 (50) | 100                   | 50/50             | 215 (50) | 85                    | 50/50             |
| 6                                                         | 267 (50) | 50/50                     | 262 (50) | 98                    | 50/50             | 268 (50) | 100                   | 50/50             | 228 (50) | 85                    | 50/50             |
| 7                                                         | 281 (50) | 50/50                     | 275 (50) | 98                    | 50/50             | 280 (50) | 100                   | 50/50             | 239 (50) | 85                    | 50/50             |
| 8                                                         | 295 (50) | 50/50                     | 289 (50) | 98                    | 50/50             | 295 (50) | 100                   | 50/50             | 248 (50) | 84                    | 50/50             |
| 9                                                         | 306 (50) | 50/50                     | 299 (50) | 98                    | 50/50             | 305 (50) | 100                   | 50/50             | 256 (50) | 84                    | 50/50             |
| 10                                                        | 315 (50) | 50/50                     | 307 (50) | 97                    | 50/50             | 313 (50) | 99                    | 50/50             | 263 (50) | 83                    | 50/50             |
| 11                                                        | 321 (50) | 50/50                     | 313 (50) | 98                    | 50/50             | 321 (50) | 100                   | 50/50             | 268 (50) | 83                    | 50/50             |
| 12                                                        | 328 (50) | 50/50                     | 320 (50) | 98                    | 50/50             | 328 (50) | 100                   | 50/50             | 273 (50) | 83                    | 50/50             |
| 13                                                        | 334 (50) | 50/50                     | 325 (50) | 97                    | 50/50             | 334 (50) | 100                   | 50/50             | 277 (50) | 83                    | 50/50             |
| 14                                                        | 339 (50) | 50/50                     | 331 (50) | 98                    | 50/50             | 338 (50) | 100                   | 50/50             | 281 (50) | 83                    | 50/50             |
| 18                                                        | 355 (50) | 50/50                     | 345 (50) | 97                    | 50/50             | 355 (50) | 100                   | 50/50             | 297 (50) | 84                    | 50/50             |
| 22                                                        | 367 (50) | 50/50                     | 358 (50) | 98                    | 50/50             | 368 (50) | 100                   | 50/50             | 310 (50) | 84                    | 50/50             |
| 26                                                        | 379 (50) | 50/50                     | 371 (50) | 98                    | 50/50             | 380 (50) | 100                   | 50/50             | 323 (50) | 85                    | 50/50             |
| 30                                                        | 392 (50) | 50/50                     | 383 (50) | 98                    | 50/50             | 393 (50) | 100                   | 50/50             | 331 (50) | 84                    | 50/50             |
| 34                                                        | 401 (50) | 50/50                     | 393 (50) | 98                    | 50/50             | 405 (50) | 101                   | 50/50             | 334 (50) | 83                    | 50/50             |
| 38                                                        | 409 (50) | 50/50                     | 401 (50) | 98                    | 50/50             | 411 (50) | 100                   | 50/50             | 345 (50) | 84                    | 50/50             |
| 42                                                        | 418 (50) | 50/50                     | 409 (50) | 98                    | 50/50             | 419 (50) | 100                   | 50/50             | 351 (50) | 84                    | 50/50             |
| 46                                                        | 422 (50) | 50/50                     | 414 (50) | 98                    | 50/50             | 424 (50) | 100                   | 50/50             | 360 (50) | 85                    | 50/50             |
| 50                                                        | 431 (50) | 50/50                     | 420 (50) | 97                    | 50/50             | 430 (50) | 100                   | 50/50             | 365 (50) | 85                    | 50/50             |
| 54                                                        | 429 (49) | 49/50                     | 422 (50) | 98                    | 50/50             | 431 (50) | 100                   | 50/50             | 369 (50) | 86                    | 50/50             |
| 58                                                        | 434 (49) | 49/50                     | 427 (50) | 98                    | 50/50             | 437 (50) | 101                   | 50/50             | 375 (50) | 86                    | 50/50             |
| 62                                                        | 436 (49) | 49/50                     | 431 (49) | 99                    | 49/50             | 437 (50) | 100                   | 50/50             | 378 (50) | 87                    | 50/50             |
| 66                                                        | 439 (49) | 49/50                     | 434 (49) | 99                    | 49/50             | 437 (50) | 100                   | 50/50             | 381 (50) | 87                    | 50/50             |
| 70                                                        | 439 (49) | 49/50                     | 434 (49) | 99                    | 49/50             | 443 (49) | 101                   | 49/50             | 383 (50) | 87                    | 50/50             |
| 74                                                        | 439 (47) | 47/50                     | 433 (47) | 99                    | 47/50             | 443 (48) | 101                   | 48/50             | 385 (50) | 88                    | 50/50             |
| 78                                                        | 438 (47) | 47/50                     | 434 (46) | 99                    | 46/50             | 444 (48) | 101                   | 48/50             | 387 (50) | 88                    | 50/50             |
| 82                                                        | 440 (46) | 46/50                     | 431 (46) | 98                    | 46/50             | 442 (48) | 100                   | 48/50             | 387 (48) | 88                    | 48/50             |
| 86                                                        | 438 (46) | 46/50                     | 428 (45) | 98                    | 45/50             | 438 (47) | 100                   | 47/50             | 386 (48) | 88                    | 48/50             |
| 90                                                        | 435 (45) | 45/50                     | 426 (43) | 98                    | 43/50             | 433 (43) | 100                   | 43/50             | 385 (48) | 89                    | 48/50             |
| 94                                                        | 434 (44) | 44/50                     | 418 (43) | 96                    | 43/50             | 428 (42) | 99                    | 42/50             | 379 (48) | 87                    | 48/50             |
| 98                                                        | 428 (44) | 44/50                     | 414 (42) | 97                    | 42/50             | 425 (39) | 99                    | 39/50             | 378 (48) | 88                    | 48/50             |
| 102                                                       | 419 (42) | 42/50                     | 410 (41) | 98                    | 41/50             | 418 (38) | 100                   | 38/50             | 376 (42) | 90                    | 42/50             |
| 104                                                       | 420 (41) | 41/50                     | 402 (40) | 96                    | 40/50             | 415 (37) | 99                    | 37/50             | 370 (42) | 88                    | 42/50             |
| < >:No. of effective animals, ( ):No. of measured animals |          |                           |          |                       |                   |          |                       |                   |          |                       |                   |
| Av. Wt. : g                                               |          |                           |          |                       |                   |          |                       |                   |          |                       |                   |

< >:No. of effective animals, ( ):No. of measured animals

Av. Wt. : g

TABLE D2

BODY WEIGHT CHANGES AND SURVIVAL ANIMAL  
NUMBERS : FEMALE

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrI CrIj [F344/DuCrj]  
 UNIT : g  
 REPORT TYPE : A1 104  
 SEX : FEMALE

MEAN BODY WEIGHTS AND SURVIVAL

PAGE : 2

| Week<br>on Study                                          | Control  |                           | 0.1ppm   |                       |                   | 0.5ppm   |                       |                   | 2ppm     |                       |                   |
|-----------------------------------------------------------|----------|---------------------------|----------|-----------------------|-------------------|----------|-----------------------|-------------------|----------|-----------------------|-------------------|
|                                                           | Av. Wt.  | No. of<br>Surviv.<br><50> | Av. Wt.  | % of<br>cont.<br><50> | No. of<br>Surviv. | Av. Wt.  | % of<br>cont.<br><50> | No. of<br>Surviv. | Av. Wt.  | % of<br>cont.<br><50> | No. of<br>Surviv. |
| 0                                                         | 95 (50)  | 50/50                     | 95 (50)  | 100                   | 50/50             | 95 (50)  | 100                   | 50/50             | 95 (50)  | 100                   | 50/50             |
| 1                                                         | 110 (50) | 50/50                     | 108 (50) | 98                    | 50/50             | 110 (50) | 100                   | 50/50             | 100 (50) | 91                    | 50/50             |
| 2                                                         | 125 (50) | 50/50                     | 123 (50) | 98                    | 50/50             | 125 (50) | 100                   | 50/50             | 114 (50) | 91                    | 50/50             |
| 3                                                         | 136 (50) | 50/50                     | 133 (50) | 98                    | 50/50             | 134 (50) | 99                    | 50/50             | 123 (50) | 90                    | 50/50             |
| 4                                                         | 144 (50) | 50/50                     | 141 (50) | 98                    | 50/50             | 143 (50) | 99                    | 50/50             | 131 (50) | 91                    | 50/50             |
| 5                                                         | 150 (50) | 50/50                     | 148 (50) | 99                    | 50/50             | 150 (50) | 100                   | 50/50             | 138 (50) | 92                    | 50/50             |
| 6                                                         | 157 (50) | 50/50                     | 154 (50) | 98                    | 50/50             | 155 (50) | 99                    | 50/50             | 143 (50) | 91                    | 50/50             |
| 7                                                         | 160 (50) | 50/50                     | 159 (50) | 99                    | 50/50             | 159 (50) | 99                    | 50/50             | 147 (50) | 92                    | 50/50             |
| 8                                                         | 165 (50) | 50/50                     | 163 (50) | 99                    | 50/50             | 163 (50) | 99                    | 50/50             | 152 (50) | 92                    | 50/50             |
| 9                                                         | 168 (50) | 50/50                     | 167 (50) | 99                    | 50/50             | 167 (50) | 99                    | 50/50             | 155 (50) | 92                    | 50/50             |
| 10                                                        | 173 (50) | 50/50                     | 171 (50) | 99                    | 50/50             | 171 (50) | 99                    | 50/50             | 160 (50) | 92                    | 50/50             |
| 11                                                        | 176 (50) | 50/50                     | 175 (50) | 99                    | 50/50             | 174 (50) | 99                    | 50/50             | 164 (50) | 93                    | 50/50             |
| 12                                                        | 179 (50) | 50/50                     | 180 (50) | 101                   | 50/50             | 178 (50) | 99                    | 50/50             | 168 (50) | 94                    | 50/50             |
| 13                                                        | 182 (50) | 50/50                     | 183 (50) | 101                   | 50/50             | 179 (50) | 98                    | 50/50             | 169 (50) | 93                    | 50/50             |
| 14                                                        | 185 (50) | 50/50                     | 184 (50) | 99                    | 50/50             | 181 (50) | 98                    | 50/50             | 171 (50) | 92                    | 50/50             |
| 18                                                        | 191 (50) | 50/50                     | 192 (50) | 101                   | 50/50             | 187 (50) | 98                    | 50/50             | 177 (50) | 93                    | 50/50             |
| 22                                                        | 195 (50) | 50/50                     | 196 (50) | 101                   | 50/50             | 190 (50) | 97                    | 50/50             | 182 (50) | 93                    | 50/50             |
| 26                                                        | 200 (50) | 50/50                     | 201 (50) | 101                   | 50/50             | 196 (50) | 98                    | 50/50             | 190 (50) | 95                    | 50/50             |
| 30                                                        | 207 (50) | 50/50                     | 206 (50) | 100                   | 50/50             | 200 (50) | 97                    | 50/50             | 194 (50) | 94                    | 50/50             |
| 34                                                        | 210 (50) | 50/50                     | 210 (50) | 100                   | 50/50             | 205 (50) | 98                    | 50/50             | 196 (50) | 93                    | 50/50             |
| 38                                                        | 212 (50) | 50/50                     | 212 (50) | 100                   | 50/50             | 208 (50) | 98                    | 50/50             | 201 (50) | 95                    | 50/50             |
| 42                                                        | 217 (50) | 50/50                     | 219 (50) | 101                   | 50/50             | 212 (50) | 98                    | 50/50             | 206 (50) | 95                    | 50/50             |
| 46                                                        | 219 (50) | 50/50                     | 223 (50) | 102                   | 50/50             | 215 (50) | 98                    | 50/50             | 212 (50) | 97                    | 50/50             |
| 50                                                        | 224 (50) | 50/50                     | 227 (50) | 101                   | 50/50             | 219 (50) | 98                    | 50/50             | 217 (50) | 97                    | 50/50             |
| 54                                                        | 228 (50) | 50/50                     | 229 (50) | 100                   | 50/50             | 224 (50) | 98                    | 50/50             | 220 (49) | 96                    | 49/50             |
| 58                                                        | 234 (49) | 49/50                     | 235 (50) | 100                   | 50/50             | 230 (50) | 98                    | 50/50             | 226 (49) | 97                    | 49/50             |
| 62                                                        | 238 (49) | 49/50                     | 240 (50) | 101                   | 50/50             | 234 (49) | 98                    | 49/50             | 229 (49) | 96                    | 49/50             |
| 66                                                        | 243 (49) | 49/50                     | 248 (50) | 102                   | 50/50             | 238 (49) | 98                    | 49/50             | 234 (49) | 96                    | 49/50             |
| 70                                                        | 246 (49) | 49/50                     | 253 (48) | 103                   | 48/50             | 242 (48) | 98                    | 48/50             | 238 (48) | 97                    | 48/50             |
| 74                                                        | 249 (49) | 49/50                     | 257 (48) | 103                   | 48/50             | 248 (47) | 100                   | 47/50             | 241 (47) | 97                    | 47/50             |
| 78                                                        | 255 (48) | 48/50                     | 264 (48) | 104                   | 48/50             | 254 (47) | 100                   | 47/50             | 246 (47) | 96                    | 47/50             |
| 82                                                        | 260 (48) | 48/50                     | 268 (48) | 103                   | 48/50             | 260 (46) | 100                   | 46/50             | 250 (46) | 96                    | 46/50             |
| 86                                                        | 265 (47) | 47/50                     | 273 (47) | 103                   | 47/50             | 264 (46) | 100                   | 46/50             | 249 (45) | 94                    | 45/50             |
| 90                                                        | 268 (47) | 47/50                     | 278 (46) | 104                   | 46/50             | 270 (43) | 101                   | 43/50             | 250 (44) | 93                    | 44/50             |
| 94                                                        | 267 (47) | 47/50                     | 278 (46) | 104                   | 46/50             | 269 (41) | 101                   | 41/50             | 250 (43) | 94                    | 43/50             |
| 98                                                        | 272 (45) | 45/50                     | 281 (46) | 103                   | 46/50             | 272 (41) | 100                   | 41/50             | 254 (41) | 93                    | 41/50             |
| 102                                                       | 275 (44) | 44/50                     | 276 (44) | 100                   | 44/50             | 271 (41) | 99                    | 41/50             | 259 (35) | 94                    | 35/50             |
| 104                                                       | 272 (43) | 43/50                     | 276 (42) | 101                   | 42/50             | 266 (41) | 98                    | 41/50             | 259 (34) | 95                    | 34/50             |
| < >:No. of effective animals, ( ):No. of measured animals |          |                           |          |                       |                   |          |                       |                   |          |                       |                   |
| Av. Wt. : g                                               |          |                           |          |                       |                   |          |                       |                   |          |                       |                   |

< >:No. of effective animals, ( ):No. of measured animals

Av. Wt. : g

TABLE D3

BODY WEIGHT CHANGES : MALE

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
UNIT : g  
REPORT TYPE : A1 104  
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)  
ALL ANIMALS

PAGE : 1

| Group | Name    | Administration |   | week |      |     |   |      |     |  |      |     |   |      |      |  |      |      |  |      |      |
|-------|---------|----------------|---|------|------|-----|---|------|-----|--|------|-----|---|------|------|--|------|------|--|------|------|
|       |         | 0              |   |      | 1    |     | 2 |      | 3   |  | 4    |     | 5 |      | 6    |  |      |      |  |      |      |
|       | Control | 119±           | 5 |      | 151± | 7   |   | 185± | 8   |  | 212± | 8   |   | 235± | 9    |  | 252± | 10   |  | 267± | 10   |
|       | 0.1ppm  | 119±           | 5 |      | 149± | 8   |   | 183± | 9   |  | 209± | 9   |   | 231± | 10   |  | 247± | 11   |  | 262± | 12   |
|       | 0.5ppm  | 119±           | 5 |      | 151± | 8   |   | 186± | 10  |  | 213± | 10  |   | 235± | 11   |  | 253± | 12   |  | 268± | 12   |
|       | 2ppm    | 119±           | 5 |      | 129± | 6** |   | 159± | 7** |  | 180± | 9** |   | 198± | 10** |  | 215± | 10** |  | 228± | 10** |

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

Test of Dunnett

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
UNIT : g  
REPORT TYPE : A1 104  
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)  
ALL ANIMALS

PAGE : 2

| Group Name | Administration week |      | 7    |      | 8    |      | 9    |      | 10   |      | 11   |      | 12   |      | 13 |  |
|------------|---------------------|------|------|------|------|------|------|------|------|------|------|------|------|------|----|--|
|            |                     |      |      |      |      |      |      |      |      |      |      |      |      |      |    |  |
| Control    | 281±                | 11   | 295± | 12   | 306± | 12   | 315± | 12   | 321± | 13   | 328± | 14   | 334± | 15   |    |  |
| 0.1ppm     | 275±                | 12   | 289± | 12   | 299± | 13*  | 307± | 14*  | 313± | 15*  | 320± | 15*  | 325± | 15*  |    |  |
| 0.5ppm     | 280±                | 13   | 295± | 14   | 305± | 15   | 313± | 14   | 321± | 15   | 328± | 15   | 334± | 16   |    |  |
| 2ppm       | 239±                | 12** | 248± | 12** | 256± | 13** | 263± | 13** | 268± | 14** | 273± | 14** | 277± | 14** |    |  |

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

Test of Dunnett

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCrI CrIj[F344/DuCrj]  
UNIT : g  
REPORT TYPE : A1 104  
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)  
ALL ANIMALS

PAGE : 3

| Group Name | Administration |      | week |      |      |      |      |      |      |      |      |      |
|------------|----------------|------|------|------|------|------|------|------|------|------|------|------|
|            | 14             |      | 18   |      | 22   |      | 26   |      | 30   |      | 34   | 38   |
| Control    | 339±           | 15   | 355± | 15   | 367± | 15   | 379± | 16   | 392± | 17   | 401± | 18   |
| 0.1ppm     | 331±           | 16*  | 345± | 17** | 358± | 18*  | 371± | 19   | 383± | 20*  | 393± | 21   |
| 0.5ppm     | 338±           | 15   | 355± | 16   | 368± | 15   | 380± | 16   | 393± | 16   | 405± | 17   |
| 2ppm       | 281±           | 14** | 297± | 15** | 310± | 16** | 323± | 18** | 331± | 18** | 334± | 19** |

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

Test of Dunnett

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCrI CrIj[F344/DuCrj]  
UNIT : g  
REPORT TYPE : A1 104  
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)  
ALL ANIMALS

PAGE : 4

| Group Name | Administration |      | week |      |      |    |      |      |  |      |      |    |      |      |  |      |      |  |      |      |
|------------|----------------|------|------|------|------|----|------|------|--|------|------|----|------|------|--|------|------|--|------|------|
|            | 42             |      |      | 46   |      | 50 |      | 54   |  | 58   |      | 62 |      | 66   |  |      |      |  |      |      |
| Control    | 418±           | 20   |      | 422± | 23   |    | 431± | 34   |  | 429± | 24   |    | 434± | 25   |  | 436± | 27   |  | 439± | 29   |
| 0.1ppm     | 409±           | 22   |      | 414± | 22   |    | 420± | 23   |  | 422± | 24   |    | 427± | 27   |  | 431± | 24   |  | 434± | 23   |
| 0.5ppm     | 419±           | 17   |      | 424± | 18   |    | 430± | 19   |  | 431± | 20   |    | 437± | 23   |  | 437± | 31   |  | 437± | 36   |
| 2ppm       | 351±           | 20** |      | 360± | 19** |    | 365± | 21** |  | 369± | 22** |    | 375± | 24** |  | 378± | 27** |  | 381± | 27** |

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

Test of Dunnett

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
UNIT : g  
REPORT TYPE : A1 104  
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)  
ALL ANIMALS

PAGE : 5

| Group Name | Administration |  | week      |  |           |  |           |  |           |  |           |           |
|------------|----------------|--|-----------|--|-----------|--|-----------|--|-----------|--|-----------|-----------|
|            | 70             |  | 74        |  | 78        |  | 82        |  | 86        |  | 90        | 94        |
| Control    | 439± 30        |  | 439± 30   |  | 438± 39   |  | 440± 27   |  | 438± 30   |  | 435± 35   | 434± 27   |
| 0.1ppm     | 434± 23        |  | 433± 25   |  | 434± 26   |  | 431± 26   |  | 428± 29   |  | 426± 28   | 418± 32*  |
| 0.5ppm     | 443± 23        |  | 443± 20   |  | 444± 21   |  | 442± 21   |  | 438± 23   |  | 433± 31   | 428± 24   |
| 2ppm       | 383± 27**      |  | 385± 28** |  | 387± 28** |  | 387± 29** |  | 386± 30** |  | 385± 30** | 379± 29** |

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

Test of Dunnett

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCrI CrIj[F344/DuCrj]  
UNIT : g  
REPORT TYPE : A1 104  
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)  
ALL ANIMALS

PAGE : 6

| Group Name | Administration |  | week      |  |           |  |
|------------|----------------|--|-----------|--|-----------|--|
|            | 98             |  | 102       |  | 104       |  |
| Control    | 428± 31        |  | 419± 39   |  | 420± 36   |  |
| 0.1ppm     | 414± 39        |  | 410± 29   |  | 402± 32*  |  |
| 0.5ppm     | 425± 24        |  | 418± 31   |  | 415± 33   |  |
| 2ppm       | 378± 33**      |  | 376± 25** |  | 370± 23** |  |

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

Test of Dunnett

**TABLE D4**

**BODY WEIGHT CHANGES : FEMALE**

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
UNIT : g  
REPORT TYPE : A1 104  
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)  
ALL ANIMALS

PAGE : 7

| Group Name | Administration |   | week | 1    |     | 2    |     | 3    |     | 4    |     | 5    |     | 6    |     |
|------------|----------------|---|------|------|-----|------|-----|------|-----|------|-----|------|-----|------|-----|
|            | 0              |   |      |      |     |      |     |      |     |      |     |      |     |      |     |
| Control    | 95±            | 3 |      | 110± | 4   | 125± | 5   | 136± | 6   | 144± | 6   | 150± | 6   | 157± | 7   |
| 0.1ppm     | 95±            | 3 |      | 108± | 4*  | 123± | 5   | 133± | 5   | 141± | 6   | 148± | 7   | 154± | 8   |
| 0.5ppm     | 95±            | 3 |      | 110± | 5   | 125± | 6   | 134± | 6   | 143± | 7   | 150± | 8   | 155± | 9   |
| 2ppm       | 95±            | 3 |      | 100± | 4** | 114± | 5** | 123± | 6** | 131± | 6** | 138± | 6** | 143± | 6** |

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

Test of Dunnett

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
UNIT : g  
REPORT TYPE : A1 104  
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)  
ALL ANIMALS

PAGE : 8

| Group Name | Administration |     | week |     |      |     |      |     |      |     |      |     |      |     |
|------------|----------------|-----|------|-----|------|-----|------|-----|------|-----|------|-----|------|-----|
|            | 7              |     | 8    |     | 9    |     | 10   |     | 11   |     | 12   |     | 13   |     |
| Control    | 160±           | 8   | 165± | 9   | 168± | 9   | 173± | 9   | 176± | 9   | 179± | 8   | 182± | 9   |
| 0.1ppm     | 159±           | 9   | 163± | 9   | 167± | 10  | 171± | 10  | 175± | 10  | 180± | 11  | 183± | 11  |
| 0.5ppm     | 159±           | 10  | 163± | 11  | 167± | 11  | 171± | 11  | 174± | 10  | 178± | 11  | 179± | 11  |
| 2ppm       | 147±           | 7** | 152± | 7** | 155± | 8** | 160± | 8** | 164± | 8** | 168± | 8** | 169± | 7** |

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

Test of Dunnett

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
UNIT : g  
REPORT TYPE : A1 104  
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)  
ALL ANIMALS

PAGE : 9

| Group Name | Administration |     | week |     |      |     |      |     |      |      |      |      |      |      |
|------------|----------------|-----|------|-----|------|-----|------|-----|------|------|------|------|------|------|
|            | 14             |     | 18   |     | 22   |     | 26   |     | 30   |      | 34   |      | 38   |      |
| Control    | 185±           | 9   | 191± | 9   | 195± | 10  | 200± | 10  | 207± | 11   | 210± | 13   | 212± | 12   |
| 0.1ppm     | 184±           | 11  | 192± | 11  | 196± | 12  | 201± | 11  | 206± | 11   | 210± | 13   | 212± | 12   |
| 0.5ppm     | 181±           | 11* | 187± | 12  | 190± | 12  | 196± | 13  | 200± | 14** | 205± | 13   | 208± | 13   |
| 2ppm       | 171±           | 7** | 177± | 8** | 182± | 9** | 190± | 9** | 194± | 11** | 196± | 10** | 201± | 10** |

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

Test of Dunnett

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCrI CrI j[F344/DuCrj]  
UNIT : g  
REPORT TYPE : A1 104  
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)  
ALL ANIMALS

PAGE : 10

| Group Name | Administration |  | week    |  |          |  |          |  |          |  |          |         |
|------------|----------------|--|---------|--|----------|--|----------|--|----------|--|----------|---------|
|            | 42             |  | 46      |  | 50       |  | 54       |  | 58       |  | 62       | 66      |
| Control    | 217± 13        |  | 219± 14 |  | 224± 15  |  | 228± 16  |  | 234± 17  |  | 238± 17  | 243± 20 |
| 0.1ppm     | 219± 15        |  | 223± 13 |  | 227± 14  |  | 229± 15  |  | 235± 14  |  | 240± 17  | 248± 20 |
| 0.5ppm     | 212± 14        |  | 215± 16 |  | 219± 16  |  | 224± 18  |  | 230± 20  |  | 234± 21  | 238± 23 |
| 2ppm       | 206± 12**      |  | 212± 13 |  | 217± 13* |  | 220± 13* |  | 226± 16* |  | 229± 16* | 234± 17 |

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

Test of Dunnett

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 UNIT : g  
 REPORT TYPE : A1 104  
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 11

| Group Name | Administration |    | week |    |      |    |      |    |      |      |      |      |
|------------|----------------|----|------|----|------|----|------|----|------|------|------|------|
|            | 70             |    | 74   |    | 78   |    | 82   |    | 86   |      | 90   |      |
| Control    | 246±           | 20 | 249± | 22 | 255± | 22 | 260± | 22 | 265± | 21   | 268± | 20   |
| 0.1ppm     | 253±           | 19 | 257± | 20 | 264± | 21 | 268± | 22 | 273± | 23   | 278± | 24   |
| 0.5ppm     | 242±           | 24 | 248± | 22 | 254± | 25 | 260± | 24 | 264± | 24   | 270± | 25   |
| 2ppm       | 238±           | 18 | 241± | 19 | 246± | 19 | 250± | 18 | 249± | 19** | 250± | 22** |

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

Test of Dunnett

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
UNIT : g  
REPORT TYPE : A1 104  
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)  
ALL ANIMALS

PAGE : 12

| Group Name | Administration |  | week      |  |          |  |
|------------|----------------|--|-----------|--|----------|--|
|            | 98             |  | 102       |  | 104      |  |
| Control    | 272± 20        |  | 275± 20   |  | 272± 22  |  |
| 0.1ppm     | 281± 33        |  | 276± 30   |  | 276± 31  |  |
| 0.5ppm     | 272± 28        |  | 271± 36   |  | 266± 37  |  |
| 2ppm       | 254± 28**      |  | 259± 23** |  | 259± 22* |  |

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

Test of Dunnett

TABLE E1

FOOD CONSUMPTION CHANGES AND SURVIVAL ANIMAL  
NUMBERS : MALE

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 UNIT : g  
 REPORT TYPE : A1 104  
 SEX : MALE

MEAN FOOD CONSUMPTION (FC) AND SURVIVAL

PAGE : 1

| Week-Day<br>on Study                                      | Control   |                           | 0.1ppm    |                       | 0.5ppm            |           | 2ppm                  |                   |           |                       |                   |
|-----------------------------------------------------------|-----------|---------------------------|-----------|-----------------------|-------------------|-----------|-----------------------|-------------------|-----------|-----------------------|-------------------|
|                                                           | Av. FC.   | No. of<br>Surviv.<br><50> | Av. FC.   | % of<br>cont.<br><50> | No. of<br>Surviv. | Av. FC.   | % of<br>cont.<br><50> | No. of<br>Surviv. | Av. FC.   | % of<br>cont.<br><50> | No. of<br>Surviv. |
| 1-7                                                       | 15.9 (50) | 50/50                     | 15.7 (50) | 99                    | 50/50             | 15.7 (50) | 99                    | 50/50             | 10.8 (50) | 68                    | 50/50             |
| 2-7                                                       | 17.9 (50) | 50/50                     | 17.4 (50) | 97                    | 50/50             | 17.7 (50) | 99                    | 50/50             | 13.9 (50) | 78                    | 50/50             |
| 3-7                                                       | 18.1 (50) | 50/50                     | 18.0 (50) | 99                    | 50/50             | 18.3 (50) | 101                   | 50/50             | 14.6 (50) | 81                    | 50/50             |
| 4-7                                                       | 18.4 (50) | 50/50                     | 17.9 (50) | 97                    | 50/50             | 18.5 (50) | 101                   | 50/50             | 15.2 (50) | 83                    | 50/50             |
| 5-7                                                       | 18.0 (50) | 50/50                     | 17.7 (50) | 98                    | 50/50             | 18.2 (50) | 101                   | 50/50             | 16.0 (50) | 89                    | 50/50             |
| 6-7                                                       | 17.7 (50) | 50/50                     | 17.2 (50) | 97                    | 50/50             | 18.0 (50) | 102                   | 50/50             | 15.6 (50) | 88                    | 50/50             |
| 7-7                                                       | 17.5 (50) | 50/50                     | 17.1 (50) | 98                    | 50/50             | 17.5 (50) | 100                   | 50/50             | 15.8 (50) | 90                    | 50/50             |
| 8-7                                                       | 17.9 (50) | 50/50                     | 17.5 (50) | 98                    | 50/50             | 17.9 (50) | 100                   | 50/50             | 15.5 (50) | 87                    | 50/50             |
| 9-7                                                       | 17.7 (50) | 50/50                     | 17.1 (50) | 97                    | 50/50             | 17.6 (50) | 99                    | 50/50             | 15.1 (50) | 85                    | 50/50             |
| 10-7                                                      | 17.6 (50) | 50/50                     | 17.0 (50) | 97                    | 50/50             | 17.5 (50) | 99                    | 50/50             | 15.1 (50) | 86                    | 50/50             |
| 11-7                                                      | 16.9 (50) | 50/50                     | 16.6 (50) | 98                    | 50/50             | 17.0 (50) | 101                   | 50/50             | 15.0 (50) | 89                    | 50/50             |
| 12-7                                                      | 17.0 (50) | 50/50                     | 16.6 (50) | 98                    | 50/50             | 16.9 (50) | 99                    | 50/50             | 14.7 (50) | 86                    | 50/50             |
| 13-7                                                      | 16.7 (50) | 50/50                     | 16.5 (50) | 99                    | 50/50             | 16.5 (50) | 99                    | 50/50             | 14.6 (50) | 87                    | 50/50             |
| 14-7                                                      | 16.5 (50) | 50/50                     | 16.2 (50) | 98                    | 50/50             | 16.6 (50) | 101                   | 50/50             | 14.6 (50) | 88                    | 50/50             |
| 18-7                                                      | 16.1 (50) | 50/50                     | 15.7 (50) | 98                    | 50/50             | 16.2 (50) | 101                   | 50/50             | 14.6 (50) | 91                    | 50/50             |
| 22-7                                                      | 16.2 (50) | 50/50                     | 15.9 (50) | 98                    | 50/50             | 16.4 (50) | 101                   | 50/50             | 14.8 (50) | 91                    | 50/50             |
| 26-7                                                      | 16.5 (50) | 50/50                     | 16.7 (50) | 101                   | 50/50             | 16.9 (50) | 102                   | 50/50             | 15.7 (50) | 95                    | 50/50             |
| 30-7                                                      | 17.1 (50) | 50/50                     | 17.1 (50) | 100                   | 50/50             | 17.2 (50) | 101                   | 50/50             | 15.8 (50) | 92                    | 50/50             |
| 34-7                                                      | 16.9 (50) | 50/50                     | 16.8 (50) | 99                    | 50/50             | 17.2 (50) | 102                   | 50/50             | 15.3 (50) | 91                    | 50/50             |
| 38-7                                                      | 16.9 (50) | 50/50                     | 16.9 (50) | 100                   | 50/50             | 16.9 (50) | 100                   | 50/50             | 15.7 (50) | 93                    | 50/50             |
| 42-7                                                      | 17.2 (50) | 50/50                     | 17.1 (50) | 99                    | 50/50             | 17.5 (50) | 102                   | 50/50             | 16.0 (50) | 93                    | 50/50             |
| 46-7                                                      | 16.9 (50) | 50/50                     | 17.0 (50) | 101                   | 50/50             | 17.4 (50) | 103                   | 50/50             | 16.3 (50) | 96                    | 50/50             |
| 50-7                                                      | 17.5 (50) | 50/50                     | 17.2 (50) | 98                    | 50/50             | 17.7 (50) | 101                   | 50/50             | 16.5 (50) | 94                    | 50/50             |
| 54-7                                                      | 17.1 (49) | 49/50                     | 17.0 (50) | 99                    | 50/50             | 17.3 (50) | 101                   | 50/50             | 16.3 (50) | 95                    | 50/50             |
| 58-7                                                      | 17.3 (49) | 49/50                     | 17.1 (50) | 99                    | 50/50             | 17.3 (50) | 100                   | 50/50             | 16.4 (50) | 95                    | 50/50             |
| 62-7                                                      | 17.2 (49) | 49/50                     | 17.1 (49) | 99                    | 49/50             | 17.3 (50) | 101                   | 50/50             | 16.1 (50) | 94                    | 50/50             |
| 66-7                                                      | 17.0 (49) | 49/50                     | 16.9 (49) | 99                    | 49/50             | 16.9 (50) | 99                    | 50/50             | 16.1 (50) | 95                    | 50/50             |
| 70-7                                                      | 17.1 (49) | 49/50                     | 16.8 (49) | 98                    | 49/50             | 17.0 (49) | 99                    | 49/50             | 16.2 (50) | 95                    | 50/50             |
| 74-7                                                      | 17.0 (47) | 47/50                     | 17.0 (47) | 100                   | 47/50             | 17.2 (48) | 101                   | 48/50             | 16.2 (50) | 95                    | 50/50             |
| 78-7                                                      | 17.0 (47) | 47/50                     | 17.1 (46) | 101                   | 46/50             | 17.5 (48) | 103                   | 48/50             | 16.3 (50) | 96                    | 50/50             |
| 82-7                                                      | 17.0 (46) | 46/50                     | 17.0 (46) | 100                   | 46/50             | 17.4 (48) | 102                   | 48/50             | 16.0 (48) | 94                    | 48/50             |
| 86-7                                                      | 17.1 (46) | 46/50                     | 17.0 (45) | 99                    | 45/50             | 17.1 (47) | 100                   | 47/50             | 16.3 (48) | 95                    | 48/50             |
| 90-7                                                      | 16.6 (45) | 45/50                     | 16.8 (43) | 101                   | 43/50             | 16.5 (43) | 99                    | 43/50             | 16.1 (48) | 97                    | 48/50             |
| 94-7                                                      | 16.9 (44) | 44/50                     | 16.6 (43) | 98                    | 43/50             | 16.7 (42) | 99                    | 42/50             | 16.3 (48) | 96                    | 48/50             |
| 98-7                                                      | 17.0 (44) | 44/50                     | 16.7 (42) | 98                    | 42/50             | 17.2 (39) | 101                   | 39/50             | 16.5 (48) | 97                    | 48/50             |
| 102-7                                                     | 16.2 (42) | 42/50                     | 16.4 (41) | 101                   | 41/50             | 16.6 (38) | 102                   | 38/50             | 16.0 (42) | 99                    | 42/50             |
| 104-7                                                     | 17.3 (41) | 41/50                     | 16.2 (40) | 94                    | 40/50             | 16.8 (37) | 97                    | 37/50             | 15.8 (42) | 91                    | 42/50             |
| < >:No. of effective animals, ( ):No. of measured animals |           |                           |           |                       |                   |           |                       |                   |           |                       |                   |
| Av. FC.: g                                                |           |                           |           |                       |                   |           |                       |                   |           |                       |                   |

< >:No. of effective animals, ( ):No. of measured animals

Av. FC. : g

TABLE E2

FOOD CONSUMPTION CHANGES AND SURVIVAL ANIMAL  
NUMBERS : FEMALE

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCrIj[F344/DuCrj]  
UNIT : g  
REPORT TYPE : A1 104  
SEX : FEMALE

MEAN FOOD CONSUMPTION (FC) AND SURVIVAL

PAGE : 2

| Week-Day<br>on Study                                      | Control   |                           | 0.1ppm    |                       | 0.5ppm            |           | 2ppm                  |                   |           |                       |                   |
|-----------------------------------------------------------|-----------|---------------------------|-----------|-----------------------|-------------------|-----------|-----------------------|-------------------|-----------|-----------------------|-------------------|
|                                                           | Av. FC.   | No. of<br>Surviv.<br><50> | Av. FC.   | % of<br>cont.<br><50> | No. of<br>Surviv. | Av. FC.   | % of<br>cont.<br><50> | No. of<br>Surviv. | Av. FC.   | % of<br>cont.<br><50> | No. of<br>Surviv. |
| 1-7                                                       | 12.5 (50) | 50/50                     | 12.0 (50) | 96                    | 50/50             | 12.1 (50) | 97                    | 50/50             | 9.1 (50)  | 73                    | 50/50             |
| 2-7                                                       | 12.6 (50) | 50/50                     | 12.0 (50) | 95                    | 50/50             | 12.3 (50) | 98                    | 50/50             | 11.1 (50) | 88                    | 50/50             |
| 3-7                                                       | 12.2 (50) | 50/50                     | 12.0 (50) | 98                    | 50/50             | 12.0 (50) | 98                    | 50/50             | 10.9 (50) | 89                    | 50/50             |
| 4-7                                                       | 12.5 (50) | 50/50                     | 12.2 (50) | 98                    | 50/50             | 12.2 (50) | 98                    | 50/50             | 11.1 (50) | 89                    | 50/50             |
| 5-7                                                       | 11.9 (50) | 50/50                     | 12.0 (50) | 101                   | 50/50             | 11.9 (50) | 100                   | 50/50             | 10.9 (50) | 92                    | 50/50             |
| 6-7                                                       | 12.1 (50) | 50/50                     | 11.9 (50) | 98                    | 50/50             | 11.7 (50) | 97                    | 50/50             | 10.6 (50) | 88                    | 50/50             |
| 7-7                                                       | 11.3 (50) | 50/50                     | 11.3 (50) | 100                   | 50/50             | 11.1 (50) | 98                    | 50/50             | 10.8 (50) | 96                    | 50/50             |
| 8-7                                                       | 11.3 (50) | 50/50                     | 11.4 (50) | 101                   | 50/50             | 11.0 (50) | 97                    | 50/50             | 10.6 (50) | 94                    | 50/50             |
| 9-7                                                       | 11.2 (50) | 50/50                     | 11.1 (50) | 99                    | 50/50             | 10.9 (50) | 97                    | 50/50             | 10.4 (50) | 93                    | 50/50             |
| 10-7                                                      | 11.2 (50) | 50/50                     | 11.2 (50) | 100                   | 50/50             | 11.1 (50) | 99                    | 50/50             | 10.8 (50) | 96                    | 50/50             |
| 11-7                                                      | 10.9 (50) | 50/50                     | 11.2 (50) | 103                   | 50/50             | 10.9 (50) | 100                   | 50/50             | 10.6 (50) | 97                    | 50/50             |
| 12-7                                                      | 11.4 (50) | 50/50                     | 11.5 (50) | 101                   | 50/50             | 11.2 (50) | 98                    | 50/50             | 10.7 (50) | 94                    | 50/50             |
| 13-7                                                      | 11.3 (50) | 50/50                     | 11.6 (50) | 103                   | 50/50             | 11.0 (50) | 97                    | 50/50             | 10.7 (50) | 95                    | 50/50             |
| 14-7                                                      | 11.4 (50) | 50/50                     | 11.2 (50) | 98                    | 50/50             | 10.7 (50) | 94                    | 50/50             | 10.7 (50) | 94                    | 50/50             |
| 18-7                                                      | 10.8 (50) | 50/50                     | 11.5 (50) | 106                   | 50/50             | 10.8 (50) | 100                   | 50/50             | 10.4 (50) | 96                    | 50/50             |
| 22-7                                                      | 10.7 (50) | 50/50                     | 10.9 (50) | 102                   | 50/50             | 10.4 (50) | 97                    | 50/50             | 10.4 (50) | 97                    | 50/50             |
| 26-7                                                      | 11.0 (50) | 50/50                     | 11.5 (50) | 105                   | 50/50             | 11.2 (50) | 102                   | 50/50             | 11.2 (50) | 102                   | 50/50             |
| 30-7                                                      | 11.2 (50) | 50/50                     | 11.2 (50) | 100                   | 50/50             | 11.0 (50) | 98                    | 50/50             | 11.5 (50) | 103                   | 50/50             |
| 34-7                                                      | 11.2 (50) | 50/50                     | 11.6 (50) | 104                   | 50/50             | 11.2 (50) | 100                   | 50/50             | 11.4 (50) | 102                   | 50/50             |
| 38-7                                                      | 11.3 (50) | 50/50                     | 11.5 (50) | 102                   | 50/50             | 10.9 (50) | 96                    | 50/50             | 11.4 (50) | 101                   | 50/50             |
| 42-7                                                      | 11.2 (50) | 50/50                     | 11.8 (50) | 105                   | 50/50             | 11.1 (50) | 99                    | 50/50             | 11.7 (50) | 104                   | 50/50             |
| 46-7                                                      | 11.1 (50) | 50/50                     | 11.8 (50) | 106                   | 50/50             | 11.3 (50) | 102                   | 50/50             | 12.1 (50) | 109                   | 50/50             |
| 50-7                                                      | 11.7 (50) | 50/50                     | 11.9 (50) | 102                   | 50/50             | 11.4 (50) | 97                    | 50/50             | 12.0 (50) | 103                   | 50/50             |
| 54-7                                                      | 11.9 (50) | 50/50                     | 12.0 (50) | 101                   | 50/50             | 11.7 (50) | 98                    | 50/50             | 12.5 (49) | 105                   | 49/50             |
| 58-7                                                      | 11.9 (49) | 49/50                     | 12.1 (50) | 102                   | 50/50             | 11.9 (50) | 100                   | 50/50             | 12.4 (49) | 104                   | 49/50             |
| 62-7                                                      | 11.5 (49) | 49/50                     | 11.9 (50) | 103                   | 50/50             | 11.7 (49) | 102                   | 49/50             | 11.8 (49) | 103                   | 49/50             |
| 66-7                                                      | 11.6 (49) | 49/50                     | 12.1 (50) | 104                   | 50/50             | 11.5 (49) | 99                    | 49/50             | 12.0 (49) | 103                   | 49/50             |
| 70-7                                                      | 11.7 (49) | 49/50                     | 12.2 (48) | 104                   | 48/50             | 11.4 (48) | 97                    | 48/50             | 12.1 (48) | 103                   | 48/50             |
| 74-7                                                      | 12.0 (49) | 49/50                     | 12.3 (48) | 103                   | 48/50             | 12.0 (47) | 100                   | 47/50             | 12.2 (47) | 102                   | 47/50             |
| 78-7                                                      | 12.4 (48) | 48/50                     | 12.9 (48) | 104                   | 48/50             | 12.4 (47) | 100                   | 47/50             | 12.5 (47) | 101                   | 47/50             |
| 82-7                                                      | 12.0 (48) | 48/50                     | 12.4 (48) | 103                   | 48/50             | 12.2 (46) | 102                   | 46/50             | 12.4 (46) | 103                   | 46/50             |
| 86-7                                                      | 12.3 (47) | 47/50                     | 12.8 (47) | 104                   | 47/50             | 12.4 (46) | 101                   | 46/50             | 12.5 (45) | 102                   | 45/50             |
| 90-7                                                      | 12.2 (47) | 47/50                     | 12.8 (46) | 105                   | 46/50             | 12.2 (43) | 100                   | 43/50             | 12.1 (44) | 99                    | 44/50             |
| 94-7                                                      | 12.3 (47) | 47/50                     | 12.6 (46) | 102                   | 46/50             | 12.4 (41) | 101                   | 41/50             | 11.9 (43) | 97                    | 43/50             |
| 98-7                                                      | 12.8 (45) | 45/50                     | 13.1 (46) | 102                   | 46/50             | 12.9 (41) | 101                   | 41/50             | 12.9 (41) | 101                   | 41/50             |
| 102-7                                                     | 12.8 (44) | 44/50                     | 12.3 (44) | 96                    | 44/50             | 12.4 (41) | 97                    | 41/50             | 12.3 (35) | 96                    | 35/50             |
| 104-7                                                     | 12.2 (43) | 43/50                     | 12.3 (42) | 101                   | 42/50             | 11.8 (41) | 97                    | 41/50             | 12.5 (34) | 102                   | 34/50             |
| < >:No. of effective animals, ( ):No. of measured animals |           |                           |           |                       |                   |           |                       |                   |           |                       |                   |
| Av. FC.: g                                                |           |                           |           |                       |                   |           |                       |                   |           |                       |                   |

< >:No. of effective animals, ( ):No. of measured animals

Av. FC. : g

**TABLE E3**

**FOOD CONSUMPTION CHANGES : MALE**

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
UNIT : g  
REPORT TYPE : A1 104  
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
ALL ANIMALS

PAGE : 1

| Group | Name    | Administration |       |         |       |         |       |         |       |         |       | week-day(effective) |       |         |       |  |  |  |  |  |  |
|-------|---------|----------------|-------|---------|-------|---------|-------|---------|-------|---------|-------|---------------------|-------|---------|-------|--|--|--|--|--|--|
|       |         | 1-7 (7)        |       | 2-7 (7) |       | 3-7 (7) |       | 4-7 (7) |       | 5-7 (7) |       | 6-7 (7)             |       | 7-7 (7) |       |  |  |  |  |  |  |
|       | Control | 15.9±          | 1.1   | 17.9±   | 1.5   | 18.1±   | 1.4   | 18.4±   | 1.3   | 18.0±   | 1.3   | 17.7±               | 1.2   | 17.5±   | 1.2   |  |  |  |  |  |  |
|       | 0.1ppm  | 15.7±          | 1.2   | 17.4±   | 1.4   | 18.0±   | 1.5   | 17.9±   | 1.3   | 17.7±   | 1.2   | 17.2±               | 1.1   | 17.1±   | 1.3   |  |  |  |  |  |  |
|       | 0.5ppm  | 15.7±          | 1.1   | 17.7±   | 1.4   | 18.3±   | 1.5   | 18.5±   | 1.5   | 18.2±   | 1.4   | 18.0±               | 1.5   | 17.5±   | 1.3   |  |  |  |  |  |  |
|       | 2ppm    | 10.8±          | 0.8** | 13.9±   | 0.8** | 14.6±   | 1.1** | 15.2±   | 1.4** | 16.0±   | 0.9** | 15.6±               | 1.1** | 15.8±   | 1.0** |  |  |  |  |  |  |

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

Test of Dunnett

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrIjCrIj[F344/DuCrj]  
 UNIT : g  
 REPORT TYPE : A1 104  
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 2

| Group Name | Administration<br>8-7 (7) | week-day(effective)<br>9-7 (7) | 10-7 (7)    | 11-7 (7)    | 12-7 (7)    | 13-7 (7)    | 14-7 (7)    |
|------------|---------------------------|--------------------------------|-------------|-------------|-------------|-------------|-------------|
| Control    | 17.9± 1.1                 | 17.7± 1.2                      | 17.6± 1.1   | 16.9± 1.0   | 17.0± 1.0   | 16.7± 1.2   | 16.5± 1.1   |
| 0.1ppm     | 17.5± 1.3                 | 17.1± 1.2*                     | 17.0± 1.4*  | 16.6± 1.2   | 16.6± 1.2   | 16.5± 1.2   | 16.2± 1.0   |
| 0.5ppm     | 17.9± 1.3                 | 17.6± 1.3                      | 17.5± 1.2   | 17.0± 1.1   | 16.9± 1.1   | 16.5± 1.1   | 16.6± 0.9   |
| 2ppm       | 15.5± 0.8**               | 15.1± 1.0**                    | 15.1± 0.9** | 15.0± 1.0** | 14.7± 0.8** | 14.6± 0.9** | 14.6± 0.9** |

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

Test of Dunnett

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
UNIT : g  
REPORT TYPE : A1 104  
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
ALL ANIMALS

PAGE : 3

| Group Name | Administration |       | week-day(effective) |       |          |       |          |       |          |       |
|------------|----------------|-------|---------------------|-------|----------|-------|----------|-------|----------|-------|
|            | 18-7 (7)       |       | 22-7 (7)            |       | 26-7 (7) |       | 30-7 (7) |       | 34-7 (7) |       |
|            |                |       |                     |       |          |       |          |       |          |       |
| Control    | 16.1±          | 1.0   | 16.2±               | 0.9   | 16.5±    | 1.0   | 17.1±    | 1.0   | 16.9±    | 0.9   |
| 0.1ppm     | 15.7±          | 1.1   | 15.9±               | 1.0   | 16.7±    | 1.1   | 17.1±    | 1.0   | 16.8±    | 0.9   |
| 0.5ppm     | 16.2±          | 1.0   | 16.4±               | 0.9   | 16.9±    | 0.9   | 17.2±    | 0.8   | 17.2±    | 0.9   |
| 2ppm       | 14.6±          | 0.9** | 14.8±               | 1.0** | 15.7±    | 1.0** | 15.8±    | 0.9** | 15.3±    | 0.9** |

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

Test of Dunnett

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrIj[F344/DuCrj]  
 UNIT : g  
 REPORT TYPE : A1 104  
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 4

| Group Name | Administration |       | week-day(effective) |       |         |       |         |       |         |       |
|------------|----------------|-------|---------------------|-------|---------|-------|---------|-------|---------|-------|
|            | 46-7(7)        |       | 50-7(7)             |       | 54-7(7) |       | 58-7(7) |       | 62-7(7) |       |
|            |                |       |                     |       |         |       |         |       |         |       |
| Control    | 16.9±          | 1.0   | 17.5±               | 1.0   | 17.1±   | 1.0   | 17.3±   | 1.2   | 17.2±   | 1.1   |
| 0.1ppm     | 17.0±          | 0.9   | 17.2±               | 1.1   | 17.0±   | 1.2   | 17.1±   | 1.3   | 17.1±   | 1.0   |
| 0.5ppm     | 17.4±          | 1.0*  | 17.7±               | 1.0   | 17.3±   | 0.9   | 17.3±   | 1.4   | 17.3±   | 1.5   |
| 2ppm       | 16.3±          | 0.8** | 16.5±               | 0.9** | 16.3±   | 0.8** | 16.4±   | 0.9** | 16.1±   | 0.9** |

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

Test of Dunnett

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrI CrIj[F344/DuCrj]  
 UNIT : g  
 REPORT TYPE : A1 104  
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 5

| Group Name | Administration |       | week-day (effective) |       |          |       |          |       |          |      |          |       |          |       |
|------------|----------------|-------|----------------------|-------|----------|-------|----------|-------|----------|------|----------|-------|----------|-------|
|            | 74-7 (7)       |       | 78-7 (7)             |       | 82-7 (7) |       | 86-7 (7) |       | 90-7 (7) |      | 94-7 (7) |       | 98-7 (7) |       |
| Control    | 17.0±          | 1.2   | 17.0±                | 2.3   | 17.0±    | 1.2   | 17.1±    | 2.3   | 16.6±    | 1.1  | 16.9±    | 1.2   | 17.0±    | 2.1   |
| 0.1ppm     | 17.0±          | 1.0   | 17.1±                | 1.2   | 17.0±    | 1.1   | 17.0±    | 1.3   | 16.8±    | 1.4  | 16.6±    | 1.3   | 16.7±    | 2.1   |
| 0.5ppm     | 17.2±          | 0.9   | 17.5±                | 1.1   | 17.4±    | 1.1   | 17.1±    | 1.6   | 16.5±    | 2.2  | 16.7±    | 1.3   | 17.2±    | 1.9   |
| 2ppm       | 16.2±          | 0.9** | 16.3±                | 0.9** | 16.0±    | 0.9** | 16.3±    | 1.0** | 16.1±    | 1.8* | 16.3±    | 2.1** | 16.5±    | 3.0** |

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

Test of Dunnett

STUDY NO. : 0816

ANIMAL : RAT F344/DuCrIj[F344/DuCrj]

UNIT : g

REPORT TYPE : A1 104

SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)

ALL ANIMALS

PAGE : 6

| Group Name | Administration |      | week-day(effective) |       |
|------------|----------------|------|---------------------|-------|
|            | 102-7 (7)      |      | 104-7 (7)           |       |
| Control    | 16.2±          | 3.1  | 17.3±               | 1.6   |
| 0.1ppm     | 16.4±          | 2.0  | 16.2±               | 1.7** |
| 0.5ppm     | 16.6±          | 2.1  | 16.8±               | 1.3   |
| 2ppm       | 16.0±          | 1.4* | 15.8±               | 1.4** |

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

Test of Dunnett

(HAN260)

BAIS 5

**TABLE E4**

**FOOD CONSUMPTION CHANGES : FEMALE**

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrIj[F344/DuCrJ]  
 UNIT : g  
 REPORT TYPE : A1 104  
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 7

| Group Name | Administration |  | week-day(effective) |  | 3-7(7)      | 4-7(7)      | 5-7(7)      | 6-7(7)      | 7-7(7)     |
|------------|----------------|--|---------------------|--|-------------|-------------|-------------|-------------|------------|
|            | 1-7(7)         |  | 2-7(7)              |  |             |             |             |             |            |
| Control    | 12.5± 0.8      |  | 12.6± 0.9           |  | 12.2± 0.9   | 12.5± 1.0   | 11.9± 1.0   | 12.1± 1.2   | 11.3± 1.0  |
| 0.1ppm     | 12.0± 0.7**    |  | 12.0± 0.9**         |  | 12.0± 0.9   | 12.2± 1.0   | 12.0± 1.1   | 11.9± 0.9   | 11.3± 0.9  |
| 0.5ppm     | 12.1± 1.1**    |  | 12.3± 1.0           |  | 12.0± 1.1   | 12.2± 1.1   | 11.9± 1.1   | 11.7± 1.2   | 11.1± 1.3  |
| 2ppm       | 9.1± 0.5**     |  | 11.1± 0.9**         |  | 10.9± 0.8** | 11.1± 1.1** | 10.9± 0.8** | 10.6± 0.7** | 10.8± 0.9* |

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

Test of Dunnett

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 UNIT : g  
 REPORT TYPE : A1 104  
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 8

| Group Name | Administration |  | week-day(effective) |  | 10-7(7)    | 11-7(7)   | 12-7(7)     | 13-7(7)     | 14-7(7)     |
|------------|----------------|--|---------------------|--|------------|-----------|-------------|-------------|-------------|
|            | 8-7(7)         |  | 9-7(7)              |  |            |           |             |             |             |
| Control    | 11.3± 0.9      |  | 11.2± 0.9           |  | 11.2± 0.8  | 10.9± 0.7 | 11.4± 0.8   | 11.3± 0.8   | 11.4± 0.9   |
| 0.1ppm     | 11.4± 1.2      |  | 11.1± 0.9           |  | 11.2± 0.9  | 11.2± 0.9 | 11.5± 0.8   | 11.6± 1.1   | 11.2± 0.9   |
| 0.5ppm     | 11.0± 1.2*     |  | 10.9± 1.1           |  | 11.1± 0.9  | 10.9± 0.9 | 11.2± 0.8   | 11.0± 1.0** | 10.7± 1.1** |
| 2ppm       | 10.6± 0.8**    |  | 10.4± 0.8**         |  | 10.8± 0.7* | 10.6± 0.8 | 10.7± 0.7** | 10.7± 0.7** | 10.7± 0.8** |

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

Test of Dunnett

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrI CrIj [F344/DuCrJ]  
 UNIT : g  
 REPORT TYPE : A1 104  
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
 ALL ANIMALS

PAGE : 9

| Group Name | Administration<br>18-7 (7) | week-day (effective)<br>22-7 (7) | 26-7 (7)   | 30-7 (7)  | 34-7 (7)  | 38-7 (7)  | 42-7 (7)   |
|------------|----------------------------|----------------------------------|------------|-----------|-----------|-----------|------------|
| Control    | 10.8± 0.9                  | 10.7± 0.9                        | 11.0± 0.7  | 11.2± 0.9 | 11.2± 1.0 | 11.3± 0.9 | 11.2± 1.0  |
| 0.1ppm     | 11.5± 1.1**                | 10.9± 0.9                        | 11.5± 0.9* | 11.2± 0.8 | 11.6± 0.9 | 11.5± 0.8 | 11.8± 1.2* |
| 0.5ppm     | 10.8± 1.2                  | 10.4± 0.8                        | 11.2± 1.0  | 11.0± 1.0 | 11.2± 1.0 | 10.9± 0.7 | 11.1± 1.0  |
| 2ppm       | 10.4± 0.7                  | 10.4± 0.8                        | 11.2± 0.8  | 11.5± 1.2 | 11.4± 0.9 | 11.4± 0.8 | 11.7± 1.1* |

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

Test of Dunnett



STUDY NO. : 0816  
ANIMAL : RAT F344/DuCrI CrIj [F344/DuCrJ]  
UNIT : g  
REPORT TYPE : A1 104  
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
ALL ANIMALS

PAGE : 11

| Group Name | Administration |  | week-day(effective) |  |           |  |           |  |           |  |
|------------|----------------|--|---------------------|--|-----------|--|-----------|--|-----------|--|
|            | 74-7 (7)       |  | 78-7 (7)            |  | 82-7 (7)  |  | 86-7 (7)  |  | 90-7 (7)  |  |
| Control    | 12.0± 1.0      |  | 12.4± 0.8           |  | 12.0± 0.8 |  | 12.3± 1.0 |  | 12.2± 0.9 |  |
| 0.1ppm     | 12.3± 0.9      |  | 12.9± 1.0           |  | 12.4± 1.1 |  | 12.8± 1.0 |  | 12.8± 1.2 |  |
| 0.5ppm     | 12.0± 1.0      |  | 12.4± 1.2           |  | 12.2± 1.3 |  | 12.4± 1.1 |  | 12.2± 1.6 |  |
| 2ppm       | 12.2± 1.6      |  | 12.5± 1.4           |  | 12.4± 1.5 |  | 12.5± 1.1 |  | 12.1± 1.5 |  |

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

Test of Dunnett

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCrIj[F344/DuCrJ]  
UNIT : g  
REPORT TYPE : A1 104  
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)  
ALL ANIMALS

PAGE : 12

| Group Name | Administration |     | week-day(effective) |     |
|------------|----------------|-----|---------------------|-----|
|            | 102-7 (7)      |     | 104-7 (7)           |     |
| Control    | 12.8±          | 1.4 | 12.2±               | 1.6 |
| 0.1ppm     | 12.3±          | 1.8 | 12.3±               | 1.8 |
| 0.5ppm     | 12.4±          | 1.7 | 11.8±               | 1.6 |
| 2ppm       | 12.3±          | 1.8 | 12.5±               | 1.2 |

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

Test of Dunnett

TABLE F1

HEMATOLOGY : MALE

STUDY NO. : 0816

ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]

MEASURE. TIME : 1

SEX : MALE

REPORT TYPE : A1

HEMATOLOGY (SUMMARY)

ALL ANIMALS (105W)

PAGE : 1

| Group Name | NO. of<br>Animals | RED BLOOD CELL<br>10 <sup>6</sup> /μl |      | HEMOGLOBIN<br>g/dl |     | HEMATOCRIT<br>% |     | MCV<br>fl |       | MCH<br>pg |       | MCHC<br>g/dl |     | PLATELET<br>10 <sup>3</sup> /μl |     |
|------------|-------------------|---------------------------------------|------|--------------------|-----|-----------------|-----|-----------|-------|-----------|-------|--------------|-----|---------------------------------|-----|
| Control    | 41                | 7.73±                                 | 1.41 | 12.5±              | 2.5 | 38.2±           | 6.2 | 50.1±     | 6.5   | 16.3±     | 2.1   | 32.5±        | 1.9 | 936±                            | 336 |
| 0.1ppm     | 40                | 8.00±                                 | 1.32 | 12.8±              | 2.4 | 39.1±           | 6.1 | 49.0±     | 2.2   | 16.0±     | 1.2   | 32.6±        | 1.7 | 858±                            | 268 |
| 0.5ppm     | 37                | 7.49±                                 | 1.75 | 11.8±              | 2.9 | 36.4±           | 7.9 | 48.9±     | 3.2   | 15.7±     | 1.4   | 32.1±        | 1.9 | 926±                            | 309 |
| 2ppm       | 42                | 8.23±                                 | 1.42 | 12.6±              | 2.7 | 38.8±           | 6.8 | 47.3±     | 3.0** | 15.2±     | 1.6** | 32.2±        | 1.9 | 948±                            | 371 |

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

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 5

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCrI CrIj [F344/DuCrJ]  
MEASURE TIME : 1  
SEX : MALE

HEMATOLOGY (SUMMARY)  
ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 2

| Group Name | NO. of<br>Animals | RETICULOCYTE<br>% |     |
|------------|-------------------|-------------------|-----|
| Control    | 41                | 4.6±              | 2.7 |
| 0.1ppm     | 40                | 4.1±              | 3.0 |
| 0.5ppm     | 37                | 5.7±              | 4.4 |
| 2ppm       | 42                | 4.2±              | 3.1 |

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

Test of Dunnett

(HCL070)

BAIS 5

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
MEASURE. TIME : 1  
SEX : MALE

HEMATOLOGY (SUMMARY)  
ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 3

| Group Name | NO. of<br>Animals | WBC<br>10 <sup>3</sup> /μl |      | Differential |    | WBC (%) |    | MONO |   | EOSINO |   | BASO |   | OTHER |    |
|------------|-------------------|----------------------------|------|--------------|----|---------|----|------|---|--------|---|------|---|-------|----|
|            |                   |                            |      | NEUTRO       |    | LYMPHO  |    |      |   |        |   |      |   |       |    |
| Control    | 41                | 4.60±                      | 3.44 | 50±          | 8  | 42±     | 8  | 4±   | 1 | 1±     | 1 | 0±   | 0 | 2±    | 1  |
| 0.1ppm     | 40                | 4.62±                      | 4.32 | 53±          | 10 | 40±     | 10 | 4±   | 1 | 1±     | 1 | 0±   | 0 | 2±    | 1  |
| 0.5ppm     | 37                | 4.15±                      | 2.34 | 52±          | 12 | 41±     | 12 | 4±   | 1 | 1±     | 1 | 0±   | 0 | 2±    | 1  |
| 2ppm       | 42                | 5.09±                      | 7.17 | 53±          | 11 | 39±     | 10 | 4±   | 1 | 1±     | 1 | 0±   | 0 | 4±    | 14 |

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

\*\* :  $P \leq 0.01$

Test of Dunnett

TABLE F2

HEMATOLOGY : FEMALE

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCrI CrIj[F344/DuCrj]  
MEASURE. TIME : 1  
SEX : FEMALE

HEMATOLOGY (SUMMARY)  
ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 4

| Group Name | NO. of<br>Animals | RED BLOOD CELL<br>10 <sup>6</sup> /μl |      | HEMOGLOBIN<br>g/dl |     | HEMATOCRIT<br>% |     | MCV<br>fl |     | MCH<br>pg |     | MCHC<br>g/dl |     | PLATELET<br>10 <sup>9</sup> /μl |     |
|------------|-------------------|---------------------------------------|------|--------------------|-----|-----------------|-----|-----------|-----|-----------|-----|--------------|-----|---------------------------------|-----|
| Control    | 43                | 8.03±                                 | 0.81 | 14.3±              | 1.5 | 41.4±           | 3.8 | 51.7±     | 3.0 | 17.9±     | 1.1 | 34.6±        | 1.0 | 599±                            | 87  |
| 0.1ppm     | 42                | 7.87±                                 | 1.29 | 14.1±              | 2.1 | 40.8±           | 5.4 | 52.8±     | 6.2 | 18.0±     | 1.2 | 34.3±        | 1.6 | 568±                            | 108 |
| 0.5ppm     | 41                | 7.93±                                 | 1.00 | 14.3±              | 1.5 | 41.4±           | 4.1 | 52.6±     | 4.4 | 18.1±     | 1.1 | 34.5±        | 0.8 | 632±                            | 124 |
| 2ppm       | 34                | 7.98±                                 | 0.90 | 14.1±              | 1.9 | 41.2±           | 4.6 | 51.6±     | 1.4 | 17.6±     | 1.1 | 34.0±        | 1.7 | 629±                            | 84* |

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

Test of Dunnett

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCrIGrlJ[F344/DuCrj]  
MEASURE. TIME : 1  
SEX : FEMALE

HEMATOLOGY (SUMMARY)  
ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 5

| Group Name | NO. of<br>Animals | RETICULOCYTE<br>% |     |
|------------|-------------------|-------------------|-----|
| Control    | 43                | 2.5±              | 2.2 |
| 0.1ppm     | 42                | 3.4±              | 5.3 |
| 0.5ppm     | 41                | 2.6±              | 2.8 |
| 2ppm       | 34                | 2.8±              | 3.9 |

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

Test of Dunnett

(HCL070)

BAIS 5

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
MEASURE. TIME : 1  
SEX : FEMALE

HEMATOLOGY (SUMMARY)  
ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 6

| Group Name | NO. of<br>Animals | WBC   |                    | Differential |    | WBC (%) |    | MONO |   | EOSINO |   | BASO |   | OTHER |    |
|------------|-------------------|-------|--------------------|--------------|----|---------|----|------|---|--------|---|------|---|-------|----|
|            |                   | 1     | 0 <sup>3</sup> /μl | NEUTRO       |    | LYMPHO  |    |      |   |        |   |      |   |       |    |
| Control    | 43                | 2.77± | 3.30               | 43±          | 13 | 50±     | 14 | 4±   | 1 | 2±     | 1 | 0±   | 0 | 1±    | 1  |
| 0.1ppm     | 42                | 7.46± | 35.54              | 45±          | 11 | 47±     | 12 | 4±   | 1 | 2±     | 1 | 0±   | 0 | 3±    | 14 |
| 0.5ppm     | 41                | 2.55± | 1.72               | 46±          | 12 | 47±     | 12 | 4±   | 1 | 2±     | 1 | 0±   | 1 | 1±    | 1  |
| 2ppm       | 34                | 2.43± | 1.59               | 49±          | 12 | 45±     | 12 | 3±   | 1 | 2±     | 1 | 0±   | 0 | 1±    | 1  |

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

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 5

TABLE G1

BIOCHEMISTRY : MALE

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
MEASURE. TIME : 1  
SEX : MALE

BIOCHEMISTRY (SUMMARY)  
ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 1

| Group Name | NO. of<br>Animals | TOTAL PROTEIN<br>g/dl |     | ALBUMIN<br>g/dl |     | A/G RATIO |       | T-BILIRUBIN<br>mg/dl |      | GLUCOSE<br>mg/dl |    | T-CHOLESTEROL<br>mg/dl |      | TRIGLYCERIDE<br>mg/dl |      |
|------------|-------------------|-----------------------|-----|-----------------|-----|-----------|-------|----------------------|------|------------------|----|------------------------|------|-----------------------|------|
| Control    | 41                | 6.5±                  | 0.2 | 2.7±            | 0.2 | 0.7±      | 0.1   | 0.08±                | 0.09 | 155±             | 25 | 170±                   | 48   | 110±                  | 86   |
| 0.1ppm     | 40                | 6.5±                  | 0.3 | 2.7±            | 0.2 | 0.7±      | 0.1   | 0.06±                | 0.03 | 161±             | 23 | 150±                   | 40   | 82±                   | 53   |
| 0.5ppm     | 37                | 6.4±                  | 0.3 | 2.7±            | 0.2 | 0.8±      | 0.1   | 0.07±                | 0.03 | 162±             | 22 | 148±                   | 22   | 81±                   | 40   |
| 2ppm       | 42                | 6.4±                  | 0.4 | 2.8±            | 0.3 | 0.8±      | 0.1** | 0.07±                | 0.03 | 162±             | 21 | 125±                   | 45** | 47±                   | 21** |

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

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 5

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
MEASURE. TIME : 1  
SEX : MALE

BIOCHEMISTRY (SUMMARY)  
ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 2

| Group Name | NO. of<br>Animals | PHOSPHOLIPID<br>mg/dl |      | AST<br>U/L |      | ALT<br>U/L |     | LDH<br>U/L |     | ALP<br>U/L |       | G-GTP<br>U/L |     | CK<br>U/L |    |
|------------|-------------------|-----------------------|------|------------|------|------------|-----|------------|-----|------------|-------|--------------|-----|-----------|----|
| Control    | 41                | 253±                  | 62   | 92±        | 57   | 36±        | 11  | 196±       | 293 | 328±       | 76    | 6.4±         | 2.8 | 120±      | 47 |
| 0.1ppm     | 40                | 229±                  | 59   | 90±        | 47   | 35±        | 13  | 136±       | 57  | 357±       | 220   | 6.0±         | 2.4 | 108±      | 33 |
| 0.5ppm     | 37                | 229±                  | 33   | 96±        | 27   | 36±        | 7   | 153±       | 50  | 344±       | 77    | 6.3±         | 2.7 | 118±      | 40 |
| 2ppm       | 42                | 197±                  | 66** | 110±       | 42** | 44±        | 16* | 138±       | 59  | 386±       | 141** | 5.9±         | 2.7 | 110±      | 43 |

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

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 5

STUDY NO. : 0816

ANIMAL : RAT F344/DuCr1Cr1J[F344/DuCrJ]

MEASURE. TIME : 1

SEX : MALE

REPORT TYPE : A1

## BIOCHEMISTRY (SUMMARY)

ALL ANIMALS (105W)

PAGE : 3

| Group Name | NO. of<br>Animals | UREA NITROGEN<br>mg/dl |     | CREATININE<br>mg/dl |        | SODIUM<br>mEq/l |   | POTASSIUM<br>mEq/l |     | CHLORIDE<br>mEq/l |     | CALCIUM<br>mg/dl |       | INORGANIC PHOSPHORUS<br>mg/dl |     |
|------------|-------------------|------------------------|-----|---------------------|--------|-----------------|---|--------------------|-----|-------------------|-----|------------------|-------|-------------------------------|-----|
| Control    | 41                | 17.8±                  | 2.9 | 0.37±               | 0.06   | 144±            | 2 | 3.9±               | 0.3 | 106±              | 2   | 10.5±            | 0.3   | 4.0±                          | 0.6 |
| 0.1ppm     | 40                | 17.6±                  | 2.1 | 0.36±               | 0.05   | 144±            | 1 | 4.0±               | 0.3 | 107±              | 2   | 10.6±            | 1.3   | 3.8±                          | 0.6 |
| 0.5ppm     | 37                | 18.3±                  | 3.3 | 0.36±               | 0.06   | 144±            | 1 | 3.9±               | 0.3 | 107±              | 2   | 10.4±            | 0.3   | 4.0±                          | 0.7 |
| 2ppm       | 42                | 18.4±                  | 5.2 | 0.33±               | 0.04** | 144±            | 2 | 4.0±               | 0.3 | 107±              | 2** | 10.2±            | 0.4** | 4.1±                          | 0.5 |

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

Test of Dunnett

(HCL074)

BAIS 5

**TABLE G2**

**BIOCHEMISTRY : FEMALE**

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 MEASURE. TIME : 1  
 SEX : FEMALE

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 4

| Group Name | NO. of<br>Animals | TOTAL PROTEIN<br>g/dl |     | ALBUMIN<br>g/dl |     | A/G RATIO |     | T-BILIRUBIN<br>mg/dl |      | GLUCOSE<br>mg/dl |     | T-CHOLESTEROL<br>mg/dl |    | TRIGLYCERIDE<br>mg/dl |     |
|------------|-------------------|-----------------------|-----|-----------------|-----|-----------|-----|----------------------|------|------------------|-----|------------------------|----|-----------------------|-----|
| Control    | 43                | 6.7±                  | 0.4 | 3.5±            | 0.3 | 1.1±      | 0.1 | 0.11±                | 0.34 | 148±             | 14  | 127±                   | 24 | 60±                   | 35  |
| 0.1ppm     | 42                | 6.8±                  | 0.5 | 3.5±            | 0.4 | 1.1±      | 0.1 | 0.09±                | 0.15 | 140±             | 24  | 142±                   | 45 | 80±                   | 93  |
| 0.5ppm     | 41                | 6.8±                  | 0.6 | 3.4±            | 0.4 | 1.0±      | 0.2 | 0.06±                | 0.03 | 136±             | 29* | 135±                   | 35 | 70±                   | 59  |
| 2ppm       | 34                | 6.8±                  | 0.5 | 3.5±            | 0.3 | 1.1±      | 0.2 | 0.05±                | 0.02 | 148±             | 14  | 137±                   | 68 | 74±                   | 120 |

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

Test of Dunnett

(HCL074)

BAIS 5

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
MEASURE. TIME : 1  
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)  
ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 5

| Group Name | NO. of<br>Animals | PHOSPHOLIPID<br>mg/dl |     | AST<br>U/L |     | ALT<br>U/L |    | LDH<br>U/L |       | ALP<br>U/L |     | G-GTP<br>U/L |     | CK<br>U/L |     |
|------------|-------------------|-----------------------|-----|------------|-----|------------|----|------------|-------|------------|-----|--------------|-----|-----------|-----|
| Control    | 43                | 236±                  | 43  | 116±       | 73  | 50±        | 23 | 124±       | 54    | 233±       | 184 | 2.4±         | 1.1 | 90±       | 32  |
| 0.1ppm     | 42                | 265±                  | 78  | 190±       | 251 | 66±        | 41 | 323±       | 1055* | 218±       | 105 | 2.7±         | 1.5 | 117±      | 119 |
| 0.5ppm     | 41                | 251±                  | 60  | 146±       | 141 | 54±        | 29 | 154±       | 81    | 219±       | 101 | 2.4±         | 1.2 | 122±      | 136 |
| 2ppm       | 34                | 252±                  | 101 | 122±       | 57  | 50±        | 16 | 147±       | 58    | 214±       | 69  | 2.4±         | 1.0 | 98±       | 28  |

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

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 5

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1J[F344/DuCrj]  
 MEASURE. TIME : 1  
 SEX : FEMALE

BIOCHEMISTRY (SUMMARY)  
 ALL ANIMALS (105W)

REPORT TYPE : A1

PAGE : 6

| Group Name | NO. of<br>Animals | UREA NITROGEN<br>mg/dl |      | CREATININE<br>mg/dl |      | SODIUM<br>mEq/l |   | POTASSIUM<br>mEq/l |     | CHLORIDE<br>mEq/l |   | CALCIUM<br>mg/dl |     | INORGANIC PHOSPHORUS<br>mg/dl |     |
|------------|-------------------|------------------------|------|---------------------|------|-----------------|---|--------------------|-----|-------------------|---|------------------|-----|-------------------------------|-----|
| Control    | 43                | 16.2±                  | 2.1  | 0.29±               | 0.04 | 142±            | 1 | 3.7±               | 0.3 | 104±              | 2 | 10.4±            | 0.3 | 3.7±                          | 0.7 |
| 0.1ppm     | 42                | 18.3±                  | 7.2  | 0.29±               | 0.03 | 143±            | 2 | 3.7±               | 0.4 | 104±              | 2 | 10.6±            | 0.5 | 3.8±                          | 0.8 |
| 0.5ppm     | 41                | 18.9±                  | 8.5* | 0.31±               | 0.06 | 143±            | 2 | 3.7±               | 0.4 | 104±              | 2 | 10.6±            | 0.5 | 3.7±                          | 0.9 |
| 2ppm       | 34                | 17.5±                  | 3.0  | 0.30±               | 0.04 | 143±            | 1 | 3.6±               | 0.3 | 105±              | 2 | 10.4±            | 0.5 | 3.5±                          | 0.7 |

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

\*\* :  $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 5

## TABLE H1

### URINALYSIS : MALE

STUDY NO. : 0816

ANIMAL : RAT F344/DuCrIj[F344/DuCrj]

MEASURE TIME : 1

SEX : MALE

REPORT TYPE : A1

## URINALYSIS

PAGE : 1

| Group Name | NO. of<br>Animals | pH  |     |     |     |     |     |     | CHI | Protein |   |   |    |    |    | CHI | Glucose |   |   |    |    |    | CHI | Ketone body |   |   |    |    |    | CHI | Bilirubin |   |    |    | CHI |
|------------|-------------------|-----|-----|-----|-----|-----|-----|-----|-----|---------|---|---|----|----|----|-----|---------|---|---|----|----|----|-----|-------------|---|---|----|----|----|-----|-----------|---|----|----|-----|
|            |                   | 5.0 | 6.0 | 6.5 | 7.0 | 7.5 | 8.0 | 8.5 |     | -       | ± | + | 2+ | 3+ | 4+ |     | -       | ± | + | 2+ | 3+ | 4+ |     | -           | ± | + | 2+ | 3+ | 4+ |     | -         | + | 2+ | 3+ |     |
| Control    | 42                | 0   | 0   | 7   | 9   | 14  | 9   | 3   |     | 0       | 0 | 2 | 19 | 18 | 3  |     | 42      | 0 | 0 | 0  | 0  | 0  |     | 38          | 3 | 1 | 0  | 0  | 0  |     | 41        | 0 | 0  | 1  |     |
| 0.1ppm     | 40                | 0   | 0   | 5   | 5   | 12  | 15  | 3   |     | 0       | 0 | 2 | 16 | 22 | 0  |     | 40      | 0 | 0 | 0  | 0  | 0  |     | 36          | 4 | 0 | 0  | 0  | 0  |     | 40        | 0 | 0  | 0  |     |
| 0.5ppm     | 38                | 0   | 1   | 1   | 8   | 12  | 7   | 9   |     | 0       | 0 | 3 | 12 | 23 | 0  |     | 38      | 0 | 0 | 0  | 0  | 0  |     | 33          | 4 | 1 | 0  | 0  | 0  |     | 38        | 0 | 0  | 0  |     |
| 2ppm       | 42                | 0   | 0   | 2   | 6   | 10  | 14  | 10  |     | 0       | 3 | 9 | 14 | 16 | 0  | *   | 42      | 0 | 0 | 0  | 0  | 0  |     | 41          | 1 | 0 | 0  | 0  | 0  |     | 42        | 0 | 0  | 0  |     |

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

Test of CHI SQUARE

(HCL101)

BAIS5

STUDY NO. : 0816

URINALYSIS

ANIMAL : RAT F344/DuCrIj[F344/DuCrj]

MEASURE. TIME : 1

SEX : MALE

REPORT TYPE : A1

PAGE : 2

| Group Name | NO. of<br>Animals | Occult blood |   |   |    |    | CHI | Urobilinogen |   |    |    |    | CHI |
|------------|-------------------|--------------|---|---|----|----|-----|--------------|---|----|----|----|-----|
|            |                   | -            | ± | + | 2+ | 3+ |     | ±            | + | 2+ | 3+ | 4+ |     |
| Control    | 42                | 37           | 1 | 3 | 0  | 1  |     | 42           | 0 | 0  | 0  | 0  |     |
| 0.1ppm     | 40                | 38           | 0 | 1 | 1  | 0  |     | 40           | 0 | 0  | 0  | 0  |     |
| 0.5ppm     | 38                | 34           | 1 | 0 | 0  | 3  |     | 38           | 0 | 0  | 0  | 0  |     |
| 2ppm       | 42                | 34           | 3 | 1 | 2  | 2  |     | 42           | 0 | 0  | 0  | 0  |     |

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

Test of CHI SQUARE

(HCL101)

BAIS5

## TABLE H2

### URINALYSIS : FEMALE

STUDY NO. : 0816

ANIMAL : RAT F344/DuCrIj[F344/DuCrj]

MEASURE. TIME : 1

SEX : FEMALE

REPORT TYPE : A1

## URINALYSIS

PAGE : 3

| Group Name | NO. of<br>Animals | pH  |     |     |     |     |     |     | CHI | Protein |   |    |    |    |    | CHI | Glucose |   |   |    |    |    | CHI | Ketone body |    |   |    |    |    | CHI | Bilirubin |   |    |    | CHI |
|------------|-------------------|-----|-----|-----|-----|-----|-----|-----|-----|---------|---|----|----|----|----|-----|---------|---|---|----|----|----|-----|-------------|----|---|----|----|----|-----|-----------|---|----|----|-----|
|            |                   | 5.0 | 6.0 | 6.5 | 7.0 | 7.5 | 8.0 | 8.5 |     | -       | ± | +  | 2+ | 3+ | 4+ |     | -       | ± | + | 2+ | 3+ | 4+ |     | -           | ±  | + | 2+ | 3+ | 4+ |     | -         | + | 2+ | 3+ |     |
| Control    | 44                | 0   | 1   | 4   | 3   | 5   | 12  | 19  |     | 4       | 8 | 11 | 16 | 5  | 0  |     | 44      | 0 | 0 | 0  | 0  | 0  |     | 27          | 17 | 0 | 0  | 0  | 0  |     | 44        | 0 | 0  | 0  |     |
| 0.1ppm     | 43                | 0   | 0   | 1   | 5   | 2   | 11  | 24  |     | 1       | 3 | 11 | 11 | 16 | 1  | *   | 43      | 0 | 0 | 0  | 0  | 0  |     | 23          | 18 | 1 | 1  | 0  | 0  |     | 42        | 0 | 1  | 0  |     |
| 0.5ppm     | 41                | 0   | 0   | 1   | 4   | 1   | 16  | 19  |     | 2       | 5 | 8  | 11 | 14 | 1  |     | 41      | 0 | 0 | 0  | 0  | 0  |     | 19          | 20 | 2 | 0  | 0  | 0  |     | 41        | 0 | 0  | 0  |     |
| 2ppm       | 34                | 0   | 0   | 0   | 2   | 7   | 10  | 15  |     | 6       | 4 | 9  | 8  | 6  | 1  |     | 34      | 0 | 0 | 0  | 0  | 0  |     | 24          | 9  | 1 | 0  | 0  | 0  |     | 34        | 0 | 0  | 0  |     |

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

Test of CHI SQUARE

(HCL101)

BAIS5

STUDY NO. : 0816

URINALYSIS

ANIMAL : RAT F344/DuCrIj[F344/DuCrj]

MEASURE TIME : 1

SEX : FEMALE

REPORT TYPE : A1

PAGE : 4

| Group Name | NO. of<br>Animals | Occult blood |   |   |    |    | CHI | Urobilinogen |   |    |    |    | CHI |
|------------|-------------------|--------------|---|---|----|----|-----|--------------|---|----|----|----|-----|
|            |                   | -            | ± | + | 2+ | 3+ |     | ±            | + | 2+ | 3+ | 4+ |     |
| Control    | 44                | 42           | 0 | 1 | 0  | 1  |     | 44           | 0 | 0  | 0  | 0  |     |
| 0.1ppm     | 43                | 43           | 0 | 0 | 0  | 0  |     | 43           | 0 | 0  | 0  | 0  |     |
| 0.5ppm     | 41                | 38           | 1 | 0 | 1  | 1  |     | 41           | 0 | 0  | 0  | 0  |     |
| 2ppm       | 34                | 33           | 0 | 1 | 0  | 0  |     | 34           | 0 | 0  | 0  | 0  |     |

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

Test of CHI SQUARE

(HCL101)

BAIS5

TABLE I 1

GROSS FINDINGS : MALE

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCrI CrIj [F344/DuCrj]  
REPORT TYPE : A1  
SEX : MALE

GROSS FINDINGS (SUMMARY)  
ALL ANIMALS (0-105W)

PAGE : 1

| Organ       | Findings            | Group Name<br>NO. of Animals | Control |       | 0.1ppm |       | 0.5ppm |       | 2ppm |      |
|-------------|---------------------|------------------------------|---------|-------|--------|-------|--------|-------|------|------|
|             |                     |                              | 50      | (%)   | 50     | (%)   | 50     | (%)   | 50   | (%)  |
| skin/app    | nodule              |                              | 3       | ( 6)  | 3      | ( 6)  | 2      | ( 4)  | 1    | ( 2) |
|             | erosion             |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1    | ( 2) |
|             | thick               |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1    | ( 2) |
|             | crust               |                              | 2       | ( 4)  | 0      | ( 0)  | 1      | ( 2)  | 0    | ( 0) |
| subcutis    | jaundice            |                              | 0       | ( 0)  | 1      | ( 2)  | 1      | ( 2)  | 0    | ( 0) |
|             | mass                |                              | 13      | ( 26) | 2      | ( 4)  | 7      | ( 14) | 3    | ( 6) |
| nasal cavit | white zone          |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1    | ( 2) |
| lung        | red                 |                              | 1       | ( 2)  | 0      | ( 0)  | 3      | ( 6)  | 0    | ( 0) |
|             | white zone          |                              | 2       | ( 4)  | 5      | ( 10) | 3      | ( 6)  | 3    | ( 6) |
|             | red zone            |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 1    | ( 2) |
|             | black zone          |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1    | ( 2) |
|             | edema               |                              | 1       | ( 2)  | 0      | ( 0)  | 1      | ( 2)  | 1    | ( 2) |
|             | nodule              |                              | 2       | ( 4)  | 1      | ( 2)  | 2      | ( 4)  | 3    | ( 6) |
|             | voluminous          |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 1    | ( 2) |
| lymph node  | enlarged            |                              | 3       | ( 6)  | 0      | ( 0)  | 4      | ( 8)  | 1    | ( 2) |
| thymus      | enlarged            |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0    | ( 0) |
| spleen      | enlarged            |                              | 5       | ( 10) | 5      | ( 10) | 11     | ( 22) | 2    | ( 4) |
|             | white zone          |                              | 2       | ( 4)  | 1      | ( 2)  | 0      | ( 0)  | 0    | ( 0) |
|             | deformed            |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 0    | ( 0) |
| heart       | white zone          |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0    | ( 0) |
| stomach     | forestomach:ulcer   |                              | 1       | ( 2)  | 0      | ( 0)  | 2      | ( 4)  | 0    | ( 0) |
|             | forestomach:erosion |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1    | ( 2) |

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCrI CrIj [F344/DuCrj]  
REPORT TYPE : A1  
SEX : MALE

GROSS FINDINGS (SUMMARY)  
ALL ANIMALS (0-105W)

PAGE : 2

| Organ       | Findings                     | Group Name<br>NO. of Animals | Control |       | 0.1ppm |       | 0.5ppm |       | 2ppm |       |
|-------------|------------------------------|------------------------------|---------|-------|--------|-------|--------|-------|------|-------|
|             |                              |                              | 50      | (%)   | 50     | (%)   | 50     | (%)   | 50   | (%)   |
| stomach     | glandular stomach:ulcer      |                              | 1       | ( 2)  | 1      | ( 2)  | 0      | ( 0)  | 0    | ( 0)  |
|             | glandular stomach:erosion    |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0    | ( 0)  |
|             | glandular stomach:nodule     |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0    | ( 0)  |
|             | glandular stomach:black zone |                              | 1       | ( 2)  | 0      | ( 0)  | 1      | ( 2)  | 1    | ( 2)  |
|             | glandular stomach:thick      |                              | 3       | ( 6)  | 2      | ( 4)  | 5      | ( 10) | 7    | ( 14) |
|             | glandular stomach:white zone |                              | 2       | ( 4)  | 0      | ( 0)  | 1      | ( 2)  | 2    | ( 4)  |
| duodenum    | nodule                       |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0    | ( 0)  |
| small intes | nodule                       |                              | 0       | ( 0)  | 1      | ( 2)  | 1      | ( 2)  | 3    | ( 6)  |
|             | dilated                      |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0    | ( 0)  |
|             | fluid:brown                  |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0    | ( 0)  |
| liver       | enlarged                     |                              | 2       | ( 4)  | 2      | ( 4)  | 5      | ( 10) | 2    | ( 4)  |
|             | white zone                   |                              | 2       | ( 4)  | 2      | ( 4)  | 1      | ( 2)  | 1    | ( 2)  |
|             | red zone                     |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0    | ( 0)  |
|             | nodule                       |                              | 0       | ( 0)  | 2      | ( 4)  | 2      | ( 4)  | 1    | ( 2)  |
|             | rough                        |                              | 1       | ( 2)  | 1      | ( 2)  | 1      | ( 2)  | 0    | ( 0)  |
|             | herniation                   |                              | 5       | ( 10) | 5      | ( 10) | 5      | ( 10) | 8    | ( 16) |
| pancreas    | nodule                       |                              | 0       | ( 0)  | 2      | ( 4)  | 2      | ( 4)  | 2    | ( 4)  |
| kidney      | white zone                   |                              | 0       | ( 0)  | 1      | ( 2)  | 1      | ( 2)  | 0    | ( 0)  |
|             | nodule                       |                              | 0       | ( 0)  | 0      | ( 0)  | 3      | ( 6)  | 0    | ( 0)  |
|             | granular                     |                              | 5       | ( 10) | 3      | ( 6)  | 4      | ( 8)  | 0    | ( 0)  |
|             | hydronephrosis               |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 0    | ( 0)  |
| ureter      | dilated                      |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1    | ( 2)  |

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCrIj[F344/DuCrj]  
REPORT TYPE : A1  
SEX : MALE

GROSS FINDINGS (SUMMARY)  
ALL ANIMALS (0-105W)

PAGE : 3

| Organ       | Findings               | Group Name<br>NO. of Animals | Control  | 0.1ppm   | 0.5ppm   | 2ppm     |
|-------------|------------------------|------------------------------|----------|----------|----------|----------|
|             |                        |                              | 50 (%)   | 50 (%)   | 50 (%)   | 50 (%)   |
| urin bladd  | urine:marked retention |                              | 1 ( 2)   | 1 ( 2)   | 1 ( 2)   | 2 ( 4)   |
| pituitary   | enlarged               |                              | 7 ( 14)  | 5 ( 10)  | 5 ( 10)  | 2 ( 4)   |
|             | red zone               |                              | 3 ( 6)   | 4 ( 8)   | 1 ( 2)   | 1 ( 2)   |
|             | nodule                 |                              | 2 ( 4)   | 0 ( 0)   | 0 ( 0)   | 0 ( 0)   |
| thyroid     | enlarged               |                              | 2 ( 4)   | 0 ( 0)   | 1 ( 2)   | 1 ( 2)   |
|             | red zone               |                              | 0 ( 0)   | 1 ( 2)   | 0 ( 0)   | 0 ( 0)   |
|             | black zone             |                              | 0 ( 0)   | 0 ( 0)   | 0 ( 0)   | 1 ( 2)   |
|             | nodule                 |                              | 5 ( 10)  | 1 ( 2)   | 3 ( 6)   | 2 ( 4)   |
| adrenal     | enlarged               |                              | 2 ( 4)   | 2 ( 4)   | 4 ( 8)   | 1 ( 2)   |
|             | black zone             |                              | 0 ( 0)   | 1 ( 2)   | 0 ( 0)   | 0 ( 0)   |
|             | nodule                 |                              | 0 ( 0)   | 0 ( 0)   | 0 ( 0)   | 1 ( 2)   |
| testis      | nodule                 |                              | 38 ( 76) | 42 ( 84) | 40 ( 80) | 44 ( 88) |
| epididymis  | nodule                 |                              | 0 ( 0)   | 0 ( 0)   | 0 ( 0)   | 1 ( 2)   |
| brain       | red zone               |                              | 0 ( 0)   | 0 ( 0)   | 2 ( 4)   | 0 ( 0)   |
| spinal cord | red zone               |                              | 0 ( 0)   | 0 ( 0)   | 1 ( 2)   | 0 ( 0)   |
| periph nerv | nodule                 |                              | 0 ( 0)   | 0 ( 0)   | 1 ( 2)   | 0 ( 0)   |
| eye         | white                  |                              | 2 ( 4)   | 4 ( 8)   | 5 ( 10)  | 3 ( 6)   |
|             | red                    |                              | 0 ( 0)   | 0 ( 0)   | 0 ( 0)   | 1 ( 2)   |
| Harder gl   | white zone             |                              | 0 ( 0)   | 0 ( 0)   | 1 ( 2)   | 0 ( 0)   |
| Zymbal gl   | nodule                 |                              | 0 ( 0)   | 3 ( 6)   | 2 ( 4)   | 1 ( 2)   |
| muscle      | nodule                 |                              | 0 ( 0)   | 1 ( 2)   | 0 ( 0)   | 0 ( 0)   |
| articulus   | swollen                |                              | 0 ( 0)   | 0 ( 0)   | 0 ( 0)   | 1 ( 2)   |

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrIj[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

GROSS FINDINGS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 4

| Organ       | Findings        | Group Name<br>NO. of Animals | Control |      | 0.1ppm |      | 0.5ppm |      | 2ppm |      |
|-------------|-----------------|------------------------------|---------|------|--------|------|--------|------|------|------|
|             |                 |                              | 50      | (%)  | 50     | (%)  | 50     | (%)  | 50   | (%)  |
| pleura      | nodule          |                              | 0       | ( 0) | 1      | ( 2) | 0      | ( 0) | 0    | ( 0) |
|             | adhesion        |                              | 0       | ( 0) | 0      | ( 0) | 0      | ( 0) | 1    | ( 2) |
|             | thick           |                              | 1       | ( 2) | 1      | ( 2) | 0      | ( 0) | 1    | ( 2) |
| mediastinum | mass            |                              | 1       | ( 2) | 0      | ( 0) | 1      | ( 2) | 0    | ( 0) |
| peritoneum  | nodule          |                              | 2       | ( 4) | 0      | ( 0) | 2      | ( 4) | 3    | ( 6) |
|             | adhesion        |                              | 0       | ( 0) | 0      | ( 0) | 0      | ( 0) | 1    | ( 2) |
|             | thick           |                              | 1       | ( 2) | 0      | ( 0) | 0      | ( 0) | 0    | ( 0) |
| retroperit  | mass            |                              | 0       | ( 0) | 0      | ( 0) | 0      | ( 0) | 1    | ( 2) |
| abdominal c | hemorrhage      |                              | 0       | ( 0) | 0      | ( 0) | 1      | ( 2) | 0    | ( 0) |
|             | ascites         |                              | 1       | ( 2) | 0      | ( 0) | 2      | ( 4) | 3    | ( 6) |
| thoracic ca | hemorrhage      |                              | 0       | ( 0) | 1      | ( 2) | 0      | ( 0) | 0    | ( 0) |
|             | pleural fluid   |                              | 2       | ( 4) | 2      | ( 4) | 3      | ( 6) | 1    | ( 2) |
| other       | tail:nodule     |                              | 0       | ( 0) | 0      | ( 0) | 1      | ( 2) | 0    | ( 0) |
|             | ear:nodule      |                              | 0       | ( 0) | 1      | ( 2) | 0      | ( 0) | 1    | ( 2) |
|             | hindlimb:nodule |                              | 0       | ( 0) | 1      | ( 2) | 0      | ( 0) | 0    | ( 0) |
|             | nose:nodule     |                              | 0       | ( 0) | 1      | ( 2) | 0      | ( 0) | 0    | ( 0) |
| whole body  | anemic          |                              | 0       | ( 0) | 2      | ( 4) | 2      | ( 4) | 2    | ( 4) |

TABLE I 2

GROSS FINDINGS : FEMALE

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

GROSS FINDINGS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 5

| Organ       | Findings                     | Group Name<br>NO. of Animals | Control |       | 0.1ppm |       | 0.5ppm |       | 2ppm |       |
|-------------|------------------------------|------------------------------|---------|-------|--------|-------|--------|-------|------|-------|
|             |                              |                              | 50      | (%)   | 50     | (%)   | 50     | (%)   | 50   | (%)   |
| skin/app    | nodule                       |                              | 2       | ( 4)  | 1      | ( 2)  | 0      | ( 0)  | 0    | ( 0)  |
|             | crust                        |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0    | ( 0)  |
| subcutis    | jaundice                     |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 1    | ( 2)  |
|             | mass                         |                              | 5       | ( 10) | 11     | ( 22) | 8      | ( 16) | 7    | ( 14) |
| lung        | red                          |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1    | ( 2)  |
|             | white zone                   |                              | 1       | ( 2)  | 0      | ( 0)  | 6      | ( 12) | 5    | ( 10) |
|             | red zone                     |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 2    | ( 4)  |
|             | nodule                       |                              | 1       | ( 2)  | 1      | ( 2)  | 1      | ( 2)  | 1    | ( 2)  |
|             | voluminous                   |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 0    | ( 0)  |
| lymph node  | enlarged                     |                              | 0       | ( 0)  | 3      | ( 6)  | 1      | ( 2)  | 2    | ( 4)  |
| spleen      | enlarged                     |                              | 3       | ( 6)  | 7      | ( 14) | 4      | ( 8)  | 5    | ( 10) |
| heart       | hypertrophy                  |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0    | ( 0)  |
| oral cavity | food                         |                              | 1       | ( 2)  | 1      | ( 2)  | 0      | ( 0)  | 0    | ( 0)  |
| tongue      | nodule                       |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 1    | ( 2)  |
| salivary gl | nodule                       |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1    | ( 2)  |
| stomach     | forestomach:ulcer            |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1    | ( 2)  |
|             | glandular stomach:ulcer      |                              | 0       | ( 0)  | 1      | ( 2)  | 1      | ( 2)  | 1    | ( 2)  |
|             | glandular stomach:nodule     |                              | 0       | ( 0)  | 0      | ( 0)  | 2      | ( 4)  | 0    | ( 0)  |
|             | glandular stomach:black zone |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 0    | ( 0)  |
|             | glandular stomach:red zone   |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0    | ( 0)  |
|             | glandular stomach:thick      |                              | 5       | ( 10) | 6      | ( 12) | 4      | ( 8)  | 2    | ( 4)  |
|             | glandular stomach:white zone |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1    | ( 2)  |

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : FEMALE

GROSS FINDINGS (SUMMARY)  
ALL ANIMALS (0-105W)

PAGE : 6

| Organ      | Findings               | Group Name<br>NO. of Animals | Control |       | 0.1ppm |       | 0.5ppm |       | 2ppm |       |
|------------|------------------------|------------------------------|---------|-------|--------|-------|--------|-------|------|-------|
|            |                        |                              | 50      | (%)   | 50     | (%)   | 50     | (%)   | 50   | (%)   |
| liver      | enlarged               |                              | 0       | ( 0)  | 2      | ( 4)  | 1      | ( 2)  | 0    | ( 0)  |
|            | white zone             |                              | 0       | ( 0)  | 1      | ( 2)  | 3      | ( 6)  | 2    | ( 4)  |
|            | red zone               |                              | 1       | ( 2)  | 1      | ( 2)  | 0      | ( 0)  | 2    | ( 4)  |
|            | nodule                 |                              | 1       | ( 2)  | 1      | ( 2)  | 2      | ( 4)  | 0    | ( 0)  |
|            | rough                  |                              | 1       | ( 2)  | 3      | ( 6)  | 2      | ( 4)  | 1    | ( 2)  |
|            | herniation             |                              | 9       | ( 18) | 10     | ( 20) | 9      | ( 18) | 9    | ( 18) |
| pancreas   | nodule                 |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0    | ( 0)  |
| kidney     | enlarged               |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 0    | ( 0)  |
|            | cyst                   |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1    | ( 2)  |
|            | granular               |                              | 0       | ( 0)  | 1      | ( 2)  | 1      | ( 2)  | 2    | ( 4)  |
| urin bladd | red zone               |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0    | ( 0)  |
|            | thick                  |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2)  | 0    | ( 0)  |
|            | urine:marked retention |                              | 0       | ( 0)  | 1      | ( 2)  | 0      | ( 0)  | 0    | ( 0)  |
| pituitary  | enlarged               |                              | 9       | ( 18) | 13     | ( 26) | 12     | ( 24) | 14   | ( 28) |
|            | white zone             |                              | 0       | ( 0)  | 1      | ( 2)  | 1      | ( 2)  | 0    | ( 0)  |
|            | red zone               |                              | 9       | ( 18) | 7      | ( 14) | 9      | ( 18) | 3    | ( 6)  |
|            | hemorrhage             |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0)  | 1    | ( 2)  |
|            | nodule                 |                              | 1       | ( 2)  | 0      | ( 0)  | 1      | ( 2)  | 1    | ( 2)  |
| thyroid    | enlarged               |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 1    | ( 2)  |
|            | red zone               |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0)  | 0    | ( 0)  |
|            | nodule                 |                              | 3       | ( 6)  | 1      | ( 2)  | 6      | ( 12) | 2    | ( 4)  |
| adrenal    | enlarged               |                              | 1       | ( 2)  | 0      | ( 0)  | 2      | ( 4)  | 2    | ( 4)  |

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCr1J[F344/DuCrJ]  
 REPORT TYPE : A1  
 SEX : FEMALE

GROSS FINDINGS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 7

| Organ       | Findings      | Group Name<br>NO. of Animals | Control |       | 0.1ppm |       | 0.5ppm |      | 2ppm |      |
|-------------|---------------|------------------------------|---------|-------|--------|-------|--------|------|------|------|
|             |               |                              | 50      | (%)   | 50     | (%)   | 50     | (%)  | 50   | (%)  |
| adrenal     | nodule        |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0) | 0    | ( 0) |
| ovary       | enlarged      |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0) | 1    | ( 2) |
|             | nodule        |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0) | 0    | ( 0) |
|             | cyst          |                              | 2       | ( 4)  | 2      | ( 4)  | 0      | ( 0) | 0    | ( 0) |
| uterus      | white zone    |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2) | 0    | ( 0) |
|             | black zone    |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0) | 1    | ( 2) |
|             | nodule        |                              | 8       | ( 16) | 2      | ( 4)  | 4      | ( 8) | 3    | ( 6) |
|             | cyst          |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2) | 1    | ( 2) |
|             | dilated lumen |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2) | 0    | ( 0) |
| vagina      | nodule        |                              | 0       | ( 0)  | 2      | ( 4)  | 0      | ( 0) | 0    | ( 0) |
| brain       | white zone    |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0) | 1    | ( 2) |
|             | red zone      |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0) | 3    | ( 6) |
|             | black zone    |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0) | 1    | ( 2) |
| spinal cord | red zone      |                              | 1       | ( 2)  | 0      | ( 0)  | 1      | ( 2) | 0    | ( 0) |
| periph nerv | thick         |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0) | 1    | ( 2) |
| eye         | turbid        |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0) | 0    | ( 0) |
|             | white         |                              | 5       | ( 10) | 7      | ( 14) | 2      | ( 4) | 1    | ( 2) |
|             | nodule        |                              | 0       | ( 0)  | 0      | ( 0)  | 0      | ( 0) | 1    | ( 2) |
| Zymbal gl   | nodule        |                              | 0       | ( 0)  | 0      | ( 0)  | 1      | ( 2) | 0    | ( 0) |
| peritoneum  | nodule        |                              | 1       | ( 2)  | 0      | ( 0)  | 2      | ( 4) | 0    | ( 0) |
|             | thick         |                              | 1       | ( 2)  | 0      | ( 0)  | 0      | ( 0) | 1    | ( 2) |
| abdominal c | hemorrhage    |                              | 1       | ( 2)  | 0      | ( 0)  | 1      | ( 2) | 0    | ( 0) |

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1J[F344/DuCrJ]  
REPORT TYPE : A1  
SEX : FEMALE

GROSS FINDINGS (SUMMARY)  
ALL ANIMALS (0-105W)

PAGE : 8

| Organ       | Findings      | Group Name<br>NO. of Animals | Control |      | 0.1ppm |      | 0.5ppm |      | 2ppm |      |
|-------------|---------------|------------------------------|---------|------|--------|------|--------|------|------|------|
|             |               |                              | 50      | (%)  | 50     | (%)  | 50     | (%)  | 50   | (%)  |
| abdominal c | ascites       |                              | 0       | ( 0) | 1      | ( 2) | 1      | ( 2) | 0    | ( 0) |
| thoracic ca | pleural fluid |                              | 0       | ( 0) | 0      | ( 0) | 3      | ( 6) | 1    | ( 2) |
| other       | lip:nodule    |                              | 0       | ( 0) | 1      | ( 2) | 0      | ( 0) | 0    | ( 0) |
|             | nose:elevated |                              | 0       | ( 0) | 0      | ( 0) | 0      | ( 0) | 1    | ( 2) |
| whole body  | anemic        |                              | 1       | ( 2) | 1      | ( 2) | 0      | ( 0) | 2    | ( 4) |

(HPT080)

BAIS 5

TABLE J1

ORGAN WEIGHT, ABSOLUTE : MALE

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrJ]  
REPORT TYPE : A1  
SEX : MALE  
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)  
SURVIVAL ANIMALS (105W)

PAGE : 1

| Group Name | NO. of<br>Animals | Body Weight | ADRENALS      | TESTES       | HEART        | LUNGS        | KIDNEYS        |
|------------|-------------------|-------------|---------------|--------------|--------------|--------------|----------------|
| Control    | 41                | 394± 36     | 0.075± 0.014  | 3.507± 1.559 | 1.237± 0.102 | 1.401± 0.254 | 2.793± 0.196   |
| 0.1ppm     | 40                | 376± 31     | 0.091± 0.090  | 3.641± 1.112 | 1.202± 0.085 | 1.323± 0.085 | 2.683± 0.190*  |
| 0.5ppm     | 37                | 389± 34     | 0.332± 1.434  | 4.221± 1.354 | 1.259± 0.168 | 1.393± 0.140 | 2.692± 0.169*  |
| 2ppm       | 42                | 346± 23**   | 0.073± 0.037* | 3.729± 1.369 | 1.200± 0.091 | 1.334± 0.151 | 2.491± 0.178** |

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

Test of Dunnett

(HCL040)

BAIS5

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrJ]  
REPORT TYPE : A1  
SEX : MALE  
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)  
SURVIVAL ANIMALS (105W)

PAGE : 2

| Group Name | NO. of<br>Animals | SPLEEN |         | LIVER   |         | BRAIN  |       |
|------------|-------------------|--------|---------|---------|---------|--------|-------|
| Control    | 41                | 1.129± | 0.810   | 11.082± | 1.447   | 2.079± | 0.048 |
| 0.1ppm     | 40                | 0.999± | 0.363   | 10.418± | 1.230   | 2.077± | 0.044 |
| 0.5ppm     | 37                | 1.091± | 0.661   | 10.746± | 1.169   | 2.074± | 0.046 |
| 2ppm       | 42                | 0.776± | 0.164** | 9.114±  | 0.889** | 2.055± | 0.052 |

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

Test of Dunnett

**TABLE J2**

**ORGAN WEIGHT, ABSOLUTE : FEMALE**

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : FEMALE  
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)  
SURVIVAL ANIMALS (105W)

PAGE : 3

| Group Name | NO. of<br>Animals | Body Weight |      | ADRENALS |       | OVARIES |       | HEART  |       | LUNGS  |       | KIDNEYS |       |
|------------|-------------------|-------------|------|----------|-------|---------|-------|--------|-------|--------|-------|---------|-------|
| Control    | 43                | 255±        | 20   | 0.075±   | 0.022 | 0.201±  | 0.385 | 0.851± | 0.053 | 0.926± | 0.099 | 1.758±  | 0.143 |
| 0.1ppm     | 42                | 258±        | 29   | 0.070±   | 0.010 | 0.193±  | 0.460 | 0.868± | 0.071 | 0.964± | 0.209 | 1.755±  | 0.131 |
| 0.5ppm     | 41                | 249±        | 36   | 0.077±   | 0.058 | 0.114±  | 0.022 | 0.836± | 0.074 | 0.931± | 0.173 | 1.782±  | 0.363 |
| 2ppm       | 34                | 240±        | 22** | 0.069±   | 0.008 | 0.178±  | 0.308 | 0.844± | 0.048 | 0.923± | 0.073 | 1.718±  | 0.159 |

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

Test of Dunnett

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : FEMALE  
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)  
SURVIVAL ANIMALS (105W)

PAGE : 4

| Group Name | NO. of<br>Animals | SPLEEN |       | LIVER  |       | BRAIN  |       |
|------------|-------------------|--------|-------|--------|-------|--------|-------|
| Control    | 43                | 0.623± | 0.610 | 6.348± | 0.875 | 1.885± | 0.049 |
| 0.1ppm     | 42                | 0.952± | 1.808 | 6.652± | 1.047 | 1.896± | 0.045 |
| 0.5ppm     | 41                | 0.597± | 0.485 | 6.201± | 1.009 | 1.871± | 0.044 |
| 2ppm       | 34                | 0.547± | 0.236 | 6.465± | 1.080 | 1.866± | 0.041 |

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

Test of Dunnett

(HCL040)

BAIS 5

TABLE K1

ORGAN WEIGHT, RELATIVE : MALE

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : MALE  
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)  
SURVIVAL ANIMALS (105W)

PAGE : 1

| Group Name | NO. of<br>Animals | Body Weight<br>(g) | ADRENALS     | TESTES        | HEART          | LUNGS          | KIDNEYS      |
|------------|-------------------|--------------------|--------------|---------------|----------------|----------------|--------------|
| Control    | 41                | 394± 36            | 0.019± 0.004 | 0.893± 0.396  | 0.316± 0.036   | 0.357± 0.062   | 0.715± 0.085 |
| 0.1ppm     | 40                | 376± 31            | 0.024± 0.023 | 0.969± 0.292  | 0.321± 0.032   | 0.354± 0.035   | 0.717± 0.072 |
| 0.5ppm     | 37                | 389± 34            | 0.106± 0.493 | 1.092± 0.352* | 0.327± 0.061   | 0.361± 0.063   | 0.697± 0.076 |
| 2ppm       | 42                | 346± 23**          | 0.021± 0.011 | 1.074± 0.392  | 0.348± 0.034** | 0.388± 0.056** | 0.724± 0.079 |

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

Test of Dunnett

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : MALE  
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)  
SURVIVAL ANIMALS (105W)

PAGE : 2

| Group Name | NO. of<br>Animals | SPLEEN         | LIVER          | BRAIN          |
|------------|-------------------|----------------|----------------|----------------|
| Control    | 41                | 0.287± 0.197   | 2.820± 0.331   | 0.532± 0.047   |
| 0.1ppm     | 40                | 0.264± 0.086   | 2.767± 0.218   | 0.556± 0.050*  |
| 0.5ppm     | 37                | 0.277± 0.150   | 2.766± 0.241   | 0.536± 0.044   |
| 2ppm       | 42                | 0.224± 0.042** | 2.647± 0.333** | 0.597± 0.036** |

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

Test of Dunnett

TABLE K2

ORGAN WEIGHT, RELATIVE : FEMALE

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : FEMALE  
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)  
SURVIVAL ANIMALS (105W)

PAGE : 3

| Group Name | NO. of<br>Animals | Body Weight<br>(g) | ADRENALS     | OVARIES      | HEART        | LUNGS         | KIDNEYS      |
|------------|-------------------|--------------------|--------------|--------------|--------------|---------------|--------------|
| Control    | 43                | 255± 20            | 0.030± 0.009 | 0.078± 0.145 | 0.335± 0.026 | 0.364± 0.046  | 0.692± 0.069 |
| 0.1ppm     | 42                | 258± 29            | 0.028± 0.006 | 0.071± 0.150 | 0.342± 0.064 | 0.385± 0.146  | 0.687± 0.089 |
| 0.5ppm     | 41                | 249± 36            | 0.032± 0.026 | 0.046± 0.007 | 0.342± 0.050 | 0.385± 0.107  | 0.750± 0.333 |
| 2ppm       | 34                | 240± 22**          | 0.029± 0.003 | 0.075± 0.128 | 0.354± 0.036 | 0.387± 0.041* | 0.720± 0.084 |

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

Test of Dunnett

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : FEMALE  
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)  
SURVIVAL ANIMALS (105W)

PAGE : 4

| Group Name | NO. of<br>Animals | SPLEEN       | LIVER        | BRAIN        |
|------------|-------------------|--------------|--------------|--------------|
| Control    | 43                | 0.246± 0.251 | 2.490± 0.316 | 0.743± 0.065 |
| 0.1ppm     | 42                | 0.424± 0.944 | 2.606± 0.523 | 0.744± 0.094 |
| 0.5ppm     | 41                | 0.243± 0.182 | 2.514± 0.353 | 0.774± 0.159 |
| 2ppm       | 34                | 0.232± 0.120 | 2.706± 0.474 | 0.783± 0.069 |

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

Test of Dunnett

TABLE L1

HISTOPATHOLOGICAL FINDINGS :  
NEOPLASTIC LESIONS : MALE

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : MALE

HISTOPATHOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)  
ALL ANIMALS (0-105W)

PAGE : 1

| Organ                            | Findings                       | Group Name<br>No. of animals on Study | Control<br>50    | 0.1ppm<br>50    | 0.5ppm<br>50    | 2ppm<br>50      |
|----------------------------------|--------------------------------|---------------------------------------|------------------|-----------------|-----------------|-----------------|
| {Integumentary system/appandage} |                                |                                       |                  |                 |                 |                 |
| skin/app                         | squamous cell papilloma        |                                       | <50><br>0 ( 0%)  | <50><br>1 ( 2%) | <50><br>1 ( 2%) | <50><br>1 ( 2%) |
|                                  | schwannoma                     |                                       | 1 ( 2%)          | 1 ( 2%)         | 0 ( 0%)         | 0 ( 0%)         |
|                                  | keratoacanthoma                |                                       | 2 ( 4%)          | 2 ( 4%)         | 2 ( 4%)         | 0 ( 0%)         |
| subcutis                         | fibroma                        |                                       | <50><br>8 ( 16%) | <50><br>1 ( 2%) | <50><br>4 ( 8%) | <50><br>3 ( 6%) |
|                                  | lipoma                         |                                       | 2 ( 4%)          | 1 ( 2%)         | 0 ( 0%)         | 0 ( 0%)         |
|                                  | schwannoma                     |                                       | 1 ( 2%)          | 1 ( 2%)         | 0 ( 0%)         | 0 ( 0%)         |
|                                  | histiocytic sarcoma            |                                       | 0 ( 0%)          | 0 ( 0%)         | 0 ( 0%)         | 1 ( 2%)         |
| {Respiratory system}             |                                |                                       |                  |                 |                 |                 |
| nasal cavit                      | chondroma                      |                                       | <50><br>1 ( 2%)  | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) |
|                                  | squamous cell carcinoma        |                                       | 0 ( 0%)          | 0 ( 0%)         | 0 ( 0%)         | 1 ( 2%)         |
| lung                             | bronchiolar-alveolar adenoma   |                                       | <50><br>4 ( 8%)  | <50><br>4 ( 8%) | <50><br>4 ( 8%) | <50><br>3 ( 6%) |
|                                  | bronchiolar-alveolar carcinoma |                                       | 0 ( 0%)          | 0 ( 0%)         | 1 ( 2%)         | 0 ( 0%)         |
| {Hematopoietic system}           |                                |                                       |                  |                 |                 |                 |
| thymus                           | thymoma:malignant              |                                       | <50><br>0 ( 0%)  | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) |

< a > a : Number of animals examined at the site  
b ( c ) b : Number of animals with neoplasm c : b / a \* 100

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : MALE

HISTOPATHOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)  
ALL ANIMALS (0-105W)

PAGE : 2

| Organ                  | Findings                  | Group Name<br>No. of animals on Study | Control<br>50   | 0.1ppm<br>50     | 0.5ppm<br>50     | 2ppm<br>50       |
|------------------------|---------------------------|---------------------------------------|-----------------|------------------|------------------|------------------|
| {Hematopoietic system} |                           |                                       |                 |                  |                  |                  |
| spleen                 | mononuclear cell leukemia |                                       | <50><br>2 ( 4%) | <50><br>5 ( 10%) | <50><br>7 ( 14%) | <50><br>1 ( 2%)  |
| {Digestive system}     |                           |                                       |                 |                  |                  |                  |
| stomach                | squamous cell papilloma   |                                       | <50><br>1 ( 2%) | <50><br>0 ( 0%)  | <50><br>0 ( 0%)  | <50><br>1 ( 2%)  |
| small intes            | fibroma                   |                                       | <50><br>0 ( 0%) | <50><br>1 ( 2%)  | <50><br>0 ( 0%)  | <50><br>0 ( 0%)  |
|                        | adenocarcinoma            |                                       | 0 ( 0%)         | 1 ( 2%)          | 0 ( 0%)          | 2 ( 4%)          |
|                        | leiomyosarcoma            |                                       | 0 ( 0%)         | 0 ( 0%)          | 1 ( 2%)          | 1 ( 2%)          |
| liver                  | hepatocellular adenoma    |                                       | <50><br>2 ( 4%) | <50><br>2 ( 4%)  | <50><br>2 ( 4%)  | <50><br>0 ( 0%)  |
| pancreas               | islet cell adenoma        |                                       | <50><br>4 ( 8%) | <50><br>5 ( 10%) | <50><br>0 ( 0%)  | <50><br>6 ( 12%) |
|                        | acinar cell adenoma       |                                       | 0 ( 0%)         | 1 ( 2%)          | 0 ( 0%)          | 0 ( 0%)          |
|                        | islet cell adenocarcinoma |                                       | 2 ( 4%)         | 1 ( 2%)          | 3 ( 6%)          | 2 ( 4%)          |
| {Urinary system}       |                           |                                       |                 |                  |                  |                  |
| kidney                 | mesenchymoma              |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%)  | <50><br>1 ( 2%)  | <50><br>0 ( 0%)  |
|                        | nephroblastoma            |                                       | 0 ( 0%)         | 0 ( 0%)          | 1 ( 2%)          | 0 ( 0%)          |

< a > a : Number of animals examined at the site  
b ( c ) b : Number of animals with neoplasm c : b / a \* 100

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 3

| Organ                 | Findings                   | Group Name<br>No. of animals on Study | Control<br>50     | 0.1ppm<br>50      | 0.5ppm<br>50      | 2ppm<br>50        |
|-----------------------|----------------------------|---------------------------------------|-------------------|-------------------|-------------------|-------------------|
| {Endocrine system}    |                            |                                       |                   |                   |                   |                   |
| pituitary             | adenoma                    |                                       | <50><br>10 ( 20%) | <50><br>8 ( 16%)  | <49><br>11 ( 22%) | <50><br>3 ( 6%)   |
|                       | adenocarcinoma             |                                       | 1 ( 2%)           | 1 ( 2%)           | 0 ( 0%)           | 0 ( 0%)           |
| thyroid               | C-cell adenoma             |                                       | <50><br>8 ( 16%)  | <50><br>10 ( 20%) | <50><br>8 ( 16%)  | <50><br>10 ( 20%) |
|                       | follicular adenoma         |                                       | 1 ( 2%)           | 1 ( 2%)           | 0 ( 0%)           | 1 ( 2%)           |
|                       | C-cell carcinoma           |                                       | 4 ( 8%)           | 0 ( 0%)           | 2 ( 4%)           | 0 ( 0%)           |
| adrenal               | pheochromocytoma           |                                       | <50><br>6 ( 12%)  | <50><br>0 ( 0%)   | <50><br>3 ( 6%)   | <50><br>1 ( 2%)   |
|                       | cortical adenoma           |                                       | 0 ( 0%)           | 1 ( 2%)           | 0 ( 0%)           | 0 ( 0%)           |
|                       | pheochromocytoma:malignant |                                       | 1 ( 2%)           | 2 ( 4%)           | 2 ( 4%)           | 1 ( 2%)           |
| {Reproductive system} |                            |                                       |                   |                   |                   |                   |
| testis                | interstitial cell tumor    |                                       | <50><br>40 ( 80%) | <50><br>43 ( 86%) | <50><br>41 ( 82%) | <50><br>46 ( 92%) |
| prostate              | adenoma                    |                                       | <50><br>1 ( 2%)   | <50><br>0 ( 0%)   | <50><br>0 ( 0%)   | <50><br>0 ( 0%)   |
| mammary gl            | fibroadenoma               |                                       | <50><br>1 ( 2%)   | <50><br>0 ( 0%)   | <50><br>1 ( 2%)   | <50><br>0 ( 0%)   |
| prep/cli gl           | adenoma                    |                                       | <50><br>2 ( 4%)   | <50><br>1 ( 2%)   | <50><br>1 ( 2%)   | <50><br>1 ( 2%)   |

< a > a : Number of animals examined at the site  
 b ( c ) b : Number of animals with neoplasm c : b / a \* 100

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 4

| Organ                            | Findings                     | Group Name<br>No. of animals on Study | Control<br>50   | 0.1ppm<br>50    | 0.5ppm<br>50    | 2ppm<br>50      |
|----------------------------------|------------------------------|---------------------------------------|-----------------|-----------------|-----------------|-----------------|
| {Nervous system}                 |                              |                                       |                 |                 |                 |                 |
| brain                            | glioma                       |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) |
| {Special sense organs/appendage} |                              |                                       |                 |                 |                 |                 |
| Harder gl                        | adenocarcinoma               |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) |
| Zymbal gl                        | Zymbal gland tumor:benign    |                                       | <50><br>0 ( 0%) | <50><br>2 ( 4%) | <50><br>1 ( 2%) | <50><br>1 ( 2%) |
|                                  | Zymbal gland tumor:malignant |                                       | <50><br>0 ( 0%) | <50><br>2 ( 4%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) |
| {Musculoskeletal system}         |                              |                                       |                 |                 |                 |                 |
| muscle                           | lipoma                       |                                       | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) |
| bone                             | osteosarcoma                 |                                       | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) |
| vertebra                         | chordoma:malignant           |                                       | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) |
| {Body cavities}                  |                              |                                       |                 |                 |                 |                 |
| pleura                           | lipoma                       |                                       | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) |
| mediastinum                      | lipoma                       |                                       | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) |
| peritoneum                       | lipoma                       |                                       | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) |

< a > a : Number of animals examined at the site  
 b ( c ) b : Number of animals with neoplasm c : b / a \* 100

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : MALE

HISTOPATHOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)  
ALL ANIMALS (0-105W)

PAGE : 5

| Organ | Findings | Group Name<br>No. of animals on Study | Control<br>50 | 0.1ppm<br>50 | 0.5ppm<br>50 | 2ppm<br>50 |
|-------|----------|---------------------------------------|---------------|--------------|--------------|------------|
|-------|----------|---------------------------------------|---------------|--------------|--------------|------------|

{Body cavities}

|            |              |  |         |         |         |         |
|------------|--------------|--|---------|---------|---------|---------|
| peritoneum |              |  | <50>    | <50>    | <50>    | <50>    |
|            | mesothelioma |  | 1 ( 2%) | 0 ( 0%) | 1 ( 2%) | 3 ( 6%) |

< a > a : Number of animals examined at the site  
b ( c ) b : Number of animals with neoplasm c : b / a \* 100

(HPT085)

BAIS5

**TABLE L2**

**HISTOPATHOLOGICAL FINDINGS :  
NEOPLASTIC LESIONS : FEMALE**

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1J[F344/DuCrJ]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 6

| Organ                            | Findings                     | Group Name<br>No. of animals on Study | Control<br>50    | 0.1ppm<br>50     | 0.5ppm<br>50    | 2ppm<br>50      |
|----------------------------------|------------------------------|---------------------------------------|------------------|------------------|-----------------|-----------------|
| {Integumentary system/appandage} |                              |                                       |                  |                  |                 |                 |
| skin/app                         | trichoepithelioma            |                                       | <50><br>1 ( 2%)  | <50><br>1 ( 2%)  | <50><br>0 ( 0%) | <50><br>0 ( 0%) |
|                                  | keratoacanthoma              |                                       | 1 ( 2%)          | 0 ( 0%)          | 0 ( 0%)         | 1 ( 2%)         |
| subcutis                         | fibroma                      |                                       | <50><br>0 ( 0%)  | <50><br>1 ( 2%)  | <50><br>0 ( 0%) | <50><br>0 ( 0%) |
|                                  | lipoma                       |                                       | 0 ( 0%)          | 0 ( 0%)          | 2 ( 4%)         | 0 ( 0%)         |
| {Respiratory system}             |                              |                                       |                  |                  |                 |                 |
| nasal cavit                      | rhabdomyoma                  |                                       | <50><br>0 ( 0%)  | <50><br>0 ( 0%)  | <50><br>0 ( 0%) | <50><br>4 ( 8%) |
|                                  | squamous cell carcinoma      |                                       | 0 ( 0%)          | 0 ( 0%)          | 0 ( 0%)         | 2 ( 4%)         |
| lung                             | bronchiolar-alveolar adenoma |                                       | <50><br>0 ( 0%)  | <50><br>2 ( 4%)  | <50><br>2 ( 4%) | <50><br>2 ( 4%) |
|                                  | squamous cell carcinoma      |                                       | 0 ( 0%)          | 0 ( 0%)          | 0 ( 0%)         | 1 ( 2%)         |
|                                  | adenocarcinoma               |                                       | 1 ( 2%)          | 0 ( 0%)          | 0 ( 0%)         | 0 ( 0%)         |
| {Hematopoietic system}           |                              |                                       |                  |                  |                 |                 |
| spleen                           | mononuclear cell leukemia    |                                       | <50><br>5 ( 10%) | <50><br>6 ( 12%) | <50><br>4 ( 8%) | <50><br>3 ( 6%) |
| {Digestive system}               |                              |                                       |                  |                  |                 |                 |
| tongue                           | squamous cell papilloma      |                                       | <50><br>1 ( 2%)  | <50><br>0 ( 0%)  | <50><br>0 ( 0%) | <50><br>1 ( 2%) |

< a > a : Number of animals examined at the site  
 b ( c ) b : Number of animals with neoplasm c : b / a \* 100

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 7

| Organ              | Findings                    | Group Name<br>No. of animals on Study | Control<br>50 | 0.1ppm<br>50 | 0.5ppm<br>50 | 2ppm<br>50 |
|--------------------|-----------------------------|---------------------------------------|---------------|--------------|--------------|------------|
| {Digestive system} |                             |                                       |               |              |              |            |
| liver              |                             |                                       | <50>          | <50>         | <50>         | <50>       |
|                    | hepatocellular adenoma      |                                       | 0 ( 0%)       | 1 ( 2%)      | 3 ( 6%)      | 0 ( 0%)    |
| pancreas           |                             |                                       | <50>          | <50>         | <50>         | <50>       |
|                    | islet cell adenoma          |                                       | 0 ( 0%)       | 1 ( 2%)      | 0 ( 0%)      | 0 ( 0%)    |
|                    | islet cell adenocarcinoma   |                                       | 1 ( 2%)       | 0 ( 0%)      | 2 ( 4%)      | 0 ( 0%)    |
| {Urinary system}   |                             |                                       |               |              |              |            |
| kidney             |                             |                                       | <50>          | <50>         | <50>         | <50>       |
|                    | renal cell adenoma          |                                       | 0 ( 0%)       | 0 ( 0%)      | 1 ( 2%)      | 0 ( 0%)    |
| urin bladd         |                             |                                       | <50>          | <50>         | <50>         | <50>       |
|                    | transitional cell papilloma |                                       | 1 ( 2%)       | 0 ( 0%)      | 0 ( 0%)      | 0 ( 0%)    |
|                    | transitional cell carcinoma |                                       | 0 ( 0%)       | 0 ( 0%)      | 1 ( 2%)      | 0 ( 0%)    |
| {Endocrine system} |                             |                                       |               |              |              |            |
| pituitary          |                             |                                       | <50>          | <50>         | <50>         | <50>       |
|                    | adenoma                     |                                       | 14 ( 28%)     | 15 ( 30%)    | 20 ( 40%)    | 17 ( 34%)  |
|                    | adenocarcinoma              |                                       | 0 ( 0%)       | 2 ( 4%)      | 1 ( 2%)      | 0 ( 0%)    |
| thyroid            |                             |                                       | <50>          | <50>         | <50>         | <50>       |
|                    | C-cell adenoma              |                                       | 12 ( 24%)     | 10 ( 20%)    | 6 ( 12%)     | 8 ( 16%)   |
|                    | C-cell carcinoma            |                                       | 1 ( 2%)       | 0 ( 0%)      | 4 ( 8%)      | 2 ( 4%)    |
|                    | follicular adenocarcinoma   |                                       | 0 ( 0%)       | 0 ( 0%)      | 0 ( 0%)      | 1 ( 2%)    |

< a > a : Number of animals examined at the site  
 b ( c ) b : Number of animals with neoplasm c : b / a \* 100

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 8

| Organ                 | Findings                    | Group Name<br>No. of animals on Study | Control<br>50   | 0.1ppm<br>50    | 0.5ppm<br>50    | 2ppm<br>50      |
|-----------------------|-----------------------------|---------------------------------------|-----------------|-----------------|-----------------|-----------------|
| {Endocrine system}    |                             |                                       |                 |                 |                 |                 |
| adrenal               | pheochromocytoma            |                                       | <50><br>1 ( 2%) | <50><br>1 ( 2%) | <50><br>2 ( 4%) | <50><br>0 ( 0%) |
|                       | pheochromocytoma:malignant  |                                       | 0 ( 0%)         | 0 ( 0%)         | 1 ( 2%)         | 1 ( 2%)         |
| {Reproductive system} |                             |                                       |                 |                 |                 |                 |
| ovary                 | cystadenoma                 |                                       | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) |
|                       | sertoli cell tumor          |                                       | 0 ( 0%)         | 0 ( 0%)         | 0 ( 0%)         | 1 ( 2%)         |
| uterus                | adenoma                     |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) |
|                       | endometrial stromal polyp   |                                       | 7 ( 14%)        | 7 ( 14%)        | 4 ( 8%)         | 10 ( 20%)       |
|                       | adenocarcinoma              |                                       | 3 ( 6%)         | 1 ( 2%)         | 0 ( 0%)         | 1 ( 2%)         |
|                       | fibrosarcoma                |                                       | 1 ( 2%)         | 0 ( 0%)         | 0 ( 0%)         | 0 ( 0%)         |
|                       | endometrial stromal sarcoma |                                       | 0 ( 0%)         | 1 ( 2%)         | 1 ( 2%)         | 0 ( 0%)         |
| mammary gl            | adenoma                     |                                       | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) |
|                       | fibroadenoma                |                                       | 4 ( 8%)         | 6 ( 12%)        | 2 ( 4%)         | 3 ( 6%)         |
|                       | adenocarcinoma              |                                       | 0 ( 0%)         | 2 ( 4%)         | 1 ( 2%)         | 1 ( 2%)         |

< a > a : Number of animals examined at the site  
 b ( c ) b : Number of animals with neoplasm c : b / a \* 100

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrI CrIj[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS : NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 9

| Organ                            | Findings                     | Group Name<br>No. of animals on Study | Control<br>50   | 0.1ppm<br>50    | 0.5ppm<br>50    | 2ppm<br>50      |
|----------------------------------|------------------------------|---------------------------------------|-----------------|-----------------|-----------------|-----------------|
| {Reproductive system}            |                              |                                       |                 |                 |                 |                 |
| prep/cli gl                      | adenoma                      |                                       | <50><br>1 ( 2%) | <50><br>2 ( 4%) | <50><br>3 ( 6%) | <50><br>2 ( 4%) |
| {Nervous system}                 |                              |                                       |                 |                 |                 |                 |
| brain                            | glioma                       |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>2 ( 4%) |
| {Special sense organs/appendage} |                              |                                       |                 |                 |                 |                 |
| Zymbal gl                        | Zymbal gland tumor:malignant |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) |
| {Musculoskeletal system}         |                              |                                       |                 |                 |                 |                 |
| muscle                           | sarcoma:NOS                  |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) |
| {Body cavities}                  |                              |                                       |                 |                 |                 |                 |
| peritoneum                       | rhabdomyosarcoma             |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) | <50><br>0 ( 0%) |
|                                  | histiocytic sarcoma          |                                       | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) |

< a > a : Number of animals examined at the site  
 b ( c ) b : Number of animals with neoplasm c : b / a \* 100

TABLE M1

NEOPLASTIC LESIONS-INCIDENCE  
AND STATISTICAL ANALYSIS : MALE

STUDY No. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 SEX : MALE

NEOPLASTIC LESIONS—INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 1

| Group Name                                                                          | Control      | 100ppb      | 500ppb      | 2000ppb    |
|-------------------------------------------------------------------------------------|--------------|-------------|-------------|------------|
| SITE : subcutis<br>TUMOR : fibroma                                                  |              |             |             |            |
| Tumor rate                                                                          |              |             |             |            |
| Overall rates(a)                                                                    | 8/50( 16.0)  | 1/50( 2.0)  | 4/50( 8.0)  | 3/50( 6.0) |
| Adjusted rates(b)                                                                   | 15.22        | 2.50        | 9.30        | 7.14       |
| Terminal rates(c)                                                                   | 6/41( 14.6)  | 1/40( 2.5)  | 3/37( 8.1)  | 3/42( 7.1) |
| Statistical analysis                                                                |              |             |             |            |
| Peto test                                                                           |              |             |             |            |
| Standard method(d)                                                                  | P = 1.0000 ? |             |             |            |
| Prevalence method(d)                                                                | P = 0.7317   |             |             |            |
| Combined analysis(d)                                                                | P = 0.7924   |             |             |            |
| Cochran-Armitage test(e)                                                            | P = 0.4545   |             |             |            |
| Fisher Exact test(e)                                                                |              | P = 0.0154* | P = 0.1783  | P = 0.0999 |
| SITE : lung<br>TUMOR : bronchiolar-alveolar adenoma                                 |              |             |             |            |
| Tumor rate                                                                          |              |             |             |            |
| Overall rates(a)                                                                    | 4/50( 8.0)   | 4/50( 8.0)  | 4/50( 8.0)  | 3/50( 6.0) |
| Adjusted rates(b)                                                                   | 9.76         | 10.00       | 10.81       | 7.14       |
| Terminal rates(c)                                                                   | 4/41( 9.8)   | 4/40( 10.0) | 4/37( 10.8) | 3/42( 7.1) |
| Statistical analysis                                                                |              |             |             |            |
| Peto test                                                                           |              |             |             |            |
| Standard method(d)                                                                  | P = ———      |             |             |            |
| Prevalence method(d)                                                                | P = 0.6879   |             |             |            |
| Combined analysis(d)                                                                | P = ———      |             |             |            |
| Cochran-Armitage test(e)                                                            | P = 0.6512   |             |             |            |
| Fisher Exact test(e)                                                                |              | P = 0.6425  | P = 0.6425  | P = 0.5000 |
| SITE : lung<br>TUMOR : bronchiolar-alveolar adenoma, bronchiolar-alveolar carcinoma |              |             |             |            |
| Tumor rate                                                                          |              |             |             |            |
| Overall rates(a)                                                                    | 4/50( 8.0)   | 4/50( 8.0)  | 5/50( 10.0) | 3/50( 6.0) |
| Adjusted rates(b)                                                                   | 9.76         | 10.00       | 13.51       | 7.14       |
| Terminal rates(c)                                                                   | 4/41( 9.8)   | 4/40( 10.0) | 5/37( 13.5) | 3/42( 7.1) |
| Statistical analysis                                                                |              |             |             |            |
| Peto test                                                                           |              |             |             |            |
| Standard method(d)                                                                  | P = ———      |             |             |            |
| Prevalence method(d)                                                                | P = 0.7024   |             |             |            |
| Combined analysis(d)                                                                | P = ———      |             |             |            |
| Cochran-Armitage test(e)                                                            | P = 0.6257   |             |             |            |
| Fisher Exact test(e)                                                                |              | P = 0.6425  | P = 0.5000  | P = 0.5000 |

STUDY No. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 SEX : MALE

NEOPLASTIC LESIONS—INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 2

| Group Name                                           | Control    | 100ppb      | 500ppb      | 2000ppb     |
|------------------------------------------------------|------------|-------------|-------------|-------------|
| SITE : spleen<br>TUMOR : mononuclear cell leukemia   |            |             |             |             |
| Tumor rate                                           |            |             |             |             |
| Overall rates(a)                                     | 2/50( 4.0) | 5/50( 10.0) | 7/50( 14.0) | 1/50( 2.0)  |
| Adjusted rates(b)                                    | 2.44       | 7.50        | 5.41        | 0.0         |
| Terminal rates(c)                                    | 1/41( 2.4) | 3/40( 7.5)  | 2/37( 5.4)  | 0/42( 0.0)  |
| Statistical analysis                                 |            |             |             |             |
| Peto test                                            |            |             |             |             |
| Standard method(d)                                   | P = 0.6891 |             |             |             |
| Prevalence method(d)                                 | P = 0.9245 |             |             |             |
| Combined analysis(d)                                 | P = 0.9048 |             |             |             |
| Cochran-Armitage test(e)                             | P = 0.2091 |             |             |             |
| Fisher Exact test(e)                                 |            | P = 0.2180  | P = 0.0798  | P = 0.5000  |
| SITE : pancreas<br>TUMOR : islet cell adenoma        |            |             |             |             |
| Tumor rate                                           |            |             |             |             |
| Overall rates(a)                                     | 4/50( 8.0) | 5/50( 10.0) | 0/50( 0.0)  | 6/50( 12.0) |
| Adjusted rates(b)                                    | 9.76       | 10.87       | 0.0         | 14.29       |
| Terminal rates(c)                                    | 4/41( 9.8) | 4/40( 10.0) | 0/37( 0.0)  | 6/42( 14.3) |
| Statistical analysis                                 |            |             |             |             |
| Peto test                                            |            |             |             |             |
| Standard method(d)                                   | P = -----  |             |             |             |
| Prevalence method(d)                                 | P = 0.2004 |             |             |             |
| Combined analysis(d)                                 | P = -----  |             |             |             |
| Cochran-Armitage test(e)                             | P = 0.3570 |             |             |             |
| Fisher Exact test(e)                                 |            | P = 0.5000  | P = 0.0587  | P = 0.3703  |
| SITE : pancreas<br>TUMOR : islet cell adenocarcinoma |            |             |             |             |
| Tumor rate                                           |            |             |             |             |
| Overall rates(a)                                     | 2/50( 4.0) | 1/50( 2.0)  | 3/50( 6.0)  | 2/50( 4.0)  |
| Adjusted rates(b)                                    | 4.88       | 2.50        | 5.41        | 2.38        |
| Terminal rates(c)                                    | 2/41( 4.9) | 1/40( 2.5)  | 2/37( 5.4)  | 1/42( 2.4)  |
| Statistical analysis                                 |            |             |             |             |
| Peto test                                            |            |             |             |             |
| Standard method(d)                                   | P = 0.1913 |             |             |             |
| Prevalence method(d)                                 | P = 0.6474 |             |             |             |
| Combined analysis(d)                                 | P = 0.4380 |             |             |             |
| Cochran-Armitage test(e)                             | P = 0.8571 |             |             |             |
| Fisher Exact test(e)                                 |            | P = 0.5000  | P = 0.5000  | P = 0.6913  |

STUDY No. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                                               | Control      | 100ppb      | 500ppb       | 2000ppb     |
|--------------------------------------------------------------------------|--------------|-------------|--------------|-------------|
| SITE : pancreas<br>TUMOR : islet cell adenoma, islet cell adenocarcinoma |              |             |              |             |
| Tumor rate                                                               |              |             |              |             |
| Overall rates(a)                                                         | 6/50( 12.0)  | 6/50( 12.0) | 3/50( 6.0)   | 8/50( 16.0) |
| Adjusted rates(b)                                                        | 14.63        | 13.04       | 5.41         | 16.67       |
| Terminal rates(c)                                                        | 6/41( 14.6)  | 5/40( 12.5) | 2/37( 5.4)   | 7/42( 16.7) |
| Statistical analysis                                                     |              |             |              |             |
| Peto test                                                                |              |             |              |             |
| Standard method(d)                                                       | P = 0.1913   |             |              |             |
| Prevalence method(d)                                                     | P = 0.3089   |             |              |             |
| Combined analysis(d)                                                     | P = 0.2210   |             |              |             |
| Cochran-Armitage test(e)                                                 | P = 0.3837   |             |              |             |
| Fisher Exact test(e)                                                     |              | P = 0.6202  | P = 0.2435   | P = 0.3871  |
| SITE : pituitary gland<br>TUMOR : adenoma                                |              |             |              |             |
| Tumor rate                                                               |              |             |              |             |
| Overall rates(a)                                                         | 10/50( 20.0) | 8/50( 16.0) | 11/49( 22.4) | 3/50( 6.0)  |
| Adjusted rates(b)                                                        | 12.20        | 10.00       | 18.18        | 4.65        |
| Terminal rates(c)                                                        | 5/41( 12.2)  | 4/40( 10.0) | 6/37( 16.2)  | 1/42( 2.4)  |
| Statistical analysis                                                     |              |             |              |             |
| Peto test                                                                |              |             |              |             |
| Standard method(d)                                                       | P = 0.9601   |             |              |             |
| Prevalence method(d)                                                     | P = 0.9156   |             |              |             |
| Combined analysis(d)                                                     | P = 0.9866   |             |              |             |
| Cochran-Armitage test(e)                                                 | P = 0.0406*  |             |              |             |
| Fisher Exact test(e)                                                     |              | P = 0.3976  | P = 0.4791   | P = 0.0357* |
| SITE : pituitary gland<br>TUMOR : adenoma, adenocarcinoma                |              |             |              |             |
| Tumor rate                                                               |              |             |              |             |
| Overall rates(a)                                                         | 11/50( 22.0) | 9/50( 18.0) | 11/49( 22.4) | 3/50( 6.0)  |
| Adjusted rates(b)                                                        | 14.63        | 12.50       | 18.18        | 4.65        |
| Terminal rates(c)                                                        | 6/41( 14.6)  | 5/40( 12.5) | 6/37( 16.2)  | 1/42( 2.4)  |
| Statistical analysis                                                     |              |             |              |             |
| Peto test                                                                |              |             |              |             |
| Standard method(d)                                                       | P = 0.9601   |             |              |             |
| Prevalence method(d)                                                     | P = 0.9563   |             |              |             |
| Combined analysis(d)                                                     | P = 0.9932   |             |              |             |
| Cochran-Armitage test(e)                                                 | P = 0.0226*  |             |              |             |
| Fisher Exact test(e)                                                     |              | P = 0.4016  | P = 0.5742   | P = 0.0204* |

STUDY No. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                                 | Control      | 100ppb       | 500ppb       | 2000ppb      |
|------------------------------------------------------------|--------------|--------------|--------------|--------------|
| SITE : thyroid<br>TUMOR : C-cell adenoma                   |              |              |              |              |
| Tumor rate                                                 |              |              |              |              |
| Overall rates(a)                                           | 8/50( 16.0)  | 10/50( 20.0) | 8/50( 16.0)  | 10/50( 20.0) |
| Adjusted rates(b)                                          | 19.51        | 25.00        | 21.62        | 21.28        |
| Terminal rates(c)                                          | 8/41( 19.5)  | 10/40( 25.0) | 8/37( 21.6)  | 8/42( 19.0)  |
| Statistical analysis                                       |              |              |              |              |
| Peto test                                                  |              |              |              |              |
| Standard method(d)                                         | P = -----    |              |              |              |
| Prevalence method(d)                                       | P = 0.4984   |              |              |              |
| Combined analysis(d)                                       | P = -----    |              |              |              |
| Cochran-Armitage test(e)                                   | P = 0.7133   |              |              |              |
| Fisher Exact test(e)                                       |              | P = 0.3976   | P = 0.6071   | P = 0.3976   |
| SITE : thyroid<br>TUMOR : C-cell carcinoma                 |              |              |              |              |
| Tumor rate                                                 |              |              |              |              |
| Overall rates(a)                                           | 4/50( 8.0)   | 0/50( 0.0)   | 2/50( 4.0)   | 0/50( 0.0)   |
| Adjusted rates(b)                                          | 8.89         | 0.0          | 2.70         | 0.0          |
| Terminal rates(c)                                          | 3/41( 7.3)   | 0/40( 0.0)   | 1/37( 2.7)   | 0/42( 0.0)   |
| Statistical analysis                                       |              |              |              |              |
| Peto test                                                  |              |              |              |              |
| Standard method(d)                                         | P = 0.3476   |              |              |              |
| Prevalence method(d)                                       | P = 0.9635   |              |              |              |
| Combined analysis(d)                                       | P = 0.9532   |              |              |              |
| Cochran-Armitage test(e)                                   | P = 0.1337   |              |              |              |
| Fisher Exact test(e)                                       |              | P = 0.0587   | P = 0.3389   | P = 0.0587   |
| SITE : thyroid<br>TUMOR : C-cell adenoma, C-cell carcinoma |              |              |              |              |
| Tumor rate                                                 |              |              |              |              |
| Overall rates(a)                                           | 12/50( 24.0) | 10/50( 20.0) | 10/50( 20.0) | 10/50( 20.0) |
| Adjusted rates(b)                                          | 26.83        | 25.00        | 24.32        | 21.28        |
| Terminal rates(c)                                          | 11/41( 26.8) | 10/40( 25.0) | 9/37( 24.3)  | 8/42( 19.0)  |
| Statistical analysis                                       |              |              |              |              |
| Peto test                                                  |              |              |              |              |
| Standard method(d)                                         | P = 0.3476   |              |              |              |
| Prevalence method(d)                                       | P = 0.7230   |              |              |              |
| Combined analysis(d)                                       | P = 0.7317   |              |              |              |
| Cochran-Armitage test(e)                                   | P = 0.7783   |              |              |              |
| Fisher Exact test(e)                                       |              | P = 0.4048   | P = 0.4048   | P = 0.4048   |

STUDY No. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                                                   | Control      | 100ppb       | 500ppb       | 2000ppb      |
|------------------------------------------------------------------------------|--------------|--------------|--------------|--------------|
| SITE : adrenal gland<br>TUMOR : pheochromocytoma                             |              |              |              |              |
| Tumor rate                                                                   |              |              |              |              |
| Overall rates(a)                                                             | 6/50( 12.0)  | 0/50( 0.0)   | 3/50( 6.0)   | 1/50( 2.0)   |
| Adjusted rates(b)                                                            | 14.63        | 0.0          | 6.67         | 2.38         |
| Terminal rates(c)                                                            | 6/41( 14.6)  | 0/40( 0.0)   | 2/37( 5.4)   | 1/42( 2.4)   |
| Statistical analysis                                                         |              |              |              |              |
| Peto test                                                                    |              |              |              |              |
| Standard method(d)                                                           | P = -----    |              |              |              |
| Prevalence method(d)                                                         | P = 0.9076   |              |              |              |
| Combined analysis(d)                                                         | P = -----    |              |              |              |
| Cochran-Armitage test(e)                                                     | P = 0.2246   |              |              |              |
| Fisher Exact test(e)                                                         |              | P = 0.0133*  | P = 0.2435   | P = 0.0559   |
| SITE : adrenal gland<br>TUMOR : pheochromocytoma, pheochromocytoma:malignant |              |              |              |              |
| Tumor rate                                                                   |              |              |              |              |
| Overall rates(a)                                                             | 7/50( 14.0)  | 2/50( 4.0)   | 5/50( 10.0)  | 2/50( 4.0)   |
| Adjusted rates(b)                                                            | 14.63        | 5.00         | 11.11        | 4.76         |
| Terminal rates(c)                                                            | 6/41( 14.6)  | 2/40( 5.0)   | 4/37( 10.8)  | 2/42( 4.8)   |
| Statistical analysis                                                         |              |              |              |              |
| Peto test                                                                    |              |              |              |              |
| Standard method(d)                                                           | P = 1.0000 ? |              |              |              |
| Prevalence method(d)                                                         | P = 0.8715   |              |              |              |
| Combined analysis(d)                                                         | P = 0.9087   |              |              |              |
| Cochran-Armitage test(e)                                                     | P = 0.2289   |              |              |              |
| Fisher Exact test(e)                                                         |              | P = 0.0798   | P = 0.3798   | P = 0.0798   |
| SITE : testis<br>TUMOR : interstitial cell tumor                             |              |              |              |              |
| Tumor rate                                                                   |              |              |              |              |
| Overall rates(a)                                                             | 40/50( 80.0) | 43/50( 86.0) | 41/50( 82.0) | 46/50( 92.0) |
| Adjusted rates(b)                                                            | 92.86        | 100.00       | 100.00       | 97.62        |
| Terminal rates(c)                                                            | 38/41( 92.7) | 40/40(100.0) | 37/37(100.0) | 41/42( 97.6) |
| Statistical analysis                                                         |              |              |              |              |
| Peto test                                                                    |              |              |              |              |
| Standard method(d)                                                           | P = -----    |              |              |              |
| Prevalence method(d)                                                         | P = 0.3974   |              |              |              |
| Combined analysis(d)                                                         | P = -----    |              |              |              |
| Cochran-Armitage test(e)                                                     | P = 0.1196   |              |              |              |
| Fisher Exact test(e)                                                         |              | P = 0.2977   | P = 0.5000   | P = 0.0739   |

STUDY No. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 SEX : MALE

NEOPLASTIC LESIONS—INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                                                            | Control    | 100ppb     | 500ppb     | 2000ppb    |
|---------------------------------------------------------------------------------------|------------|------------|------------|------------|
| SITE : Zymbal gland<br>TUMOR : Zmbal gland tumor:benign ,Zymbal gland tumor:malignant |            |            |            |            |
| Tumor rate                                                                            |            |            |            |            |
| Overall rates(a)                                                                      | 0/50( 0.0) | 4/50( 8.0) | 2/50( 4.0) | 1/50( 2.0) |
| Adjusted rates(b)                                                                     | 0.0        | 7.50       | 2.70       | 0.0        |
| Terminal rates(c)                                                                     | 0/41( 0.0) | 3/40( 7.5) | 1/37( 2.7) | 0/42( 0.0) |
| Statistical analysis                                                                  |            |            |            |            |
| Peto test                                                                             |            |            |            |            |
| Standard method(d)                                                                    | P = 0.3206 |            |            |            |
| Prevalence method(d)                                                                  | P = 0.8775 |            |            |            |
| Combined analysis(d)                                                                  | P = 0.7033 |            |            |            |
| Cochran-Armitage test(e)                                                              | P = 0.5809 |            |            |            |
| Fisher Exact test(e)                                                                  |            | P = 0.0587 | P = 0.2475 | P = 0.5000 |
| SITE : peritoneum<br>TUMOR : mesothelioma                                             |            |            |            |            |
| Tumor rate                                                                            |            |            |            |            |
| Overall rates(a)                                                                      | 1/50( 2.0) | 0/50( 0.0) | 1/50( 2.0) | 3/50( 6.0) |
| Adjusted rates(b)                                                                     | 2.44       | 0.0        | 2.70       | 4.76       |
| Terminal rates(c)                                                                     | 1/41( 2.4) | 0/40( 0.0) | 1/37( 2.7) | 2/42( 4.8) |
| Statistical analysis                                                                  |            |            |            |            |
| Peto test                                                                             |            |            |            |            |
| Standard method(d)                                                                    | P = 0.1802 |            |            |            |
| Prevalence method(d)                                                                  | P = 0.1422 |            |            |            |
| Combined analysis(d)                                                                  | P = 0.0547 |            |            |            |
| Cochran-Armitage test(e)                                                              | P = 0.0663 |            |            |            |
| Fisher Exact test(e)                                                                  |            | P = 0.5000 | P = 0.7525 | P = 0.3087 |

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- (a): Number of tumor-bearing animals/number of animals examined at the site.  
 (b): Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.  
 (c): Observed tumor incidence at terminal kill.  
 (d): Beneath the control incidence are the P-values associated with the trend test.  
     Standard method : Death analysis  
     Prevalence method : Incidental tumor test  
     Combined analysis : Death analysis + Incidental tumor test  
 (e): The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.  
 ? : The conditional probabilities of the largest and smallest possible outcomes cannot be estimated or this P-value is beyond the estimated P-value.  
 — : There is no data which should be statistical analysis.  
 Significant difference : \* :  $P \leq 0.05$     \*\* :  $P \leq 0.01$   
 N.C.:Statistical value cannot be calculated and was not significant.

**TABLE M2**

**NEOPLASTIC LESIONS-INCIDENCE  
AND STATISTICAL ANALYSIS : FEMALE**

STUDY No. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 SEX : FEMALE

NEOPLASTIC LESIONS—INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                                                                   | Control       | 100ppb     | 500ppb     | 2000ppb     |
|----------------------------------------------------------------------------------------------|---------------|------------|------------|-------------|
| SITE : nasal cavity<br>TUMOR : rhabdomyoma                                                   |               |            |            |             |
| Tumor rate                                                                                   |               |            |            |             |
| Overall rates(a)                                                                             | 0/50( 0.0)    | 0/50( 0.0) | 0/50( 0.0) | 4/50( 8.0)  |
| Adjusted rates(b)                                                                            | 0.0           | 0.0        | 0.0        | 11.76       |
| Terminal rates(c)                                                                            | 0/43( 0.0)    | 0/42( 0.0) | 0/41( 0.0) | 4/34( 11.8) |
| Statistical analysis                                                                         |               |            |            |             |
| Peto test                                                                                    |               |            |            |             |
| Standard method(d)                                                                           | P = -----     |            |            |             |
| Prevalence method(d)                                                                         | P = 0.0001**? |            |            |             |
| Combined analysis(d)                                                                         | P = -----     |            |            |             |
| Cochran-Armitage test(e)                                                                     | P = 0.0007**  |            |            |             |
| Fisher Exact test(e)                                                                         |               | P = N. C.  | P = N. C.  | P = 0.0587  |
| SITE : nasal cavity<br>TUMOR : rhabdomyoma, squamous cell carcinoma                          |               |            |            |             |
| Tumor rate                                                                                   |               |            |            |             |
| Overall rates(a)                                                                             | 0/50( 0.0)    | 0/50( 0.0) | 0/50( 0.0) | 6/50( 12.0) |
| Adjusted rates(b)                                                                            | 0.0           | 0.0        | 0.0        | 14.71       |
| Terminal rates(c)                                                                            | 0/43( 0.0)    | 0/42( 0.0) | 0/41( 0.0) | 5/34( 14.7) |
| Statistical analysis                                                                         |               |            |            |             |
| Peto test                                                                                    |               |            |            |             |
| Standard method(d)                                                                           | P = 0.1398    |            |            |             |
| Prevalence method(d)                                                                         | P < 0.0001**? |            |            |             |
| Combined analysis(d)                                                                         | P < 0.0001**? |            |            |             |
| Cochran-Armitage test(e)                                                                     | P < 0.0001**  |            |            |             |
| Fisher Exact test(e)                                                                         |               | P = N. C.  | P = N. C.  | P = 0.0133* |
| SITE : lung<br>TUMOR : bronchiolar-alveolar adenoma, squamous cell carcinoma, adenocarcinoma |               |            |            |             |
| Tumor rate                                                                                   |               |            |            |             |
| Overall rates(a)                                                                             | 1/50( 2.0)    | 2/50( 4.0) | 2/50( 4.0) | 3/50( 6.0)  |
| Adjusted rates(b)                                                                            | 2.33          | 4.76       | 4.88       | 6.82        |
| Terminal rates(c)                                                                            | 1/43( 2.3)    | 2/42( 4.8) | 2/41( 4.9) | 2/34( 5.9)  |
| Statistical analysis                                                                         |               |            |            |             |
| Peto test                                                                                    |               |            |            |             |
| Standard method(d)                                                                           | P = -----     |            |            |             |
| Prevalence method(d)                                                                         | P = 0.1745    |            |            |             |
| Combined analysis(d)                                                                         | P = -----     |            |            |             |
| Cochran-Armitage test(e)                                                                     | P = 0.3679    |            |            |             |
| Fisher Exact test(e)                                                                         |               | P = 0.5000 | P = 0.5000 | P = 0.3087  |

STUDY No. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                         | Control      | 100ppb       | 500ppb       | 2000ppb      |
|----------------------------------------------------|--------------|--------------|--------------|--------------|
| SITE : spleen<br>TUMOR : mononuclear cell leukemia |              |              |              |              |
| Tumor rate                                         |              |              |              |              |
| Overall rates(a)                                   | 5/50( 10.0)  | 6/50( 12.0)  | 4/50( 8.0)   | 3/50( 6.0)   |
| Adjusted rates(b)                                  | 6.98         | 4.76         | 4.88         | 0.0          |
| Terminal rates(c)                                  | 3/43( 7.0)   | 2/42( 4.8)   | 2/41( 4.9)   | 0/34( 0.0)   |
| Statistical analysis                               |              |              |              |              |
| Peto test                                          |              |              |              |              |
| Standard method(d)                                 | P = 0.3998   |              |              |              |
| Prevalence method(d)                               | P = 0.9416   |              |              |              |
| Combined analysis(d)                               | P = 0.7503   |              |              |              |
| Cochran-Armitage test(e)                           | P = 0.3393   |              |              |              |
| Fisher Exact test(e)                               |              | P = 0.5000   | P = 0.5000   | P = 0.3575   |
| SITE : liver<br>TUMOR : hepatocellular adenoma     |              |              |              |              |
| Tumor rate                                         |              |              |              |              |
| Overall rates(a)                                   | 0/50( 0.0)   | 1/50( 2.0)   | 3/50( 6.0)   | 0/50( 0.0)   |
| Adjusted rates(b)                                  | 0.0          | 2.38         | 7.32         | 0.0          |
| Terminal rates(c)                                  | 0/43( 0.0)   | 1/42( 2.4)   | 3/41( 7.3)   | 0/34( 0.0)   |
| Statistical analysis                               |              |              |              |              |
| Peto test                                          |              |              |              |              |
| Standard method(d)                                 | P = -----    |              |              |              |
| Prevalence method(d)                               | P = 0.6346   |              |              |              |
| Combined analysis(d)                               | P = -----    |              |              |              |
| Cochran-Armitage test(e)                           | P = 0.5286   |              |              |              |
| Fisher Exact test(e)                               |              | P = 0.5000   | P = 0.1212   | P = N. C.    |
| SITE : pituitary gland<br>TUMOR : adenoma          |              |              |              |              |
| Tumor rate                                         |              |              |              |              |
| Overall rates(a)                                   | 14/50( 28.0) | 15/50( 30.0) | 20/50( 40.0) | 17/50( 34.0) |
| Adjusted rates(b)                                  | 25.58        | 31.25        | 44.19        | 29.41        |
| Terminal rates(c)                                  | 11/43( 25.6) | 12/42( 28.6) | 18/41( 43.9) | 10/34( 29.4) |
| Statistical analysis                               |              |              |              |              |
| Peto test                                          |              |              |              |              |
| Standard method(d)                                 | P = 0.0115*  |              |              |              |
| Prevalence method(d)                               | P = 0.5619   |              |              |              |
| Combined analysis(d)                               | P = 0.1619   |              |              |              |
| Cochran-Armitage test(e)                           | P = 0.6257   |              |              |              |
| Fisher Exact test(e)                               |              | P = 0.5000   | P = 0.1456   | P = 0.3329   |

STUDY No. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                                | Control       | 100ppb        | 500ppb        | 2000ppb       |
|-----------------------------------------------------------|---------------|---------------|---------------|---------------|
| SITE : pituitary gland<br>TUMOR : adenoma, adenocarcinoma |               |               |               |               |
| Tumor rate                                                |               |               |               |               |
| Overall rates(a)                                          | 14/50 ( 28.0) | 17/50 ( 34.0) | 21/50 ( 42.0) | 17/50 ( 34.0) |
| Adjusted rates(b)                                         | 25.58         | 34.04         | 46.51         | 29.41         |
| Terminal rates(c)                                         | 11/43 ( 25.6) | 13/42 ( 31.0) | 19/41 ( 46.3) | 10/34 ( 29.4) |
| Statistical analysis                                      |               |               |               |               |
| Peto test                                                 |               |               |               |               |
| Standard method(d)                                        | P = 0.0215*   |               |               |               |
| Prevalence method(d)                                      | P = 0.6199    |               |               |               |
| Combined analysis(d)                                      | P = 0.2243    |               |               |               |
| Cochran-Armitage test(e)                                  | P = 0.8022    |               |               |               |
| Fisher Exact test(e)                                      |               | P = 0.3329    | P = 0.1041    | P = 0.3329    |
| SITE : thyroid<br>TUMOR : C-cell adenoma                  |               |               |               |               |
| Tumor rate                                                |               |               |               |               |
| Overall rates(a)                                          | 12/50 ( 24.0) | 10/50 ( 20.0) | 6/50 ( 12.0)  | 8/50 ( 16.0)  |
| Adjusted rates(b)                                         | 27.91         | 23.81         | 12.24         | 23.53         |
| Terminal rates(c)                                         | 12/43 ( 27.9) | 10/42 ( 23.8) | 5/41 ( 12.2)  | 8/34 ( 23.5)  |
| Statistical analysis                                      |               |               |               |               |
| Peto test                                                 |               |               |               |               |
| Standard method(d)                                        | P = -----     |               |               |               |
| Prevalence method(d)                                      | P = 0.6088    |               |               |               |
| Combined analysis(d)                                      | P = -----     |               |               |               |
| Cochran-Armitage test(e)                                  | P = 0.4350    |               |               |               |
| Fisher Exact test(e)                                      |               | P = 0.4048    | P = 0.0961    | P = 0.2270    |
| SITE : thyroid<br>TUMOR : C-cell carcinoma                |               |               |               |               |
| Tumor rate                                                |               |               |               |               |
| Overall rates(a)                                          | 1/50 ( 2.0)   | 0/50 ( 0.0)   | 4/50 ( 8.0)   | 2/50 ( 4.0)   |
| Adjusted rates(b)                                         | 2.08          | 0.0           | 9.76          | 5.26          |
| Terminal rates(c)                                         | 0/43 ( 0.0)   | 0/42 ( 0.0)   | 4/41 ( 9.8)   | 1/34 ( 2.9)   |
| Statistical analysis                                      |               |               |               |               |
| Peto test                                                 |               |               |               |               |
| Standard method(d)                                        | P = -----     |               |               |               |
| Prevalence method(d)                                      | P = 0.2221    |               |               |               |
| Combined analysis(d)                                      | P = -----     |               |               |               |
| Cochran-Armitage test(e)                                  | P = 0.4864    |               |               |               |
| Fisher Exact test(e)                                      |               | P = 0.5000    | P = 0.1811    | P = 0.5000    |

STUDY No. : 0816  
 ANIMAL : RAT F344/DuCrI CrIj [F344/DuCrj]  
 SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                                                   | Control       | 100ppb        | 500ppb        | 2000ppb       |
|------------------------------------------------------------------------------|---------------|---------------|---------------|---------------|
| SITE : thyroid<br>TUMOR : C-cell adenoma, C-cell carcinoma                   |               |               |               |               |
| Tumor rate                                                                   |               |               |               |               |
| Overall rates(a)                                                             | 13/50 ( 26.0) | 10/50 ( 20.0) | 10/50 ( 20.0) | 10/50 ( 20.0) |
| Adjusted rates(b)                                                            | 27.91         | 23.81         | 21.95         | 26.47         |
| Terminal rates(c)                                                            | 12/43 ( 27.9) | 10/42 ( 23.8) | 9/41 ( 22.0)  | 9/34 ( 26.5)  |
| Statistical analysis                                                         |               |               |               |               |
| Peto test                                                                    |               |               |               |               |
| Standard method(d)                                                           | P = -----     |               |               |               |
| Prevalence method(d)                                                         | P = 0.4971    |               |               |               |
| Combined analysis(d)                                                         | P = -----     |               |               |               |
| Cochran-Armitage test(e)                                                     | P = 0.6754    |               |               |               |
| Fisher Exact test(e)                                                         |               | P = 0.3176    | P = 0.3176    | P = 0.3176    |
| SITE : adrenal gland<br>TUMOR : pheochromocytoma, pheochromocytoma:malignant |               |               |               |               |
| Tumor rate                                                                   |               |               |               |               |
| Overall rates(a)                                                             | 1/50 ( 2.0)   | 1/50 ( 2.0)   | 3/50 ( 6.0)   | 1/50 ( 2.0)   |
| Adjusted rates(b)                                                            | 2.33          | 2.38          | 4.17          | 0.0           |
| Terminal rates(c)                                                            | 1/43 ( 2.3)   | 1/42 ( 2.4)   | 1/41 ( 2.4)   | 0/34 ( 0.0)   |
| Statistical analysis                                                         |               |               |               |               |
| Peto test                                                                    |               |               |               |               |
| Standard method(d)                                                           | P = 0.1587    |               |               |               |
| Prevalence method(d)                                                         | P = 0.8072    |               |               |               |
| Combined analysis(d)                                                         | P = 0.5072    |               |               |               |
| Cochran-Armitage test(e)                                                     | P = 0.8767    |               |               |               |
| Fisher Exact test(e)                                                         |               | P = 0.7525    | P = 0.3087    | P = 0.7525    |
| SITE : uterus<br>TUMOR : endometrial stromal polyp                           |               |               |               |               |
| Tumor rate                                                                   |               |               |               |               |
| Overall rates(a)                                                             | 7/50 ( 14.0)  | 7/50 ( 14.0)  | 4/50 ( 8.0)   | 10/50 ( 20.0) |
| Adjusted rates(b)                                                            | 14.58         | 16.67         | 9.52          | 22.50         |
| Terminal rates(c)                                                            | 6/43 ( 14.0)  | 7/42 ( 16.7)  | 3/41 ( 7.3)   | 7/34 ( 20.6)  |
| Statistical analysis                                                         |               |               |               |               |
| Peto test                                                                    |               |               |               |               |
| Standard method(d)                                                           | P = -----     |               |               |               |
| Prevalence method(d)                                                         | P = 0.1148    |               |               |               |
| Combined analysis(d)                                                         | P = -----     |               |               |               |
| Cochran-Armitage test(e)                                                     | P = 0.2526    |               |               |               |
| Fisher Exact test(e)                                                         |               | P = 0.6129    | P = 0.2623    | P = 0.2977    |

STUDY No. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                       | Control    | 100ppb      | 500ppb     | 2000ppb    |
|--------------------------------------------------|------------|-------------|------------|------------|
| SITE : uterus<br>TUMOR : adenocarcinoma          |            |             |            |            |
| Tumor rate                                       |            |             |            |            |
| Overall rates(a)                                 | 3/50( 6.0) | 1/50( 2.0)  | 0/50( 0.0) | 1/50( 2.0) |
| Adjusted rates(b)                                | 6.98       | 2.38        | 0.0        | 2.94       |
| Terminal rates(c)                                | 3/43( 7.0) | 1/42( 2.4)  | 0/41( 0.0) | 1/34( 2.9) |
| Statistical analysis                             |            |             |            |            |
| Peto test                                        |            |             |            |            |
| Standard method(d)                               | P = -----  |             |            |            |
| Prevalence method(d)                             | P = 0.6425 |             |            |            |
| Combined analysis(d)                             | P = -----  |             |            |            |
| Cochran-Armitage test(e)                         | P = 0.5158 |             |            |            |
| Fisher Exact test(e)                             |            | P = 0.3087  | P = 0.1212 | P = 0.3087 |
| SITE : uterus<br>TUMOR : adenoma, adenocarcinoma |            |             |            |            |
| Tumor rate                                       |            |             |            |            |
| Overall rates(a)                                 | 3/50( 6.0) | 1/50( 2.0)  | 1/50( 2.0) | 1/50( 2.0) |
| Adjusted rates(b)                                | 6.98       | 2.38        | 2.44       | 2.94       |
| Terminal rates(c)                                | 3/43( 7.0) | 1/42( 2.4)  | 1/41( 2.4) | 1/34( 2.9) |
| Statistical analysis                             |            |             |            |            |
| Peto test                                        |            |             |            |            |
| Standard method(d)                               | P = -----  |             |            |            |
| Prevalence method(d)                             | P = 0.6495 |             |            |            |
| Combined analysis(d)                             | P = -----  |             |            |            |
| Cochran-Armitage test(e)                         | P = 0.5014 |             |            |            |
| Fisher Exact test(e)                             |            | P = 0.3087  | P = 0.3087 | P = 0.3087 |
| SITE : mammary gland<br>TUMOR : fibroadenoma     |            |             |            |            |
| Tumor rate                                       |            |             |            |            |
| Overall rates(a)                                 | 4/50( 8.0) | 6/50( 12.0) | 2/50( 4.0) | 3/50( 6.0) |
| Adjusted rates(b)                                | 9.30       | 11.11       | 4.88       | 8.82       |
| Terminal rates(c)                                | 4/43( 9.3) | 4/42( 9.5)  | 2/41( 4.9) | 3/34( 8.8) |
| Statistical analysis                             |            |             |            |            |
| Peto test                                        |            |             |            |            |
| Standard method(d)                               | P = 0.4846 |             |            |            |
| Prevalence method(d)                             | P = 0.6254 |             |            |            |
| Combined analysis(d)                             | P = 0.6826 |             |            |            |
| Cochran-Armitage test(e)                         | P = 0.4715 |             |            |            |
| Fisher Exact test(e)                             |            | P = 0.3703  | P = 0.3389 | P = 0.5000 |

STUDY No. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                                            | Control    | 100ppb      | 500ppb     | 2000ppb    |
|-----------------------------------------------------------------------|------------|-------------|------------|------------|
| SITE : mammary gland<br>TUMOR : adenoma, fibroadenoma                 |            |             |            |            |
| Tumor rate                                                            |            |             |            |            |
| Overall rates(a)                                                      | 4/50( 8.0) | 7/50( 14.0) | 3/50( 6.0) | 3/50( 6.0) |
| Adjusted rates(b)                                                     | 9.30       | 12.77       | 7.32       | 8.82       |
| Terminal rates(c)                                                     | 4/43( 9.3) | 4/42( 9.5)  | 3/41( 7.3) | 3/34( 8.8) |
| Statistical analysis                                                  |            |             |            |            |
| Peto test                                                             |            |             |            |            |
| Standard method(d)                                                    | P = 0.4846 |             |            |            |
| Prevalence method(d)                                                  | P = 0.7313 |             |            |            |
| Combined analysis(d)                                                  | P = 0.7754 |             |            |            |
| Cochran-Armitage test(e)                                              | P = 0.3673 |             |            |            |
| Fisher Exact test(e)                                                  |            | P = 0.2623  | P = 0.5000 | P = 0.5000 |
| SITE : mammary gland<br>TUMOR : adenoma, fibroadenoma, adenocarcinoma |            |             |            |            |
| Tumor rate                                                            |            |             |            |            |
| Overall rates(a)                                                      | 4/50( 8.0) | 9/50( 18.0) | 4/50( 8.0) | 4/50( 8.0) |
| Adjusted rates(b)                                                     | 9.30       | 17.02       | 9.76       | 8.82       |
| Terminal rates(c)                                                     | 4/43( 9.3) | 6/42( 14.3) | 4/41( 9.8) | 3/34( 8.8) |
| Statistical analysis                                                  |            |             |            |            |
| Peto test                                                             |            |             |            |            |
| Standard method(d)                                                    | P = 0.2184 |             |            |            |
| Prevalence method(d)                                                  | P = 0.8200 |             |            |            |
| Combined analysis(d)                                                  | P = 0.7240 |             |            |            |
| Cochran-Armitage test(e)                                              | P = 0.4287 |             |            |            |
| Fisher Exact test(e)                                                  |            | P = 0.1168  | P = 0.6425 | P = 0.6425 |

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STUDY No. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

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| Group Name                                         | Control    | 100ppb     | 500ppb     | 2000ppb    |
|----------------------------------------------------|------------|------------|------------|------------|
| SITE : preputial/clitoral gland<br>TUMOR : adenoma |            |            |            |            |
| Tumor rate                                         |            |            |            |            |
| Overall rates(a)                                   | 1/50( 2.0) | 2/50( 4.0) | 3/50( 6.0) | 2/50( 4.0) |
| Adjusted rates(b)                                  | 2.33       | 4.76       | 7.32       | 4.08       |
| Terminal rates(c)                                  | 1/43( 2.3) | 2/42( 4.8) | 3/41( 7.3) | 1/34( 2.9) |
| Statistical analysis                               |            |            |            |            |
| Peto test                                          |            |            |            |            |
| Standard method(d)                                 | P = -----  |            |            |            |
| Prevalence method(d)                               | P = 0.3623 |            |            |            |
| Combined analysis(d)                               | P = -----  |            |            |            |
| Cochran-Armitage test(e)                           | P = 0.8219 |            |            |            |
| Fisher Exact test(e)                               |            | P = 0.5000 | P = 0.3087 | P = 0.5000 |

(HPT360A)

BAIS5

(a): Number of tumor-bearing animals/number of animals examined at the site.  
 (b): Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.  
 (c): Observed tumor incidence at terminal kill.  
 (d): Beneath the control incidence are the P-values associated with the trend test.  
     Standard method : Death analysis  
     Prevalence method : Incidental tumor test  
     Combined analysis : Death analysis + Incidental tumor test  
 (e): The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.  
 ? : The conditional probabilities of the largest and smallest possible out comes can not estimated or this P-value is beyond the estimated P-value.  
 ----- : There is no data which should be statistical analysis.  
 Significant difference : \* :  $P \leq 0.05$     \*\* :  $P \leq 0.01$   
 N.C.:Statistical value cannot be calculated and was not significant.

**TABLE N1**

**HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC  
LESIONS IN JAPAN BIOASSAY RESEARCH CENTER :  
F344/DuCr1Cr1j MALE RATS**

TABLE N1 HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN  
JAPAN BIOASSAY RESEARCH CENTER : F344/DuCr1Cr1j MALE RATS

| Organs<br>Tumors                        | No. of animals<br>examined | No. of animals<br>bearing tumor | Incidence<br>(%) | Min. - Max.<br>(%) |
|-----------------------------------------|----------------------------|---------------------------------|------------------|--------------------|
| Nasal cavity<br>Squamous cell carcinoma | 599                        | 0                               | 0.0              | 0 - 0              |

12 carcinogenicity studies examined in Japan Bioassay Research Center were used.

Study No. : 0457, 0535, 0560, 0610, 0667, 0675, 0686, 0704, 0731, 0753, 0774, 0794

**TABLE N2**

**HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC  
LESIONS IN JAPAN BIOASSAY RESEARCH CENTER :  
F344/DuCr1Cr1j FEMALE RATS**

TABLE N2 HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN  
JAPAN BIOASSAY RESEARCH CENTER : F344/DuCr1Cr1j FEMALE RATS

| Organs<br>Tumors        | No. of animals<br>examined | No. of animals<br>bearing tumor | Incidence<br>(%) | Min. - Max.<br>(%) |
|-------------------------|----------------------------|---------------------------------|------------------|--------------------|
| Nasal cavity            | 600                        |                                 |                  |                    |
| Rhabdomyoma             |                            | 0                               | 0.0              | 0 - 0              |
| Squamous cell carcinoma |                            | 0                               | 0.0              | 0 - 0              |
| Pituitary               | 599                        |                                 |                  |                    |
| Adenoma                 |                            | 165                             | 27.5             | 22 - 42            |

12 carcinogenicity studies examined in Japan Bioassay Research Center were used.

Study No. : 0457, 0535, 0560, 0610, 0667, 0675, 0686, 0704, 0731, 0753, 0774, 0794

TABLE O1

HISTOPATHOLOGICAL FINDINGS :  
NON-NEOPLASTIC LESIONS : MALE

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrIj[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 1

| Organ                            | Findings                                 | Group Name              | Control      |              |            |            | 0. 1ppm      |              |            |            | 0. 5ppm      |              |            |            | 2ppm         |              |             |            |
|----------------------------------|------------------------------------------|-------------------------|--------------|--------------|------------|------------|--------------|--------------|------------|------------|--------------|--------------|------------|------------|--------------|--------------|-------------|------------|
|                                  |                                          | No. of Animals on Study | 50           |              |            |            | 50           |              |            |            | 50           |              |            |            | 50           |              |             |            |
|                                  |                                          | Grade                   | 1+           | 2+           | 3+         | 4+         | 1+           | 2+           | 3+         | 4+         | 1+           | 2+           | 3+         | 4+         | 1+           | 2+           | 3+          | 4+         |
|                                  |                                          |                         | (%)          | (%)          | (%)        | (%)        | (%)          | (%)          | (%)        | (%)        | (%)          | (%)          | (%)        | (%)        | (%)          | (%)          | (%)         | (%)        |
| {Integumentary system/appandage} |                                          |                         |              |              |            |            |              |              |            |            |              |              |            |            |              |              |             |            |
| skin/app                         |                                          |                         | <50>         |              |            |            | <50>         |              |            |            | <50>         |              |            |            | <50>         |              |             |            |
|                                  | ulcer                                    |                         | 0<br>( 0 )   | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )   | 1<br>( 2 )   | 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 ) |
|                                  | scab                                     |                         | 1<br>( 2 )   | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )   | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 )   | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 )   | 0<br>( 0 )   | 0<br>( 0 )  | 0<br>( 0 ) |
| {Respiratory system}             |                                          |                         |              |              |            |            |              |              |            |            |              |              |            |            |              |              |             |            |
| nasal cavit                      |                                          |                         | <50>         |              |            |            | <50>         |              |            |            | <50>         |              |            |            | <50>         |              |             |            |
|                                  | exudate                                  |                         | 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 ) | 1<br>( 2 )   | 0<br>( 0 )   | 0<br>( 0 )  | 0<br>( 0 ) |
|                                  | thrombus                                 |                         | 1<br>( 2 )   | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 )   | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 )   | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 )   | 0<br>( 0 )   | 0<br>( 0 )  | 0<br>( 0 ) |
|                                  | mineralization                           |                         | 16<br>( 32 ) | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 22<br>( 44 ) | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 22<br>( 44 ) | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 16<br>( 32 ) | 0<br>( 0 )   | 0<br>( 0 )  | 0<br>( 0 ) |
|                                  | goblet cell hyperplasia                  |                         | 2<br>( 4 )   | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 )   | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 )   | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 35<br>( 70 ) | 1<br>( 2 )   | 0<br>( 0 )  | 0<br>( 0 ) |
|                                  | eosinophilic change:olfactory epithelium |                         | 16<br>( 32 ) | 15<br>( 30 ) | 4<br>( 8 ) | 0<br>( 0 ) | 22<br>( 44 ) | 11<br>( 22 ) | 3<br>( 6 ) | 0<br>( 0 ) | 27<br>( 54 ) | 12<br>( 24 ) | 3<br>( 6 ) | 0<br>( 0 ) | 16<br>( 32 ) | 26<br>( 52 ) | 6<br>( 12 ) | 0<br>( 0 ) |

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

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCrIj[F344/DuCrj]  
REPORT TYPE : A1  
SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
ALL ANIMALS (0-105W)

PAGE : 2

| Organ                                           | Findings                                   | Group Name              | Control |      |      |       | 0.1ppm |      |      |       | 0.5ppm |      |      |       | 2ppm  |       |      |      |
|-------------------------------------------------|--------------------------------------------|-------------------------|---------|------|------|-------|--------|------|------|-------|--------|------|------|-------|-------|-------|------|------|
|                                                 |                                            | No. of Animals on Study | 50      |      |      |       | 50     |      |      |       | 50     |      |      |       | 50    |       |      |      |
|                                                 |                                            | Grade                   | 1+      | 2+   | 3+   | 4+    | 1+     | 2+   | 3+   | 4+    | 1+     | 2+   | 3+   | 4+    | 1+    | 2+    | 3+   | 4+   |
|                                                 |                                            |                         | (%)     | (%)  | (%)  | (%)   | (%)    | (%)  | (%)  | (%)   | (%)    | (%)  | (%)  | (%)   | (%)   | (%)   | (%)  | (%)  |
| [Respiratory system]                            |                                            |                         |         |      |      |       |        |      |      |       |        |      |      |       |       |       |      |      |
| nasal cavit                                     |                                            |                         | <50>    |      |      |       | <50>   |      |      |       | <50>   |      |      |       | <50>  |       |      |      |
|                                                 | eosinophilic change:respiratory epithelium |                         | 0       | 0    | 0    | 0     | 0      | 0    | 0    | 0     | 4      | 0    | 0    | 0     | 0     | 0     | 0    | 0    |
|                                                 |                                            |                         | ( 0)    | ( 0) | ( 0) | ( 0)  | ( 0)   | ( 0) | ( 0) | ( 0)  | ( 8)   | ( 0) | ( 0) | ( 0)  | ( 0)  | ( 0)  | ( 0) | ( 0) |
|                                                 | inflammation:foreign body                  |                         | 13      | 1    | 0    | 0     | 11     | 0    | 0    | 0     | 11     | 3    | 0    | 0     | 26    | 17    | 0    | 0 ** |
|                                                 |                                            |                         | ( 26)   | ( 2) | ( 0) | ( 0)  | ( 22)  | ( 0) | ( 0) | ( 0)  | ( 22)  | ( 6) | ( 0) | ( 0)  | ( 52) | ( 34) | ( 0) | ( 0) |
|                                                 | inflammation:respiratory epithelium        |                         | 13      | 1    | 0    | 0     | 16     | 0    | 0    | 0     | 10     | 0    | 0    | 0     | 31    | 3     | 0    | 0 ** |
|                                                 |                                            |                         | ( 26)   | ( 2) | ( 0) | ( 0)  | ( 32)  | ( 0) | ( 0) | ( 0)  | ( 20)  | ( 0) | ( 0) | ( 0)  | ( 62) | ( 6)  | ( 0) | ( 0) |
|                                                 | inflammation:olfactory epithelium          |                         | 0       | 0    | 0    | 0     | 0      | 0    | 0    | 0     | 0      | 0    | 0    | 0     | 1     | 1     | 0    | 0    |
|                                                 |                                            |                         | ( 0)    | ( 0) | ( 0) | ( 0)  | ( 0)   | ( 0) | ( 0) | ( 0)  | ( 0)   | ( 0) | ( 0) | ( 0)  | ( 2)  | ( 2)  | ( 0) | ( 0) |
| respiratory metaplasia:olfactory epithelium     |                                            | 0                       | 0       | 0    | 0    | 0     | 0      | 0    | 0    | 0     | 0      | 0    | 0    | 29    | 20    | 0     | 0 ** |      |
|                                                 |                                            | ( 0)                    | ( 0)    | ( 0) | ( 0) | ( 0)  | ( 0)   | ( 0) | ( 0) | ( 0)  | ( 0)   | ( 0) | ( 0) | ( 58) | ( 40) | ( 0)  | ( 0) |      |
| respiratory metaplasia:gland                    |                                            | 15                      | 0       | 0    | 0    | 12    | 0      | 0    | 0    | 17    | 0      | 0    | 0    | 27    | 10    | 1     | 0 ** |      |
|                                                 |                                            | ( 30)                   | ( 0)    | ( 0) | ( 0) | ( 24) | ( 0)   | ( 0) | ( 0) | ( 34) | ( 0)   | ( 0) | ( 0) | ( 54) | ( 20) | ( 2)  | ( 0) |      |
| squamous cell metaplasia:respiratory epithelium |                                            | 0                       | 0       | 0    | 0    | 1     | 0      | 0    | 0    | 0     | 1      | 0    | 0    | 35    | 3     | 0     | 0 ** |      |
|                                                 |                                            | ( 0)                    | ( 0)    | ( 0) | ( 0) | ( 2)  | ( 0)   | ( 0) | ( 0) | ( 0)  | ( 2)   | ( 0) | ( 0) | ( 70) | ( 6)  | ( 0)  | ( 0) |      |
| ulcer:respiratory epithelium                    |                                            | 0                       | 0       | 0    | 0    | 0     | 0      | 0    | 0    | 0     | 0      | 0    | 1    | 0     | 0     | 0     | 0    |      |
|                                                 |                                            | ( 0)                    | ( 0)    | ( 0) | ( 0) | ( 0)  | ( 0)   | ( 0) | ( 0) | ( 0)  | ( 0)   | ( 0) | ( 2) | ( 0)  | ( 0)  | ( 0)  | ( 0) |      |

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

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrIj[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 3

| Organ_____           | Findings_____                       | Group Name              | Control |       |       |       | 0. 1ppm |       |       |       | 0. 5ppm |       |       |        | 2ppm   |       |       |       |
|----------------------|-------------------------------------|-------------------------|---------|-------|-------|-------|---------|-------|-------|-------|---------|-------|-------|--------|--------|-------|-------|-------|
|                      |                                     | No. of Animals on Study | 50      |       |       |       | 50      |       |       |       | 50      |       |       |        | 50     |       |       |       |
|                      |                                     | Grade                   | 1+      | 2+    | 3+    | 4+    | 1+      | 2+    | 3+    | 4+    | 1+      | 2+    | 3+    | 4+     | 1+     | 2+    | 3+    | 4+    |
|                      |                                     |                         | (%)     | (%)   | (%)   | (%)   | (%)     | (%)   | (%)   | (%)   | (%)     | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)   |
| [Respiratory system] |                                     |                         |         |       |       |       |         |       |       |       |         |       |       |        |        |       |       |       |
| nasal cavit          |                                     |                         | <50>    |       |       |       | <50>    |       |       |       | <50>    |       |       |        | <50>   |       |       |       |
|                      | hyperplasia:transitional epithelium |                         | 0       | 0     | 0     | 0     | 0       | 0     | 0     | 0     | 0       | 0     | 0     | 0      | 41     | 1     | 0     | 0 **  |
|                      |                                     |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 )  | ( 82 ) | ( 2 ) | ( 0 ) | ( 0 ) |
|                      | atrophy:olfactory epithelium        |                         | 0       | 0     | 0     | 0     | 0       | 0     | 0     | 0     | 0       | 0     | 0     | 0      | 28     | 2     | 0     | 0 **  |
|                      |                                     |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 )  | ( 56 ) | ( 4 ) | ( 0 ) | ( 0 ) |
|                      | edema:lamina propria                |                         | 0       | 0     | 0     | 0     | 0       | 0     | 0     | 0     | 0       | 0     | 0     | 0      | 17     | 9     | 0     | 0 **  |
|                      |                                     | ( 0 )                   | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 34 ) | ( 18 ) | ( 0 ) | ( 0 ) |       |
|                      | adhesion:turbinate                  |                         | 0       | 0     | 0     | 0     | 0       | 0     | 0     | 0     | 0       | 0     | 0     | 10     | 0      | 0     | 0 **  |       |
|                      |                                     |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 20 ) | ( 0 )  | ( 0 ) | ( 0 ) |       |
|                      | proliferation:striated muscle       |                         | 0       | 0     | 0     | 0     | 0       | 0     | 0     | 0     | 0       | 0     | 0     | 3      | 3      | 0     | 0 *   |       |
|                      |                                     |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 6 )  | ( 6 )  | ( 0 ) | ( 0 ) |       |
| larynx               |                                     |                         | <50>    |       |       |       | <50>    |       |       |       | <50>    |       |       |        | <50>   |       |       |       |
|                      | inflammation                        |                         | 4       | 0     | 0     | 0     | 2       | 0     | 0     | 0     | 5       | 0     | 0     | 0      | 0      | 0     | 0     | 0     |
|                      |                                     |                         | ( 8 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 10 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
| lung                 |                                     |                         | <50>    |       |       |       | <50>    |       |       |       | <50>    |       |       |        | <50>   |       |       |       |
|                      | hemorrhage                          |                         | 0       | 3     | 0     | 0     | 0       | 2     | 0     | 0     | 2       | 0     | 0     | 0      | 1      | 0     | 0     | 0     |
|                      |                                     |                         | ( 0 )   | ( 6 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 4 ) | ( 0 ) | ( 0 ) | ( 4 )   | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) |

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe  
 < a > a : Number of animals examined at the site  
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STUDY NO. : 0816  
ANIMAL : RAT F344/DuCrIj[F344/DuCrj]  
REPORT TYPE : A1  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
ALL ANIMALS (0-105W)

PAGE : 4

| Organ                  | Findings                              | Group Name              | Control    |            |            |            | 0.1ppm     |            |            |            | 0.5ppm      |            |            |            | 2ppm        |            |            |            |
|------------------------|---------------------------------------|-------------------------|------------|------------|------------|------------|------------|------------|------------|------------|-------------|------------|------------|------------|-------------|------------|------------|------------|
|                        |                                       | No. of Animals on Study | 50         |            |            |            | 50         |            |            |            | 50          |            |            |            | 50          |            |            |            |
|                        |                                       | Grade                   | 1+<br>(%)  | 2+<br>(%)  | 3+<br>(%)  | 4+<br>(%)  | 1+<br>(%)  | 2+<br>(%)  | 3+<br>(%)  | 4+<br>(%)  | 1+<br>(%)   | 2+<br>(%)  | 3+<br>(%)  | 4+<br>(%)  | 1+<br>(%)   | 2+<br>(%)  | 3+<br>(%)  | 4+<br>(%)  |
| {Respiratory system}   |                                       |                         |            |            |            |            |            |            |            |            |             |            |            |            |             |            |            |            |
| lung                   | edema                                 |                         | 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 ) | 1<br>( 2 )  | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |
|                        | inflammatory infiltration             |                         | 2<br>( 4 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 2<br>( 4 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 2<br>( 4 )  | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 2<br>( 4 )  | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |
|                        | osseous metaplasia                    |                         | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 ) | 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 ) |
|                        | accumulation of foamy cells           |                         | 3<br>( 6 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 4<br>( 8 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 2<br>( 4 )  | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |
|                        | bronchiolar-alveolar cell hyperplasia |                         | 3<br>( 6 ) | 1<br>( 2 ) | 1<br>( 2 ) | 0<br>( 0 ) | 4<br>( 8 ) | 2<br>( 4 ) | 1<br>( 2 ) | 0<br>( 0 ) | 8<br>( 16 ) | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) | 5<br>( 10 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |
| {Hematopoietic system} |                                       |                         |            |            |            |            |            |            |            |            |             |            |            |            |             |            |            |            |
| bone marrow            | granulation                           |                         | 3<br>( 6 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 4<br>( 8 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 6<br>( 12 ) | 0<br>( 0 ) | 2<br>( 4 ) | 0<br>( 0 ) | 2<br>( 4 )  | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |
|                        | erythropoiesis:increased              |                         | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 4<br>( 8 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 4<br>( 8 )  | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 6<br>( 12 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe  
< a > a : Number of animals examined at the site  
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STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrIj[F344/DuCrj]  
 REPORT TYPE : A1  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 5

| Organ_____             | Findings_____                | Group Name              | Control      |            |            |             | 0.1ppm       |            |            |            | 0.5ppm       |            |            |            | 2ppm         |            |            |            |
|------------------------|------------------------------|-------------------------|--------------|------------|------------|-------------|--------------|------------|------------|------------|--------------|------------|------------|------------|--------------|------------|------------|------------|
|                        |                              | No. of Animals on Study | 50           |            |            |             | 50           |            |            |            | 50           |            |            |            | 50           |            |            |            |
|                        |                              | Grade                   | 1+<br>(%)    | 2+<br>(%)  | 3+<br>(%)  | 4+<br>(%)   | 1+<br>(%)    | 2+<br>(%)  | 3+<br>(%)  | 4+<br>(%)  | 1+<br>(%)    | 2+<br>(%)  | 3+<br>(%)  | 4+<br>(%)  | 1+<br>(%)    | 2+<br>(%)  | 3+<br>(%)  | 4+<br>(%)  |
| {Hematopoietic system} |                              |                         |              |            |            |             |              |            |            |            |              |            |            |            |              |            |            |            |
| bone marrow            | granulopoiesis:increased     |                         | <50>         |            |            |             | <50>         |            |            |            | <50>         |            |            |            | <50>         |            |            |            |
|                        |                              | 1<br>( 2 )              | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 )  | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 4<br>( 8 ) | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 4<br>( 8 ) | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) |            |
| lymph node             | granulation                  |                         | <50>         |            |            |             | <50>         |            |            |            | <50>         |            |            |            | <50>         |            |            |            |
|                        |                              | 0<br>( 0 )              | 1<br>( 2 )   | 0<br>( 0 ) | 0<br>( 0 ) | 2<br>( 4 )  | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 3<br>( 6 ) | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 ) | 1<br>( 2 )   | 0<br>( 0 ) | 0<br>( 0 ) |            |
|                        | lymphadenitis                |                         | 1<br>( 2 )   | 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 )   | 0<br>( 0 ) | 0<br>( 0 ) |            |
| spleen                 | deposit of hemosiderin       |                         | <50>         |            |            |             | <50>         |            |            |            | <50>         |            |            |            | <50>         |            |            |            |
|                        |                              | 3<br>( 6 )              | 1<br>( 2 )   | 0<br>( 0 ) | 0<br>( 0 ) | 5<br>( 10 ) | 2<br>( 4 )   | 0<br>( 0 ) | 0<br>( 0 ) | 3<br>( 6 ) | 1<br>( 2 )   | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 ) | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) |            |
|                        | fibrosis:focal               |                         | 0<br>( 0 )   | 2<br>( 4 ) | 0<br>( 0 ) | 0<br>( 0 )  | 0<br>( 0 )   | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 )   | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 2<br>( 4 )   | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) |
|                        | extramedullary hematopoiesis |                         | 15<br>( 30 ) | 3<br>( 6 ) | 0<br>( 0 ) | 0<br>( 0 )  | 12<br>( 24 ) | 4<br>( 8 ) | 1<br>( 2 ) | 0<br>( 0 ) | 17<br>( 34 ) | 2<br>( 4 ) | 3<br>( 6 ) | 0<br>( 0 ) | 13<br>( 26 ) | 2<br>( 4 ) | 1<br>( 2 ) | 0<br>( 0 ) |
| {Circulatory system}   |                              |                         |              |            |            |             |              |            |            |            |              |            |            |            |              |            |            |            |
| heart                  | mineralization               |                         | <50>         |            |            |             | <50>         |            |            |            | <50>         |            |            |            | <50>         |            |            |            |
|                        |                              | 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>( 2 ) | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |

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

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrI CrI j [F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 6

| Organ                | Findings                  | Group Name              | Control |      |      |      | 0.1ppm |      |      |      | 0.5ppm |      |      |      | 2ppm  |      |      |      |
|----------------------|---------------------------|-------------------------|---------|------|------|------|--------|------|------|------|--------|------|------|------|-------|------|------|------|
|                      |                           | No. of Animals on Study | 50      |      |      |      | 50     |      |      |      | 50     |      |      |      | 50    |      |      |      |
|                      |                           | Grade                   | 1+      | 2+   | 3+   | 4+   | 1+     | 2+   | 3+   | 4+   | 1+     | 2+   | 3+   | 4+   | 1+    | 2+   | 3+   | 4+   |
|                      |                           |                         | (%)     | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  | (%)    | (%)  | (%)  | (%)  | (%)   | (%)  | (%)  | (%)  |
| {Circulatory system} |                           |                         |         |      |      |      |        |      |      |      |        |      |      |      |       |      |      |      |
| heart                | myocardial fibrosis       |                         | <50>    |      |      |      | <50>   |      |      |      | <50>   |      |      |      | <50>  |      |      |      |
|                      |                           |                         | 25      | 1    | 0    | 0    | 26     | 0    | 0    | 0    | 33     | 1    | 0    | 0    | 23    | 0    | 0    | 0    |
|                      |                           |                         | ( 50)   | ( 2) | ( 0) | ( 0) | ( 52)  | ( 0) | ( 0) | ( 0) | ( 66)  | ( 2) | ( 0) | ( 0) | ( 46) | ( 0) | ( 0) | ( 0) |
| {Digestive system}   |                           |                         |         |      |      |      |        |      |      |      |        |      |      |      |       |      |      |      |
| tongue               | mineralization            |                         | <50>    |      |      |      | <50>   |      |      |      | <50>   |      |      |      | <50>  |      |      |      |
|                      |                           |                         | 1       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0     | 0    | 0    | 0    |
|                      |                           |                         | ( 2)    | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)  | ( 0) | ( 0) | ( 0) |
| stomach              | mineralization            |                         | <50>    |      |      |      | <50>   |      |      |      | <50>   |      |      |      | <50>  |      |      |      |
|                      |                           |                         | 0       | 1    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0     | 0    | 0    | 0    |
|                      |                           |                         | ( 0)    | ( 2) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)  | ( 0) | ( 0) | ( 0) |
|                      | inflammatory infiltration |                         | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 1      | 0    | 0    | 0    | 0     | 0    | 0    | 0    |
|                      |                           |                         | ( 0)    | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 2)   | ( 0) | ( 0) | ( 0) | ( 0)  | ( 0) | ( 0) | ( 0) |
|                      | erosion:forestomach       |                         | 0       | 0    | 0    | 0    | 1      | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0     | 0    | 0    | 0    |
|                      |                           |                         | ( 0)    | ( 0) | ( 0) | ( 0) | ( 2)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)  | ( 0) | ( 0) | ( 0) |
|                      | ulcer:forestomach         |                         | 1       | 0    | 0    | 0    | 0      | 0    | 0    | 0    | 0      | 3    | 0    | 0    | 0     | 1    | 0    | 0    |
|                      |                           |                         | ( 2)    | ( 0) | ( 0) | ( 0) | ( 0)   | ( 0) | ( 0) | ( 0) | ( 0)   | ( 6) | ( 0) | ( 0) | ( 0)  | ( 2) | ( 0) | ( 0) |

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

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 7

| Organ_____         | Findings_____                 | Group Name              | Control |       |       |       | 0. 1ppm |       |       |       | 0. 5ppm |       |       |       | 2ppm   |       |       |       |
|--------------------|-------------------------------|-------------------------|---------|-------|-------|-------|---------|-------|-------|-------|---------|-------|-------|-------|--------|-------|-------|-------|
|                    |                               | No. of Animals on Study | 50      |       |       |       | 50      |       |       |       | 50      |       |       |       | 50     |       |       |       |
|                    |                               | Grade                   | 1+      | 2+    | 3+    | 4+    | 1+      | 2+    | 3+    | 4+    | 1+      | 2+    | 3+    | 4+    | 1+     | 2+    | 3+    | 4+    |
|                    |                               |                         | (%)     | (%)   | (%)   | (%)   | (%)     | (%)   | (%)   | (%)   | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   |
| [Digestive system] |                               |                         |         |       |       |       |         |       |       |       |         |       |       |       |        |       |       |       |
| stomach            |                               |                         | <50>    |       |       |       | <50>    |       |       |       | <50>    |       |       |       | <50>   |       |       |       |
|                    | hyperplasia:forestomach       |                         | 4       | 0     | 0     | 0     | 1       | 0     | 0     | 0     | 2       | 0     | 0     | 0     | 1      | 1     | 0     | 0     |
|                    |                               |                         | ( 8 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 2 ) | ( 0 ) | ( 0 ) |
|                    | erosion:glandular stomach     |                         | 4       | 0     | 0     | 0     | 4       | 0     | 0     | 0     | 2       | 0     | 0     | 0     | 2      | 0     | 0     | 0     |
|                    |                               |                         | ( 8 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 8 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                    | ulcer:glandular stomach       |                         | 2       | 1     | 0     | 0     | 0       | 0     | 0     | 0     | 3       | 0     | 0     | 0     | 2      | 0     | 0     | 0     |
|                    |                               |                         | ( 4 )   | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 6 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 4 ) | ( 0 )  | ( 0 ) | ( 0 ) |       |
|                    | hyperplasia:glandular stomach |                         | 1       | 0     | 0     | 0     | 0       | 0     | 0     | 2     | 0       | 0     | 0     | 1     | 0      | 0     | 0     |       |
|                    |                               |                         | ( 2 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 4 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 2 ) | ( 0 )  | ( 0 ) | ( 0 ) |       |
| small intes        |                               |                         | <50>    |       |       |       | <50>    |       |       |       | <50>    |       |       |       | <50>   |       |       |       |
|                    | inflammation                  |                         | 0       | 0     | 0     | 0     | 0       | 1     | 0     | 0     | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     |
|                    |                               |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
| liver              |                               |                         | <50>    |       |       |       | <50>    |       |       |       | <50>    |       |       |       | <50>   |       |       |       |
|                    | herniation                    |                         | 5       | 0     | 0     | 0     | 5       | 0     | 0     | 0     | 5       | 0     | 0     | 0     | 8      | 0     | 0     | 0     |
|                    |                               |                         | ( 10 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 10 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 10 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 16 ) | ( 0 ) | ( 0 ) | ( 0 ) |
|                    | necrosis:central              |                         | 0       | 0     | 0     | 0     | 1       | 0     | 0     | 0     | 0       | 1     | 0     | 0     | 0      | 1     | 0     | 0     |
|                    |                               |                         | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 ) | ( 0 ) | ( 0 ) |

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

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrIj[F344/DuCrj]  
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 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 8

| Organ_____                   | Findings_____             | Group Name              | Control |      |      |       | 0. 1ppm |      |      |       | 0. 5ppm |      |      |       | 2ppm |      |      |      |
|------------------------------|---------------------------|-------------------------|---------|------|------|-------|---------|------|------|-------|---------|------|------|-------|------|------|------|------|
|                              |                           | No. of Animals on Study | 50      |      |      |       | 50      |      |      |       | 50      |      |      |       | 50   |      |      |      |
|                              |                           | Grade                   | 1+      | 2+   | 3+   | 4+    | 1+      | 2+   | 3+   | 4+    | 1+      | 2+   | 3+   | 4+    | 1+   | 2+   | 3+   | 4+   |
|                              |                           |                         | (%)     | (%)  | (%)  | (%)   | (%)     | (%)  | (%)  | (%)   | (%)     | (%)  | (%)  | (%)   | (%)  | (%)  | (%)  | (%)  |
| {Digestive system}           |                           |                         |         |      |      |       |         |      |      |       |         |      |      |       |      |      |      |      |
| liver                        |                           |                         | <50>    |      |      |       | <50>    |      |      |       | <50>    |      |      |       | <50> |      |      |      |
|                              | necrosis:peripheral       |                         | 1       | 0    | 0    | 0     | 0       | 0    | 0    | 0     | 0       | 0    | 0    | 0     | 0    | 0    | 0    | 0    |
|                              |                           |                         | ( 2)    | ( 0) | ( 0) | ( 0)  | ( 0)    | ( 0) | ( 0) | ( 0)  | ( 0)    | ( 0) | ( 0) | ( 0)  | ( 0) | ( 0) | ( 0) | ( 0) |
|                              | necrosis:focal            |                         | 1       | 0    | 0    | 0     | 1       | 2    | 0    | 0     | 0       | 0    | 0    | 0     | 0    | 0    | 0    | 0    |
|                              |                           |                         | ( 2)    | ( 0) | ( 0) | ( 0)  | ( 2)    | ( 4) | ( 0) | ( 0)  | ( 0)    | ( 0) | ( 0) | ( 0)  | ( 0) | ( 0) | ( 0) | ( 0) |
|                              | cyst                      |                         | 0       | 0    | 0    | 0     | 0       | 0    | 0    | 0     | 1       | 0    | 0    | 0     | 0    | 0    | 0    | 0    |
|                              |                           |                         | ( 0)    | ( 0) | ( 0) | ( 0)  | ( 0)    | ( 0) | ( 0) | ( 0)  | ( 2)    | ( 0) | ( 0) | ( 0)  | ( 0) | ( 0) | ( 0) | ( 0) |
|                              | inflammatory infiltration |                         | 0       | 1    | 0    | 0     | 0       | 0    | 0    | 0     | 0       | 0    | 0    | 0     | 0    | 0    | 0    | 0    |
|                              |                           |                         | ( 0)    | ( 2) | ( 0) | ( 0)  | ( 0)    | ( 0) | ( 0) | ( 0)  | ( 0)    | ( 0) | ( 0) | ( 0)  | ( 0) | ( 0) | ( 0) | ( 0) |
| lymphocytic infiltration     |                           | 0                       | 0       | 0    | 0    | 0     | 0       | 0    | 0    | 1     | 0       | 0    | 0    | 1     | 0    | 0    | 0    |      |
|                              |                           | ( 0)                    | ( 0)    | ( 0) | ( 0) | ( 0)  | ( 0)    | ( 0) | ( 0) | ( 2)  | ( 0)    | ( 0) | ( 0) | ( 2)  | ( 0) | ( 0) | ( 0) |      |
| granulation                  |                           | 6                       | 0       | 0    | 0    | 6     | 1       | 0    | 0    | 5     | 0       | 0    | 0    | 1     | 0    | 0    | 0    |      |
|                              |                           | ( 12)                   | ( 0)    | ( 0) | ( 0) | ( 12) | ( 2)    | ( 0) | ( 0) | ( 10) | ( 0)    | ( 0) | ( 0) | ( 2)  | ( 0) | ( 0) | ( 0) |      |
| inflammatory cell nest       |                           | 4                       | 0       | 0    | 0    | 3     | 3       | 0    | 0    | 2     | 1       | 1    | 0    | 7     | 0    | 0    | 0    |      |
|                              |                           | ( 8)                    | ( 0)    | ( 0) | ( 0) | ( 6)  | ( 6)    | ( 0) | ( 0) | ( 4)  | ( 2)    | ( 2) | ( 0) | ( 14) | ( 0) | ( 0) | ( 0) |      |
| extramedullary hematopoiesis |                           | 0                       | 0       | 0    | 0    | 0     | 0       | 0    | 0    | 0     | 0       | 0    | 0    | 1     | 0    | 0    | 0    |      |
|                              |                           | ( 0)                    | ( 0)    | ( 0) | ( 0) | ( 0)  | ( 0)    | ( 0) | ( 0) | ( 0)  | ( 0)    | ( 0) | ( 0) | ( 2)  | ( 0) | ( 0) | ( 0) |      |

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

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrI CrI j [F344/DuCrj]  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 9

| Organ_____         | Findings_____              | Group Name              | Control |      |      |       | 0.1ppm |      |      |       | 0.5ppm |      |      |       | 2ppm |      |      |      |
|--------------------|----------------------------|-------------------------|---------|------|------|-------|--------|------|------|-------|--------|------|------|-------|------|------|------|------|
|                    |                            | No. of Animals on Study | 50      |      |      |       | 50     |      |      |       | 50     |      |      |       | 50   |      |      |      |
|                    |                            | Grade                   | 1+      | 2+   | 3+   | 4+    | 1+     | 2+   | 3+   | 4+    | 1+     | 2+   | 3+   | 4+    | 1+   | 2+   | 3+   | 4+   |
|                    |                            |                         | (%)     | (%)  | (%)  | (%)   | (%)    | (%)  | (%)  | (%)   | (%)    | (%)  | (%)  | (%)   | (%)  | (%)  | (%)  | (%)  |
| {Digestive system} |                            |                         |         |      |      |       |        |      |      |       |        |      |      |       |      |      |      |      |
| liver              |                            |                         | <50>    |      |      |       | <50>   |      |      |       | <50>   |      |      |       | <50> |      |      |      |
|                    | clear cell focus           | 3                       | 0       | 0    | 0    | 0     | 0      | 0    | 0    | 0     | 1      | 0    | 0    | 0     | 0    | 0    | 0    | 0    |
|                    |                            | ( 6)                    | ( 0)    | ( 0) | ( 0) | ( 0)  | ( 0)   | ( 0) | ( 0) | ( 0)  | ( 2)   | ( 0) | ( 0) | ( 0)  | ( 0) | ( 0) | ( 0) | ( 0) |
|                    | acidophilic cell focus     | 30                      | 4       | 3    | 0    | 18    | 4      | 1    | 0 *  | 20    | 3      | 2    | 0    | 16    | 0    | 0    | 0    | 0 ** |
|                    |                            | ( 60)                   | ( 8)    | ( 6) | ( 0) | ( 36) | ( 8)   | ( 2) | ( 0) | ( 40) | ( 6)   | ( 4) | ( 0) | ( 32) | ( 0) | ( 0) | ( 0) | ( 0) |
|                    | basophilic cell focus      | 6                       | 1       | 0    | 0    | 4     | 0      | 0    | 0    | 5     | 0      | 0    | 0    | 6     | 0    | 0    | 0    | 0    |
|                    |                            | ( 12)                   | ( 2)    | ( 0) | ( 0) | ( 8)  | ( 0)   | ( 0) | ( 0) | ( 10) | ( 0)   | ( 0) | ( 0) | ( 12) | ( 0) | ( 0) | ( 0) | ( 0) |
|                    | spongiosis hepatitis       | 2                       | 0       | 0    | 0    | 1     | 0      | 0    | 0    | 2     | 1      | 0    | 0    | 2     | 0    | 0    | 0    | 0    |
|                    | ( 4)                       | ( 0)                    | ( 0)    | ( 0) | ( 2) | ( 0)  | ( 0)   | ( 0) | ( 4) | ( 2)  | ( 0)   | ( 0) | ( 4) | ( 0)  | ( 0) | ( 0) | ( 0) |      |
|                    | bile duct hyperplasia      | 39                      | 2       | 0    | 0    | 41    | 0      | 1    | 0    | 42    | 1      | 0    | 0    | 42    | 0    | 0    | 0    | 0    |
|                    |                            | ( 78)                   | ( 4)    | ( 0) | ( 0) | ( 82) | ( 0)   | ( 2) | ( 0) | ( 84) | ( 2)   | ( 0) | ( 0) | ( 84) | ( 0) | ( 0) | ( 0) | ( 0) |
|                    | focal fatty change         | 2                       | 0       | 0    | 0    | 2     | 0      | 0    | 0    | 2     | 0      | 0    | 0    | 6     | 0    | 0    | 0    | 0    |
|                    |                            | ( 4)                    | ( 0)    | ( 0) | ( 0) | ( 4)  | ( 0)   | ( 0) | ( 0) | ( 4)  | ( 0)   | ( 0) | ( 0) | ( 12) | ( 0) | ( 0) | ( 0) | ( 0) |
|                    | vacuolic change:peripheral | 0                       | 0       | 1    | 0    | 0     | 0      | 0    | 0    | 0     | 0      | 0    | 0    | 1     | 0    | 0    | 0    | 0    |
|                    |                            | ( 0)                    | ( 0)    | ( 2) | ( 0) | ( 0)  | ( 0)   | ( 0) | ( 0) | ( 0)  | ( 0)   | ( 0) | ( 0) | ( 2)  | ( 0) | ( 0) | ( 0) | ( 0) |
| bile duct          |                            |                         | <50>    |      |      |       | <50>   |      |      |       | <50>   |      |      |       | <50> |      |      |      |
|                    | dilatation                 | 0                       | 0       | 0    | 0    | 0     | 0      | 1    | 0    | 0     | 0      | 0    | 0    | 0     | 0    | 0    | 0    | 0    |
|                    |                            | ( 0)                    | ( 0)    | ( 0) | ( 0) | ( 0)  | ( 0)   | ( 2) | ( 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  
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ANIMAL : RAT F344/DuCrI CrI j [F344/DuCrj]  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
ALL ANIMALS (0-105W)

PAGE : 10

| Organ_____         | Findings_____                       | Group Name              | Control    |            |            |            | 0.1ppm      |            |            |            | 0.5ppm     |            |            |            | 2ppm       |            |            |            |
|--------------------|-------------------------------------|-------------------------|------------|------------|------------|------------|-------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
|                    |                                     | No. of Animals on Study | 50         |            |            |            | 50          |            |            |            | 50         |            |            |            | 50         |            |            |            |
|                    |                                     | Grade                   | 1+<br>(%)  | 2+<br>(%)  | 3+<br>(%)  | 4+<br>(%)  | 1+<br>(%)   | 2+<br>(%)  | 3+<br>(%)  | 4+<br>(%)  | 1+<br>(%)  | 2+<br>(%)  | 3+<br>(%)  | 4+<br>(%)  | 1+<br>(%)  | 2+<br>(%)  | 3+<br>(%)  | 4+<br>(%)  |
| {Digestive system} |                                     |                         |            |            |            |            |             |            |            |            |            |            |            |            |            |            |            |            |
| pancreas           |                                     |                         | <50>       |            |            |            | <50>        |            |            |            | <50>       |            |            |            | <50>       |            |            |            |
|                    | atrophy                             |                         | 4<br>( 8 ) | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) | 5<br>( 10 ) | 1<br>( 2 ) | 1<br>( 2 ) | 0<br>( 0 ) | 3<br>( 6 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 3<br>( 6 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |
|                    | islet cell hyperplasia              |                         | 1<br>( 2 ) | 2<br>( 4 ) | 0<br>( 0 ) | 0<br>( 0 ) | 2<br>( 4 )  | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 ) | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) | 3<br>( 6 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |
|                    | hyperplasia:acinar cell             |                         | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 )  | 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 ) |
| {Urinary system}   |                                     |                         |            |            |            |            |             |            |            |            |            |            |            |            |            |            |            |            |
| kidney             |                                     |                         | <50>       |            |            |            | <50>        |            |            |            | <50>       |            |            |            | <50>       |            |            |            |
|                    | hyperplasia:tubular epithelial cell |                         | 1<br>( 2 ) | 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 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |
|                    | thrombus                            |                         | 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>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |
|                    | basophilic change                   |                         | 1<br>( 2 ) | 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 ) | 0<br>( 0 ) | 0<br>( 0 ) |            |
|                    | deposit of hemosiderin              |                         | 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>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |            |

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

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrI CrI j [F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 11

| Organ_____         | Findings_____                        | Group Name              | Control |        |        |       | 0. 1ppm |        |        |       | 0. 5ppm |        |        |       | 2ppm   |        |       |       |
|--------------------|--------------------------------------|-------------------------|---------|--------|--------|-------|---------|--------|--------|-------|---------|--------|--------|-------|--------|--------|-------|-------|
|                    |                                      | No. of Animals on Study | 50      |        |        |       | 50      |        |        |       | 50      |        |        |       | 50     |        |       |       |
|                    |                                      | Grade                   | 1+      | 2+     | 3+     | 4+    | 1+      | 2+     | 3+     | 4+    | 1+      | 2+     | 3+     | 4+    | 1+     | 2+     | 3+    | 4+    |
|                    |                                      |                         | (%)     | (%)    | (%)    | (%)   | (%)     | (%)    | (%)    | (%)   | (%)     | (%)    | (%)    | (%)   | (%)    | (%)    | (%)   | (%)   |
| {Urinary system}   |                                      |                         |         |        |        |       |         |        |        |       |         |        |        |       |        |        |       |       |
| kidney             |                                      |                         | <50>    |        |        |       | <50>    |        |        |       | <50>    |        |        |       | <50>   |        |       |       |
|                    | chronic nephropathy                  |                         | 15      | 19     | 11     | 2     | 13      | 21     | 16     | 0     | 12      | 18     | 16     | 2     | 27     | 14     | 3     | 0 *   |
|                    |                                      |                         | ( 30 )  | ( 38 ) | ( 22 ) | ( 4 ) | ( 26 )  | ( 42 ) | ( 32 ) | ( 0 ) | ( 24 )  | ( 36 ) | ( 32 ) | ( 4 ) | ( 54 ) | ( 28 ) | ( 6 ) | ( 0 ) |
|                    | papillary necrosis                   |                         | 0       | 0      | 0      | 0     | 0       | 1      | 0      | 0     | 0       | 0      | 0      | 0     | 0      | 0      | 0     | 0     |
|                    |                                      |                         | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )   | ( 2 )  | ( 0 )  | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |
| urin bladd         |                                      |                         | <50>    |        |        |       | <50>    |        |        |       | <50>    |        |        |       | <50>   |        |       |       |
|                    | dilatation                           |                         | 2       | 0      | 0      | 0     | 1       | 0      | 0      | 0     | 1       | 0      | 0      | 0     | 2      | 0      | 0     | 0     |
|                    |                                      |                         | ( 4 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 2 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 2 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 4 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                    | inflammation                         |                         | 0       | 0      | 0      | 0     | 1       | 0      | 0      | 0     | 0       | 0      | 0      | 0     | 0      | 0      | 0     | 0     |
|                    |                                      |                         | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 2 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                    | papillary and/or nodular hyperplasia |                         | 0       | 1      | 0      | 0     | 1       | 0      | 0      | 0     | 0       | 0      | 0      | 0     | 1      | 0      | 0     | 0     |
|                    |                                      |                         | ( 0 )   | ( 2 )  | ( 0 )  | ( 0 ) | ( 2 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 2 )  | ( 0 )  | ( 0 ) | ( 0 ) |
| {Endocrine system} |                                      |                         |         |        |        |       |         |        |        |       |         |        |        |       |        |        |       |       |
| pituitary          |                                      |                         | <50>    |        |        |       | <50>    |        |        |       | <49>    |        |        |       | <50>   |        |       |       |
|                    | congestion                           |                         | 0       | 0      | 0      | 0     | 0       | 0      | 0      | 0     | 0       | 0      | 0      | 0     | 1      | 0      | 0     | 0     |
|                    |                                      |                         | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 )  | ( 0 ) | ( 2 )  | ( 0 )  | ( 0 ) | ( 0 ) |

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

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCrI CrIj [F344/DuCrj]  
REPORT TYPE : A1  
SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
ALL ANIMALS (0-105W)

PAGE : 12

| Organ              | Findings               | Group Name              | Control    |           |           |           | 0.1ppm     |            |           |           | 0.5ppm     |           |           |           | 2ppm       |           |           |           |
|--------------------|------------------------|-------------------------|------------|-----------|-----------|-----------|------------|------------|-----------|-----------|------------|-----------|-----------|-----------|------------|-----------|-----------|-----------|
|                    |                        | No. of Animals on Study | 50         |           |           |           | 50         |            |           |           | 50         |           |           |           | 50         |           |           |           |
|                    |                        | Grade                   | 1+<br>(%)  | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) | 1+<br>(%)  | 2+<br>(%)  | 3+<br>(%) | 4+<br>(%) | 1+<br>(%)  | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) | 1+<br>(%)  | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) |
| [Endocrine system] |                        |                         |            |           |           |           |            |            |           |           |            |           |           |           |            |           |           |           |
| pituitary          |                        |                         | <50>       |           |           |           | <50>       |            |           |           | <49>       |           |           |           | <50>       |           |           |           |
|                    | angiectasis            |                         | 0<br>( 0)  | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 2)  | 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) |
|                    | cyst                   |                         | 3<br>( 6)  | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 6<br>( 12) | 0<br>( 0)  | 0<br>( 0) | 0<br>( 0) | 3<br>( 6)  | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 2<br>( 4)  | 1<br>( 2) | 0<br>( 0) | 0<br>( 0) |
|                    | hyperplasia            |                         | 7<br>( 14) | 3<br>( 6) | 1<br>( 2) | 0<br>( 0) | 7<br>( 14) | 2<br>( 4)  | 2<br>( 4) | 0<br>( 0) | 9<br>( 18) | 4<br>( 8) | 0<br>( 0) | 0<br>( 0) | 8<br>( 16) | 2<br>( 4) | 1<br>( 2) | 0<br>( 0) |
|                    | Rathke pouch           |                         | 5<br>( 10) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 2<br>( 4)  | 0<br>( 0)  | 0<br>( 0) | 0<br>( 0) | 5<br>( 10) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 3<br>( 6)  | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
| thyroid            |                        |                         | <50>       |           |           |           | <50>       |            |           |           | <50>       |           |           |           | <50>       |           |           |           |
|                    | cyst                   |                         | 1<br>( 2)  | 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)  | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
|                    | follicular hyperplasia |                         | 0<br>( 0)  | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)  | 0<br>( 0)  | 1<br>( 2) | 0<br>( 0) | 1<br>( 2)  | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 2)  | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
|                    | C-cell hyperplasia     |                         | 9<br>( 18) | 1<br>( 2) | 1<br>( 2) | 0<br>( 0) | 7<br>( 14) | 5<br>( 10) | 4<br>( 8) | 0<br>( 0) | 8<br>( 16) | 1<br>( 2) | 1<br>( 2) | 0<br>( 0) | 7<br>( 14) | 2<br>( 4) | 0<br>( 0) | 0<br>( 0) |
| adrenal            |                        |                         | <50>       |           |           |           | <50>       |            |           |           | <50>       |           |           |           | <50>       |           |           |           |
|                    | hemorrhage             |                         | 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) | 1<br>( 2)  | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |

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( c ) c : b / a \* 100  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 13

| Organ_____            | Findings_____                          | Group Name              | Control     |           |           |           | 0.1ppm      |           |           |           | 0.5ppm      |           |           |           | 2ppm        |           |           |           |
|-----------------------|----------------------------------------|-------------------------|-------------|-----------|-----------|-----------|-------------|-----------|-----------|-----------|-------------|-----------|-----------|-----------|-------------|-----------|-----------|-----------|
|                       |                                        | No. of Animals on Study | 50          |           |           |           | 50          |           |           |           | 50          |           |           |           | 50          |           |           |           |
|                       |                                        | Grade                   | 1+<br>(%)   | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) | 1+<br>(%)   | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) | 1+<br>(%)   | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) | 1+<br>(%)   | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) |
| {Endocrine system}    |                                        |                         |             |           |           |           |             |           |           |           |             |           |           |           |             |           |           |           |
| adrenal               |                                        |                         |             |           |           |           |             |           |           |           |             |           |           |           |             |           |           |           |
|                       | cyst                                   |                         | <50>        |           |           |           | <50>        |           |           |           | <50>        |           |           |           | <50>        |           |           |           |
|                       |                                        |                         | 0<br>( 0)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 2)   | 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) |
|                       | hyperplasia:medulla                    |                         | 2<br>( 4)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 2<br>( 4)   | 0<br>( 0) | 1<br>( 2) | 0<br>( 0) | 2<br>( 4)   | 1<br>( 2) | 0<br>( 0) | 0<br>( 0) | 3<br>( 6)   | 1<br>( 2) | 0<br>( 0) | 0<br>( 0) |
|                       | focal fatty change:cortex              |                         | 0<br>( 0)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 2<br>( 4)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 2<br>( 4)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 3<br>( 6)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
|                       | cortical vacuolation:diffuse           |                         | 0<br>( 0)   | 0<br>( 0) | 1<br>( 2) | 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) | 0<br>( 0) |
|                       | fatty change:corticomedullary junction |                         | 1<br>( 2)   | 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)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
| {Reproductive system} |                                        |                         |             |           |           |           |             |           |           |           |             |           |           |           |             |           |           |           |
| testis                |                                        |                         |             |           |           |           |             |           |           |           |             |           |           |           |             |           |           |           |
|                       | atrophy                                |                         | <50>        |           |           |           | <50>        |           |           |           | <50>        |           |           |           | <50>        |           |           |           |
|                       |                                        |                         | 38<br>( 76) | 1<br>( 2) | 0<br>( 0) | 0<br>( 0) | 45<br>( 90) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 39<br>( 78) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 46<br>( 92) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
|                       | interstitial cell hyperplasia          |                         | 2<br>( 4)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 2)   | 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) |

Grade 1+ : Slight 2+ : Moderate 3+ : Marked 4+ : Severe  
 < a > a : Number of animals examined at the site  
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 ( c ) c : b / a \* 100  
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STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrIj[F344/DuCrIj]  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 14

| Organ_____            | Findings_____    | Group Name              | Control      |            |            |            | 0.1ppm       |            |            |            | 0.5ppm       |             |            |            | 2ppm         |            |            |            |
|-----------------------|------------------|-------------------------|--------------|------------|------------|------------|--------------|------------|------------|------------|--------------|-------------|------------|------------|--------------|------------|------------|------------|
|                       |                  | No. of Animals on Study | 50           |            |            |            | 50           |            |            |            | 50           |             |            |            | 50           |            |            |            |
|                       |                  | Grade                   | 1+<br>(%)    | 2+<br>(%)  | 3+<br>(%)  | 4+<br>(%)  | 1+<br>(%)    | 2+<br>(%)  | 3+<br>(%)  | 4+<br>(%)  | 1+<br>(%)    | 2+<br>(%)   | 3+<br>(%)  | 4+<br>(%)  | 1+<br>(%)    | 2+<br>(%)  | 3+<br>(%)  | 4+<br>(%)  |
| {Reproductive system} |                  |                         |              |            |            |            |              |            |            |            |              |             |            |            |              |            |            |            |
| epididymis            | inflammation     |                         | <50>         |            |            |            | <50>         |            |            |            | <50>         |             |            |            | <50>         |            |            |            |
|                       |                  | 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>( 2 )   | 0<br>( 0 )  | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 )   | 0<br>( 0 ) | 0<br>( 0 ) |            |
| prostate              | inflammation     |                         | <50>         |            |            |            | <50>         |            |            |            | <50>         |             |            |            | <50>         |            |            |            |
|                       |                  | 11<br>( 22 )            | 1<br>( 2 )   | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 15<br>( 30 ) | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) | 12<br>( 24 ) | 0<br>( 0 )  | 0<br>( 0 ) | 0<br>( 0 ) | 14<br>( 28 ) | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) |
|                       | hyperplasia      |                         | 15<br>( 30 ) | 2<br>( 4 ) | 1<br>( 2 ) | 0<br>( 0 ) | 12<br>( 24 ) | 2<br>( 4 ) | 3<br>( 6 ) | 0<br>( 0 ) | 6<br>( 12 )  | 3<br>( 6 )  | 0<br>( 0 ) | 0<br>( 0 ) | 11<br>( 22 ) | 3<br>( 6 ) | 0<br>( 0 ) | 0<br>( 0 ) |
|                       |                  | mammary gl              | cyst         |            | <50>       |            |              |            | <50>       |            |              |             | <50>       |            |              |            | <50>       |            |
| 0<br>( 0 )            | 1<br>( 2 )       |                         |              | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 )   | 0<br>( 0 )  | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |
|                       | hyperplasia      |                         | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 )   | 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 ) |
|                       |                  | galactoceles            |              | 4<br>( 8 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )   | 3<br>( 6 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )   | 5<br>( 10 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |
|                       | {Nervous system} |                         |              |            |            |            |              |            |            |            |              |             |            |            |              |            |            |            |
|                       | brain            | hemorrhage              |              | <50>       |            |            |              | <50>       |            |            |              | <50>        |            |            |              | <50>       |            |            |
| 0<br>( 0 )            |                  |                         | 0<br>( 0 )   | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 )   | 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 ) |

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 ANIMAL : RAT F344/DuCrIj[F344/DuCrj]  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 15

| Organ_____                       | Findings_____             | Group Name              | Control    |            |            |            | 0.1ppm     |            |            |            | 0.5ppm     |            |            |            | 2ppm       |            |            |            |            |
|----------------------------------|---------------------------|-------------------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
|                                  |                           | No. of Animals on Study | 50         |            |            |            | 50         |            |            |            | 50         |            |            |            | 50         |            |            |            |            |
|                                  |                           | Grade                   | 1+<br>(%)  | 2+<br>(%)  | 3+<br>(%)  | 4+<br>(%)  | 1+<br>(%)  | 2+<br>(%)  | 3+<br>(%)  | 4+<br>(%)  | 1+<br>(%)  | 2+<br>(%)  | 3+<br>(%)  | 4+<br>(%)  | 1+<br>(%)  | 2+<br>(%)  | 3+<br>(%)  | 4+<br>(%)  |            |
|                                  |                           |                         |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |
| {Nervous system}                 |                           |                         |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |
| brain                            |                           |                         |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |
|                                  | gliosis                   |                         | <50>       |            |            |            | <50>       |            |            |            | <50>       |            |            |            | <50>       |            |            |            |            |
|                                  |                           |                         | 1<br>( 2 ) | 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 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |            |
| {Special sense organs/appendage} |                           |                         |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |
| eye                              |                           |                         |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |
|                                  | cataract                  |                         | <50>       |            |            |            | <50>       |            |            |            | <50>       |            |            |            | <50>       |            |            |            |            |
|                                  |                           |                         | 2<br>( 4 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 4<br>( 8 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 4<br>( 8 ) | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) | 3<br>( 6 ) | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) |
|                                  | retinal atrophy           |                         | 0<br>( 0 ) | 1<br>( 2 ) | 1<br>( 2 ) | 0<br>( 0 ) | 1<br>( 2 ) | 0<br>( 0 ) | 4<br>( 8 ) | 0<br>( 0 ) | 1<br>( 2 ) | 1<br>( 2 ) | 3<br>( 6 ) | 0<br>( 0 ) | 1<br>( 2 ) | 1<br>( 2 ) | 2<br>( 4 ) | 0<br>( 0 ) |            |
|                                  | keratitis                 |                         | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 ) | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) | 2<br>( 4 ) | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 ) | 1<br>( 2 ) | 0<br>( 0 ) |            |
| Harder gl                        |                           |                         |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |
|                                  | degeneration              |                         | <50>       |            |            |            | <50>       |            |            |            | <50>       |            |            |            | <50>       |            |            |            |            |
|                                  |                           |                         | 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 ) | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |            |
|                                  | inflammatory 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 ) | 3<br>( 6 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |            |

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

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrIj[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 16

|                                  |                           | Group Name              | Control    |            |            |            | 0.1ppm     |            |            |            | 0.5ppm     |            |            |            | 2ppm       |            |            |           |
|----------------------------------|---------------------------|-------------------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|-----------|
|                                  |                           | No. of Animals on Study | 50         |            |            |            | 50         |            |            |            | 50         |            |            |            | 50         |            |            |           |
| Organ_____                       | Findings_____             | Grade                   | 1+<br>(%)  | 2+<br>(%)  | 3+<br>(%)  | 4+<br>(%)  | 1+<br>(%)  | 2+<br>(%)  | 3+<br>(%)  | 4+<br>(%)  | 1+<br>(%)  | 2+<br>(%)  | 3+<br>(%)  | 4+<br>(%)  | 1+<br>(%)  | 2+<br>(%)  | 3+<br>(%)  | 4+<br>(%) |
| {Special sense organs/appendage} |                           |                         |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |           |
| Harder gl                        | granulation               |                         | <50>       |            |            |            | <50>       |            |            |            | <50>       |            |            |            | <50>       |            |            |           |
|                                  |                           | 0<br>( 0 )              | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |           |
| nasolacr d                       | inflammation              |                         | <50>       |            |            |            | <50>       |            |            |            | <50>       |            |            |            | <50>       |            |            |           |
|                                  |                           | 0<br>( 0 )              | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 ) | 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 ) |           |
| {Musculoskeletal system}         |                           |                         |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |           |
| muscle                           | mineralization            |                         | <50>       |            |            |            | <50>       |            |            |            | <50>       |            |            |            | <50>       |            |            |           |
|                                  |                           | 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>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |           |
| {Body cavities}                  |                           |                         |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |           |
| pleura                           | inflammatory infiltration |                         | <50>       |            |            |            | <50>       |            |            |            | <50>       |            |            |            | <50>       |            |            |           |
|                                  |                           | 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 ) | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |           |
| peritoneum                       | inflammatory infiltration |                         | <50>       |            |            |            | <50>       |            |            |            | <50>       |            |            |            | <50>       |            |            |           |
|                                  |                           | 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 ) | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |           |

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

TABLE O2

HISTOPATHOLOGICAL FINDINGS :  
NON-NEOPLASTIC LESIONS : FEMALE

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 17

|                                  |                                            | Group Name              | Control |       |       |      | 0. 1ppm |       |       |      | 0. 5ppm |       |       |      | 2ppm  |       |       |      |
|----------------------------------|--------------------------------------------|-------------------------|---------|-------|-------|------|---------|-------|-------|------|---------|-------|-------|------|-------|-------|-------|------|
|                                  |                                            | No. of Animals on Study | 50      |       |       |      | 50      |       |       |      | 50      |       |       |      | 50    |       |       |      |
| Organ_____                       | Findings_____                              | Grade                   | 1+      | 2+    | 3+    | 4+   | 1+      | 2+    | 3+    | 4+   | 1+      | 2+    | 3+    | 4+   | 1+    | 2+    | 3+    | 4+   |
|                                  |                                            |                         | (%)     | (%)   | (%)   | (%)  | (%)     | (%)   | (%)   | (%)  | (%)     | (%)   | (%)   | (%)  | (%)   | (%)   | (%)   | (%)  |
| {Integumentary system/appandage} |                                            |                         |         |       |       |      |         |       |       |      |         |       |       |      |       |       |       |      |
| skin/app                         |                                            |                         | <50>    |       |       |      | <50>    |       |       |      | <50>    |       |       |      | <50>  |       |       |      |
|                                  | scab                                       |                         | 0       | 0     | 0     | 0    | 1       | 0     | 0     | 0    | 1       | 0     | 0     | 0    | 0     | 0     | 0     | 0    |
|                                  |                                            |                         | ( 0)    | ( 0)  | ( 0)  | ( 0) | ( 2)    | ( 0)  | ( 0)  | ( 0) | ( 2)    | ( 0)  | ( 0)  | ( 0) | ( 0)  | ( 0)  | ( 0)  | ( 0) |
| {Respiratory system}             |                                            |                         |         |       |       |      |         |       |       |      |         |       |       |      |       |       |       |      |
| nasal cavit                      |                                            |                         | <50>    |       |       |      | <50>    |       |       |      | <50>    |       |       |      | <50>  |       |       |      |
|                                  | exudate                                    |                         | 0       | 0     | 0     | 0    | 0       | 0     | 0     | 0    | 0       | 0     | 0     | 0    | 1     | 0     | 0     | 0    |
|                                  |                                            |                         | ( 0)    | ( 0)  | ( 0)  | ( 0) | ( 0)    | ( 0)  | ( 0)  | ( 0) | ( 0)    | ( 0)  | ( 0)  | ( 0) | ( 2)  | ( 0)  | ( 0)  | ( 0) |
|                                  | thrombus                                   |                         | 2       | 0     | 0     | 0    | 3       | 0     | 0     | 0    | 0       | 0     | 0     | 0    | 3     | 0     | 0     | 0    |
|                                  |                                            |                         | ( 4)    | ( 0)  | ( 0)  | ( 0) | ( 6)    | ( 0)  | ( 0)  | ( 0) | ( 0)    | ( 0)  | ( 0)  | ( 0) | ( 6)  | ( 0)  | ( 0)  | ( 0) |
|                                  | mineralization                             |                         | 7       | 0     | 0     | 0    | 9       | 0     | 0     | 0    | 8       | 0     | 0     | 0    | 5     | 0     | 0     | 0    |
|                                  |                                            |                         | ( 14)   | ( 0)  | ( 0)  | ( 0) | ( 18)   | ( 0)  | ( 0)  | ( 0) | ( 16)   | ( 0)  | ( 0)  | ( 0) | ( 10) | ( 0)  | ( 0)  | ( 0) |
|                                  | goblet cell hyperplasia                    |                         | 5       | 0     | 0     | 0    | 11      | 0     | 0     | 0    | 1       | 0     | 0     | 0    | 18    | 0     | 0     | 0 ** |
|                                  |                                            |                         | ( 10)   | ( 0)  | ( 0)  | ( 0) | ( 22)   | ( 0)  | ( 0)  | ( 0) | ( 2)    | ( 0)  | ( 0)  | ( 0) | ( 36) | ( 0)  | ( 0)  | ( 0) |
|                                  | eosinophilic change:olfactory epithelium   |                         | 4       | 20    | 24    | 0    | 3       | 18    | 29    | 0    | 4       | 21    | 24    | 0    | 3     | 15    | 29    | 0    |
|                                  |                                            |                         | ( 8)    | ( 40) | ( 48) | ( 0) | ( 6)    | ( 36) | ( 58) | ( 0) | ( 8)    | ( 42) | ( 48) | ( 0) | ( 6)  | ( 30) | ( 58) | ( 0) |
|                                  | eosinophilic change:respiratory epithelium |                         | 10      | 0     | 0     | 0    | 2       | 0     | 0     | 0 *  | 1       | 0     | 0     | 0 *  | 0     | 0     | 0     | 0 ** |
|                                  |                                            |                         | ( 20)   | ( 0)  | ( 0)  | ( 0) | ( 4)    | ( 0)  | ( 0)  | ( 0) | ( 2)    | ( 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 : Number of animals with lesion  
 ( c ) c : b / a \* 100  
 Significant difference : \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
ALL ANIMALS (0-105W)

PAGE : 18

| Organ                | Findings                                        | Control                 |       |       |       | 0.1ppm |       |       |       | 0.5ppm |       |       |       | 2ppm   |        |       |       |
|----------------------|-------------------------------------------------|-------------------------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|--------|-------|-------|
|                      |                                                 | No. of Animals on Study |       |       |       | 50     |       |       |       | 50     |       |       |       | 50     |        |       |       |
|                      |                                                 | 1+                      | 2+    | 3+    | 4+    | 1+     | 2+    | 3+    | 4+    | 1+     | 2+    | 3+    | 4+    | 1+     | 2+     | 3+    | 4+    |
|                      |                                                 | (%)                     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   |
| [Respiratory system] |                                                 |                         |       |       |       |        |       |       |       |        |       |       |       |        |        |       |       |
| nasal cavit          |                                                 |                         |       |       |       |        |       |       |       |        |       |       |       |        |        |       |       |
|                      | inflammation:foreign body                       | 2                       | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 2      | 0     | 0     | 0     | 14     | 6      | 0     | 0 **  |
|                      |                                                 | ( 4 )                   | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 28 ) | ( 12 ) | ( 0 ) | ( 0 ) |
|                      | inflammation:respiratory epithelium             | 5                       | 0     | 0     | 0     | 8      | 0     | 0     | 0     | 8      | 0     | 0     | 0     | 13     | 3      | 0     | 0 *   |
|                      |                                                 | ( 10 )                  | ( 0 ) | ( 0 ) | ( 0 ) | ( 16 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 16 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 26 ) | ( 6 )  | ( 0 ) | ( 0 ) |
|                      | respiratory metaplasia:olfactory epithelium     | 1                       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 31     | 7      | 0     | 0 **  |
|                      |                                                 | ( 2 )                   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 62 ) | ( 14 ) | ( 0 ) | ( 0 ) |
|                      | respiratory metaplasia:gland                    | 38                      | 0     | 0     | 0     | 31     | 2     | 0     | 0     | 32     | 1     | 0     | 0     | 23     | 12     | 1     | 0 **  |
|                      |                                                 | ( 76 )                  | ( 0 ) | ( 0 ) | ( 0 ) | ( 62 ) | ( 4 ) | ( 0 ) | ( 0 ) | ( 64 ) | ( 2 ) | ( 0 ) | ( 0 ) | ( 46 ) | ( 24 ) | ( 2 ) | ( 0 ) |
|                      | squamous cell metaplasia:respiratory epithelium | 0                       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 39     | 7      | 0     | 0 **  |
|                      |                                                 | ( 0 )                   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 78 ) | ( 14 ) | ( 0 ) | ( 0 ) |
|                      | ulcer:respiratory epithelium                    | 0                       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 0      | 0     | 0     |
|                      |                                                 | ( 0 )                   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                      | hyperplasia:transitional epithelium             | 0                       | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 28     | 0      | 0     | 0 **  |
|                      |                                                 | ( 0 )                   | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 56 ) | ( 0 )  | ( 0 ) | ( 0 ) |
|                      | atrophy:olfactory epithelium                    | 0                       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 26     | 5      | 1     | 0 **  |
|                      |                                                 | ( 0 )                   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 52 ) | ( 10 ) | ( 2 ) | ( 0 ) |

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

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrIj[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 19

|                                                                        |                                            | Group Name              | Control     |             |       |       | 0.1ppm |       |       |       | 0.5ppm |       |       |       | 2ppm   |        |       |       |
|------------------------------------------------------------------------|--------------------------------------------|-------------------------|-------------|-------------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|--------|-------|-------|
|                                                                        |                                            | No. of Animals on Study | 50          |             |       |       | 50     |       |       |       | 50     |       |       |       | 50     |        |       |       |
| Organ_____                                                             | Findings_____                              | Grade                   | 1+          | 2+          | 3+    | 4+    | 1+     | 2+    | 3+    | 4+    | 1+     | 2+    | 3+    | 4+    | 1+     | 2+     | 3+    | 4+    |
|                                                                        |                                            |                         | (%)         | (%)         | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   |
| {Respiratory system}                                                   |                                            |                         |             |             |       |       |        |       |       |       |        |       |       |       |        |        |       |       |
| nasal cavit                                                            |                                            |                         | <50>        |             |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |        |       |       |
|                                                                        | edema:lamina propria                       |                         | 0           | 0           | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 15     | 0      | 0     | 0 **  |
|                                                                        |                                            |                         | ( 0 )       | ( 0 )       | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 30 ) | ( 0 )  | ( 0 ) | ( 0 ) |
|                                                                        | adhesion:turbinate                         |                         | 0           | 0           | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 3      | 0      | 0     | 0     |
|                                                                        |                                            |                         | ( 0 )       | ( 0 )       | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 6 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                                                                        | proliferation:striated muscle              |                         | 0           | 0           | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 4      | 1      | 1     | 0     |
|                                                                        |                                            |                         | ( 0 )       | ( 0 )       | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 8 )  | ( 2 )  | ( 2 ) | ( 0 ) |
| nasopharynx                                                            |                                            |                         | <50>        |             |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |        |       |       |
|                                                                        | goblet cell hyperplasia                    |                         | 1           | 0           | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0      | 0     | 0     |
|                                                                        |                                            |                         | ( 2 )       | ( 0 )       | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |
| larynx                                                                 |                                            |                         | <50>        |             |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |        |       |       |
|                                                                        | inflammation                               |                         | 1           | 0           | 0     | 0     | 2      | 0     | 0     | 0     | 2      | 0     | 0     | 0     | 0      | 0      | 0     | 0     |
|                                                                        |                                            |                         | ( 2 )       | ( 0 )       | ( 0 ) | ( 0 ) | ( 4 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |
| lung                                                                   |                                            |                         | <50>        |             |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |        |       |       |
|                                                                        | congestion                                 |                         | 0           | 1           | 0     | 0     | 1      | 0     | 0     | 0     | 3      | 0     | 0     | 0     | 0      | 1      | 0     | 0     |
|                                                                        |                                            |                         | ( 0 )       | ( 2 )       | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 6 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 )  | ( 0 ) | ( 0 ) |
|                                                                        | hemorrhage                                 |                         | 0           | 2           | 0     | 0     | 0      | 2     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 7      | 0     | 0     |
|                                                                        |                                            |                         | ( 0 )       | ( 4 )       | ( 0 ) | ( 0 ) | ( 0 )  | ( 4 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 14 ) | ( 0 ) | ( 0 ) |
| Grade                                                                  | 1+ : Slight                                | 2+ : Moderate           | 3+ : Marked | 4+ : Severe |       |       |        |       |       |       |        |       |       |       |        |        |       |       |
| < a >                                                                  | a : Number of animals examined at the site |                         |             |             |       |       |        |       |       |       |        |       |       |       |        |        |       |       |
| b                                                                      | b : Number of animals with lesion          |                         |             |             |       |       |        |       |       |       |        |       |       |       |        |        |       |       |
| ( c )                                                                  | c : b / a * 100                            |                         |             |             |       |       |        |       |       |       |        |       |       |       |        |        |       |       |
| Significant difference : * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square |                                            |                         |             |             |       |       |        |       |       |       |        |       |       |       |        |        |       |       |

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

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| Organ_____                                                             | Findings_____                              | Group Name              | Control     |             |      |      | 0. 1ppm |      |      |      | 0. 5ppm |      |      |      | 2ppm  |      |      |      |
|------------------------------------------------------------------------|--------------------------------------------|-------------------------|-------------|-------------|------|------|---------|------|------|------|---------|------|------|------|-------|------|------|------|
|                                                                        |                                            | No. of Animals on Study | 50          |             |      |      | 50      |      |      |      | 50      |      |      |      | 50    |      |      |      |
|                                                                        |                                            | Grade                   | 1+          | 2+          | 3+   | 4+   | 1+      | 2+   | 3+   | 4+   | 1+      | 2+   | 3+   | 4+   | 1+    | 2+   | 3+   | 4+   |
|                                                                        |                                            |                         | (%)         | (%)         | (%)  | (%)  | (%)     | (%)  | (%)  | (%)  | (%)     | (%)  | (%)  | (%)  | (%)   | (%)  | (%)  | (%)  |
| {Respiratory system}                                                   |                                            |                         |             |             |      |      |         |      |      |      |         |      |      |      |       |      |      |      |
| lung                                                                   | edema                                      |                         | <50>        |             |      |      | <50>    |      |      |      | <50>    |      |      |      | <50>  |      |      |      |
|                                                                        |                                            |                         | 1           | 0           | 0    | 0    | 0       | 0    | 0    | 0    | 1       | 1    | 0    | 0    | 0     | 0    | 0    | 0    |
|                                                                        |                                            |                         | ( 2)        | ( 0)        | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) | ( 2)    | ( 2) | ( 0) | ( 0) | ( 0)  | ( 0) | ( 0) | ( 0) |
|                                                                        | inflammatory infiltration                  |                         | 2           | 0           | 0    | 0    | 0       | 0    | 0    | 0    | 0       | 1    | 0    | 0    | 0     | 0    | 0    | 0    |
|                                                                        |                                            |                         | ( 4)        | ( 0)        | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) | ( 0)    | ( 2) | ( 0) | ( 0) | ( 0)  | ( 0) | ( 0) | ( 0) |
|                                                                        | osseous metaplasia                         |                         | 1           | 0           | 0    | 0    | 1       | 0    | 0    | 0    | 0       | 0    | 0    | 0    | 1     | 0    | 0    | 0    |
|                                                                        |                                            |                         | ( 2)        | ( 0)        | ( 0) | ( 0) | ( 2)    | ( 0) | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) | ( 2)  | ( 0) | ( 0) | ( 0) |
|                                                                        | accumulation of foamy cells                |                         | 4           | 0           | 0    | 0    | 9       | 0    | 0    | 0    | 10      | 0    | 0    | 0    | 7     | 0    | 0    | 0    |
|                                                                        |                                            |                         | ( 8)        | ( 0)        | ( 0) | ( 0) | ( 18)   | ( 0) | ( 0) | ( 0) | ( 20)   | ( 0) | ( 0) | ( 0) | ( 14) | ( 0) | ( 0) | ( 0) |
|                                                                        | bronchiolar-alveolar cell hyperplasia      |                         | 2           | 0           | 0    | 0    | 2       | 0    | 0    | 0    | 2       | 0    | 0    | 0    | 2     | 0    | 0    | 0    |
|                                                                        |                                            |                         | ( 4)        | ( 0)        | ( 0) | ( 0) | ( 4)    | ( 0) | ( 0) | ( 0) | ( 4)    | ( 0) | ( 0) | ( 0) | ( 4)  | ( 0) | ( 0) | ( 0) |
| {Hematopoietic system}                                                 |                                            |                         |             |             |      |      |         |      |      |      |         |      |      |      |       |      |      |      |
| bone marrow                                                            | hemorrhage                                 |                         | <50>        |             |      |      | <50>    |      |      |      | <50>    |      |      |      | <50>  |      |      |      |
|                                                                        |                                            |                         | 0           | 0           | 0    | 0    | 0       | 0    | 0    | 0    | 0       | 0    | 0    | 0    | 1     | 0    | 0    | 0    |
|                                                                        |                                            |                         | ( 0)        | ( 0)        | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 0) | ( 0)    | ( 0) | ( 0) | ( 2) | ( 0)  | ( 0) | ( 0) |      |
|                                                                        | granulation                                |                         | 10          | 2           | 0    | 0    | 10      | 3    | 0    | 0    | 8       | 1    | 1    | 0    | 9     | 1    | 1    | 0    |
|                                                                        |                                            |                         | ( 20)       | ( 4)        | ( 0) | ( 0) | ( 20)   | ( 6) | ( 0) | ( 0) | ( 16)   | ( 2) | ( 2) | ( 0) | ( 18) | ( 2) | ( 2) | ( 0) |
| Grade                                                                  | 1+ : Slight                                | 2+ : Moderate           | 3+ : Marked | 4+ : Severe |      |      |         |      |      |      |         |      |      |      |       |      |      |      |
| < a >                                                                  | a : Number of animals examined at the site |                         |             |             |      |      |         |      |      |      |         |      |      |      |       |      |      |      |
| b                                                                      | b : Number of animals with lesion          |                         |             |             |      |      |         |      |      |      |         |      |      |      |       |      |      |      |
| ( c )                                                                  | c : b / a * 100                            |                         |             |             |      |      |         |      |      |      |         |      |      |      |       |      |      |      |
| Significant difference : * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square |                                            |                         |             |             |      |      |         |      |      |      |         |      |      |      |       |      |      |      |

STUDY NO. : 0816  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

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| Organ                  | Findings                     | Control |        |       |       | 0.1ppm |        |       |       | 0.5ppm |        |       |       | 2ppm   |        |       |       |
|------------------------|------------------------------|---------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|
|                        |                              | 50      |        |       |       | 50     |        |       |       | 50     |        |       |       | 50     |        |       |       |
|                        |                              | 1+      | 2+     | 3+    | 4+    | 1+     | 2+     | 3+    | 4+    | 1+     | 2+     | 3+    | 4+    | 1+     | 2+     | 3+    | 4+    |
|                        |                              | (%)     | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   |
| {Hematopoietic system} |                              |         |        |       |       |        |        |       |       |        |        |       |       |        |        |       |       |
| bone marrow            |                              | <50>    |        |       |       | <50>   |        |       |       | <50>   |        |       |       | <50>   |        |       |       |
|                        | erythropoiesis:increased     | 0       | 0      | 0     | 0     | 2      | 0      | 0     | 0     | 1      | 0      | 0     | 0     | 1      | 0      | 0     | 0     |
|                        |                              | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 4 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                        | granulopoiesis:increased     | 0       | 0      | 0     | 0     | 2      | 0      | 0     | 0     | 1      | 1      | 0     | 0     | 3      | 1      | 0     | 0     |
|                        |                              | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 4 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 2 )  | ( 2 )  | ( 0 ) | ( 0 ) | ( 6 )  | ( 2 )  | ( 0 ) | ( 0 ) |
| lymph node             |                              | <50>    |        |       |       | <50>   |        |       |       | <50>   |        |       |       | <50>   |        |       |       |
|                        | hemorrhage                   | 0       | 0      | 0     | 0     | 1      | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0     | 0     |
|                        |                              | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                        | granulation                  | 0       | 0      | 0     | 0     | 1      | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 2      | 0      | 0     | 0     |
|                        |                              | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 4 )  | ( 0 )  | ( 0 ) | ( 0 ) |
| spleen                 |                              | <50>    |        |       |       | <50>   |        |       |       | <50>   |        |       |       | <50>   |        |       |       |
|                        | deposit of hemosiderin       | 28      | 10     | 0     | 0     | 29     | 7      | 0     | 0     | 23     | 13     | 0     | 0     | 29     | 11     | 0     | 0     |
|                        |                              | ( 56 )  | ( 20 ) | ( 0 ) | ( 0 ) | ( 58 ) | ( 14 ) | ( 0 ) | ( 0 ) | ( 46 ) | ( 26 ) | ( 0 ) | ( 0 ) | ( 58 ) | ( 22 ) | ( 0 ) | ( 0 ) |
|                        | extramedullary hematopoiesis | 33      | 4      | 0     | 0     | 32     | 9      | 0     | 0     | 32     | 6      | 3     | 0     | 25     | 4      | 3     | 0     |
|                        |                              | ( 66 )  | ( 8 )  | ( 0 ) | ( 0 ) | ( 64 ) | ( 18 ) | ( 0 ) | ( 0 ) | ( 64 ) | ( 12 ) | ( 6 ) | ( 0 ) | ( 50 ) | ( 8 )  | ( 6 ) | ( 0 ) |
| {Circulatory system}   |                              |         |        |       |       |        |        |       |       |        |        |       |       |        |        |       |       |
| heart                  |                              | <50>    |        |       |       | <50>   |        |       |       | <50>   |        |       |       | <50>   |        |       |       |
|                        | dilatation                   | 0       | 0      | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 1      | 0     | 0     | 0      | 0      | 0     | 0     |
|                        |                              | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 )  | ( 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 : Number of animals with lesion  
 ( c ) c : b / a \* 100  
 Significant difference : \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

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| Organ                                                                  | Findings                                   | Group Name              | Control     |             |       |       | 0.1ppm |       |       |       | 0.5ppm |       |       |       | 2ppm   |       |       |    |
|------------------------------------------------------------------------|--------------------------------------------|-------------------------|-------------|-------------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|----|
|                                                                        |                                            | No. of Animals on Study | 50          |             |       |       | 50     |       |       |       | 50     |       |       |       | 50     |       |       |    |
|                                                                        |                                            | Grade                   | 1+          | 2+          | 3+    | 4+    | 1+     | 2+    | 3+    | 4+    | 1+     | 2+    | 3+    | 4+    | 1+     | 2+    | 3+    | 4+ |
|                                                                        |                                            |                         | (%)         | (%)         | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   |    |
| {Circulatory system}                                                   |                                            |                         |             |             |       |       |        |       |       |       |        |       |       |       |        |       |       |    |
| heart                                                                  | inflammatory infiltration                  |                         | <50>        |             |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |       |       |    |
|                                                                        |                                            | 0                       | 0           | 0           | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 0     | 0     |    |
|                                                                        |                                            |                         | ( 0 )       | ( 0 )       | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) |    |
|                                                                        | myocardial fibrosis                        |                         | 15          | 1           | 0     | 0     | 21     | 0     | 0     | 0     | 18     | 0     | 0     | 0     | 21     | 0     | 0     |    |
|                                                                        |                                            |                         | ( 30 )      | ( 2 )       | ( 0 ) | ( 0 ) | ( 42 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 36 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 42 ) | ( 0 ) | ( 0 ) |    |
| {Digestive system}                                                     |                                            |                         |             |             |       |       |        |       |       |       |        |       |       |       |        |       |       |    |
| tongue                                                                 | inflammatory infiltration                  |                         | <50>        |             |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |       |       |    |
|                                                                        |                                            | 0                       | 0           | 0           | 0     | 0     | 0      | 1     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     |    |
|                                                                        |                                            |                         | ( 0 )       | ( 0 )       | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) |    |
| stomach                                                                | basal cell hyperplasia                     |                         | <50>        |             |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |       |       |    |
|                                                                        |                                            | 2                       | 0           | 0           | 0     | 1     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     |    |
|                                                                        |                                            |                         | ( 4 )       | ( 0 )       | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) |    |
|                                                                        | ulcer:forestomach                          |                         | 0           | 1           | 0     | 0     | 1      | 2     | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 1     | 0     |    |
|                                                                        |                                            |                         | ( 0 )       | ( 2 )       | ( 0 ) | ( 0 ) | ( 2 )  | ( 4 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 ) | ( 0 ) |    |
|                                                                        | hyperplasia:forestomach                    |                         | 0           | 0           | 0     | 0     | 4      | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 4      | 0     | 0     |    |
|                                                                        |                                            |                         | ( 0 )       | ( 0 )       | ( 0 ) | ( 0 ) | ( 8 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 8 )  | ( 0 ) | ( 0 ) |    |
| Grade                                                                  | 1+ : Slight                                | 2+ : Moderate           | 3+ : Marked | 4+ : Severe |       |       |        |       |       |       |        |       |       |       |        |       |       |    |
| < a >                                                                  | a : Number of animals examined at the site |                         |             |             |       |       |        |       |       |       |        |       |       |       |        |       |       |    |
| b                                                                      | b : Number of animals with lesion          |                         |             |             |       |       |        |       |       |       |        |       |       |       |        |       |       |    |
| ( c )                                                                  | c : b / a * 100                            |                         |             |             |       |       |        |       |       |       |        |       |       |       |        |       |       |    |
| Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square |                                            |                         |             |             |       |       |        |       |       |       |        |       |       |       |        |       |       |    |

STUDY NO. : 0816  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

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| Organ              | Findings                              | Group Name<br>No. of Animals on Study |           |           |           | Control     |           |           |           | 0.1ppm      |           |           |           | 0.5ppm      |           |           |           | 2ppm        |           |           |           |
|--------------------|---------------------------------------|---------------------------------------|-----------|-----------|-----------|-------------|-----------|-----------|-----------|-------------|-----------|-----------|-----------|-------------|-----------|-----------|-----------|-------------|-----------|-----------|-----------|
|                    |                                       | Grade                                 |           |           |           | 50          |           |           |           | 50          |           |           |           | 50          |           |           |           | 50          |           |           |           |
|                    |                                       | 1+                                    | 2+        | 3+        | 4+        | 1+          | 2+        | 3+        | 4+        | 1+          | 2+        | 3+        | 4+        | 1+          | 2+        | 3+        | 4+        | 1+          | 2+        | 3+        | 4+        |
|                    |                                       | (%)                                   | (%)       | (%)       | (%)       | (%)         | (%)       | (%)       | (%)       | (%)         | (%)       | (%)       | (%)       | (%)         | (%)       | (%)       | (%)       | (%)         | (%)       | (%)       | (%)       |
| {Digestive system} |                                       |                                       |           |           |           |             |           |           |           |             |           |           |           |             |           |           |           |             |           |           |           |
| stomach            |                                       |                                       |           |           |           |             |           |           |           |             |           |           |           |             |           |           |           |             |           |           |           |
|                    | erosion:glandular stomach             | 1<br>( 2)                             | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 2)   | 1<br>( 2) | 0<br>( 0) | 0<br>( 0) | 3<br>( 6)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 2)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 2)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
|                    | ulcer:glandular stomach               | 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>( 2)   | 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) |
|                    | hyperplasia:glandular stomach         | 1<br>( 2)                             | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 2<br>( 4)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 2<br>( 4)   | 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) |
|                    | neuroendocrine cell hyperplasia:focal | 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>( 2) | 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) |
| liver              |                                       |                                       |           |           |           |             |           |           |           |             |           |           |           |             |           |           |           |             |           |           |           |
|                    | herniation                            | 9<br>( 18)                            | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 10<br>( 20) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 10<br>( 20) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 10<br>( 20) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 10<br>( 20) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
|                    | necrosis:central                      | 1<br>( 2)                             | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 2)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)   | 1<br>( 2) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)   | 1<br>( 2) | 0<br>( 0) | 0<br>( 0) | 2<br>( 4)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
|                    | necrosis:focal                        | 0<br>( 0)                             | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 2)   | 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>( 2)   | 1<br>( 2) | 0<br>( 0) | 0<br>( 0) |
|                    | fatty change:peripheral               | 1<br>( 2)                             | 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)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |

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

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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

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| Organ              | Findings                  | Group Name<br>No. of Animals on Study |       |       |       | Control |        |       |       | 0.1ppm |       |       |       | 0.5ppm |        |       |       | 2ppm   |        |       |       |
|--------------------|---------------------------|---------------------------------------|-------|-------|-------|---------|--------|-------|-------|--------|-------|-------|-------|--------|--------|-------|-------|--------|--------|-------|-------|
|                    |                           | Grade                                 |       |       |       | 50      |        |       |       | 50     |       |       |       | 50     |        |       |       | 50     |        |       |       |
|                    |                           | 1+                                    | 2+    | 3+    | 4+    | 1+      | 2+     | 3+    | 4+    | 1+     | 2+    | 3+    | 4+    | 1+     | 2+     | 3+    | 4+    | 1+     | 2+     | 3+    | 4+    |
|                    |                           | (%)                                   | (%)   | (%)   | (%)   | (%)     | (%)    | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   |
| {Digestive system} |                           |                                       |       |       |       |         |        |       |       |        |       |       |       |        |        |       |       |        |        |       |       |
| liver              |                           |                                       |       |       |       |         |        |       |       |        |       |       |       |        |        |       |       |        |        |       |       |
|                    | cyst                      | <50>                                  |       |       |       | <50>    |        |       |       | <50>   |       |       |       | <50>   |        |       |       | <50>   |        |       |       |
|                    |                           | 1                                     | 0     | 0     | 0     | 0       | 0      | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0     | 0     |
|                    |                           | ( 2 )                                 | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                    | inflammatory infiltration | 0                                     | 1     | 0     | 0     | 0       | 0      | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0     | 0     |
|                    |                           | ( 0 )                                 | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                    | lymphocytic infiltration  | 0                                     | 0     | 0     | 0     | 0       | 0      | 0     | 0     | 2      | 0     | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0     | 0     |
|                    |                           | ( 0 )                                 | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 4 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                    | granulation               | 1                                     | 0     | 0     | 0     | 1       | 1      | 0     | 0     | 2      | 0     | 0     | 0     | 2      | 0      | 0     | 0     | 2      | 2      | 0     | 0     |
|                    |                           | ( 2 )                                 | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )   | ( 2 )  | ( 0 ) | ( 0 ) | ( 4 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 4 )  | ( 4 )  | ( 0 ) | ( 0 ) |
|                    | inflammatory cell nest    | 15                                    | 3     | 0     | 0     | 13      | 5      | 2     | 0     | 12     | 2     | 0     | 0     | 7      | 5      | 1     | 0     | 7      | 5      | 1     | 0     |
|                    |                           | ( 30 )                                | ( 6 ) | ( 0 ) | ( 0 ) | ( 26 )  | ( 10 ) | ( 4 ) | ( 0 ) | ( 24 ) | ( 4 ) | ( 0 ) | ( 0 ) | ( 14 ) | ( 10 ) | ( 2 ) | ( 0 ) | ( 14 ) | ( 10 ) | ( 2 ) | ( 0 ) |
|                    | clear cell focus          | 1                                     | 0     | 0     | 0     | 0       | 0      | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0      | 0     | 0     |
|                    |                           | ( 2 )                                 | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )   | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) |
|                    | acidophilic cell focus    | 1                                     | 1     | 1     | 0     | 2       | 0      | 1     | 0     | 1      | 0     | 1     | 0     | 3      | 2      | 0     | 0     | 3      | 2      | 0     | 0     |
|                    |                           | ( 2 )                                 | ( 2 ) | ( 2 ) | ( 0 ) | ( 4 )   | ( 0 )  | ( 2 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 2 ) | ( 0 ) | ( 6 )  | ( 4 )  | ( 0 ) | ( 0 ) | ( 6 )  | ( 4 )  | ( 0 ) | ( 0 ) |
|                    | basophilic cell focus     | 23                                    | 2     | 0     | 0     | 19      | 1      | 0     | 0     | 21     | 3     | 0     | 0     | 18     | 2      | 0     | 0     | 18     | 2      | 0     | 0     |
|                    |                           | ( 46 )                                | ( 4 ) | ( 0 ) | ( 0 ) | ( 38 )  | ( 2 )  | ( 0 ) | ( 0 ) | ( 42 ) | ( 6 ) | ( 0 ) | ( 0 ) | ( 36 ) | ( 4 )  | ( 0 ) | ( 0 ) | ( 36 ) | ( 4 )  | ( 0 ) | ( 0 ) |

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

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 25

| Organ_____         | Findings_____               | Group Name              | Control    |            |            |            | 0.1ppm     |            |            |            | 0.5ppm     |            |            |            | 2ppm       |            |            |            |
|--------------------|-----------------------------|-------------------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
|                    |                             | No. of Animals on Study | 50         |            |            |            | 50         |            |            |            | 50         |            |            |            | 50         |            |            |            |
|                    |                             | Grade                   | 1+         | 2+         | 3+         | 4+         | 1+         | 2+         | 3+         | 4+         | 1+         | 2+         | 3+         | 4+         | 1+         | 2+         | 3+         | 4+         |
|                    |                             |                         | (%)        | (%)        | (%)        | (%)        | (%)        | (%)        | (%)        | (%)        | (%)        | (%)        | (%)        | (%)        | (%)        | (%)        | (%)        | (%)        |
| [Digestive system] |                             |                         |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |
| liver              |                             |                         | <50>       |            |            |            | <50>       |            |            |            | <50>       |            |            |            | <50>       |            |            |            |
|                    | bile duct hyperplasia       |                         | 3<br>( 6 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 3<br>( 6 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 3<br>( 6 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |
|                    | bile ductular proliferation |                         | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 ) | 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 ) |
|                    | cholangiofibrosis           |                         | 1<br>( 2 ) | 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 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |
|                    | focal fatty change          |                         | 1<br>( 2 ) | 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 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |
| pancreas           |                             |                         | <50>       |            |            |            | <50>       |            |            |            | <50>       |            |            |            | <50>       |            |            |            |
|                    | atrophy                     |                         | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 2<br>( 4 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |
|                    | islet cell hyperplasia      |                         | 0<br>( 0 ) | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |
| [Urinary system]   |                             |                         |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |            |
| kidney             |                             |                         | <50>       |            |            |            | <50>       |            |            |            | <50>       |            |            |            | <50>       |            |            |            |
|                    | cyst                        |                         | 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 ) | 1<br>( 2 ) | 0<br>( 0 ) | 0<br>( 0 ) | 0<br>( 0 ) |

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 < a > a : Number of animals examined at the site  
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 ( c ) c : b / a \* 100  
 Significant difference : \* : P ≤ 0.05 \*\* : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 26

| Organ            | Findings                                  | Group Name              | Control     |              |           |           | 0. 1ppm     |              |           |           | 0. 5ppm     |              |           |           | 2ppm        |              |           |             |
|------------------|-------------------------------------------|-------------------------|-------------|--------------|-----------|-----------|-------------|--------------|-----------|-----------|-------------|--------------|-----------|-----------|-------------|--------------|-----------|-------------|
|                  |                                           | No. of Animals on Study | 50          |              |           |           | 50          |              |           |           | 50          |              |           |           | 50          |              |           |             |
|                  |                                           | Grade                   | 1+<br>(%)   | 2+<br>(%)    | 3+<br>(%) | 4+<br>(%) | 1+<br>(%)   | 2+<br>(%)    | 3+<br>(%) | 4+<br>(%) | 1+<br>(%)   | 2+<br>(%)    | 3+<br>(%) | 4+<br>(%) | 1+<br>(%)   | 2+<br>(%)    | 3+<br>(%) | 4+<br>(%)   |
| {Urinary system} |                                           |                         |             |              |           |           |             |              |           |           |             |              |           |           |             |              |           |             |
| kidney           | chronic nephropathy                       |                         | 31<br>( 62) | 3<br>( 6)    | 0<br>( 0) | 0<br>( 0) | 29<br>( 58) | 4<br>( 8)    | 2<br>( 4) | 0<br>( 0) | 20<br>( 40) | 8<br>( 16)   | 2<br>( 4) | 1<br>( 2) | 15<br>( 30) | 6<br>( 12)   | 2<br>( 4) | 1 *<br>( 2) |
|                  | papillary necrosis                        |                         | 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) | 0<br>( 0)   | 1<br>( 2)    | 0<br>( 0) | 0<br>( 0)   |
|                  | mineralization:cortico-medullary junction |                         | 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) | 1<br>( 2)   | 0<br>( 0)    | 0<br>( 0) | 0<br>( 0)   |
|                  | mineralization:pelvis                     |                         | 1<br>( 2)   | 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)   | 0<br>( 0)    | 0<br>( 0) | 0<br>( 0)   |
|                  | urothelial hyperplasia:pelvis             |                         | 0<br>( 0)   | 0<br>( 0)    | 0<br>( 0) | 0<br>( 0) | 1<br>( 2)   | 0<br>( 0)    | 0<br>( 0) | 0<br>( 0) | 1<br>( 2)   | 0<br>( 0)    | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)   | 0<br>( 0)    | 0<br>( 0) | 0<br>( 0)   |
|                  | eosinophilic droplet:proximal tubule      |                         | 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) | 1<br>( 2)   | 0<br>( 0)    | 0<br>( 0) | 0<br>( 0)   |
| urin bladd       | dilatation                                |                         | 0<br>( 0)   | <50><br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 2)   | <50><br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)   | <50><br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)   | <50><br>( 0) | 0<br>( 0) | 0<br>( 0)   |
|                  | hemorrhage                                |                         | 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>( 2)   | 0<br>( 0)    | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)   | 0<br>( 0)    | 0<br>( 0) | 0<br>( 0)   |

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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
ALL ANIMALS (0-105W)

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| Organ_____         | Findings_____                       | Group Name              | Control     |           |           |           | 0. 1ppm    |           |           |           | 0. 5ppm     |           |           |           | 2ppm        |           |           |           |
|--------------------|-------------------------------------|-------------------------|-------------|-----------|-----------|-----------|------------|-----------|-----------|-----------|-------------|-----------|-----------|-----------|-------------|-----------|-----------|-----------|
|                    |                                     | No. of Animals on Study | 50          |           |           |           | 50         |           |           |           | 50          |           |           |           | 50          |           |           |           |
|                    |                                     | Grade                   | 1+<br>(%)   | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) | 1+<br>(%)  | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) | 1+<br>(%)   | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) | 1+<br>(%)   | 2+<br>(%) | 3+<br>(%) | 4+<br>(%) |
|                    |                                     |                         |             |           |           |           |            |           |           |           |             |           |           |           |             |           |           |           |
| {Urinary system}   |                                     |                         |             |           |           |           |            |           |           |           |             |           |           |           |             |           |           |           |
| urin bladd         |                                     |                         | <50>        |           |           |           | <50>       |           |           |           | <50>        |           |           |           | <50>        |           |           |           |
|                    | hyperplasia:transitional epithelium |                         | 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>( 2)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
|                    |                                     |                         |             |           |           |           |            |           |           |           |             |           |           |           |             |           |           |           |
| {Endocrine system} |                                     |                         |             |           |           |           |            |           |           |           |             |           |           |           |             |           |           |           |
| pituitary          |                                     |                         | <50>        |           |           |           | <50>       |           |           |           | <50>        |           |           |           | <50>        |           |           |           |
|                    | cyst                                |                         | 17<br>( 34) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 8<br>( 16) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 11<br>( 22) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 11<br>( 22) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
|                    | hyperplasia                         |                         | 11<br>( 22) | 4<br>( 8) | 0<br>( 0) | 0<br>( 0) | 5<br>( 10) | 3<br>( 6) | 2<br>( 4) | 0<br>( 0) | 8<br>( 16)  | 3<br>( 6) | 1<br>( 2) | 0<br>( 0) | 5<br>( 10)  | 2<br>( 4) | 2<br>( 4) | 0<br>( 0) |
|                    | Rathke pouch                        |                         | 3<br>( 6)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 2)  | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 2<br>( 4)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 3<br>( 6)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
| thyroid            |                                     |                         | <50>        |           |           |           | <50>       |           |           |           | <50>        |           |           |           | <50>        |           |           |           |
|                    | ultimobranchial body remanet        |                         | 0<br>( 0)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 2)  | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 1<br>( 2)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) | 0<br>( 0)   | 0<br>( 0) | 0<br>( 0) | 0<br>( 0) |
|                    | C-cell hyperplasia                  |                         | 7<br>( 14)  | 2<br>( 4) | 0<br>( 0) | 0<br>( 0) | 9<br>( 18) | 1<br>( 2) | 1<br>( 2) | 0<br>( 0) | 11<br>( 22) | 1<br>( 2) | 0<br>( 0) | 0<br>( 0) | 6<br>( 12)  | 1<br>( 2) | 0<br>( 0) | 0<br>( 0) |

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HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

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| Organ                 | Findings                  | Control |       |       |       | 0.1ppm |       |       |       | 0.5ppm |       |       |       | 2ppm   |       |       |       |
|-----------------------|---------------------------|---------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|--------|-------|-------|-------|
|                       |                           | 50      |       |       |       | 50     |       |       |       | 50     |       |       |       | 50     |       |       |       |
|                       |                           | 1+      | 2+    | 3+    | 4+    | 1+     | 2+    | 3+    | 4+    | 1+     | 2+    | 3+    | 4+    | 1+     | 2+    | 3+    | 4+    |
|                       |                           | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   |
| {Endocrine system}    |                           |         |       |       |       |        |       |       |       |        |       |       |       |        |       |       |       |
| adrenal               |                           | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |       |       |       |
|                       | necrosis                  | 0       | 0     | 1     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     |
|                       |                           | ( 0 )   | ( 0 ) | ( 2 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                       |                           |         |       |       |       |        |       |       |       |        |       |       |       |        |       |       |       |
|                       |                           | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |       |       |       |
|                       | degeneration:cortex       | 0       | 1     | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 0     | 0     | 0     |
|                       |                           | ( 0 )   | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
|                       |                           |         |       |       |       |        |       |       |       |        |       |       |       |        |       |       |       |
|                       |                           | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |       |       |       |
|                       | hyperplasia:medulla       | 0       | 0     | 0     | 0     | 1      | 2     | 1     | 0     | 0      | 0     | 0     | 0     | 1      | 1     | 0     | 0     |
|                       |                           | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 4 ) | ( 2 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 2 ) | ( 0 ) | ( 0 ) |
|                       |                           |         |       |       |       |        |       |       |       |        |       |       |       |        |       |       |       |
|                       |                           | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |       |       |       |
|                       | focal fatty change:cortex | 10      | 0     | 0     | 0     | 6      | 1     | 0     | 0     | 6      | 1     | 0     | 0     | 10     | 2     | 0     | 0     |
|                       |                           | ( 20 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 12 ) | ( 2 ) | ( 0 ) | ( 0 ) | ( 12 ) | ( 2 ) | ( 0 ) | ( 0 ) | ( 20 ) | ( 4 ) | ( 0 ) | ( 0 ) |
|                       |                           |         |       |       |       |        |       |       |       |        |       |       |       |        |       |       |       |
| {Reproductive system} |                           |         |       |       |       |        |       |       |       |        |       |       |       |        |       |       |       |
| ovary                 |                           | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |       |       |       |
|                       | cyst                      | 2       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 0      | 0     | 0     | 0     |
|                       |                           | ( 4 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |
| uterus                |                           | <50>    |       |       |       | <50>   |       |       |       | <50>   |       |       |       | <50>   |       |       |       |
|                       | dilatation                | 0       | 0     | 0     | 0     | 0      | 0     | 0     | 0     | 1      | 0     | 0     | 0     | 0      | 0     | 0     | 0     |
|                       |                           | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) |

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

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
ALL ANIMALS (0-105W)

PAGE : 29

| Organ                            | Findings                       | Control |       |       |       | 0.1ppm |        |       |       | 0.5ppm |       |       |       | 2ppm  |       |       |       |
|----------------------------------|--------------------------------|---------|-------|-------|-------|--------|--------|-------|-------|--------|-------|-------|-------|-------|-------|-------|-------|
|                                  |                                | 50      |       |       |       | 50     |        |       |       | 50     |       |       |       | 50    |       |       |       |
|                                  |                                | 1+      | 2+    | 3+    | 4+    | 1+     | 2+     | 3+    | 4+    | 1+     | 2+    | 3+    | 4+    | 1+    | 2+    | 3+    | 4+    |
|                                  |                                | (%)     | (%)   | (%)   | (%)   | (%)    | (%)    | (%)   | (%)   | (%)    | (%)   | (%)   | (%)   | (%)   | (%)   | (%)   | (%)   |
| {Reproductive system}            |                                |         |       |       |       |        |        |       |       |        |       |       |       |       |       |       |       |
| uterus                           | hemorrhage                     | <50>    |       |       |       | <50>   |        |       |       | <50>   |       |       |       | <50>  |       |       |       |
|                                  |                                | 0       | 0     | 0     | 0     | 0      | 0      | 0     | 0     | 0      | 0     | 0     | 0     | 0     | 1     | 0     | 0     |
|                                  |                                | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 ) | ( 0 ) | ( 0 ) |
|                                  | cystic endometrial hyperplasia | <50>    |       |       |       | <50>   |        |       |       | <50>   |       |       |       | <50>  |       |       |       |
|                                  |                                | 1       | 0     | 0     | 0     | 1      | 0      | 0     | 0     | 2      | 0     | 0     | 0     | 0     | 0     | 0     | 0     |
|                                  |                                | ( 2 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 4 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) |
| mammary gl                       | galactoceles                   | <50>    |       |       |       | <50>   |        |       |       | <50>   |       |       |       | <50>  |       |       |       |
|                                  |                                | 1       | 0     | 0     | 0     | 0      | 0      | 0     | 0     | 1      | 0     | 0     | 0     | 2     | 0     | 0     | 0     |
|                                  |                                | ( 2 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 ) | ( 0 ) | ( 0 ) | ( 0 ) |
| {Nervous system}                 |                                |         |       |       |       |        |        |       |       |        |       |       |       |       |       |       |       |
| brain                            | hemorrhage                     | <50>    |       |       |       | <50>   |        |       |       | <50>   |       |       |       | <50>  |       |       |       |
|                                  |                                | 0       | 0     | 0     | 0     | 0      | 0      | 0     | 0     | 1      | 0     | 0     | 0     | 4     | 0     | 0     | 0     |
|                                  |                                | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 8 ) | ( 0 ) | ( 0 ) | ( 0 ) |
|                                  | necrosis:focal                 | <50>    |       |       |       | <50>   |        |       |       | <50>   |       |       |       | <50>  |       |       |       |
|                                  |                                | 0       | 0     | 0     | 0     | 1      | 0      | 0     | 0     | 0      | 0     | 0     | 0     | 0     | 0     | 0     | 0     |
|                                  |                                | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) |
| {Special sense organs/appendage} |                                |         |       |       |       |        |        |       |       |        |       |       |       |       |       |       |       |
| eye                              | cataract                       | <50>    |       |       |       | <50>   |        |       |       | <50>   |       |       |       | <50>  |       |       |       |
|                                  |                                | 5       | 3     | 0     | 0     | 3      | 5      | 0     | 0     | 1      | 1     | 0     | 0     | 0     | 1     | 0     | 0 *   |
|                                  |                                | ( 10 )  | ( 6 ) | ( 0 ) | ( 0 ) | ( 6 )  | ( 10 ) | ( 0 ) | ( 0 ) | ( 2 )  | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 ) | ( 0 ) | ( 0 ) |

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

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrIj[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 30

| Organ                            | Findings                  | Control |       |       |       | 0.1ppm |       |        |       | 0.5ppm |       |       |       | 2ppm  |       |       |       |
|----------------------------------|---------------------------|---------|-------|-------|-------|--------|-------|--------|-------|--------|-------|-------|-------|-------|-------|-------|-------|
|                                  |                           | 50      |       |       |       | 50     |       |        |       | 50     |       |       |       | 50    |       |       |       |
|                                  |                           | 1+      | 2+    | 3+    | 4+    | 1+     | 2+    | 3+     | 4+    | 1+     | 2+    | 3+    | 4+    | 1+    | 2+    | 3+    | 4+    |
|                                  |                           | (%)     | (%)   | (%)   | (%)   | (%)    | (%)   | (%)    | (%)   | (%)    | (%)   | (%)   | (%)   | (%)   | (%)   | (%)   | (%)   |
| {Special sense organs/appendage} |                           |         |       |       |       |        |       |        |       |        |       |       |       |       |       |       |       |
| eye                              | retinal atrophy           | <50>    |       |       |       | <50>   |       |        |       | <50>   |       |       |       | <50>  |       |       |       |
|                                  |                           | 1       | 2     | 3     | 0     | 1      | 0     | 7      | 0     | 0      | 1     | 1     | 0     | 0     | 0     | 1     | 0     |
|                                  |                           | ( 2 )   | ( 4 ) | ( 6 ) | ( 0 ) | ( 2 )  | ( 0 ) | ( 14 ) | ( 0 ) | ( 0 )  | ( 2 ) | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 ) | ( 0 ) |
|                                  | keratitis                 | <50>    |       |       |       | <50>   |       |        |       | <50>   |       |       |       | <50>  |       |       |       |
|                                  |                           | 0       | 0     | 0     | 0     | 0      | 1     | 0      | 0     | 0      | 0     | 0     | 0     | 0     | 0     | 0     | 0     |
|                                  |                           | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 )  | ( 2 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) |
| Harder gl                        | degeneration              | <50>    |       |       |       | <50>   |       |        |       | <50>   |       |       |       | <50>  |       |       |       |
|                                  |                           | 0       | 0     | 0     | 0     | 2      | 0     | 0      | 0     | 1      | 0     | 0     | 0     | 0     | 0     | 0     | 0     |
|                                  |                           | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) |
|                                  | inflammatory infiltration | <50>    |       |       |       | <50>   |       |        |       | <50>   |       |       |       | <50>  |       |       |       |
|                                  |                           | 2       | 0     | 0     | 0     | 5      | 0     | 0      | 0     | 0      | 0     | 1     | 0     | 3     | 0     | 0     | 0     |
|                                  |                           | ( 4 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 10 ) | ( 0 ) | ( 0 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 2 ) | ( 0 ) | ( 6 ) | ( 0 ) | ( 0 ) | ( 0 ) |
|                                  | granulation               | <50>    |       |       |       | <50>   |       |        |       | <50>   |       |       |       | <50>  |       |       |       |
|                                  |                           | 0       | 0     | 0     | 0     | 2      | 0     | 0      | 0     | 3      | 1     | 0     | 0     | 3     | 0     | 0     | 0     |
|                                  |                           | ( 0 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 6 )  | ( 2 ) | ( 0 ) | ( 0 ) | ( 6 ) | ( 0 ) | ( 0 ) | ( 0 ) |
| nasolacr d                       | inflammation              | <50>    |       |       |       | <50>   |       |        |       | <50>   |       |       |       | <50>  |       |       |       |
|                                  |                           | 0       | 1     | 0     | 0     | 2      | 0     | 0      | 0     | 1      | 0     | 0     | 0     | 0     | 0     | 0     | 0     |
|                                  |                           | ( 0 )   | ( 2 ) | ( 0 ) | ( 0 ) | ( 4 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 2 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) | ( 0 ) |
| {Musculoskeletal system}         |                           |         |       |       |       |        |       |        |       |        |       |       |       |       |       |       |       |
| bone                             | osteosclerosis            | <50>    |       |       |       | <50>   |       |        |       | <50>   |       |       |       | <50>  |       |       |       |
|                                  |                           | 2       | 0     | 0     | 0     | 2      | 0     | 0      | 0     | 3      | 0     | 0     | 0     | 1     | 0     | 0     | 0     |
|                                  |                           | ( 4 )   | ( 0 ) | ( 0 ) | ( 0 ) | ( 4 )  | ( 0 ) | ( 0 )  | ( 0 ) | ( 6 )  | ( 0 ) | ( 0 ) | ( 0 ) | ( 2 ) | ( 0 ) | ( 0 ) | ( 0 ) |

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

**TABLE P1**

**HISTOPATHOLOGICAL FINDINGS :**

**METASTASIS OF TUMOR :**

**MALE**

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1J[F344/DuCrJ]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 1

| Organ                                      | Findings                         | Group Name<br>No. of Animals on Study | Control<br>50 | 0.1ppm<br>50 | 0.5ppm<br>50 | 2ppm<br>50 |
|--------------------------------------------|----------------------------------|---------------------------------------|---------------|--------------|--------------|------------|
| {Integumentary system/appandage}           |                                  |                                       |               |              |              |            |
| skin/app                                   | metastasis:subcutis tumor        |                                       | <50><br>0     | <50><br>0    | <50><br>0    | <50><br>1  |
| {Respiratory system}                       |                                  |                                       |               |              |              |            |
| nasal cavit                                | leukemic cell infiltration       |                                       | <50><br>0     | <50><br>0    | <50><br>1    | <50><br>0  |
| lung                                       | leukemic cell infiltration       |                                       | <50><br>2     | <50><br>3    | <50><br>6    | <50><br>1  |
|                                            | metastasis:adrenal tumor         |                                       | 0             | 0            | 1            | 1          |
|                                            | metastasis:subcutis tumor        |                                       | 0             | 0            | 0            | 1          |
|                                            | metastasis:Zymbal gland tumor    |                                       | 0             | 2            | 1            | 0          |
|                                            | metastasis:vertebra tumor        |                                       | 0             | 1            | 0            | 0          |
| {Hematopoietic system}                     |                                  |                                       |               |              |              |            |
| bone marrow                                | leukemic cell infiltration       |                                       | <50><br>1     | <50><br>1    | <50><br>5    | <50><br>1  |
| lymph node                                 | leukemic cell infiltration       |                                       | <50><br>1     | <50><br>2    | <50><br>5    | <50><br>1  |
|                                            | metastasis:lung tumor            |                                       | 0             | 0            | 1            | 0          |
|                                            | metastasis:small intestine tumor |                                       | 0             | 0            | 1            | 0          |
| {Circulatory system}                       |                                  |                                       |               |              |              |            |
| heart                                      | leukemic cell infiltration       |                                       | <50><br>1     | <50><br>1    | <50><br>1    | <50><br>0  |
| < a ><br>b : Number of animals with lesion |                                  |                                       |               |              |              |            |

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : MALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 2

| Group Name<br>No. of Animals on Study                                                   |                                  | Control<br>50 | 0.1ppm<br>50 | 0.5ppm<br>50 | 2ppm<br>50 |
|-----------------------------------------------------------------------------------------|----------------------------------|---------------|--------------|--------------|------------|
| Organ                                                                                   | Findings                         |               |              |              |            |
| {Digestive system}                                                                      |                                  |               |              |              |            |
| liver                                                                                   |                                  | <50>          | <50>         | <50>         | <50>       |
|                                                                                         | leukemic cell infiltration       | 1             | 1            | 5            | 1          |
|                                                                                         | metastasis:subcutis tumor        | 0             | 0            | 0            | 1          |
|                                                                                         | metastasis:small intestine tumor | 0             | 0            | 1            | 0          |
| pancreas                                                                                |                                  | <50>          | <50>         | <50>         | <50>       |
|                                                                                         | leukemic cell infiltration       | 1             | 1            | 2            | 0          |
|                                                                                         | metastasis:small intestine tumor | 0             | 0            | 1            | 0          |
| {Urinary system}                                                                        |                                  |               |              |              |            |
| kidney                                                                                  |                                  | <50>          | <50>         | <50>         | <50>       |
|                                                                                         | leukemic cell infiltration       | 0             | 0            | 3            | 0          |
| {Endocrine system}                                                                      |                                  |               |              |              |            |
| pituitary                                                                               |                                  | <50>          | <50>         | <49>         | <50>       |
|                                                                                         | leukemic cell infiltration       | 0             | 0            | 1            | 0          |
| adrenal                                                                                 |                                  | <50>          | <50>         | <50>         | <50>       |
|                                                                                         | leukemic cell infiltration       | 0             | 0            | 1            | 0          |
| {Nervous system}                                                                        |                                  |               |              |              |            |
| brain                                                                                   |                                  | <50>          | <50>         | <50>         | <50>       |
|                                                                                         | leukemic cell infiltration       | 0             | 1            | 3            | 0          |
|                                                                                         | metastasis:pituitary tumor       | 0             | 1            | 0            | 0          |
|                                                                                         | metastasis:nasal tumor           | 0             | 0            | 0            | 1          |
| < a > a : Number of animals examined at the site<br>b b : Number of animals with lesion |                                  |               |              |              |            |

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : MALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
ALL ANIMALS (0-105W)

PAGE : 3

|                                  |                                            | Group Name              | Control   | 0.1ppm    | 0.5ppm    | 2ppm      |
|----------------------------------|--------------------------------------------|-------------------------|-----------|-----------|-----------|-----------|
| Organ                            | Findings                                   | No. of Animals on Study | 50        | 50        | 50        | 50        |
| {Nervous system}                 |                                            |                         |           |           |           |           |
| spinal cord                      | leukemic cell infiltration                 |                         | <50><br>0 | <50><br>0 | <50><br>2 | <50><br>0 |
| periph nerv                      | metastasis:Zymbal gland tumor              |                         | <50><br>0 | <50><br>0 | <50><br>1 | <50><br>0 |
| {Special sense organs/appendage} |                                            |                         |           |           |           |           |
| Harder gl                        | leukemic cell infiltration                 |                         | <50><br>0 | <50><br>0 | <50><br>1 | <50><br>0 |
| {Body cavities}                  |                                            |                         |           |           |           |           |
| pleura                           | metastasis:bone tumor                      |                         | <50><br>0 | <50><br>1 | <50><br>0 | <50><br>0 |
| mediastinum                      | leukemic cell infiltration                 |                         | <50><br>0 | <50><br>0 | <50><br>1 | <50><br>0 |
| peritoneum                       | metastasis:small intestine tumor           |                         | <50><br>0 | <50><br>0 | <50><br>1 | <50><br>0 |
| < a >                            | a : Number of animals examined at the site |                         |           |           |           |           |
| b                                | b : Number of animals with lesion          |                         |           |           |           |           |

(JPT150)

BA1S5

**TABLE P2**

**HISTOPATHOLOGICAL FINDINGS :**

**METASTASIS OF TUMOR :**

**FEMALE**

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
REPORT TYPE : A1  
SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
ALL ANIMALS (0-105W)

PAGE : 4

| Group Name              |                                            | Control | 0.1ppm | 0.5ppm | 2ppm |
|-------------------------|--------------------------------------------|---------|--------|--------|------|
| No. of Animals on Study |                                            | 50      | 50     | 50     | 50   |
| Organ                   | Findings                                   |         |        |        |      |
| {Respiratory system}    |                                            |         |        |        |      |
| lung                    |                                            | <50>    | <50>   | <50>   | <50> |
|                         | leukemic cell infiltration                 | 3       | 6      | 3      | 3    |
|                         | metastasis:uterus tumor                    | 2       | 0      | 0      | 0    |
|                         | metastasis:thyroid tumor                   | 0       | 0      | 2      | 0    |
|                         | metastasis:peritoneum tumor                | 0       | 0      | 1      | 1    |
|                         | metastasis:muscle tumor                    | 0       | 0      | 0      | 1    |
| {Hematopoietic system}  |                                            |         |        |        |      |
| bone marrow             |                                            | <50>    | <50>   | <50>   | <50> |
|                         | leukemic cell infiltration                 | 1       | 6      | 3      | 2    |
| lymph node              |                                            | <50>    | <50>   | <50>   | <50> |
|                         | leukemic cell infiltration                 | 0       | 3      | 1      | 1    |
|                         | metastasis:uterus tumor                    | 1       | 0      | 0      | 0    |
|                         | metastasis:peritoneum tumor                | 0       | 0      | 0      | 1    |
|                         | metastasis:muscle tumor                    | 0       | 0      | 0      | 1    |
| spleen                  |                                            | <50>    | <50>   | <50>   | <50> |
|                         | metastasis:peritoneum tumor                | 0       | 0      | 0      | 1    |
| {Digestive system}      |                                            |         |        |        |      |
| salivary gl             |                                            | <50>    | <50>   | <50>   | <50> |
|                         | metastasis:muscle tumor                    | 0       | 0      | 0      | 1    |
| small intes             |                                            | <50>    | <50>   | <50>   | <50> |
|                         | leukemic cell infiltration                 | 0       | 1      | 0      | 0    |
| < a >                   | a : Number of animals examined at the site |         |        |        |      |
| b                       | b : Number of animals with lesion          |         |        |        |      |

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrIGrlj[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 5

| Group Name              |                             | Control | 0.1ppm | 0.5ppm | 2ppm |
|-------------------------|-----------------------------|---------|--------|--------|------|
| No. of Animals on Study |                             | 50      | 50     | 50     | 50   |
| Organ                   | Findings                    |         |        |        |      |
| {Digestive system}      |                             |         |        |        |      |
| large intes             |                             | <50>    | <50>   | <50>   | <50> |
|                         | leukemic cell infiltration  | 0       | 1      | 0      | 0    |
| liver                   |                             | <50>    | <50>   | <50>   | <50> |
|                         | leukemic cell infiltration  | 5       | 6      | 3      | 2    |
|                         | metastasis:uterus tumor     | 0       | 0      | 0      | 1    |
|                         | metastasis:peritoneum tumor | 0       | 0      | 0      | 1    |
| pancreas                |                             | <50>    | <50>   | <50>   | <50> |
|                         | leukemic cell infiltration  | 0       | 1      | 0      | 0    |
|                         | metastasis:uterus tumor     | 1       | 0      | 0      | 0    |
|                         | metastasis:peritoneum tumor | 0       | 0      | 0      | 1    |
| {Urinary system}        |                             |         |        |        |      |
| kidney                  |                             | <50>    | <50>   | <50>   | <50> |
|                         | leukemic cell infiltration  | 1       | 0      | 0      | 1    |
|                         | metastasis:uterus tumor     | 1       | 0      | 0      | 0    |
| {Endocrine system}      |                             |         |        |        |      |
| pituitary               |                             | <50>    | <50>   | <50>   | <50> |
|                         | leukemic cell infiltration  | 0       | 0      | 0      | 1    |
| {Reproductive system}   |                             |         |        |        |      |
| ovary                   |                             | <50>    | <50>   | <50>   | <50> |
|                         | leukemic cell infiltration  | 0       | 1      | 0      | 0    |

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

STUDY NO. : 0816  
 ANIMAL : RAT F344/DuCrIGrlj[F344/DuCrj]  
 REPORT TYPE : A1  
 SEX : FEMALE

HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)  
 ALL ANIMALS (0-105W)

PAGE : 6

| Group Name                       |                                            | Control | 0.1ppm | 0.5ppm | 2ppm |
|----------------------------------|--------------------------------------------|---------|--------|--------|------|
| No. of Animals on Study          |                                            | 50      | 50     | 50     | 50   |
| Organ                            | Findings                                   |         |        |        |      |
| {Reproductive system}            |                                            |         |        |        |      |
| ovary                            |                                            | <50>    | <50>   | <50>   | <50> |
|                                  | metastasis:uterus tumor                    | 1       | 0      | 0      | 0    |
| uterus                           |                                            | <50>    | <50>   | <50>   | <50> |
|                                  | leukemic cell infiltration                 | 0       | 1      | 0      | 0    |
| {Nervous system}                 |                                            |         |        |        |      |
| brain                            |                                            | <50>    | <50>   | <50>   | <50> |
|                                  | leukemic cell infiltration                 | 1       | 2      | 1      | 2    |
|                                  | metastasis:pituitary tumor                 | 0       | 2      | 1      | 0    |
| spinal cord                      |                                            | <50>    | <50>   | <50>   | <50> |
|                                  | leukemic cell infiltration                 | 1       | 1      | 2      | 0    |
| {Special sense organs/appendage} |                                            |         |        |        |      |
| Harder gl                        |                                            | <50>    | <50>   | <50>   | <50> |
|                                  | metastasis:muscle tumor                    | 0       | 0      | 0      | 1    |
| {Body cavities}                  |                                            |         |        |        |      |
| pleura                           |                                            | <50>    | <50>   | <50>   | <50> |
|                                  | metastasis:peritoneum tumor                | 0       | 0      | 1      | 0    |
| peritoneum                       |                                            | <50>    | <50>   | <50>   | <50> |
|                                  | leukemic cell infiltration                 | 0       | 0      | 1      | 0    |
|                                  | metastasis:uterus tumor                    | 1       | 0      | 0      | 0    |
| < a >                            | a : Number of animals examined at the site |         |        |        |      |
| b                                | b : Number of animals with lesion          |         |        |        |      |

**TABLE Q1**

**CAUSE OF DEATH : MALE**

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
SEX : MALE

COUSE OF DEATH (SUMMARY)  
(0-105W)

PAGE : 1

| Group Name                         | Control | 0.1ppm | 0.5ppm | 2ppm |
|------------------------------------|---------|--------|--------|------|
| Number of Dead and Moribund Animal | 9       | 10     | 13     | 8    |
| hepatic lesion                     | 0       | 1      | 0      | 0    |
| tumor d:leukemia                   | 1       | 2      | 5      | 1    |
| tumor d:subcutis                   | 1       | 0      | 0      | 1    |
| tumor d:nasal cavit                | 0       | 0      | 0      | 1    |
| tumor d:small intes                | 0       | 0      | 1      | 0    |
| tumor d:pancreas                   | 0       | 0      | 1      | 1    |
| tumor d:kidney                     | 0       | 0      | 1      | 0    |
| tumor d:pituitary                  | 5       | 4      | 3      | 1    |
| tumor d:thyroid                    | 0       | 0      | 1      | 0    |
| tumor d:adrenal                    | 1       | 0      | 0      | 0    |
| tumor d:prostate                   | 1       | 0      | 0      | 0    |
| tumor d:prep/eli gl                | 0       | 1      | 0      | 0    |
| tumor d:Zymbal gl                  | 0       | 1      | 1      | 1    |
| tumor d:bone                       | 0       | 1      | 0      | 1    |
| tumor d:peritoneum                 | 0       | 0      | 0      | 1    |

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**TABLE Q2**

**CAUSE OF DEATH : FEMALE**

STUDY NO. : 0816  
ANIMAL : RAT F344/DuCr1Cr1j[F344/DuCrj]  
SEX : FEMALE

COUSE OF DEATH (SUMMARY)  
(0-105W)

PAGE : 2

| Group Name                         | Control | 0.1ppm | 0.5ppm | 2ppm |
|------------------------------------|---------|--------|--------|------|
| Number of Dead and Moribund Animal | 7       | 8      | 9      | 16   |
| no microscop confirm               | 1       | 0      | 1      | 0    |
| respiratory sy les                 | 0       | 0      | 1      | 0    |
| deglutition disorder               | 0       | 1      | 0      | 0    |
| tumor d:leukemia                   | 2       | 4      | 2      | 3    |
| tumor d:nasal cavit                | 0       | 0      | 0      | 1    |
| tumor d:urin bladd                 | 0       | 0      | 1      | 0    |
| tumor d:pituitary                  | 3       | 1      | 1      | 6    |
| tumor d:adrenal                    | 0       | 0      | 1      | 1    |
| tumor d:uterus                     | 1       | 1      | 1      | 0    |
| tumor d:mammary gl                 | 0       | 1      | 0      | 1    |
| tumor d:brain                      | 0       | 0      | 0      | 2    |
| tumor d:muscle                     | 0       | 0      | 0      | 1    |
| tumor d:peritoneum                 | 0       | 0      | 1      | 1    |

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