2-メチル-1-プロパノールのマウスを用いた 経口投与によるがん原性試験(混水試験)報告書

試験番号:0613

# TABLES

### TABLES

- TABLE A 1SURVIVAL ANIMAL NUMBERS: MALE
- TABLE A 2SURVIVAL ANIMAL NUMBERS: FEMALE
- TABLE B 1 CLINICAL OBSERVATION: MALE
- TABLE B 2CLINICAL OBSERVATION: FEMALE
- TABLE C 1 BODY WEIGHT CHANGES AND SURVIVAL ANIMAL NUMBERS: MALE
- TABLE C 2BODY WEIGHT CHANGES AND SURVIVAL ANIMAL NUMBERS:<br/>FEMALE
- TABLE C 3 BODY WEIGHT CHANGES: MALE
- TABLE C 4BODY WEIGHT CHANGES: FEMALE
- TABLE D 1
   FOOD
   CONSUMPTION
   CHANGES
   AND
   SURVIVAL
   ANIMAL

   NUMBERS:
   MALE
- TABLE D 2FOODCONSUMPTIONCHANGESANDSURVIVALANIMALNUMBERS:FEMALE
- TABLE D 3 FOOD CONSUMPTION CHANGES: MALE
- TABLE D 4FOOD CONSUMPTION CHANGES: FEMALE
- TABLE E 1
   WATER
   CONSUMPTION
   CHANGES
   AND
   SURVIVAL
   ANIMAL

   NUMBERS:
   MALE
- TABLE E 2WATER CONSUMPTION CHANGES AND SURVIVAL ANIMAL<br/>NUMBERS: FEMALE
- TABLE E 3WATER CONSUMPTION CHANGES: MALE
- TABLE E 4WATER CONSUMPTION CHANGES: FEMALE
- TABLE F 1
   CHEMICAL INTAKE CHANGES: MALE
- TABLE F 2CHEMICAL INTAKE CHANGES: FEMALE

### TABLES (CONTINUED)

- TABLE G 1 HEMATOLOGY: MALE
- TABLE G 2
   HEMATOLOGY: FEMALE
- TABLE H 1 BIOCHEMISTRY: MALE
- TABLE H 2BIOCHEMISTRY: FEMALE
- TABLE I 1 URINALYSIS: MALE
- TABLE I 2URINALYSIS: FEMALE
- TABLE J 1GROSS FINDINGS: MALE: ALL ANIMALS
- TABLE J 2GROSS FINDINGS: MALE : DEAD AND MORIBUND ANIMALS
- TABLE J 3
   GROSS FINDINGS: MALE: SACRIFICED ANIMALS
- TABLE J 4
   GROSS FINDINGS: FEMALE: ALL ANIMALS
- TABLE J 5GROSS FINDINGS: FEMALE: DEAD AND MORIBUND ANIMALS
- TABLE J 6
   GROSS FINDINGS: FEMALE: SACRIFICED ANIMALS
- TABLE K 1 ORGAN WEIGHT, ABSOLUTE: MALE
- TABLE K 2ORGAN WEIGHT, ABSOLUTE: FEMALE
- TABLE L 1 ORGAN WEIGHT, RELATIVE: MALE
- TABLE L 2ORGAN WEIGHT, RELATIVE: FEMALE
- TABLE M 1HISTOPATHOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS:<br/>MALE: ALL ANIMALS
- TABLE M 2HISTOPATHOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS:<br/>MALE: DEAD AND MORIBUND ANIMALS
- TABLE M 3HISTOPATHOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS:<br/>MALE: SACRIFICED ANIMALS

### TABLES (CONTINUED)

- TABLE M 4HISTOPATHOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS:<br/>FEMALE: ALL ANIMALS
- TABLE M 5HISTOPATHOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS:<br/>FEMALE: DEAD AND MORIBUND ANIMALS
- TABLE M 6HISTOPATHOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS:<br/>FEMALE: SACRIFICED ANIMALS
- TABLE N 1NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF<br/>TUMORS-TIME RELATED: MALE
- TABLE N 2NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF<br/>TUMORS-TIME RELATED: FEMALE
- TABLE O 1
   HISTOPATHOLOGICAL FINDINGS: NEOPLASTIC LESIONS: MALE
- TABLE O 2HISTOPATHOLOGICAL FINDINGS: NEOPLASTIC LESIONS:<br/>FEMALE
- TABLE P 1
   NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS:

   MALE
- TABLE P 2NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS:<br/>FEMALE
- TABLE Q 1 HISTOPATHOLOGICAL FINDINGS: METASTASIS OF TUMOR: MALE
- TABLE Q 2HISTOPATHOLOGICAL FINDINGS: METASTASIS OF TUMOR:<br/>FEMALE
- TABLE R 1CAUSE OF DEATH: MALE
- TABLE R 2 CAUSE OF DEATH: FEMALE

## TABLE A 1

# SURVIVAL ANIMAL NUMBERS: MALE

~

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1] REPORT TYPE : A1 104 SEX : MALE

| Group Name | Animals  | Administ | tration (Wee | eks)  |        |       |       |        |        |        |       |       |       |        |        |
|------------|----------|----------|--------------|-------|--------|-------|-------|--------|--------|--------|-------|-------|-------|--------|--------|
|            | At start | 0        | 1            | 2     | 3      | 4     | 5     | 6      | 7      | 8      | 9     | 10    | 11    | 12     | 13     |
| ontrol     | 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  |
| 5000 ppm   | 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 |
| 0000 ppm   | 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  |
| 20000 ppm  | 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)

| Group Name | Animals  | Administ | tration (Wee | ks)   |        | •     |       |       |       |       |       |       |       |       |       |
|------------|----------|----------|--------------|-------|--------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
|            | At start | 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 |
| 5000 ppm   | 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 |
| 10000 ppm  | 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)

STUDY NO. : 0613

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 104 SEX : MALE

| SEX : MALE |                     |                |                   |           |        |       |       |       |       |       |       |        |       |        | PAGE : : |
|------------|---------------------|----------------|-------------------|-----------|--------|-------|-------|-------|-------|-------|-------|--------|-------|--------|----------|
| Group Name | Animals<br>At start | Administ<br>28 | ration (Wee<br>29 | ks)<br>30 | 31     | 32    |       | 0.4   |       | 00    | 07    |        | 00    | 40     |          |
|            | AL SLALL            | 20             | 29                | 50        | 91     | 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    |
| 000 ppm    | 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     |
| 0000 ppm   | 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   |
| 20000 ppm  | 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)

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 104 SEX : MALE

| Group Name | Animals  | Administ | tration (Wee | eks)  |        |       |       |        |        |       |       |       |       |       |       |
|------------|----------|----------|--------------|-------|--------|-------|-------|--------|--------|-------|-------|-------|-------|-------|-------|
|            | At start | 42       | 43           | 44    | 45     | 46    | 47    | 48     | 49     | 50    | 51    | 52    | 53    | 54    | 55    |
| ontrol     | 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 |
| 5000 ppm   | 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  |
| .0000 ppm  | 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 | 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 | 100.0 | 98.0  |
| 20000 ppm  | 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)

BAIS4

,

#### STUDY NO. : 0613 SURVIVAL ANIMAL NUMBERS ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 104 SEX : MALE

| Group Name | Animals  | Administ | ration (Wee | ks)   |        |        |       |        |        |       |       |        |       |       |       |
|------------|----------|----------|-------------|-------|--------|--------|-------|--------|--------|-------|-------|--------|-------|-------|-------|
|            | At start | 56       | 57          | 58    | 59     | 60     | 61    | 62     | 63     | 64    | 65    | 66     | 67    | 68    | 69    |
| 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 | 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  |
| 5000 ppm   | 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 | 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  | 98.0  | 96.0  |
| 10000 ppm  | 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  |
| 20000 ppm  | 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  |

-

Number of survival/ Number of effective animals Survival rate(%)

(HAN360)

BAIS4

PAGE: 5

#### SURVIVAL ANIMAL NUMBERS

| Group Name | Animals  | Administ | ration (Wee | ks)   |       |       |       |       |       | -     |       |       |       |       |       |
|------------|----------|----------|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
|            | At start | 70       | 71          | 72    | 73    | 74    | 75    | 76    | 77    | 78    | 79    | 80    | 81    | 82    | 83    |
| Control    | 50       | 49/50    | 48/50       | 48/50 | 47/50 | 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  | 94.0  | 94.0  | 94.0  | 94.0  | 94. 0 | 94. 0 | 94.0  | 92.0  | 92.0  | 92.0  | 92.0  |
| 5000 ppm   | 50       | 47/50    | 47/50       | 47/50 | 47/50 | 47/50 | 47/50 | 47/50 | 46/50 | 46/50 | 44/50 | 44/50 | 44/50 | 43/50 | 42/50 |
|            |          | 94.0     | 94.0        | 94.0  | 94.0  | 94.0  | 94.0  | 94.0  | 92.0  | 92.0  | 88.0  | 88.0  | 88.0  | 86.0  | 84.0  |
| 0000 ppm   | 50       | 49/50    | 49/50       | 49/50 | 48/50 | 48/50 | 48/50 | 48/50 | 48/50 | 48/50 | 47/50 | 47/50 | 47/50 | 46/50 | 46/50 |
|            |          | 98.0     | 98.0        | 98.0  | 96.0  | 96.0  | 96.0  | 96.0  | 96.0  | 96.0  | 94.0  | 94.0  | 94.0  | 92.0  | 92.0  |
| 20000 ppm  | 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 | 48/50 | 48/50 |
|            |          | 98.0     | 98.0        | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 96.0  | 96.0  | 96.0  | 96.0  |

Number of survival/ Number of effective animals

Survival rate(%)

(HAN360)

.

~~~

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 104 SEX : MALE

| Group Name | Animals  | Administ | ration (Wee | ks)   |       |       |       | -     |       |       |       |       |       |       |       |
|------------|----------|----------|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
|            | At start | 84       | 85          | 86    | 87    | 88    | 89    | 90    | 91    | 92    | 93    | 94    | 95    | 96    | 97    |
| Control    | 50       | 45/50    | 44/50       | 44/50 | 44/50 | 43/50 | 42/50 | 41/50 | 40/50 | 40/50 | 40/50 | 40/50 | 40/50 | 40/50 | 40/50 |
|            |          | 90. 0    | 88.0        | 88.0  | 88.0  | 86.0  | 84.0  | 82.0  | 80.0  | 80.0  | 80.0  | 80.0  | 80.0  | 80.0  | 80.0  |
| 5000 ppm   | 50       | 42/50    | 42/50       | 41/50 | 41/50 | 41/50 | 40/50 | 40/50 | 40/50 | 39/50 | 39/50 | 38/50 | 38/50 | 37/50 | 36/50 |
|            |          | 84.0     | 84.0        | 82.0  | 82.0  | 82.0  | 80.0  | 80.0  | 80.0  | 78.0  | 78.0  | 76.0  | 76.0  | 74.0  | 72.0  |
| .0000 ppm  | 50       | 46/50    | 45/50       | 45/50 | 45/50 | 44/50 | 43/50 | 43/50 | 43/50 | 43/50 | 43/50 | 41/50 | 41/50 | 38/50 | 37/50 |
|            |          | 92.0     | 90.0        | 90.0  | 90.0  | 88.0  | 86.0  | 86.0  | 86.0  | 86.0  | 86.0  | 82.0  | 82.0  | 76.0  | 74.0  |
| mqq 0000   | 50       | 48/50    | 48/50       | 48/50 | 47/50 | 45/50 | 45/50 | 45/50 | 45/50 | 45/50 | 45/50 | 45/50 | 45/50 | 45/50 | 45/50 |
|            |          | 96.0     | 96.0        | 96.0  | 94.0  | 90.0  | 90.0  | 90.0  | 90.0  | 90.0  | 90.0  | 90.0  | 90.0  | 90.0  | 90.0  |

Number of survival/ Number of effective animals

Survival rate(%)

(HAN360)

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 104 SEX : MALE

| Group Name | Animals  | Administ | ration (Wee | ks)   |       |       |       | **    |                                       |  |
|------------|----------|----------|-------------|-------|-------|-------|-------|-------|---------------------------------------|--|
|            | At start | 98       | 99          | 100   | 101   | 102   | 103   | 104   |                                       |  |
|            |          |          |             |       |       |       |       |       | · · · · · · · · · · · · · · · · · · · |  |
| Control    | 50       | 38/50    | 36/50       | 35/50 | 35/50 | 35/50 | 35/50 | 35/50 |                                       |  |
|            |          | 76.0     | 72.0        | 70.0  | 70.0  | 70.0  | 70.0  | 70.0  |                                       |  |
| 5000 ppm   | 50       | 36/50    | 36/50       | 35/50 | 35/50 | 35/50 | 33/50 | 33/50 |                                       |  |
|            |          | 72.0     | 72.0        | 70.0  | 70.0  | 70.0  | 66.0  | 66.0  |                                       |  |
| 10000 ppm  | 50       | 36/50    | 36/50       | 36/50 | 36/50 | 36/50 | 36/50 | 36/50 |                                       |  |
|            |          | 72.0     | 72.0        | 72.0  | 72.0  | 72.0  | 72.0  | 72.0  |                                       |  |
| 20000 ppm  | 50       | 45/50    | 45/50       | 45/50 | 43/50 | 41/50 | 41/50 | 41/50 |                                       |  |
|            |          | 90.0     | 90.0        | 90.0  | 86.0  | 82.0  | 82.0  | 82.0  |                                       |  |

Number of survival/ Number of effective animals Survival rate(%)

Survivar rat

(HAN360)

TABLE A 2

SURVIVAL ANIMAL NUMBERS: FEMALE

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 104 SEX : FEMALE

| Group Name | Animals  | Administ | ration (Wee | ks)   |        |       |       |        |       |       |       |        |        |        |        |
|------------|----------|----------|-------------|-------|--------|-------|-------|--------|-------|-------|-------|--------|--------|--------|--------|
|            | At start | 0        | 1           | 2     | 3      | 4     | 5     | 6      | 7     | 8     | 9     | 10     | 11     | 12     | 13     |
| ontrol     | 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  |
| 500 ppm    | 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  |
| 000 ppm    | 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 |
| 0000 ppm   | 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)

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 104 SEX : FEMALE

#### SURVIVAL ANIMAL NUMBERS

| Group Name | Animals  | Administ    | tration (Wee | ks)   |        |       |       |       |        |       |       |        |        |        |        |
|------------|----------|-------------|--------------|-------|--------|-------|-------|-------|--------|-------|-------|--------|--------|--------|--------|
|            | At start | 14          | 15           | 16    | 17     | 18    | . 19  | 20    | 21     | 22    | 23    | 24     | 25     | 26     | 27     |
|            |          | <del></del> |              | · .   |        |       |       |       |        |       |       |        |        |        |        |
| 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  |
| 2500 ppm   | 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  |
| 5000 ppm   | 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 |
| 10000 ppm  | 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  | 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  | 100.0  | 98.0   |

Number of survival/ Number of effective animals Survival rate(%)

(HAN360)

 $\overline{\phantom{a}}$ 

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 104 SEX : FEMALE

| Group Name | Animals  | Administ | ration (Wee | ks)   |        |       |       |        |        |        |       |        |        |       |       |
|------------|----------|----------|-------------|-------|--------|-------|-------|--------|--------|--------|-------|--------|--------|-------|-------|
|            | At start | 28       | 29          | 30    | 31     | 32    | 33    | 34     | 35     | 36     | 37    | 38     | 39     | 40    | 41    |
| ontrol     | 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 |
| 2500 ppm   | 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 |
| 000 ppm    | 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 |
| 0000 ppm   | 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  |

 $\sim$ 

Number of survival/ Number of effective animals Survival rate(%)

(HAN360)

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 104 SEX : FEMALE

| roup Name | Animals  | Administ | ration (Wee | ks)   |        | 1     |       |       |       |       |       |        |        |       |       |
|-----------|----------|----------|-------------|-------|--------|-------|-------|-------|-------|-------|-------|--------|--------|-------|-------|
|           | At start | 42       | 43          | 44    | 45     | 46    | 47    | 48    | 49    | 50    | 51    | 52     | 53     | 54    | 55    |
| ontrol    | 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 |
| 500 ppm   | 50       | 50/50    | 50/50       | 50/50 | 50/50  | 50/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 48/50  | 48/50  | 48/50 | 47/50 |
|           |          | 100.0    | 100.0       | 100.0 | 100. 0 | 100.0 | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  | 96.0   | 96.0   | 96.0  | 94. 0 |
| 000 ppm   | 50       | 50/50    | 50/50       | 50/50 | 50/50  | 50/50 | 50/50 | 49/50 | 49/50 | 49/50 | 48/50 | 48/50  | 48/50  | 48/50 | 48/50 |
|           |          | 100.0    | 100. 0      | 100.0 | 100. 0 | 100.0 | 100.0 | 98.0  | 98.0  | 98.0  | 96.0  | 96.0   | 96.0   | 96.0  | 96.0  |
| 0000 µpm  | 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  |

Number of survival/ Number of effective animals Survival rate(%)

(HAN360)



•

-----

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 104 SEX : FEMALE

| Group Name | Animals  | Administ | ration (Wee | ks)    |       |       |       |       |        |        |       |       |       |       |       |
|------------|----------|----------|-------------|--------|-------|-------|-------|-------|--------|--------|-------|-------|-------|-------|-------|
|            | At start | 56       | 57          | 58     | 59    | 60    | 61    | 62    | 63     | 64     | 65    | 66    | 67    | 68    | 69    |
| 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 | 98.0  | 98.0  | 98.0  | 98.0  | 98.0  |
| 2500 ppm   | 50       | 47/50    | 47/50       | 47/50  | 47/50 | 47/50 | 47/50 | 46/50 | 46/50  | 46/50  | 46/50 | 45/50 | 45/50 | 44/50 | 41/50 |
|            |          | 94.0     | 94.0        | 94.0   | 94. 0 | 94.0  | 94.0  | 92.0  | 92.0   | 92.0   | 92.0  | 90.0  | 90.0  | 88.0  | 82.0  |
| 5000 ppm   | 50       | 48/50    | 48/50       | 48/50  | 48/50 | 48/50 | 48/50 | 47/50 | 46/50  | 46/50  | 46/50 | 46/50 | 46/50 | 46/50 | 46/50 |
|            |          | 96.0     | 96.0        | 96.0   | 96.0  | 96.0  | 96.0  | 94.0  | 92.0   | 92.0   | 92.0  | 92.0  | 92.0  | 92.0  | 92.0  |
| 10000 ppm  | 50       | 49/50    | 49/50       | 49/50  | 49/50 | 49/50 | 49/50 | 49/50 | 49/50  | 48/50  | 48/50 | 48/50 | 48/50 | 48/50 | 48/50 |
|            |          | 98.0     | 98.0        | 98.0   | 98.0  | 98.0  | 98.0  | 98.0  | 98.0   | 96.0   | 96.0  | 96.0  | 96.0  | 96.0  | 96.0  |

Number of survival/ Number of effective animals

.

Survival rate(%)

(HAN360)

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 104 SEX : FEMALE

| Group Name | Animals  | Administ | ration (Wee | ks)   |       |       |       |       |       |       |       |       |       |       |       |
|------------|----------|----------|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
|            | At start | 70       | 71          | 72    | 73    | 74    | 75    | 76    | 77    | 78    | 79    | 80    | 81    | 82    | 83    |
| Control    | 50       | 49/50    | 48/50       | 47/50 | 47/50 | 47/50 | 46/50 | 45/50 | 45/50 | 44/50 | 44/50 | 44/50 | 44/50 | 44/50 | 44/50 |
|            |          | 98.0     | 96.0        | 94.0  | 94. 0 | 94.0  | 92.0  | 90. 0 | 90.0  | 88.0  | 88.0  | 88. 0 | 88.0  | 88.0  | 88.0  |
| 2500 ppm   | 50       | 41/50    | 41/50       | 41/50 | 41/50 | 40/50 | 40/50 | 40/50 | 40/50 | 39/50 | 39/50 | 37/50 | 37/50 | 36/50 | 36/50 |
|            |          | 82.0     | 82.0        | 82.0  | 82.0  | 80.0  | 80.0  | 80.0  | 80.0  | 78.0  | 78.0  | 74.0  | 74.0  | 72.0  | 72.0  |
| 000 ppm    | 50       | 46/50    | 46/50       | 46/50 | 45/50 | 44/50 | 44/50 | 44/50 | 44/50 | 44/50 | 42/50 | 42/50 | 42/50 | 41/50 | 41/50 |
|            |          | 92.0     | 92.0        | 92.0  | 90.0  | 88.0  | 88.0  | 88.0  | 88.0  | 88.0  | 84.0  | 84. 0 | 84.0  | 82.0  | 82.0  |
| 10000 ppm  | 50       | 48/50    | 48/50       | 48/50 | 48/50 | 48/50 | 47/50 | 47/50 | 46/50 | 46/50 | 44/50 | 44/50 | 44/50 | 42/50 | 42/50 |
|            |          | 96.0     | 96.0        | 96.0  | 96. 0 | 96.0  | 94.0  | 94.0  | 92.0  | 92.0  | 88.0  | 88.0  | 88.0  | 84.0  | 84.0  |

Number of survival/ Number of effective animals

Survival rate(%)

(HAN360)

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 104 SEX : FEMALE

| Group Name | Animals  | Administ | ration (Wee | ks)   |       |       |       |       |       |       |       |       |       |       |       |
|------------|----------|----------|-------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
|            | At start | 84       | 85          | 86    | 87    | 88    | 89    | 90    | 91    | 92    | 93    | 94    | 95    | 96    | 97    |
| Control    | 50       | 42/50    | 41/50       | 41/50 | 41/50 | 41/50 | 40/50 | 40/50 | 40/50 | 40/50 | 39/50 | 39/50 | 38/50 | 38/50 | 34/50 |
|            |          | 84.0     | 82.0        | 82.0  | 82.0  | 82.0  | 80.0  | 80.0  | 80.0  | 80.0  | 78.0  | 78.0  | 76.0  | 76.0  | 68.0  |
| 500 ppm    | 50       | 34/50    | 34/50       | 34/50 | 34/50 | 34/50 | 34/50 | 34/50 | 34/50 | 34/50 | 33/50 | 33/50 | 31/50 | 31/50 | 30/50 |
|            |          | 68.0     | 68.0        | 68.0  | 68.0  | 68.0  | 68.0  | 68.0  | 68.0  | 68.0  | 66.0  | 66.0  | 62.0  | 62.0  | 60.0  |
| 000 ppm    | 50       | 41/50    | 41/50       | 40/50 | 40/50 | 40/50 | 40/50 | 38/50 | 38/50 | 37/50 | 36/50 | 36/50 | 36/50 | 35/50 | 34/50 |
|            |          | 82.0     | 82.0        | 80.0  | 80. 0 | 80.0  | 80.0  | 76.0  | 76.0  | 74.0  | 72.0  | 72.0  | 72.0  | 70.0  | 68.0  |
| 0000 ppm   | 50       | 42/50    | 40/50       | 39/50 | 37/50 | 37/50 | 36/50 | 36/50 | 36/50 | 33/50 | 33/50 | 32/50 | 32/50 | 32/50 | 31/50 |
|            |          | 84.0     | 80.0        | 78.0  | 74.0  | 74.0  | 72.0  | 72.0  | 72.0  | 66.0  | 66.0  | 64.0  | 64.0  | 64.0  | 62.0  |

Number of survival/ Number of effective animals

Survival rate(%)

(HAN360)

BAIS4

.

#### STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 104 SEX : FEMALE

#### SURVIVAL ANIMAL NUMBERS

Group Name Animals Administration (Weeks)\_ 98 99 At start 100 101 102 103 104 Control 50 34/5034/50 34/50 32/5032/50 30/50 29/5068.0 68.0 68.0 64.0 64.0 60.0 58.0 2500 ppm 50 30/50 30/50 30/50 29/50 28/50 26/5026/50 60.0 60.0 60.0 58.0 56.0 52.0 52.0 5000 ppm 50 34/50 34/50 34/50 33/50 32/5032/50 31/50 68.0 68.0 68.0 66.0 64.0 64.0 62.0 10000 ppm 50 30/50 28/50 26/5024/5024/5023/5020/5060.0 56.0 52.0 48.0 48.0 46.0 40.0

.

Number of survival/ Number of effective animals Survival rate(%)

.

(HAN360)

BAIS4

PAGE : 16

## TABLE B 1

# CLINICAL OBSERVATION: MALE

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

 $\sim \sim$ 

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 104

•

#### SEX : MALE

| Clinical sign          | Group Name | Admini | stration We | eek-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                  | Centrel    | 0      | 0           | 0       | 0      | 0      | 0      |        |        | 0   | 0    | <u>^</u> | <u>^</u> |        |        |
| JEATH                  | Control    |        | 0           | 0       | 0      | 0      | 0      | 0      | 0      | 0   | 0    | 0        | 0        | 0      | 0      |
|                        | 5000 ppm   | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0      | 0   | 0    | 0        | 0        | 0      | 0      |
|                        | 10000 ppm  | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0      | 0   | 0    | 0        | 0        | 0      | 0      |
|                        | 20000 ppm  | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0      | 0   | 0    | 0        | 0        | 0      | 0      |
| ORIBUND SACRIFICE      | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0      | 0   | 0    | 0        | 0        | 0      | 0      |
|                        | 5000 ppm   | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0      | 0   | 0    | 0        | 0        | 0      | 0      |
|                        | 10000 ppm  | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0      | 0   | 0    | 0        | 0        | 0      | 0      |
|                        | 20000 ppm  | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0      | 0   | 0    | 0        | õ        | Ő      | 0      |
| OCOMOTOR MOVEMENT DECR | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0      | 0   | 0    | 0        | 0        | 0      | 0      |
|                        | 5000 ppm   | ů      | Ő           | 0<br>0  | 0      | 0      | 0      | 0<br>0 | 0      | 0   | 0    | 0        | 0        | 0      | 0      |
|                        | 10000 ppm  | Ő      | ů           | ů       | 0      | 0      | 0      | 0<br>0 | 0      | 0   | 0    | 0        | 0        | 0      | 0      |
|                        | 20000 ppm  | 0      | ° Õ         | Ő       | 0      | 0      | 0      | 0      | 0      | 0   | 0    | 0        | 0        | 0      | 0      |
| UNCHBACK POSITION      | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0      | 0   | 0    | 0        | 0        | 0      | 0      |
|                        | 5000 ppm   | Ő      | 0           | 0       | 0      | 0      | 0      | 0      | 0      | 0   | 0    | 0        |          |        | 0      |
|                        | 10000 ppm  | 0      | 0           | 0       | 0      | 0      |        |        | -      |   | . •  | -        | 0        | 0      | •      |
|                        | 20000 ppm  | 0      | 0           | 0       | 0      | 0      | 0      | 0<br>0 | 0<br>0 | 0<br>0  | 0    | 0        | 0<br>0   | 0<br>0 | 0<br>0 |
|                        | Deese ppm  | · ·    | Ŭ           | 0       | Ũ      | Ū      | Ū      | v      | 0      | v   | Ū    | 0        |          | 0      | Ū      |
| TAXIC GAIT             | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0      | 0   | . 0  | 0        | 0        | 0      | 0      |
|                        | 5000 ppm   | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0      | 0   | 0    | 0        | 0        | 0      | 0      |
|                        | 10000 ppm  | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0      | 0   | 0    | 0        | 0        | 0      | 0      |
|                        | 20000 ppm  | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0      | 0   | 0    | 0        | 0        | 0      | 0      |
| OILED                  | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0      | 0   | 0    | 0        | 0        | 0      | 0      |
|                        | 5000 ppm   | 0      | 0           | õ       | Ő      | ů<br>0 | Ő      | Ő      | 0<br>0 | 0   | ŏ    | 0        | 0<br>0   | 0      | 0      |
|                        | 10000 ppm  | õ      | Õ           | ŏ       | ů<br>0 | 0      | 0      | Ő      | õ      | 0   | 0    | 0        | 0        | 0      | 0      |
|                        | 20000 ppm  | Õ      | Õ           | õ       | 0      | 0      | 0      | 0      | 0      | 0   | 0    | 0        | 0        | 0      | 0      |
|                        |            | -      | -           | -       | · ·    | Ū.     | Ŭ      | ·      | Ũ      | , in the second s | v    | Ũ        | Ŭ.       | Ū      | Ū      |
| ILOERECTION            | Control    | 0      | 0           | 0       | 0      | 0      | ~ 0    | 0      | 0      | 0   | 0    | 0        | 0        | 0      | 0      |
|                        | 5000 ppm   | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0      | 0   | 0    | 0        | 0        | 0      | 0      |
|                        | 10000 ppm  | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0      | 0   | 0    | 0        | 0        | 0      | 0      |
|                        | 20000 ppm  | 0      | 0           | 1       | 1      | 0      | 0      | 0      | 0      | 0   | 0    | 0        | 0        | 0      | 0      |
| ROG BELLY              | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0      | 0   | 0    | 0        | 0        | 0      | 0      |
|                        | 5000 ppm   | 0      | 0           | 0       | ů<br>0 | 0      | 0<br>0 | Ő      | 0      | 0   | 0    | 0        | 0        | 0      | 0      |
|                        | 10000 ppm  | ů      | ů           | Ő       | 0      | 0      | 0      | 0      | 0      | 0   | 0    | 0        | 0        | 0      | 0      |
|                        | 20000 ppm  | ů<br>0 | 0<br>0      | Ő       | 0      | 0      | 0      | 0      | 0      | 0   | 0    | 0        | 0        | 0      | 0      |
| OILED PERI-GENITALIA   | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0      | 0   | 0    | 0        | 0        | 0      | 0      |
| OTDED TENT VENTILETA   | 5000 ppm   | 0      | 0           |         |        |        |        | -      |        | -   | -    | •        | 0        | 0      | 0      |
|                        |            | •      |             | 0       | 0      | 0      | 0      | 0      | 0      | 0   | 0    | 0        | 0        | 0      | 0      |
|                        | 10000 ppm  | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0      | 0   | 0    | 0        | 0        | 0      | 0      |
|                        | 20000 ppm  | 0      | 0           | 0       | 0      | 0      | . 0    | 0      | 0      | 0   | 0    | 0        | 0        | 0      | 0      |

PAGE: 1

(HAN190)

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : MALE

| Clinical sign         | Group Name | Admini | stration W | eek-dav |      |      |      |      |      |      |      |      |      |      |      |
|-----------------------|------------|--------|------------|---------|------|------|------|------|------|------|------|------|------|------|------|
|                       |            | 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 |
|                       |            | -      | ,          |         |      |      |      |      |      |      |      |      |      |      |      |
| EATH                  | Control    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | .0   | 0    | 0    | 0    | 0    | 1    |
|                       | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 20000 ppm  | 0      | 0          | Q       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| RIBUND SACRIFICE      | Control    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | . 0  | 0    | 0    | 0    | . 0  | 0    |
|                       | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 20000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| COMOTOR MOVEMENT DECR | Control    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 10000 ppm  | 0      | 0          | Ó       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 20000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| NCHBACK POSITION      | Control    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 20000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| XIC GAIT              | Control    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 20000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ILED                  | Control    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 20000 ррт  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LOERECTION            | Control    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 20000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| OG BELLY              | Control    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | . 0  | 0    | 0    | 0    | 0    |
|                       | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 20000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LED PERI-GENITALIA    | Control    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                       | 20000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

(HAN190)

PAGE : 2

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : MALE

PAGE : 3

| Clinical sign          | Group Name | Admini | stration W | eek-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    |
|                        | 5000 ppm   | 1      | 1          | 1       | 1      | 1    | 1    | 1      | 1    | 1    | 1      | 1      | 1      | 1      | 1    |
|                        | 10000 ppm  | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |
|                        | 20000 ppm  | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |
| ORIBUND SACRIFICE      | Control    | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |
|                        | 5000 ppm   | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |
|                        | 10000 ppm  | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |
|                        | 20000 ppm  | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |
| OCOMOTOR MOVEMENT DECR | Control    | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |
|                        | 5000 ppm   | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |
|                        | 10000 ppm  | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |
|                        | 20000 ppm  | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0    | Ō      | Õ      | Õ      | 0      | Õ    |
| UNCHBACK POSITION      | Control    | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |
|                        | 5000 ppm   | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |
|                        | 10000 ppm  | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |
|                        | 20000 ррт  | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |
| TAXIC GAIT             | Control    | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0    | · 0    | 0      | 0      | 0      | 0    |
|                        | 5000 ppm   | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |
|                        | 10000 ppm  | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |
|                        | 20000 ppm  | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |
| SOILED                 | Control    | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |
|                        | 5000 ppm   | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |
|                        | 10000 ppm  | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0    | Ō      | Ō      | Ő      | õ      | Ő    |
|                        | 20000 ppm  | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | Ő    | 0<br>0 | ů<br>0 | õ      | õ      | Ő    |
| ILOERECTION            | Control    | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0    | . 0    | 0      | 0      | 0      | 0    |
|                        | 5000 ppm   | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0    | Ō      | 0      | 0      | 0      | õ    |
|                        | 10000 ppm  | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0    | 0      | õ      | ŏ      | ů      | ů    |
|                        | 20000 ppm  | 0      | 0          | 0       | 0      | 0    | 0    | 0      | Û,   | 0    | 0<br>0 | ů<br>0 | Ő      | Ő      | 0    |
| ROG BELLY              | Control    | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |
|                        | 5000 ppm   | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0    | Ō      | 0      | 0      | Ő      | Ő    |
|                        | 10000 ppm  | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0    | Õ      | õ      | Ő      | Ő      | ů    |
|                        | 20000 ppm  | 0      | 0          | 0       | 0      | 0    | 0    | 0      | Õ    | Ō    | Ő      | ů<br>0 | ů      | ů      | 0    |
| OILED PERI-GENITALIA   | Control    | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |
|                        | 5000 ppm   | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | õ      | Ő    |
|                        | 10000 ppm  | 0      | 0          | 0       | Ō      | Ő    | . 0  | 0<br>0 | ů    | Õ    | ů<br>0 | ů      | ů<br>0 | 0<br>0 | Ő    |
|                        | 20000 ppm  | 0      | 0          | 0       | 0<br>0 | Ő    | 0    | Ő      | ů    | ů    | õ      | ů<br>0 | ŏ      | 0<br>0 | õ    |

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

#### SEX : MALE

PAGE : 4

-

| Clinical sign         | Group Name | Admini | stration W | eek-dav |      |        |        |        |      |        |        |        |        |        |        |
|-----------------------|------------|--------|------------|---------|------|--------|--------|--------|------|--------|--------|--------|--------|--------|--------|
|                       |            | 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    | 0      | 0      | 0      | 0      | 0      | 0      |
|                       | 5000 ppm   | 1      | 1          | 1       | 1    | 1      | 1      | 1      | 1    | 1      | 1      | 1      | 1      | 1      | 1      |
|                       | 10000 ррт  | 0      | 0          | 0       | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 1      | 1      |
|                       | 20000 ppm  | 0      | 0          | 0       | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 1      |
| DRIBUND SACRIFICE     | Control    | 0      | 0          | 0       | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
|                       | 5000 ppm   | 0      | 0          | 0       | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
|                       | 10000 ppm  | 0      | 0          | 0       | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
|                       | 20000 ppm  | 0      | 0          | 0       | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
| COMOTOR MOVEMENT DECR | Control    | 0      | 0          | 0       | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
|                       | 5000 ppm   | 0      | 0          | 0       | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
|                       | 10000 ppm  | 0      | 0          | 0       | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
|                       | 20000 ppm  | 0      | 0          | 0       | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | Ő      | 0      | ů      |
| JNCHBACK POSITION     | Control    | 0      | 0          | 0       | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0.     | 0      | 0      |
|                       | 5000 ppm   | 0      | 0          | 0       | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
|                       | 10000 ppm  | 0      | 0          | 0       | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | õ      | õ      |
|                       | 20000 ppm  | 0      | 0          | 0 -     | 0    | 0      | 0      | 0      | 0    | 0<br>0 | Ő      | Ő      | ů<br>0 | 0      | Ő      |
| FAXIC GAIT            | Control    | 0      | 0          | 0       | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
|                       | 5000 ppm   | 0      | 0          | 0       | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
|                       | 10000 ppm  | 0      | 0          | 0       | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
|                       | 20000 ppm  | 0      | 0          | 0       | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
| DILED                 | Control    | 0      | 0          | 0       | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
|                       | 5000 ppm   | 0      | 0          | 0       | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | Ō      | 0      | ŏ      |
|                       | 10000 ppm  | 0      | 0          | Ō       | 0    | Ō      | 0      | ů<br>0 | õ    | õ      | õ      | õ      | Ő      | Ő      | ŏ      |
|                       | 20000 ppm  | 0      | 0          | 0       | 0    | õ      | ů<br>0 | 0      | Õ    | Õ      | õ      | 0      | 0      | 0      | 0      |
| ILOERECTION           | Control    | 0      | 0          | 0       | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
|                       | 5000 ppm   | 0      | 0          | Ō       | Ō    | õ      | Ő      | Ő      | ů    | õ      | ŏ      | õ      | 0<br>0 | Õ      | 0      |
|                       | 10000 ppm  | 0      | ů          | 0       | õ    | õ      | 0<br>0 | 0<br>0 | 0    | Ő      | 0      | 0<br>0 | 0      | 0      | 0      |
|                       | 20000 ppm  | ů<br>0 | ů<br>0     | 0       | 0    | , Ö    | Ő      | 0      | 0    | 0      | 0<br>0 | 0      | 0      | . 0    | 0      |
| OG BELLY              | Control    | 0      | 0          | 0       | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
|                       | 5000 ppm   | 0      | Õ          | Ő       | õ    | 0<br>0 | 0      | 0      | 0    | 0      | 0      | ő      | 0      | 0      | 0      |
|                       | 10000 ppm  | ů      | ů          | 0       | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
|                       | 20000 ppm  | ő      | Ő          | Ő       | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
| )ILED PERI-GENITALIA  | Control    | 0      | 0          | 0       | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
|                       | 5000 ppm   | Ő      | Ô          | Ő       | õ    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
|                       | 10000 ppm  | 0      | 0          | 0       | 0    | 0      | 0      | 0      | 0    | 0      |        | -      | 0      |        | -      |
|                       | 20000 ppm  | 0      | 0          | 0       | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0<br>0 | 0      | 0<br>0 | 0<br>0 |
|                       |            |        |            |         |      |        |        |        |      |        |        |        |        |        |        |

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

#### SEX : MALE

| Clinical sign            | Group Name | Admini | stration W | eek-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      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    | 1    | 1      | 1    |
|                          | 5000 ppm   | 1      | 1          | 1       | 1      | 1    | 1      | 1      | 1    | 1      | 1      | 1    | 1    | 1      | 1    |
|                          | 10000 ppm  | 1      | 1          | 1       | 1      | 1    | 1      | 1      | 1    | 1      | 1      | ī    | 1    | - 1    | · 1  |
|                          | 20000 ppm  | 1      | 1          | 1       | 1      | 1    | 1      | 1      | 1    | 1      | 1      | 1    | 1    | 1      | 1    |
| MORIBUND SACRIFICE       | Control    | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    | 0    | 0      | 0    |
|                          | 5000 ppm   | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    | 0    | 1      | 2    |
|                          | 10000 ppm  | õ      | ů          | ů       | 0      | 0    | 0      | ů<br>0 | 0    | 0      | 0      | 0    | 0    | 0      | 0    |
|                          | 20000 ppm  | 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    |
| Booomoron mortanian Mion | 5000 ppm   | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    | 0    | 0      |      |
|                          | 10000 ppm  | 0      | 0          | -       |        | -    |        | -      | -    | -      |        |      |      | -      | 0    |
|                          | 20000 ppm  |        |            | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    | 0    | 0      | 0    |
|                          | 20000 ppm  | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    | 0    | 0      | 0    |
| HUNCHBACK POSITION       | Control    | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    | 0    | 0      | 0    |
|                          | 5000 ppm   | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    | 0    | 0      | 0    |
|                          | 10000 ppm  | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    | 0    | 0      | 0    |
|                          | 20000 ppm  | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    | 0    | 0      | 0    |
| ATAXIC GAIT              | Control    | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    | 0    | 0      | 0    |
|                          | 5000 ppm   | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    | 0    | 0      | 0    |
|                          | 10000 ppm  | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    | 0    | 0      | 0    |
|                          | 20000 ppm  | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    | 0    | 0      | 0    |
| SOILED                   | Control    | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    | 0    | 0      | 0    |
|                          | 5000 ppm   | 0      | 0          | 0       | 0      | 0    | 0      | Ō      | 0    | 0      | 0      | 0    | õ    | õ      | Ő    |
|                          | 10000 ppm  | 0      | 0          | 0       | 0      | 0    | 0      | Ō      | Ő    | ů      | ů      | Ő    | ŏ    | õ      | ů    |
|                          | 20000 ppm  | 0      | 0          | 0       | 0      | Õ    | 0      | Õ      | õ    | õ      | 0      | õ    | 0    | õ      | Ő    |
| PILOERECTION             | Control    | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    | 0    | 0      | 1    |
|                          | 5000 ppm   | 0      | 0          | 0       | 0      | Ő    | Ő      | ŏ      | Ő    | ů<br>0 | ů<br>0 | õ    | ů    | 0<br>0 | 0    |
|                          | 10000 ppm  | 0      | 0          | õ       | 0<br>0 | ů    | ů      | ů      | ů    | 0      | 0      | 0    | Ő    | 0      | 0    |
|                          | 20000 ppm  | 0      | 0          | 0       | Ő      | õ    | ů<br>0 | ů<br>0 | ő    | ů      | 0      | õ    | Ő    | 0      | 0    |
| FROG BELLY               | Control    | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    | 0    | 0      | 0    |
|                          | 5000 ppm   | 0      | ů<br>0     | õ       | ů<br>0 | 0    | 0      | 0<br>0 | 0    | 0      | 0      | 0    | 0    | 0      | 0    |
| •                        | 10000 ppm  | 0      | ů          | 0<br>0  | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    | 0    | 0      | 0    |
|                          | 20000 ppm  | 0      | Ő          | õ       | 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    |
|                          | 5000 ppm   | Ő      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      |        | 0    |      |        |      |
|                          | 10000 ppm  | 0      | 0          | 0       | 0      | 0    | 0      |        | -    | 0      | 0      |      | . 0  | 0      | 0    |
|                          | 20000 ppm  | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | -      | 0      | 0    | 0    | 0      | 0    |
|                          | 20000 ppm  | U      | U          | U       | U      | U    | U      | 0      | 0    | 0      | 0      | 0    | 0    | 0      | 0    |

PAGE : 5

~~~

(HAN190)

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

#### SEX : MALE

| Clinical sign          | Group Name             | Admini | stration W | eek-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   |
| - Amu                  |                        | 0      | 0          | 2       | 0    |      |        |        | _    | _      |        |        |      |        | _      |
| EATH                   | Control                | 2      | 2          | 3       | 3    | 3    | 3      | 3      | 3    | 3      | 4      | 4      | 4    | 4      | 5      |
|                        | 5000 ppm               | 1      | 1          | 1       | 1    | 1    | 1      | 2      | 2    | 4      | 4      | 4      | 5    | 6      | 6      |
|                        | 10000 ppm              | 1      | 1          | 2       | 2    | 2    | 2      | 2      | 2    | 3      | 3      | 3      | 4    | 4      | 4      |
|                        | 20000 ppm              | 1      | 1          | 1       | 1    | 1    | 1      | 1      | 1    | 1      | 2      | 2      | 2    | 2      | 2      |
| ORIBUND SACRIFICE      | Control                | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      |
|                        | 5000 ppm               | 2      | 2          | 2       | 2    | 2    | 2      | 2      | 2    | 2      | 2      | 2      | 2    | 2      | 2      |
|                        | 10000 ppm              | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      |
|                        | 20000 ppm              | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      |
| OCOMOTOR MOVEMENT DECR | Control                | 0      | 0          | 0       | 1    | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      |
|                        | 5000 ppm               | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      |
|                        | 10000 ppm              | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      |
|                        | 20000 ppm              | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      |
| UNCHBACK POSITION      | Control                | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      |
|                        | 5000 ppm               | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      |
|                        | 10000 ppm              | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      |
|                        | 20000 ppm              | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      |
| TAXIC GAIT             | Control                | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      |
|                        | 5000 ppm               | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | Ő      | 0<br>0 |
|                        | 10000 ppm              | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | õ      | 0<br>0 |
|                        | 20000 ppm              | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      |
| OILED                  | Control                | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      |
|                        | 5000 ppm               | ŏ      | õ          | 0       | ŏ    | 0    | 0<br>0 | õ      | Ő    | 0      | 0      | 0      | 0    | ŏ      | 0      |
|                        | 10000 ppm              | ŏ      | Ő          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      |
|                        | 20000 ppm              | 0      | Ő          | 0       | õ    | 0    | Ő      | 0<br>0 | 0    | 0      | 0      | 0      | 0    | 0      | 0      |
| ILOERECTION            | Control                | 0      | 0          | . 0     | 0    | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      |
|                        | 5000 ppm               | 0      | 0          | 0       | 0    | 0    | 1      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      |
|                        | 10000 ppm              | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0      | -      | 0    |        | 0      |
|                        | 20000 ppm              | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 1<br>0 | 1<br>0 | 1<br>0 | 0    | 0<br>0 | 0<br>0 |
| ROG BELLY              | Control                | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      |
|                        | 5000 ppm               | 0      | 0          | 0       | 0    |      |        |        | 0    | 0      | 0      | 0      | 0    | 0      | 0      |
|                        | 10000 ppm<br>10000 ppm | 0      | 0          | . 0     | 0    | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      |
|                        | 20000 ppm<br>20000 ppm | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      |
|                        | 20000 ppm              | U      | U          | U       | U    | Ų    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      |
| DILED PERI-GENITALIA   | Control                | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      |
|                        | 5000 ppm               | 0      | 0          | 0       | 0    | 0    | 1      | 0      | 1    | 0      | 0      | 0      | 0    | 0      | 0      |
|                        | 10000 ppm              | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | · 1    | 1      | 1 .    | 0    | 0      | 0      |
|                        | 20000 ppm              | 0      | 0          | . 0     | 0    | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      |

BAIS 4

PAGE : 6

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : MALE

PAGE : 7

| linical sign          | Group Name | Admini | stration W | eek-dav |      |      |      |      |      |      |      |        |      |      |        |
|-----------------------|------------|--------|------------|---------|------|------|------|------|------|------|------|--------|------|------|--------|
|                       |            | 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   |
|                       |            |        |            |         |      |      |      |      |      |      |      |        |      |      |        |
| EATH                  | Control    | 6      | 6          | 6       | 6    | 6    | 7    | 8    | 8    | 8    | 8    | 8      | 8    | 8    | 9      |
|                       | 5000 ppm   | 6      | 7          | 7       | 7    | 8    | 8    | 8    | 8    | 8    | 9    | 9      | 10   | 11   | 11     |
|                       | 10000 ppm  | 5      | 5          | 5       | 6    | 7    | 7    | 7    | 7    | 7    | 9    | 9      | 12   | 13   | 14     |
|                       | 20000 ppm  | 2      | 2          | 3       | 5    | 5    | 5    | 5    | 5    | 5    | 5    | 5      | 5    | 5    | 5      |
| RIBUND SACRIFICE      | Control    | 0      | 0          | 0       | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 2      | 2    | 2    | 3      |
|                       | 5000 ppm   | 2      | 2          | 2       | 2    | 2    | 2    | 2    | 3    | 3    | 3    | 3      | 3    | 3    | 3      |
|                       | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      |
|                       | 20000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      |
| COMOTOR MOVEMENT DECR | Control    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      |
|                       | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      |
|                       | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      |
|                       | 20000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      |
| NCHBACK POSITION      | Control    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      |
|                       | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      |
|                       | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      |
|                       | 20000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      |
| AXIC GAIT             | Control    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0    | : 0    |
|                       | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      |
|                       | 10000 թթա  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      |
|                       | 20000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      |
| DILED                 | Control    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 1    | 1      |
|                       | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0 .  | 0      | 0    | 0    | 0      |
|                       | 10000 ppm  | 0.     | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 1    | 0      |
|                       | 20000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | Ō    | 0      |
| LOERECTION            | Control    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 1    | 2    | 2      |
|                       | 5000 ppm   | 0      | 0          | 0       | 1    | 0    | 1    | 1    | 1    | 1    | 1    | 1      | 1    | . 0  | 0      |
|                       | 10000 ppm  | 0      | 0          | 0       | 1    | 0    | 0    | 0    | 0    | 1    | 1    | 1      | 2    | 1    | Ő      |
|                       | 20000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | ō    | ō      | 0    | 0    | ů      |
| OG BELLY              | Control    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 1      |
|                       | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | Ő    | 0    | ò      |
|                       | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | Õ    | Ő    | õ    | õ      | ů    | Ő    | 0      |
|                       | 20000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | Ō    | Ő    | Ő      | Õ    | 0    | Ő      |
| ILED PERI-GENITALIA   | Control    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      |
|                       | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      | Ő    | Õ    | õ      |
|                       | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | Ō    | Õ    | õ    | õ    | Ő      | õ    | 0    | 0<br>0 |
|                       | 20000 ppm  | 0      | 0          | 0       | 0    | Ö    | Ő    | Õ    | õ    | õ    | ů    | ů<br>0 | õ    | ŏ    | ŏ      |

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

#### SEX : MALE

PAGE : 8

| Clinical sign                         | Group Name | Admin | istration N | Veek-dav |       |       |       |  |
|---------------------------------------|------------|-------|-------------|----------|-------|-------|-------|--|
|                                       | ever vene  | 99-7  | 100-7       | 101-7    | 102-7 | 103-7 | 104-7 |  |
| · · · · · · · · · · · · · · · · · · · |            |       |             |          |       |       |       |  |
|                                       |            |       |             |          |       |       |       |  |
| EATH                                  | Control    | 11    | 12          | 12       | 12    | 12    | 12    |  |
|                                       | 5000 ppm   | 11    | 12          | 12       | 12    | 14    | 14    |  |
|                                       | 10000 ppm  | 14    | 14          | 14       | 14    | 14    | 14    |  |
|                                       | 20000 ppm  | 5     | 5           | 7        | 9     | 9     | 9     |  |
| ORIBUND SACRIFICE                     | Control    | 3     | 3           | 3        | 3     | 3     | 3     |  |
| Internet Enternet 105                 | 5000 ppm   | 3     | 3           | 3        | 3     | 3     | 3     |  |
|                                       |            |       | 0           | Ó        | 0     |       |       |  |
|                                       | 10000 ppm  | 0     |             |          |       | 0     | 0     |  |
|                                       | 20000 ррт  | 0     | 0           | 0 .      | 0     | 0     | 0     |  |
| OCOMOTOR MOVEMENT DECR                | Control    | 0     | 0           | 0        | 0     | 0     | 0     |  |
|                                       | 5000 ppm   | 0     | 0           | 0        | 0     | 0     | 0     |  |
|                                       | 10000 ppm  | 0     | 0           | 0        | 0     | 0     | 0     |  |
|                                       | 20000 ppm  | 0     | 0           | 0        | 0     | 0     | 0     |  |
| UNCHBACK POSITION                     | Control    | 0     | 0           | 1        | 1     | 1     | 1     |  |
|                                       | 5000 ppm   | 0     | Ő           | Ô        | 0     | 0     | 0     |  |
|                                       |            |       | -           |          |       |       |       |  |
|                                       | 10000 ppm  | 0     | 0           | 0        | 0     | 0     | 0     |  |
|                                       | 20000 ppm  | 0     | 0           | 0        | 0     | 0     | 0     |  |
| TAXIC GAIT                            | Control    | 0     | 0           | 0        | 0     | 0     | 0     |  |
|                                       | 5000 ppm   | 0     | 0           | 0        | 0     | 0     | 0     |  |
|                                       | 10000 ppm  | 0     | 0           | 0        | 0     | 0     | 0     |  |
|                                       | 20000 ppm  | 0     | 0           | 0        | 0     | 1     | 1     |  |
| OILED                                 | Control    | 0     | 0           | 0        | 0     | 0     | 0     |  |
|                                       | 5000 ppm   | 0     | Ő           | Ő        | 0     | 0     | 0     |  |
|                                       |            |       |             |          |       |       |       |  |
|                                       | 10000 ppm  | 0     | 0           | 0        | 0     | 0     | 0     |  |
|                                       | 20000 ppm  | 0     | 0           | 0        | 0     | 0     | 0     |  |
| ILOERECTION                           | Control    | 1     | 0           | 2        | 2     | 2     | 2     |  |
|                                       | 5000 ррт   | 0     | 0           | 0        | 1     | 1     | 1     |  |
|                                       | 10000 ppm  | 0     | 0           | 0        | 0     | 0     | 1     |  |
|                                       | 20000 ppm  | 0     | 0           | 2        | 2     | 2     | 2     |  |
| ROG BELLY                             | Control    | 1     | 0           | 0        | 0     | 0     | 0     |  |
| 100 10051                             |            | 1     |             |          | 0     | 0     | 0     |  |
|                                       | 5000 ppm   | 0     | 0           | 0        | 0     | 0     | 0     |  |
|                                       | 10000 ppm  | 0     | 0           | 0        | 0     | 0     | 0     |  |
|                                       | 20000 ррт  | 0     | 0           | 0        | 0     | 0     | 0     |  |
| DILED PERI-GENITALIA                  | Control    | 0     | 0           | 0        | 0     | 0     | 0     |  |
|                                       | 5000 ppm   | 0     | 0           | 0        | 0     | 0     | 0     |  |
|                                       | 10000 ppm  | 0     | 0           | 0        | Õ     | Ő     | ů     |  |
|                                       | 20000 ppm  | Ů     | ů           | õ        | 1     | 1     | 1     |  |
|                                       | Boood bbm  | v     | v           | •        | r     | 1     | T     |  |

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

#### SEX : MALE

| PAGE |  |
|------|--|
|      |  |

| linical 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 |
|                  |            |                         |     |     |     |     |     |     |     |     |      |      |      |      |      |
| EXOPHTHALMOS     | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                  | 5000 ppm   | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                  | 10000 ppm  | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                  | 20000 ppm  | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| TERNAL MASS      | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                  | 5000 ppm   | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                  | 10000 ppm  | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                  | 20000 ppm  | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| VTERNAL MASS     | Control    | 0                       | 0   | 0   | .0  | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                  | 5000 ppm   | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 1    | 1    | 1    | 1    |
|                  | 10000 ppm  | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                  | 20000 ppm  | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| EYE              | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                  | 5000 ppm   | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                  | 10000 ppm  | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                  | 20000 ppm  | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| . EAR            | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | · 0 | 0    | 0    | 0    | 0    | 0    |
|                  | 5000 թթո   | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                  | 10000 թթա  | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                  | 20000 ppm  | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| HEAD             | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                  | 5000 ppm   | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                  | 10000 ppm  | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                  | 20000 ppm  | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| NECK             | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                  | 5000 ppm   | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                  | 10000 ppm  | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                  | 20000 ppm  | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| ABDOMEN          | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                  | 5000 ppm   | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | -0   | 0    | 0    |
|                  | 10000 ppm  | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                  | 20000 ppm  | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| ANTERIOR. DORSUM | Control    | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | . 0  | 0    | 0    | 0    |
|                  | 5000 ppm   | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                  | 10000 ppm  | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                  | 20000 ppm  | 0                       | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0   | 0    | Õ    | Õ    | õ    | Ő    |

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

~~~

#### SEX : MALE

PAGE : 10

| Clinical sign    | Group Name | Admini | stration W | eek-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 |
|                  |            |        |            |           |        |        |        |        |      |        |      |      |        |        |      |
| XOPHTHALMOS      | Control    | 0      | 0          | 0         | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    |
|                  | 5000 ppm   | 0      | 0          | 0         | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    |
|                  | 10000 ppm  | 0      | 0          | 0         | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    |
|                  | 20000 ррт  | 0      | 0          | 0         | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    |
| XTERNAL MASS     | Control    | 0      | 0          | 0         | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    |
|                  | 5000 ppm   | 0      | 0          | 0         | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    |
|                  | 10000 ppm  | 0      | 0          | 0         | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    |
|                  | 20000 ppm  | 0      | 0          | 0         | 0      | 0      | 0      | 0      | 0    | 0      | 1    | 1    | 1      | 1      | 1    |
| NTERNAL MASS     | Control    | 0      | 0          | 0         | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    |
|                  | 5000 ppm   | 1      | 1          | 1         | 1      | 1      | 1      | 2      | 2    | 2      | 2    | 2    | 2      | 2      | 1    |
|                  | 10000 ppm  | 0      | 0          | 0         | 0      | 0      | 0      | 0      | 0    | • 0    | 0    | 0    | 0      | 0      | 0    |
|                  | 20000 ppm  | 0      | 0          | 0         | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    |
| . EYE            | Control    | 0      | 0          | 0         | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    |
|                  | 5000 ppm   | 0      | 0          | 0         | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    |
|                  | 10000 ppm  | 0      | 0          | 0         | 0      | 0      | 0      | 0.     | 0    | 0      | 0    | 0    | 0      | 0      | 0    |
|                  | 20000 ppm  | 0      | 0          | 0         | 0      | 0      | 0      | 0      | 0    | Ō      | Ő    | õ    | 0      | õ      | 0    |
| 1. EAR           | Control    | 0      | 0          | 0         | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    |
|                  | 5000 ppm   | 0      | 0          | 0         | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | Ō    |
|                  | 10000 ppm  | 0      | 0          | 0         | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | Ő    |
|                  | 20000 ppm  | 0      | 0          | 0         | 0      | 0      | 0      | 0      | 0    | 0      | 1    | 1    | 1      | 1      | 1    |
| . HEAD           | Control    | 0      | 0          | 0         | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    |
|                  | 5000 ppm   | 0      | 0          | 0         | 0      | 0      | 0      | 0      | 0    | 0      | Õ    | õ    | Ő      | ů<br>0 | Ő    |
|                  | 10000 ppm  | 0      | 0          | 0         | 0      | 0      | 0      | õ      | Ő    | ů<br>0 | Ő    | õ    | ů      | 0      | 0 ·  |
|                  | 20000 ppm  | Ő      | Ő          | 0         | õ      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    |
| . NECK           | Control    | . 0 .  | 0          | 0         | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    |
|                  | 5000 ppm   | 0      | Ő          | õ         | 0      | 0<br>0 | õ      | ů      | 0    | 0      | 0    | 0    | õ      | 0      | 0    |
|                  | 10000 ppm  | ů<br>0 | ů          | õ         | Ő      | 0      | 0      | Ő      | 0    | 0      | 0    | 0    | 0<br>0 | 0      | 0    |
|                  | 20000 ppm  | ů      | 0          | 0         | ŏ      | 0      | ő      | ŏ      | õ    | 0<br>0 | 0    | 0    | Ő      | 0      | 0    |
| ABDOMEN          | Control    | 0      | 0          | 0         | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    |
|                  | 5000 ppm   | 0      | 0          | õ         | Ő      | 0      | ů<br>0 | ů      | 0    | 0      | 0    | 0    | 0      | 0      | Ő    |
|                  | 10000 ppm  | 0      | Ô          | Ő         | ů      | 0      | 0      | 0<br>0 | 0    | 0      | 0    | 0    | 0      | 0      | 0    |
|                  | 20000 ppm  | Õ      | 0          | 0<br>0    | Õ      | 0      | ŏ      | Õ      | Ő    | õ      | 0    | 0    | 0      | 0      | Ő    |
| ANTERIOR. DORSUM | Control    | 0      | 0          | 0         | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | . 0  |
|                  | 5000 ppm   | 0<br>0 | Ő          | Ő         | 0<br>0 | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    |
|                  | 10000 ppm  | 0      | 0          | 0         | 0      | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0      | 0    |
|                  | 20000 ppm  | 0      | õ          | 0         | 0      | 0      | 0      | 0      | 0    |        | 0    |      |        |        |      |
|                  | 20000 ppm  | v      | U          | 0         | U      | U      | U      | U      | U    | 0      | U    | 0    | 0      | 0      | 0    |

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

#### SEX : MALE

| Clinical sign    | Group Name |      |      |      |        |        |        |        |      |        |        |      |        |        |      |
|------------------|------------|------|------|------|--------|--------|--------|--------|------|--------|--------|------|--------|--------|------|
|                  |            | 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 |
|                  |            |      |      |      |        |        |        |        |      |        |        |      |        |        |      |
| EXOPHTHALMOS     | Control    | 0    | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    |
|                  | 5000 ppm   | 0    | 0    | 0    | 0      | Ó      | 0      | 0      | 0    | 0      | Õ      | Õ    | Õ      | . 0    | ů    |
|                  | 10000 ppm  | 0    | 0    | 0    | 0      | 0      | 0      | 0      | Õ    | 0<br>0 | Õ      | Õ    | õ      | Ő      | ŏ    |
|                  | 20000 ppm  | Ő    | Ő    | Ő    | õ      | Ö      | Ő      | 0<br>0 | õ    | 0      | 0<br>0 | õ    | õ      | õ      | ŏ    |
|                  |            |      |      |      |        |        |        |        |      |        | -      | -    | ·      | -      | ·    |
| XTERNAL MASS     | Control    | 0    | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    |
|                  | 5000 ppm   | 0    | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    |
|                  | 10000 ppm  | 0    | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    |
|                  | 20000 ppm  | 1    | 1    | 1    | 1      | 1      | 1      | 1      | 1    | 1      | 1      | 1    | 1      | 1      | 1    |
| VTERNAL MASS     | Control    | 0    | 0    | 0    | 0      | ٥      | 0      |        | 0    | 0      | 0      | 0    | 0      | 0      | 0    |
|                  | 5000 ppm   | 1    | 0    | 0    | 0      | 0<br>0 | 0<br>0 | 0<br>0 | 0    | 0<br>0 | 0<br>0 | 0    | 0<br>0 | 0      | 0    |
|                  |            | 1    | 0    |      |        |        |        |        |      |        |        |      |        | 0      | 0    |
|                  | 10000 ppm  |      |      | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    |
|                  | 20000 ppm  | 0    | 0    | 1    | 1      | 1      | 1      | 1      | 1    | 1      | 1      | 0    | 0      | 0      | 0    |
| M. EYÉ           | Control    | 0    | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    |
|                  | 5000 ppm   | 0    | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0      | 0      | Ő    |
|                  | 10000 ppm  | 0    | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0      | 0<br>0 | Ő    |
|                  | 20000 ppm  | 0    | 0    | 0    | 0      | 0      | 0      | õ      | 0    | Ő      | Ő      | ů    | ů      | 0      | 0    |
| E ( D            |            |      | _    | _    |        |        |        |        |      |        |        |      |        |        |      |
| I. EAR           | Control    | 0    | 0    | 0    | 0      | 0      | 0      | . 0    | 0    | 0      | 0      | 0    | 0      | 0      | 0    |
|                  | 5000 թթա   | 0    | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    |
|                  | 10000 ppm  | 0    | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    |
|                  | 20000 ppm  | 1    | 1    | 1    | 1      | 1      | 1      | 1      | 1    | 1      | 1      | 1    | 1      | 1      | 1    |
| . HEAD           | Control    | 0    | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0      | 0      | Ö    |
|                  | 5000 ppm   | õ    | Ő    | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    |
|                  | 10000 ppm  | 0    | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0      | -      | -    |
|                  | 20000 ppm  | 0    | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    |
|                  | 20000 ppm  | v    | v    | v    | U      | U      | U      | U      | U    | U      | U      | U    | U      | U      | 0    |
| NECK             | Control    | 0    | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    |
|                  | 5000 ppm   | 0    | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0 .  | 0      | 0      | 0    |
|                  | 10000 ppm  | 0    | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    |
|                  | 20000 ppm  | 0    | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0      | 0      | Ő    |
| ABDOMEN          | Control    | 0    | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0      |        | 0    |
| THE PARTY WALLET | 5000 ppm   | 0    | 0    | 0 -  | 0      | 0      | 0      |        |      |        |        | 0    | 0      | 0      | 0    |
|                  | 10000 ppm  | -    |      |      |        |        |        | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    |
|                  |            | 0    | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    |
|                  | 20000 ppm  | 0    | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    |
| ANTERIOR. DORSUM | Control    | 0    | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0    |
|                  | 5000 ppm   | 0    | 0    | 0    | 0      | 0      | 0      | Ő      | Õ    | õ      | õ      | Õ    | õ      | Õ      | 0    |
|                  | 10000 ppm  | õ    | ů    | õ    | ů<br>0 | 0      | 0<br>0 | ů<br>0 | 0    | 0      | 0      | 0    | 0      | 0      | 0    |
|                  | 20000 ppm  | ő    | ů    | Õ    | 0      | Ő      | 0      | 0<br>0 | 0    | 0      | Ő      | 0    | 0      | 0      | 0    |

(HAN190)

PAGE : 11

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : MALE

.

| Clinical sign    | Group Name             | Admini | stration W | 'eek-dav |        |        |        |        |        |        |        |        |        |        |        |
|------------------|------------------------|--------|------------|----------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|                  |                        | 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   |
|                  | 6 1                    | •      |            |          |        |        | _      |        | _      | _      | _      |        |        |        |        |
| (OPHTHALMOS      | Control                | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 5000 ppm               | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 10000 ppm              | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 20000 ppm              | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
| TERNAL MASS      | Control                | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 5000 ppm               | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 10000 ppm              | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 20000 ppm              | 1      | L          | 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      |
|                  | 5000 ppm               | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 10000 ppm              | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 20000 ppm              | 0      | 0          | 0        | 0      | 0      | 1      | 1      | 0      | ů<br>0 | ů      | 0      | 0      | 0      | 0      |
| EYE              | Control                | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 5000 ppm               | ŏ      | ů          | õ        | Ő      | ů      | õ      | õ      | 0      | õ      | 0      | Ő      | ŏ      | 0      | 0      |
|                  | 10000 ppm              | 0      | 0          | õ        | Ő      | ŏ      | õ      | Õ      | ů      | õ      | ů      | Ő      | ŏ      | 0      | 0<br>0 |
|                  | 20000 ppm              | 0      | ů<br>0     | ů        | Ő      | Õ      | 0      | Ő      | Õ      | Õ      | 0      | 0      | Ő      | 0      | 0      |
| . EAR            | Control                | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 5000 ppm               | 0      | 0          | 0        | Ő      | õ      | õ      | Ő      | õ      | õ      | õ      | õ      | ŏ      | 0      | ŏ      |
|                  | 10000 ppm              | ů      | õ          | ů        | ů      | ő      | ů      | Ő      | 0<br>0 | 0      | 0<br>0 | õ      | ŏ      | 0      | 0      |
|                  | 20000 ppm              | 1      | 1          | 1        | 1      | 1      | 1      | 1      | 1      | 1      | 1      | 1      | 1      | 1      | 1      |
| HEAD             | Control                | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 5000 ppm               | õ      | ů          | ŏ        | Ő      | Ő      | ŏ      | Ő      | 0      | 0      | 0      | 0      | 0      |        |        |
|                  | 10000 ppm              | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0      |        | 0      |        |        | 0      | 0      |
|                  | 20000 ppm              | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0      | 0<br>0 | 0      | 0<br>0 | 0<br>0 | 0      | 0<br>0 |
| NECK             | Control                | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | •      | 0      | •      | 0      |
| 1.5Vh            | 5000 ppm               | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  |                        | -      | 0          | 0        |        |        |        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 10000 ppm<br>20000 ppm | 0<br>0 | 0          | 0        | 0<br>0 |
| ABDOMEN          | Control                | 0      | 0          | 0        | ^      | ~      | •      | •      | •      |        |        |        |        |        |        |
| TDROMEN          | Control                | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 5000 ppm               | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | . 0    | 0      |
|                  | 10000 ppm              | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 20000 ppm              | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
| ANTERIOR. DORSUM | Control                | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 5000 ppm               | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 10000 ppm              | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 20000 ppm              | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |

(HAN190)

#### PAGE : 12

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

#### SEX : MALE

| PAGE | : | 13 |  |
|------|---|----|--|
|      |   |    |  |

.

| 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   |
|                    |            |                         |      |      |      |      |        |        |      |      |        |      |        |        |        |
| EXOPHTHALMOS       | Control    | 0                       | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    | 0      | 0    | 0      | 0      | 0      |
|                    | 5000 ppm   | 0                       | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    | 0      | 0    | 0      | 0      | 0      |
|                    | 10000 ppm  | 0                       | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    | 0      | 0    | 0      | 0      | 0      |
|                    | 20000 ррт  | 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      | 1    | 1      | 1      | 1      |
|                    | 5000 ppm   | 0                       | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    | 1      | 1    | 1      | 1      | 0      |
|                    | 10000 ppm  | 0                       | 0    | 0    | 0    | 0    | 0      | 0      | 0    | · 0  | 0      | 0    | 0      | 0      | 0      |
|                    | 20000 ppm  | 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    | 2    | 2      | 2    | 1      | 1      | 2      |
|                    | 5000 ppm   | 0                       | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    | 0      | 1    | 1      | 1      | 3      |
|                    | 10000 ppm  | 0                       | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    | 0      | 0    | 0      | 0      | 1      |
|                    | 20000 ppm  | 0                       | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    | 0      | 0    | 0      | 0      | 0      |
| I. EYE             | Control    | 0                       | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    | 0      | 0    | 0      | 0      | 0      |
|                    | 5000 ppm   | 0                       | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    | 0      | 0    | 0      | 0      | 0      |
|                    | 10000 ppm  | 0                       | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    | 0      | 0    | 0      | 0      | 0      |
|                    | 20000 ppm  | 0                       | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    | 0      | 0    | 0      | 0      | 0      |
| M. EAR             | Control    | 0                       | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    | 0      | 0    | 0      | . 0    | 0      |
|                    | 5000 թթա   | 0                       | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    | 0      | 0    | 0      | 0      | 0      |
|                    | 10000 ppm  | 0                       | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    | 0      | 0    | 0      | 0      | 0      |
|                    | 20000 ррт  | 1                       | 1    | 1    | 1    | 1    | 1      | 1      | 1    | 1    | 1      | 1    | 1      | 1      | 1      |
| I. HEAD            | Control    | 0                       | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    | 0      | 0    | 0      | 0      | 0      |
|                    | 5000 ppm   | 0                       | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    | 1      | 1    | 1      | 1      | 0      |
|                    | 10000 ppm  | 0                       | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    | 0      | 0    | 0      | 0      | 0      |
|                    | 20000 ppm  | 0                       | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    | 0      | 0    | 0      | Õ      | 0<br>0 |
| I. NECK            | Control    | 0                       | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    | 0      | 1    | 1      | 1      | 1      |
|                    | 5000 ppm   | 0                       | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    | 0      | 0    | 0      | ō      | Ō      |
|                    | 10000 ppm  | 0                       | 0    | 0    | 0    | 0    | 0      | Ō      | 0    | 0    | ů      | 0    | 0      | 0<br>0 | õ      |
|                    | 20000 ppm  | 0                       | 0    | 0    | Ő    | Ő    | ò      | Õ      | õ    | 0    | ő      | ů    | õ      | õ      | Ő      |
| . ABDOMEN          | Control    | 0                       | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    | 0      | 0    | 0      | 0      | 0      |
|                    | 5000 ppm   | 0                       | 0    | 0    | 0    | 0    | 0      | 0      | Ő    | 0    | õ      | õ    | ů      | ů<br>0 | Ő      |
|                    | 10000 ppm  | 0                       | 0    | 0    | 0    | 0    | 0<br>0 | ő      | ů    | Ő    | Ő      | õ    | 0<br>0 | 0      | 0      |
|                    | 20000 ppm  | 0                       | 0    | 0    | 0    | Õ    | Ő      | Õ      | Ő    | Ő    | ő      | õ    | õ      | õ      | õ      |
| . ANTERIOR. DORSUM | Control    | 0                       | 0    | 0    | 0    | 0    | 0      | 0      | 0    | 0    | 0      | 0    | 0      | 0      | 0      |
|                    | 5000 ppm   | 0                       | 0    | 0    | Ő    | Õ    | Ő      | Ő      | 0    | õ    | 0<br>0 | õ    | Õ      | 0      | Ő      |
|                    | 10000 ppm  | 0                       | 0    | 0    | 0    | Õ    | 0      | Ő      | Ő    | Ő    | ů<br>0 | õ    | ů      | 0      | 0<br>0 |
|                    | 20000 ppm  | 0<br>0                  | 0    | õ    | Õ    | 0    | õ      | ů<br>0 | 0    | õ    | 0      | Ő    | 0<br>0 | v      | õ      |

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

## SEX : MALE

PAGE : 14

| Clinical sign    | Group Name |        | stration W | eer uay |        |      |      |        |      |        |      |      |        |      |        |
|------------------|------------|--------|------------|---------|--------|------|------|--------|------|--------|------|------|--------|------|--------|
|                  |            | 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   |
|                  |            |        |            |         |        |      |      |        |      |        |      |      |        |      |        |
| EXOPHTHALMOS     | Contro1    | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0      |
|                  | 5000 ppm   | 0      | 0          | 0       | 0      | 0    | 0    | 0.     | 0    | 0      | 0    | 0    | 0      | 0    | 0      |
|                  | 10000 ppm  | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0      |
|                  | 20000 ppm  | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0      |
| KTERNAL MASS     | Control    | 1      | 1          | 1       | 1      | 1    | 1    | 1      | 1    | 1      | 2    | 2    | 2      | 2 ·  | 1      |
|                  | 5000 ppm   | 0      | 0          | 0       | 0      | 1    | 2    | 2      | 2    | 2      | 2    | 3    | 3      | 3    | 2      |
|                  | 10000 ppm  | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 1    | 1      | 1    | 1    | 1      | 1    | 2      |
|                  | 20000 ppm  | 1      | 1          | 1       | 1      | 1    | 1    | 1      | 1    | 1      | 1    | 1    | 1      | 1    | 1      |
| NTERNAL MASS     | Control    | 1      | 1          | 1       | 1      | 1    | 1    | 1      | 2    | 2      | 2    | 2    | 3      | 3    | 3      |
|                  | 5000 ppm   | 3      | 3          | 3       | 3      | 3    | 4    | 3      | 3    | 3      | 2    | 3    | 3      | 2    | 3      |
|                  | 10000 ppm  | 2      | 2          | 1       | 1      | 1    | 1    | 1      | 2    | 3      | 1    | 1    | 1      | 1    | 1      |
|                  | 20000 ppm  | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0      | 0    | 0    | 2      | 2    | 3      |
| . EYE            | Control    | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0      |
|                  | 5000 ppm   | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0      |
|                  | 10000 ppm  | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 1    | 1      | 1    | 1    | 0      | 0    | õ      |
|                  | 20000 ppm  | 0      | 0          | 0       | 0      | 0    | 0    | 0      | ō    | õ      | Ō    | 0    | 0      | 0    | ů      |
| . EAR            | Control    | 0      | 0.         | 0       | 0      | 0    | 0    | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0      |
|                  | 5000 թթա   | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0      | Õ    | Ő    | 0<br>0 | Ő    | Ő      |
|                  | 10000 ppm  | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0      | Ő    | 0    | 0<br>0 | Õ    | Ő      |
|                  | 20000 ppm  | 1      | 1          | 1       | 1      | 1    | 1    | 1      | 1    | 1      | 1    | 1    | 1      | 1    | 1      |
| . HEAD           | Control    | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0      |
|                  | 5000 ppm   | 0      | 0          | 0       | 0      | 1    | 1    | ĩ      | 1    | 1      | 1    | 1    | 1      | 1    | 0      |
|                  | 10000 ppm  | 0      | 0          | õ       | Ő      | ò    | Ô    | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0      |
|                  | 20000 ppm  | 0      | 0          | 0       | 0      | Ő    | Ő    | ů<br>0 | Õ    | Õ      | Õ    | 0    | 0<br>0 | 0    | Ő      |
| . NECK           | Control    | 1      | 1          | 1       | 1      | 1    | 1    | 1      | 1    | 1      | 1    | 1    | 1      | 1    | 0      |
|                  | 5000 ppm   | Ō .    | Õ          | Ô       | Ō      | ô    | Ô    | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0      |
|                  | 10000 ppm  | ů      | ů<br>0     | õ       | 0<br>0 | 0    | 0    | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0      |
|                  | 20000 ppm  | ů      | ů<br>0     | Õ       | õ      | õ    | 0    | 0      | õ    | 0      | 0    | 0    | 0      | 0    | 0      |
| ABDOMEN          | Control    | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0      |
|                  | 5000 ppm   | Õ      | ů          | ő       | 0<br>0 | Ő    | 0    | 0      | 0    | 0      | 0    | 0    | 1      | 1    | 1      |
|                  | 10000 ppm  | 0      | Õ          | õ       | ů<br>0 | ů    | 0    | 0      | 0    | 0<br>0 | 0    | 0    | 0      | 0    | 0      |
|                  | 20000 ppm  | 0      | Ő          | , Õ     | õ      | Ő    | Ő    | Ő      | 0    | 0      | 0    | 0    | 0      | 0    | 0      |
| ANTERIOR. DORSUM | Control    | 0      | 0          | 0       | 0      | 0    | 0    | 0      | 0    | 0      | 1    | . 1  | 1      | 1    | 1      |
|                  | 5000 ppm   | õ      | Õ          | õ       | 0<br>0 | Ő    | 0    | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0      |
|                  | 10000 ppm  | 0      | 0          | 0       | 0      | 0    | 0.   | 0      | 0    | 0      | 0    | 0    | 0      | 0    |        |
|                  | 20000 ppm  | 0<br>0 | 0<br>0     | 0       | 0      | 0    | 0    | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 1<br>0 |

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

~\_\_\_\_

#### SEX : MALE

PAGE : 15

| Clinical sign    | Group Name          | Admini | istration W | eek-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 |
|                  |                     | 0      |             |           | 0    | 0    | 0      |      |        |        |        |      |      |      |      |
| XOPHTHALMOS      | Control             | 0      | 0           | 0         | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0    | 0    |
|                  | 5000 ppm            | 0      | 0           | 0         | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0    | 0    |
|                  | 10000 ppm           | 0      | 0           | 0         | 0    | 0    | 1      | 1    | 1      | 1      | 0      | 0    | 1    | 1    | 1    |
|                  | 20000 ррт           | 0      | 0           | 0         | 0    | . 0  | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0    | 0    |
| XTERNAL MASS     | Contro1             | 1      | 1           | 1         | 1    | 1    | 1      | 1    | 2      | 2      | 2      | 3    | 4    | 3    | 3    |
|                  | 5000 ppm            | 2      | 2           | 2         | 2    | 2    | 2      | 2    | 2      | 2      | 2      | 4    | 4    | 4    | 4    |
|                  | 10000 ppm           | 2      | 1           | 1         | 1    | 1    | 1      | 1    | 1      | 1      | 1      | 1    | 1    | 1    | 1    |
|                  | 20000 ppm           | 1      | 1           | 0         | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0    | 0    |
| NTERNAL MASS     | Control             | 1      | 1           | 1         | 2    | 3    | 6      | 6    | 7      | 7      | 10     | 11   | 11   | 11   | 9    |
|                  | 5000 ppm            | 3      | 3           | 3         | 3    | 2    | 2      | 2    | 2      | 2      | 2      | 2    | 2    | 1    | 1    |
|                  | 10000 ppm           | 1      | 3           | 4         | 3    | 2    | 2      | 3    | 3      | 4      | 5      | 7    | 6    | 5    | 5    |
|                  | 20000 ppm           | 4      | 3           | 3         | 2    | 2    | 2      | 3    | 3      | 4      | 3      | 3    | 3    | 3    | 3    |
| . EYE            | Control             | 0      | 0           | 0         | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0    | 0    |
|                  | 5000 ppm            | 0      | 0           | 0         | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0    | 0    |
|                  | 10000 ppm           | 0      | 0           | 0         | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0    | 0.   |
|                  | 20000 ppm           | 0      | 0           | 0         | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0    | 0    |
| . EAR            | Control             | 0      | 0           | 0         | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 1    | 2    | 1    | - 1  |
|                  | 5000 թթա            | 0      | 0           | 0         | 0    | 0    | 0      | 0    | 0      | 0      | 0      | Ō    | 0    | 0    | ō    |
|                  | 10000 ppm           | 0      | 0           | 0         | 0    | 0    | 0      | õ    | 0<br>0 | ů<br>0 | 0<br>0 | ů    | ů    | ů    | Ő    |
|                  | 20000 ppm           | 1      | 1           | 0         | 0    | 0    | 0      | 0    | 0      | 0      | Ő      | õ    | 0    | 0    | 0    |
| . HEAD           | Control             | 0      | 0           | 0         | 0    | 0    | 0      | 0    | 0      | 0      | . 0    | 0    | 0    | 0    | 0    |
|                  | 5000 ppm            | 0      | 0           | 0         | 0    | Õ    | 0<br>0 | ŏ    | 0      | Ő      | ů      | õ    | õ    | 0    | 0    |
|                  | 10000 ppm           | 0      | 0           | 0         | 0    | 0    | 0<br>0 | ŏ    | Ő      | 0      | ů      | õ    | õ    | 0    | 0    |
|                  | 20000 ppm           | 0      | 0           | 0         | 0    | 0    | 0      | Ő    | ů      | 0      | Õ      | Ő    | ő    | 0    | 0    |
| . NECK           | Control             | 0      | 0           | 0         | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0    | 0    |
|                  | 5000 ppm            | 0      | 0           | 0         | 0    | õ    | ů<br>0 | ů    | ů      | 0<br>0 | 0      | Õ    | 0    | Ő    | Ő    |
|                  | 10000 ppm           | ů      | ů           | 0         | 0    | 0    | 0      | ŏ    | 0      | 0      | 0      | 0    | 0    | 0    | 0    |
|                  | 20000 ppm           | 0      | ů           | 0         | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0    | 0    |
| ABDOMEN          | Control             | 0      | 0           | 0         | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0    | 0    |
|                  | 5000 ppm            | 1      | 1           | 1         | 1    | 1    | 1      | 1    | 1      | 1      | 1      | 2    | 2    | 2    | 2    |
|                  | 10000 ppm           | 0      | 0           | . 0       | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 2    | 2    | 0    |
|                  | 20000 ppm           | 0      | 0           | 0         | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0    | 0    |
|                  |                     | v      | v           | v         | v    | v    | v      | v    | U      |        | v      |      | U    | U    | U    |
| ANTERIOR. DORSUM | Control<br>5000 ppm | 1      | 1           | 1         | 1    | 1    | 1      | 1    | 1      | 1      | 1      | 1    | 1    | 1    | 1    |
|                  |                     | •      |             | 0         | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0    | 0    |
|                  | 10000 ppm           | .1     | 0           | 0         | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0    | 0    |
|                  | 20000 ppm           | 0      | 0           | 0         | 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0    | 0    |

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

 $\sim$  .

## SEX : MALE

PAGE : 16

| Clinical sign       | Group Name | Admin | istration | Week-dav |       |       |       |   |  | <br> |  |  |
|---------------------|------------|-------|-----------|----------|-------|-------|-------|---|--|------|--|--|
|                     |            | 99-7  | 100-7     | 101-7    | 102-7 | 103-7 | 104-7 |   |  |      |  |  |
|                     |            |       |           |          |       |       |       |   |  |      |  |  |
| EXOPHTHALMOS        | Control    | 0     | 0         | 0        | 0     | 0     | 0     |   |  |      |  |  |
|                     | 5000 ppm   | 0     | 0         | 0        | 0     | 0     | 0     |   |  |      |  |  |
|                     | 10000 ppm  | 1     | 1         | 1        | 1     | 1     | 1     |   |  |      |  |  |
|                     | 20000 ppm  | 0     | 0         | 0        | 0     | 0     | 0     |   |  |      |  |  |
| EXTERNAL MASS       | Control    | 3     | 3         | 3        | 4     | 4     | 4     |   |  |      |  |  |
|                     | 5000 ppm   | 4     | 4         | 4        | 4     | 3     | 4     |   |  |      |  |  |
|                     | 10000 ppm  | 1     | 1         | 2        | 2     | 2     | 2     |   |  |      |  |  |
|                     | 20000 ppm  | 0     | 0         | 0        | 0     | 0     | 0     |   |  |      |  |  |
| INTERNAL MASS       | Control    | 7     | 7         | 8        | 8     | 9     | 10    |   |  |      |  |  |
|                     | 5000 ppm   | 1     | 2         | 2        | 2     | 3     | 3     |   |  |      |  |  |
|                     | 10000 ppm  | 5     | 5         | 5        | 5     | 8     | 7     |   |  |      |  |  |
|                     | 20000 ppm  | 3     | 4         | 4        | 5     | 6     | 6     | - |  |      |  |  |
| M. EYE              | Control    | 0     | 0         | 0        | 0     | 0     | 0     |   |  |      |  |  |
|                     | 5000 ppm   | 0     | 0         | 0        | 0     | 0     | 0     |   |  |      |  |  |
|                     | 10000 ppm  | 0     | 0         | 0        | 0     | 0     | 0     |   |  |      |  |  |
|                     | 20000 ppm  | 0     | 0         | 0        | 0     | 0     | 0     |   |  |      |  |  |
| I. EAR              | Control    | 1     | 1         | 1        | 1     | 1     | 1     |   |  |      |  |  |
|                     | 5000 ррт   | 0     | 0         | 0        | 0     | 0     | 0     |   |  |      |  |  |
|                     | 10000 ppm  | 0     | 0         | 0        | 0     | 0     | 0     |   |  |      |  |  |
|                     | 20000 ppm  | 0     | 0         | 0        | 0     | 0     | 0     |   |  |      |  |  |
| A. HEAD             | Control    | 0     | 0         | 0        | 0     | 0     | 0     |   |  |      |  |  |
|                     | 5000 ppm   | 0     | 0         | 0        | 0     | 0     | 0     |   |  |      |  |  |
|                     | 10000 ppm  | 0 .   | 0         | 0        | 0     | 0     | 0     |   |  |      |  |  |
|                     | 20000 ppm  | 0     | 0         | 0        | 0     | 0     | 0     |   |  |      |  |  |
| M. NECK             | Control    | 0     | 0         | 0        | 0     | 0     | 0     |   |  |      |  |  |
|                     | 5000 ppm   | 0     | 0         | 0        | 0     | 0     | 0     |   |  |      |  |  |
|                     | 10000 ppm  | 0     | 0         | 0        | 0     | 0     | 0     |   |  |      |  |  |
|                     | 20000 ppm  | 0     | 0         | 0        | 0     | 0     | 0     |   |  |      |  |  |
| I. ABDOMEN          | Control    | 0     | 0         | 0        | 0     | 0     | 0     |   |  |      |  |  |
|                     | 5000 ppm   | 2     | 2         | 2        | 2     | 1     | 1     |   |  |      |  |  |
|                     | 10000 ppm  | 0     | 0         | 0        | 0     | 0     | 0     |   |  |      |  |  |
|                     | 20000 ppm  | 0     | 0         | 0        | 0     | 0     | 0     |   |  |      |  |  |
| A. ANTERIOR. DORSUM | Control    | 1     | 1         | 1        | 1     | 1     | 1     |   |  |      |  |  |
|                     | 5000 ppm   | 0     | 0         | 0        | 0     | 0     | 1     |   |  |      |  |  |
|                     | 10000 ppm  | 0     | 0         | 0        | 0     | 0     | . 0   |   |  |      |  |  |
|                     | 20000 ppm  | 0     | 0         | 0        | 0     | 0     | 0     |   |  |      |  |  |

(HAN190)

# CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

# SEX : MALE

| Clinical sign      | Group Name | Admini | stration We | eek-dav |        |        |        |     |     |        |        |        |        |      |      |
|--------------------|------------|--------|-------------|---------|--------|--------|--------|-----|-----|--------|--------|--------|--------|------|------|
|                    |            | 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 |
| . POSTERIOR DORSUM | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0      | 0      |        | 0      | 0    | 0    |
| POSTERIOR DORSOM   | Control    |        | 0<br>0      | 0       | 0      | 0      | 0      | 0   | 0   | 0      | 0      | 0      | 0      | 0    | 0    |
|                    | 5000 ppm   | 0      |             | 0       | 0      | 0      | 0      | 0   | 0   | 0      | 0      | 0      | 0      | 0    | 0    |
|                    | 10000 ppm  | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0      | 0      | 0      | 0      | 0    | 0    |
|                    | 20000 ppm  | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0      | 0      | 0      | 0      | 0    | 0    |
| GENITALIA          | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0      | 0      | 0      | 0      | 0    | 0    |
|                    | 5000 ppm   | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0      | 0      | 0      | 0      | 0    | 0    |
|                    | 10000 ppm  | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0      | 0      | 0      | 0      | 0    | 0    |
|                    | 20000 ppm  | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0      | 0      | 0      | 0      | 0    | 0    |
| . TAIL             | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0      | 0      | 0      | 0      | 0    | 0    |
|                    | 5000 ppm   | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0      | 0      | 0      | 0      | 0    | 0    |
|                    | 10000 ppm  | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0      | ō      | 0      | ů      | ů    | 0    |
|                    | 20000 ppm  | 0      | 0           | 0       | 0      | 0      | 0      | Ō   | õ   | 0      | Õ      | ů      | ů      | 0    | 0    |
| DEMA               | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0      | 0      | 0      | 0      | 0    | 0    |
|                    | 5000 ppm   | 0      | 0           | 0       | 0      | 0      | 0      | Ō   | Õ   | 0      | õ      | ů<br>0 | Ő      | Ő    | õ    |
|                    | 10000 ppm  | õ      | Ŏ           | Õ       | ů<br>0 | 0      | ů      | ů   | 0   | 0      | ů<br>0 | 0      | Ő      | 0    | 0    |
|                    | 20000 ppm  | 0      | 0           | Õ       | 0      | ů<br>0 | 0      | õ   | 0   | ů<br>0 | ů<br>0 | ů      | ŏ      | 0    | 0    |
| NEMIA              | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0      | 0      | 0      | 0      | 0    | 0    |
|                    | 5000 ppm   | õ      | Õ           | ů       | Õ      | 0<br>0 | õ      | ů   | 0   | 0<br>0 | Ő      | Ő      | Õ      | õ    | 0    |
|                    | 10000 ppm  | õ      | õ           | õ       | 0      | 0      | 0<br>0 | 0   | 0   | 0      | 0      | 0      | 0<br>0 | 0    | 0    |
|                    | 20000 ppm  | 0      | 0           | Ő       | 0      | 0      | 0      | 0   | 0   | 0      | 0      | 0      | 0      | 0    | 0    |
| LCER               | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0      | 0      | 0      | 0      | 0    | 0    |
| Bolk               | 5000 ppm   | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0      |        | 0      |        | 0    | 0    |
|                    | 10000 ppm  | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   |        | 0      | -      | 0      | 0    | 0    |
|                    | 20000 ppm  | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0<br>0 | 0      | 0      | 0      | 0    | 0    |
|                    | 20000 ppm  | U      | U           | U       | U      | 0      | U      | U   | Ų   | U      | 0      | 0      | 0      | 0    | 0    |
| ROSION             | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0      | 0      | 0      | 0      | 0    | 0    |
|                    | 5000 ppm   | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0      | 0      | 0      | 0      | 0    | 0    |
|                    | 10000 ppm  | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0      | 0      | 0      | 0      | 0    | 0    |
|                    | 20000 ppm  | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0      | 0      | 0      | 0      | 0    | 0    |
| RUSTA              | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0      | 0      | 0      | 0      | 0 .  | 0    |
|                    | 5000 ppm   | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0      | Ō      | 0      | 0      | 0    | 0    |
|                    | 10000 ppm  | 0      | 0           | 0       | 0      | 0      | 0      | 0   | õ   | õ      | õ      | 0      | ů      | õ    | õ    |
|                    | 20000 ppm  | 0      | 0           | 0       | 0      | Ō      | 0      | 0   | õ   | õ      | Ő      | ŏ      | Ő      | 0    | 0    |
| ORTICOLLIS         | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0      | 0      | 0      | 0      | 0    | 0    |
|                    | 5000 ppm   | 0      | Õ           | õ       | õ      | Ő      | Ő      | õ   | 0   | Õ      | 0      | 0      | 0      | Ő    | 0    |
|                    | 10000 ppm  | ő      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0      | 0      | 0      | 0      | 0    | 0    |
|                    | Toore bbm  | •      |             | ~       | ~      |        | v      | v   |     |        | ~      | v      | ~ ~    | 0    | 0    |

PAGE : 17

(HAN190)

# CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

#### SEX : MALE

\_\_\_\_\_

| Clinical sign      | Group Name             | Admin: | istration W | eek-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   |
|                    |                        |        |             |         |      |        |        |        |        |        |        |        |        |        |        |
| . POSTERIOR DORSUM | Control                | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                    | 5000 ppm               | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                    | 10000 ppm              | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | · 0    |
|                    | 20000 ppm              | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
| I. GENITALIA       | Control                | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                    | 5000 ppm               | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                    | 10000 ppm              | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                    | 20000 ppm              | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
| I. TAIL            | Control                | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | • 0    | 0      | 0      |
|                    | 5000 ppm               | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                    | 10000 ppm              | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | ů<br>0 |
|                    | 20000 ppm              | 0      | 0           | 0       | 0    | 0      | 0      | Ő      | ů      | õ      | õ      | ő      | õ      | õ      | ů      |
| DEMA               | Control                | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                    | 5000 ppm               | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | õ      | Õ      | Õ      |
|                    | 10000 ppm              | 0      | 0           | 0       | 0    | 0      | 0      | 0<br>0 | 0<br>0 | õ      | Ő      | 0      | ů      | 0<br>0 | 0<br>0 |
|                    | 20000 ppm              | .0     | 0           | 0       | 0    | 0      | 0      | 0      | 0      | Ō      | õ      | 0      | 0      | õ      | ů      |
| NEMIA              | Control                | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                    | 5000 ppm               | 0      | 0           | 0       | 0    | 0      | 0      | Ő      | õ      | 0<br>0 | õ      | Õ      | ů<br>0 | ů      | õ      |
|                    | 10000 ppm              | 0      | 0           | õ       | Õ    | Õ      | õ      | ů<br>0 | 0      | 0<br>0 | 0<br>0 | ů<br>0 | ů      | 0      | 0      |
|                    | 20000 ppm              | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | ů<br>0 | 0      | 0      | Ő      | Ő      | 0      |
| LCER               | Control                | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                    | 5000 ppm               | õ      | õ           | õ       | õ    | 0<br>0 | õ      | Ő      | 0      | õ      | 0      | 0      | ŏ      | ŏ      | 0      |
|                    | 10000 ppm              | Ő      | õ           | õ       | õ    | 0      | õ      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | . 0    |
|                    | 20000 ppm              | ů<br>0 | ů           | Õ       | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
| ROSION             | Control                | . 0    | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
| · ·                | 5000 ppm               | ů      | Ő           | 0       | õ    | Ő      | 0      | 0      | 0      | Ő      | 0      | 0      | 0      | 0      | 0      |
|                    | 10000 ppm              | ů      | Õ           | õ       | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |
|                    | 20000 ppm              | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0<br>0 |
| RUSTA              | Control                | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                    | 5000 ppm               | 0      | 0           | 0<br>0  | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                    | 10000 ppm              | 0<br>0 | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |        |        |
|                    | 20000 ppm              | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0<br>0 | 0<br>0 |
| ORTICOLLIS         | Control                | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
| SATTODDID          | 5000 ppm               | 0      | 0           | 0       | 0    | 0      | 0      | 0      | 0      | 0      | 0      |        | -      | 0      | 0      |
|                    | 10000 ppm              | 0      | 0           | 0       | 0    | 0      |        | -      | -      |        |        | 0      | 0      | 0      | 0      |
|                    | 20000 ppm<br>20000 ppm | 0      | 0           | 0       | 0    | 0      | 0<br>0 | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                    | 20000 ppm              | U      | U           | U       | U    | U      | U      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |

(HAN190)

# CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

 $\sim \sim$ 

SEX : MALE

PAGE : 19

| Clinical sign       | Group Name | Admini | stration W | eek-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      |
| A. TOSTERIOR DORDOW | 5000 ppm   | 0      | 0          | 0       | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0    | 0      |
|                     | 10000 ppm  | . 0    | 0          | 0       | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0    |        |
|                     |            | 0      | 0          | 0       | 0      | 0      | 0    |        | 0    |      |        |      | -    |      | 0      |
|                     | 20000 ppm  | U      | U          | U       | 0      | U      | U    | 0      | 0    | 0    | 0      | 0    | 0    | 0    | 0      |
| 1. GENITALIA        | Control    | 0      | 0          | 0       | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0    | 0      |
|                     | 5000 ppm   | 0      | 0          | 0       | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0    | 0      |
|                     | 10000 ppm  | 0.     | 0          | 0       | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0    | 0      |
|                     | 20000 ppm  | 0      | 0          | 0       | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0    | 0      |
| A. TAIL             | Control    | 0      | 0          | 0       | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0    | 0      |
|                     | 5000 ppm   | 0      | 0          | 0       | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0    | 0      |
|                     | 10000 ppm  | 0      | 0          | 0       | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0    | 0      |
|                     | 20000 ppm  | 0      | 0          | 0       | 0      | 0      | 0    | 0      | 0    | Ő    | õ      | 0    | õ    | 0    | 0      |
| DEMA                | Control    | 0      | 0          | 0       | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0    | 0      |
|                     | 5000 ppm   | õ      | ů<br>0     | ů<br>0  | 0<br>0 | 0<br>0 | õ    | ŏ      | 0    | 0    | 0      | 0    | 0    | 0    | 0      |
|                     | 10000 ppm  | ů      | 0          | ů<br>0  | 0      | ů      | 0    | Ő      | 0    | 0    | 0      | 0    | 0    | 0    | 0      |
|                     | 20000 ppm  | Ö      | 0          | 0       | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0    | 0      |
|                     | 20000 ppm  |        | 0          | Ũ       | Ū      | 0      | 0    | U      | U    | 0    | 0      | 0    | U    | 0    | 0      |
| NEMIA               | Control    | 0      | 0          | 0       | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0    | 0      |
|                     | 5000 թթա   | 0      | 0          | 0       | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0    | 0      |
|                     | 10000 ppm  | 0      | 0          | 0       | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0    | 0      |
|                     | 20000 ppm  | 0      | 0          | 0       | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0    | 0      |
| ILCER               | Control    | 0      | 0          | 0       | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0    | 0      |
|                     | 5000 ppm   | • 0    | 0          | 0       | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | Ő    | 0<br>0 |
|                     | 10000 ppm  | 0      | 0          | 0       | 0      | . 0    | 0    | 0      | 0    | 0    | 0      | 0    | 0    | Ō    | 0      |
|                     | 20000 ppm  | 0      | 0          | 0       | 0      | 0      | 0    | Ō      | õ    | 0    | Õ      | ů    | Õ    | ů    | Ő      |
| BROSION             | Control    | 0      | 0          | 0       | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0    | 0      |
|                     | 5000 ppm   | ů      | 0          | ů       | 0      | 0<br>0 | 0    | 0<br>0 | 0    | 0    | 0<br>0 | 0    | 0    | 0    | 0      |
|                     | 10000 ppm  | ů<br>0 | 0          | ů<br>0  | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0    | 0      |
|                     | 20000 ppm  | ů      | 0          | 0       | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0    | 0      |
|                     | 20000 ppm  | v      | v          | v       | v      | v      | v    | v      | U    | U    | U      | v    | v    | υ.   | U      |
| RUSTA               | Control    | 0      | 0          | 0       | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0    | 0      |
|                     | 5000 ppm   | 0      | 0          | 0       | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0    | 0      |
|                     | 10000 ppm  | 0      | 0          | 0       | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0    | 0      |
|                     | 20000 ppm  | 0      | 0          | 0       | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0    | 0      |
| ORTICOLLIS          | Control    | 0      | 0          | 0       | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0    | 0      |
|                     | 5000 ppm   | 0      | 0          | 0       | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0    | 0      |
|                     | 10000 ppm  | 0      | 0          | 0       | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0    | 0      |
|                     | 20000 ppm  | 0      | 0          | 0       | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0    | 0      |

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

# SEX : MALE Clinical sign

PAGE : 20 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<br>5000 ppm    | 0<br>0 |
|---------------------|------------------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|                     | 10000 ррт<br>20000 ррт | 0<br>0 | 0<br>0 | 0<br>0 | 0<br>0 | 0<br>0 | 0      | 0<br>0 | 0<br>0 | 0<br>0 | 00     | 0<br>0 | 0<br>0 | 0<br>0 | 0<br>0 |
| M. GENITALIA        | Control                | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                     | 5000 ppm               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                     | 10000 ppm              | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                     | 20000 ppm              | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
| M. TAIL             | Control                | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                     | 5000 ppm               | 0      | 0      | 0      | 0.     | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                     | 10000 ppm              | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                     | 20000 ppm              | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
| EDEMA               | Control                | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                     | 5000 ppm               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                     | 10000 ppm              | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                     | 20000 ppm              | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
| ANEMIA              | Control                | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                     | 5000 ppm               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                     | 10000 ppm              | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                     | 20000 ppm              | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
| ULCER               | Control                | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                     | 5000 ppm               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                     | 10000 ppm              | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                     | 20000 ppm              | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | Θ      | 0      |
| EROSION             | Control                | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                     | 5000 ppm               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                     | 10000 ppm              | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                     | 20000 ppm              | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
| CRUSTA              | Control                | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                     | 5000 ppm               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                     | 10000 ppm              | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                     | 20000 ррт              | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
| TORTICOLLIS         | Control                | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                     | 5000 ppm               | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                     | 10000 ppm              | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                     | 20000 ppm              | 0      | 1      | 1      | 1      | 1      | 1      | 1      | 1      | 1      | 1      | 1      | 1      | 1      | 1      |

(HAN190)

•

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

1-----

SEX : MALE

| Clinical sign    | Group Name |      | istration W |      |        |      |      |      |      |      |      |      |      |      |      |
|------------------|------------|------|-------------|------|--------|------|------|------|------|------|------|------|------|------|------|
|                  |            | 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 |
| POSTERIOR DORSUM | Control    | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| TODIERION DONDOM | 5000 ppm   | 0    | 0           | 0    | 0<br>0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 10000 ppm  | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 20000 ppm  | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| GENITALIA        | Control    | 0    | 0           | 0    | . 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 5000 ppm   | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 10000 ppm  | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 20000 ppm  | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| TAIL             | Control    | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 5000 ppm   | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | . 0  | 0    | 0    |
|                  | 10000 ppm  | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 20000 ppm  | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| DEMA             | Control    | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 5000 ррт   | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 10000 ppm  | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 20000 ppm  | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| NEMIA            | Control    | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 5000 ppm   | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 10000 ppm  | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 20000 ppm  | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LCER             | Control    | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 5000 ppm   | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 10000 ppm  | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 20000 ppm  | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ROSION           | Control    | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 5000 ppm   | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 10000 ppm  | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 20000 ppm  | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | . 0  | . 0  | 0    | 0    | 0    |
| RUSTA            | Control    | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 5000 ppm   | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 10000 ppm  | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | · 0  | 0    | 0    | 0    |
|                  | 20000 ppm  | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| DRTICOLLIS       | Control    | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 5000 ppm   | 0    | 0           | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 10000 ppm  | 0    | 0           | 0    | 0      | 0    | . 0  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 20000 ppm  | 1    | 1           | 1    | 1      | 1    | 1    | 1    | 1    | 2    | 2    | 2    | 2    | 2    | 2    |

PAGE : 21

(HAN190)

# ALL ANIMALS

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 104

#### SEX : MALE

# CLINICAL OBSERVATION (SUMMARY)

| <br> | <br> |  |
|------|------|--|
|      |      |  |
|      |      |  |

|                     |           | 71-7   | <b>TO T</b> |        |        |        |        |      |      |        |        |        |        |      |        |
|---------------------|-----------|--------|-------------|--------|--------|--------|--------|------|------|--------|--------|--------|--------|------|--------|
|                     |           | 1-1    | 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   |
|                     |           |        |             |        |        |        |        |      |      |        |        |        |        |      |        |
| 1. POSTERIOR DORSUM | Control   | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      |
|                     | 5000 ppm  | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      |
|                     | 10000 ppm | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      |
|                     | 20000 ppm | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      |
| . GENITALIA         | Control   | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      |
|                     | 5000 ppm  | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      |
|                     | 10000 ppm | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      |
|                     | 20000 ppm | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | • 0    | 0    | 0      |
| . TAIL              | Control   | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      |
|                     | 5000 ppm  | 0      | 0           | 0      | 0      | 0      | 1      | 1    | 1    | 1      | 1      | 2      | 2      | 2    | 2      |
|                     | 10000 ppm | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 1      | 1    | 1      |
|                     | 20000 ppm | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | Ō      | 0    | 0      |
| DEMA                | Control   | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      |
|                     | 5000 ppm  | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      |
|                     | 10000 ppm | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    | Õ      |
|                     | 20000 ppm | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | Ō      | 0    | ů      |
| NEMIA               | Control   | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      |
|                     | 5000 ppm  | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | Ō      | Õ    | ŏ      |
|                     | 10000 ppm | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0    | õ      | 0      | 0<br>0 | ů      | Õ    | ŏ      |
|                     | 20000 ppm | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | ů      | 0    | 0      |
| LCER                | Control   | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      |
|                     | 5000 ppm  | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0    | 0 -    | Ō      | Õ      | Ő      | õ    | Ő      |
|                     | 10000 ppm | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0    | õ      | ů<br>0 | ů<br>0 | ů      | 0    | 0<br>0 |
|                     | 20000 ppm | 0      | 0           | 0      | 0      | 1      | 0      | 0    | ů    | 0<br>0 | Ő      | ů      | Õ      | 0    | Ő      |
| ROSION              | Control   | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      |
|                     | 5000 ppm  | 0      | Ő           | Ő      | õ      | ů      | ° 0    | 0    | 0    | 0<br>0 | 0      | 0      | 0      | 0    | 0      |
|                     | 10000 ppm | 0<br>0 | ů           | 0<br>0 | ů      | ů      | ů<br>0 | 0    | 0    | Ő      | · 0    | 0      | 0<br>0 | 0    | 0      |
|                     | 20000 ppm | ů<br>0 | ů<br>0      | 0      | õ      | õ      | Ő      | 0    | 0    | 0      | 0      | 0      | o      | 0    | 0      |
| RUSTA               | Control   | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      |
|                     | 5000 ppm  | Ő      | Ő           | 0<br>0 | 0<br>0 | 0      | 0      | 1    | 1    | 1      | 1      | 1      | 1      | 1    | 1      |
|                     | 10000 ppm | 0      | 0<br>0      | 0      | ů<br>0 | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      |
|                     | 20000 ppm | 0      | 0           | 0      | Ő      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      |
| ORTICOLLIS          | Control   | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    | 0      |
|                     | 5000 ppm  | 0      | 0           | 0      | 0<br>0 | 0<br>0 | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0    |        |
|                     | 10000 ppm | 0      | 0           | 0      | 0      | 0      | 0      | 0    | 0    |        | 0      | •      |        |      | 0      |
|                     | 20000 ppm | •      | v           | U      | v      | v      | U      | U    | v    | 0      | v      | 0      | 0      | 0    | 0<br>2 |

(HAN190)

# CLINICAL OBSERVATION (SUMMARY)

SEX : MALE

| ODT: | (TOUR | ODDDMITTON | (DOILING) |
|------|-------|------------|-----------|
| ALL  | ANIM  | ALS        |           |

| Clinical sign       | Group Name | Admini | stration W | eek-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 |
|                     |            | · .    |            |         |        |        |        |      |      |      |        |      |        |          |      |
| A. POSTERIOR DORSUM | Control    | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0    | 0      | 0        | 0    |
|                     | 5000 ppm   | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0    | 0      | 0        | 0    |
|                     | 10000 ppm  | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0    | 0      | 0        | 0    |
|                     | 20000 ppm  | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0    | 0    | õ      | õ    | Õ      | õ        | Ő    |
| . GENITALIA         | Control    | . 0    | 0          | 0       | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0    | 0      | 0        | 0    |
|                     | 5000 ppm   | 0      | 0          | 0       | 0      | 0      | 0      | 0    | · 0  | 0    | 0      | 0    | 0      | Õ        | Ő.   |
|                     | 10000 ppm  | ů<br>0 | Ő          | 0       | ů<br>0 | ů      | ů      | ů    | 0    | Ő    | ů      | ů    | õ      | 0        | 0    |
|                     | 20000 ppm  | 0      | õ          | õ       | 0      | 0<br>0 | 0 -    | 0.   | 0    | 0    | Ő      | ů    | Õ      | Ő        | Õ    |
| I. TAIL             | Control    | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 1    | 1    | 1      | 1    | 1 ·    | 1        | 1    |
|                     | 5000 ppm   | 2      | 2          | 2       | 2      | 2      | 2      | 2    | 2    | 2    | 2      | 3    | 3      | 3        | 3    |
|                     | 10000 ppm  | 1      | 1          | 1       | 1      | 1      | 1      | 1    | 1    | 1    | 1      | 1    | 1      | 1        | 3    |
|                     | 20000 ppm  | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0    | 1<br>0 | 0        | 1    |
| IDEMA               | Control    | 0      | 0          | 0       | 0      | ^      | ^      | ^    | ^    | ^    | ^      | ^    | ^      | ^        | •    |
| 1711011             |            | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0    | 0      | 0        | 0    |
|                     | 5000 ppm   |        |            | -       |        | 0      | 0      | 0    | 0    | 0    | 0      | 1    | 1      | 1        | 1    |
|                     | 10000 ppm  | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0    | 0      | 0        | 0    |
|                     | 20000 ррт  | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0    | 0      | 0        | 0    |
| NEMIA               | Control    | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0    | 0      | 0        | 0    |
|                     | 5000 թթա   | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0    | 0      | 0        | 0    |
|                     | 10000 ppm  | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0    | 1    | 0      | 0    | 1      | 1        | 0    |
|                     | 20000 ppm  | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0    | 0      | 0        | 0    |
| LCER                | Control    | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0    | 0      | 0        | 0    |
|                     | 5000 ppm   | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0    | 0      | 0        | 0    |
|                     | 10000 ppm  | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0    | 0    | Ō      | 0    | Ō      | Ő        | õ    |
|                     | 20000 ppm  | 0      | 0          | 0       | 0      | 0      | 0      | 0    | . 0  | 0    | 0      | 0    | 0      | 0        | Ő    |
| ROSION              | Control    | 0      | 0          | 0       | 0      | 0      | 2      | 2    | 2    | 3    | 3      | 3    | 4      | . 4      | 3    |
|                     | 5000 ppm   | 0      | 0          | 0       | 0<br>0 | Ő      | Ō      | . 0  | 0    | Ő    | õ      | Ő    | 0      | 0        | 0    |
|                     | 10000 ppm  | Ő      | ů<br>0     | Ő       | 0<br>0 | ů      | ů<br>I | . 0  | 1    | 1    | ů<br>1 | 1    | 1<br>I | 0<br>0   | 0    |
|                     | 20000 ppm  | 0      | õ          | 0       | 0<br>0 | ů      | 0      | 0    | 0    | 0    | 0      | 0    | 0      | 0<br>0   | 0    |
| RUSTA               | Control    | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0    | 1      | 1        | 1    |
|                     | 5000 ppm   | 1      | 1          | 1       | 2      | 2      | 2      | 2    | 2    | 2    | 1      | 1    | 1      | 1        | 1    |
|                     | 10000 ppm  | 0      | 0          | 0       | 0      | 0      | 0      | õ    | 0    | 0    | 0      | 0    | 0      | 0        | 0    |
|                     | 20000 ppm  | 0<br>0 | Ő          | 0       | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 1    | 1      | 1        | 1    |
| ORTICOLLIS          | Control    | 0      | ٥          | ٥       | 0      | 0      | 0      | 0    | 0    |      | 0      | 0    | 0      | <u>^</u> | c    |
| 0111002210          | Control    |        | 0          | 0       | 0      | 0      | 0      | 0    | 0    | . 0  | 0      | 0    | 0      | 0        | 0    |
|                     | 5000 ppm   | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0    | 0      | 0        | 0    |
|                     | 10000 ppm  | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0    | 0      | 0        | 0    |
|                     | 20000 ppm  | 2      | 2          | 2       | 2      | 2      | 2      | 2    | 2    | 2    | 2      | 2    | 2      | 2        | 2    |

# CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

----

# SEX : MALE

| Clinical sign       | Group Name | Admin  | istration | Veek-day _ |       |       |       | <br> | <br> |   | <br> |                                       |
|---------------------|------------|--------|-----------|------------|-------|-------|-------|------|------|---|------|---------------------------------------|
|                     |            | 99-7   | 100-7     | 101-7      | 102-7 | 103-7 | 104-7 |      | <br> |   |      |                                       |
|                     |            |        |           |            |       |       |       |      |      |   |      | · · · · · · · · · · · · · · · · · · · |
|                     |            |        |           |            |       |       |       |      |      |   |      |                                       |
| . POSTERIOR DORSUM  | Control    | 0      | 0         | 0          | 1     | 1     | 1     |      |      |   |      |                                       |
| I. FOSTERIOR DORSOM |            |        | 0         | 0          | 1     |       |       |      |      |   |      |                                       |
|                     | 5000 ppm   | 0      |           |            |       | . 0   | 0     |      |      |   |      |                                       |
|                     | 10000 ppm  | 0      | 0         | 0          | 0     | 0     | 0     |      |      |   |      |                                       |
|                     | 20000 ppm  | 0      | 0         | 0          | 0     | 0     | 0     |      |      |   |      |                                       |
| I. GENITALIA        | Control    | 0      | 0         | 0          | 0     | 0     | 0     |      |      |   |      |                                       |
|                     | 5000 ppm   | Ő      | Õ         | õ          | õ     | 0     | 0     |      |      |   |      |                                       |
|                     |            |        |           | 1          |       |       |       |      |      |   |      |                                       |
|                     | 10000 ppm  | 0      | 0         | -          | 1     | 1     | 1     |      |      |   |      |                                       |
|                     | 20000 ppm  | 0      | 0         | 0          | 0     | 0     | 0     |      |      |   |      |                                       |
| M. TAIL             | Control    | 1      | 1         | 1          | 1     | 1     | 1     |      |      |   |      |                                       |
|                     | 5000 ppm   | 3      | 3         | 3          | 3     | 2     | 2     |      |      |   |      |                                       |
|                     | 10000 ppm  | 1      | ĩ         | 1          | 1     | 1     | 1     |      |      |   |      |                                       |
|                     | 20000 ppm  | 0      | 0         | 0          | 0     | 0     | 0     |      |      |   |      | •                                     |
|                     | 20000 ppm  | 0      | 0         | U          | U     | 0     | 0     |      |      |   |      |                                       |
| EDEMA               | Control    | 0      | 0         | 0          | 0     | 0     | 0     |      |      |   |      |                                       |
|                     | 5000 ppm   | 1      | 1         | 1          | 1     | 1     | 1     |      |      |   |      |                                       |
|                     | 10000 ppm  | 0      | 0         | Ô          | Ō     | 0     | ō     |      |      |   |      |                                       |
|                     | 20000 ppm  | ů<br>0 | Ő         | Ő          | õ     | 0     | õ     |      |      |   |      |                                       |
|                     | 20000 ppm  | v      | v         | Ū          | v     | Ū     | v     |      |      |   |      |                                       |
| ANEMIA              | Control    | 0      | 0         | 0          | 0     | · 0   | 0     |      |      |   |      |                                       |
|                     | 5000 ppm   | 0      | 0         | 0          | 0     | 0     | 0     |      |      |   |      |                                       |
|                     | 10000 ppm  | 0      | 0         | 0          | 0     | 0     | 0     |      |      |   |      |                                       |
|                     | 20000 ppm  | 0      | 0         | 1          | 0     | 1     | 1     |      |      |   |      |                                       |
|                     | 11         | -      | -         | -          | -     | -     | •     |      |      |   |      |                                       |
| ULCER               | Control    | 0      | 0         | 0          | 0     | 0     | 0     |      |      |   |      |                                       |
|                     | 5000 ppm   | 0      | 0         | 0          | 0     | 0     | 0     |      |      | • |      |                                       |
|                     | 10000 ppm  | 0      | 0         | 0          | 0     | 0     | 0     |      |      |   |      |                                       |
|                     | 20000 ppm  | 0      | 0         | 0          | 0     | 0     | 0     |      |      |   |      |                                       |
| PROCION             | 0 . 1      |        |           |            |       | _     |       |      |      |   |      |                                       |
| EROSION             | Control    | 2      | 2         | 2          | 2     | 2     | 2     |      |      |   |      |                                       |
|                     | 5000 ppm   | 0      | 0         | 0          | 0     | 0     | 0     |      |      |   |      |                                       |
|                     | 10000 ppm  | 0      | 0         | 0          | 0     | 0     | .0    |      |      |   |      |                                       |
|                     | 20000 ppm  | 0      | 0         | 0          | 0     | 0     | 0     |      |      |   |      |                                       |
| CRUSTA              | Control    | 1      | 1         | 1          | 1     | 1     | 1     |      |      |   |      |                                       |
| 000017              |            | 1<br>0 | -         | - 1        | 1     | 1     | 1     |      |      |   |      |                                       |
|                     | 5000 ppm   | 2      | 2         | 2          | 2     | 2     | 3     |      |      |   |      |                                       |
|                     | 10000 ppm  | 0      | 0         | 1          | 1     | 1     | 1     |      |      |   |      |                                       |
|                     | 20000 ppm  | 1      | 1         | 1          | 1     | 2     | 1     |      |      |   |      |                                       |
| TORTICOLLIS         | Control    | 0      | 0         | 0          | 0     | 0     | 0     |      |      |   |      |                                       |
|                     | 5000 ppm   | 0      | 0         | 0          | 0     |       |       |      |      |   |      |                                       |
|                     |            |        |           |            |       | 0     | 0     |      |      |   |      |                                       |
|                     | 10000 ppm  | 0      | 0         | 0          | 0     | 0     | 0     |      |      |   |      |                                       |
|                     | 20000 ppm  | 2      | 2         | 2          | 2     | 2     | 2     |      |      |   |      |                                       |

# CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : MALE

| Clinical sign      | Group Name | Admini | stration W | eek-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 |
|                    |            |        |            |         |     |     |     |     |     |     |      |      |      |      |      |
| RREGULAR BREATHING | Control    | 0      | 0          | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 5000 ppm   | 0      | 0          | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 10000 ppm  | 0      | 0          | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 20000 ppm  | 0      | 0          | 0       | 0   | 0   | 0   | 0   | 0   | 0   | - 0  | 0    | 0    | 0    | 0    |
| MALL STOOL         | Control    | 0      | 0          | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 5000 ppm   | 0      | 0          | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 10000 ppm  | 0      | 0          | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 20000 ppm  | 0      | 0          | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 1    | 0    | 0    | 0    | 0    |
| LIGO-STOOL         | Control    | 0      | 0          | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 5000 ppm   | 1      | 1          | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 10000 ppm  | 1      | L          | 1       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 1    |
|                    | 20000 ppm  | 0      | 0          | 0       | 0   | 0.  | 0   | 0   | 0   | 0   | 1    | 0    | 0    | 0    | Ô    |
| UBNORMAL TEMP      | Control    | 0      | 0          | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 5000 ppm   | 0      | 0          | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 10000 ppm  | 0      | 0          | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                    | 20000 ppm  | 0      | 0          | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| ON REMARKABLE      | Control    | 50     | 50         | 50      | 50  | 50  | 50  | 50  | 50  | 50  | 50   | 50   | 50   | 50   | 50   |
|                    | 5000 թթա   | 49     | 49         | 50      | 50  | 50  | 50  | 50  | 50  | 50  | 50   | 49   | 49   | 49   | 49   |
|                    | 10000 ppm  | 49     | 49         | 49      | 50  | 50  | 50  | 50  | 50  | 50  | 50   | 50   | 50   | 50   | 49   |
|                    | 20000 ppm  | 50     | 50         | 49      | 49  | 50  | 50  | 50  | 50  | 50  | 49   | 50   | 50   | 50   | 50   |

.

(HAN190)

.

.

BAIS 4

.

# CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : MALE

| linical sign       | Group Name | Admini | stration W | eek-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 |
|                    | *          |        |            |         |      |      |      |      |      |      |      |      |      |      |      |
| RREGULAR BREATHING | Control    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 20000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| MALL STOOL         | Control    | 0      | 0          | 0       | 0 .  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 20000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| JGO-STOOL          | Control    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | . 0  | 0    | 0    | 0    |
|                    | 20000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| BNORMAL TEMP       | Control    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | Ō    | Ő    |
|                    | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | ů.   |
|                    | 20000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ON REMARKABLE      | Control    | 50     | 50         | 50      | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 50   |
|                    | 5000 ppm   | 49     | 49         | 49      | 49   | 49   | 49   | 48   | 48   | 48   | 48   | 48   | 48   | 48   | 48   |
|                    | 10000 ppm  | 50     | 50         | 50      | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 50   |
|                    | 20000 ppm  | 50     | 50         | 50      | 50   | 50   | 50   | 50   | 50   | 50   | 49   | 49   | 49   | 49   | 49   |

(HAN190)

BAIS 4

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : MALE

PAGE : 27

| Clinical sign      | Group Name | Admini | istration W | /eek-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 |
|                    |            |        |             |          |      |      |      |      |      |      |      |      |      |      |      |
| RREGULAR BREATHING | Control    | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | · 0  | 0    | 0    |
|                    | 5000 ppm   | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 10000 ppm  | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 20000 ppm  | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| MALL STOOL         | Control    | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 5000 ppm   | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 10000 ppm  | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 20000 ppm  | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LIGO-STOOL         | Control    | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 5000 ppm   | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 10000 ppm  | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 20000 ррт  | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    |
| UBNORMAL TEMP      | Control    | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 5000 ppm   | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 10000 ppm  | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | . 0  | 0    | 0    | 0    |
|                    | 20000 ppm  | 0      | 0           | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ON REMARKABLE      | Control    | 50     | 50          | 50       | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 50   |
|                    | 5000 թթա   | 48     | 48          | 49       | 49   | 49   | 49   | 49   | 49   | 49   | 49   | 49   | 49   | 49   | 49   |
|                    | 10000 ppm  | 50     | 50          | 50       | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 50   | - 50 | 50   |
|                    | 20000 ppm  | 49     | 49          | 48       | 48   | 48   | 48   | 48   | 48   | 48   | 47   | 49   | 49   | 49   | 49   |

(HAN190)

~

-

# CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

| OBV | 1441 5 |  |
|-----|--------|--|
| SEX | MALE   |  |

| пьь | ANT MALO |  |
|-----|----------|--|
|     |          |  |
|     |          |  |
|     |          |  |
|     |          |  |

| 43-7         44-7         45-7         46-7         47-7         48-7         49-7         50-7         51-7         52-7         53-7         54-7           IRREGULAR BREATHING         Control         0  |               | Group Name | Admini | stration W | eek-day |      |      |      |      |      |      |      |      |      |      |      |
|--|---------------|------------|--------|------------|---------|------|------|------|------|------|------|------|------|------|------|------|
| 5000 ppm         0<  |               |            | 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 |
| 5000 ppm         0<  |               |            |        |            |         |      |      |      |      |      |      |      |      |      |      |      |
| 10000 ppm         0  | LAR BREATHING | Control    | - 0    | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| 2000 ppm         0<  |               | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| MALL STOOL         Control         0   |               | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| 5000 ppm         0<  |               | 20000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| 10000 ppm       0  | STOOL         | Control    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| 20000 ppm         0  |               | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| 20000 ppm         0  |               | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| 5000 ppm         0<  |               | 20000 ppm  | 0      | 0          | 0       | 0    | 0    | 0.   | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| 10000 ppm       0  | STOOL         | Control    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| 2000 ppm       0       1       1       1       1       1       1       0       0       0       0       0         UBNORMAL TEMP       Control       0 <td< td=""><td></td><td>5000 ppm</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td></td<> |               | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| UBNORMAL TEMP         Control         0  |               | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| 5000 ppm       0<  |               | 20000 ppm  | 0      | 1          | 1       | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    |
| 10000 ppm       0  | MAL TEMP      | Control    | 0      | 0          | 0       | • 0  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| 20000 ppm         0  |               | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ON REMARKABLE Control 50 50 50 50 50 50 50 50 50 50 50 50 50   |               |            | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| 5000 ppm 49 49 49 49 49 49 49 49 49 49 49 49 49  |               | 20000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| 5000 ppm 49 49 49 49 49 49 49 49 49 49 49 49 49  | MARKABLE      | Control    | 50     | 50         | 50      | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 50   |
|  |               | 5000 ppm   | 49     | 49         | 49      | 49   | 49   | 49   | 49   | 49   | 49   | 49   |      |      | 49   | 49   |
|  |               | 10000 ppm  | 50     | 50         | 50      | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 49   | 49   |
| 20000 ppm 49 48 48 48 48 47 47 48 48 48 48 48 48   |               |            | 49     | 48         |         |      |      |      |      |      |      | 48   |      |      | 48   | 47   |

(HAN190)

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : MALE

PAGE : 29

| Clinical sign      | Group Name | Admini | stration W | Veek-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 |
|                    |            |        |            |          |      |      |      |      |      |      |      |      |      |      |      |
| RREGULAR BREATHING | Control    | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 5000 ppm   | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    |
|                    | 10000 ppm  | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 20000 ppm  | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| MALL STOOL         | Control    | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 5000 ppm   | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0.   | 0    |
|                    | 10000 ppm  | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 20000 ppm  | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LIGO-STOOL         | Control    | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 1    | 2    | 1    | 0    | . 0  | 0    |
|                    | 5000 ppm   | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1    | 1    | 0    |
|                    | 10000 ppm  | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 20000 ppm  | 0      | 0          | 0        | 0    | 0    | 0    | 0    | . 0  | 0    | 1    | 0    | 0    | 0    | 0    |
| JBNORMAL TEMP      | Control    | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 5000 ppm   | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 10000 ppm  | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 20000 ppm  | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ON REMARKABLE      | Control    | 50     | 50         | 50       | 50   | 50   | 50   | 50   | 50   | 48   | 48   | 47   | 47   | 47   | 46   |
|                    | 5000 րրա   | 49     | 49         | 49       | 49   | 49   | 49   | 49   | 49   | 49   | 48   | 47   | 47   | 46   | 44   |
|                    | 10000 ppm  | 49     | 49         | 49       | 49   | 49   | 49   | 49   | 49   | 49   | 49   | 49   | 49   | 49   | 48   |
|                    | 20000 ppm  | 47     | 47         | 47       | 47   | 47   | 47   | 47   | 47   | 46   | 46   | 46   | 46   | 46   | 46   |
|                    |            |        |            |          |      |      |      |      |      |      |      |      |      |      |      |

(HAN190)

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : MALE

| linical sign       | Group Name | Admini | stration W | eek-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 |
| RREGULAR BREATHING | Control    | 0      | 0          | 0         | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 1    | 1    | 1    |
| MEDOCLAR DREATHING | 5000 ppm   | 0      | 0          | 0         | 0    | 0      | 0    | Ő      | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                    | 10000 ppm  | 1      | 1          | 0         | 0    | 0      | 0    | ő      | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 20000 ppm  | 0      | 0          | 0         | 0    | 0      | 0    | 0<br>0 | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| IALL STOOL         | Control    | 0      | 0          | 0         | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 1    | . 0  | 0    |
| MILLE STOOL        | 5000 ppm   | 0      | 0          | 0         | 0    | 0      | 0    | 0      | 1    | 0    | 0    | 0    | 1    | 0    | 0    |
|                    | 10000 ppm  | 0      | 0          | 0         | 0    | 0      | 0    | 0      | 1    | 0    | 1    | 0    | 1    | 0    | 0    |
|                    | 20000 ppm  | ů<br>0 | 0          | 0         | õ    | 0<br>0 | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                    | Booot ppm  | Ū      | •          | v         | Ŷ    | 0      |      | v      | v    | v    | Ū    | v    | v    | v    | r    |
| LIGO-STOOL         | Control    | Ó      | 0          | 0         | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 1    | 0    | 0    |
|                    | 5000 ppm   | 0      | 0          | 0         | 0    | 0      | • 1  | 1      | 1    | 0    | 0    | 0    | 1    | 0    | 0    |
|                    | 10000 ppm  | 1      | - 1        | 0         | 1    | 0      | 0    | 1      | 1    | 2    | 0    | 0    | 0    | 0    | 0    |
|                    | 20000 ppm  | 0      | 0          | 0         | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
| JBNORMAL TEMP      | Control    | 0      | 0          | 0         | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 5000 ppm   | 0      | 0          | 0         | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 10000 ppm  | 0      | 0          | 0         | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                    | 20000 ppm  | 0      | 0          | 0         | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ON REMARKABLE      | Control    | 46     | 46         | 45        | 44   | 45     | 45   | 45     | 44   | 44   | 42   | 42   | 40   | 40   | 40   |
|                    | 5000 ppm   | 44     | 44         | 44        | 44   | 43     | 41   | 40     | 40   | 39   | 40   | 38   | 37   | 37   | 37   |
|                    | 10000 ppm  | 47     | 47         | 47        | 46   | 47     | 47   | 46     | 45   | 44   | 46   | 46   | 44   | 44   | 43   |
|                    | 20000 ppm  | 46     | 46         | 46        | 46   | 46     | 46   | 46     | 46   | 46   | 45   | 45   | 43   | 43   | 42   |

(HAN190)

# CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

# SEX : MALE

| SEX : MALE          |            |       |             |            |      |      |      |      |      |      |      |      |      |      | PAGE : |  |
|---------------------|------------|-------|-------------|------------|------|------|------|------|------|------|------|------|------|------|--------|--|
| Clinical sign       | Group Name | Admin | istration W | leek-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   |  |
|                     |            |       |             |            |      |      |      |      |      |      |      |      |      |      |        |  |
| IRREGULAR BREATHING | Control    | 1     | 0           | 0          | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 1      |  |
|                     | 5000 ppm   | 0     | 0           | 0          | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0      |  |
|                     | 10000 ppm  | 0     | 0           | 0          | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 1    | 1    | 0      |  |
|                     | 20000 ppm  | 0     | 0           | 0          | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0      |  |
| SMALL STOOL         | Control    | 0     | 0           | 0          | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      |  |
|                     | 5000 ppm   | 0     | 0           | 0          | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0      |  |
|                     | 10000 ppm  | 0     | 0           | 0          | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 1    | 1    | 0      |  |
|                     | 20000 ppm  | 0     | 0           | 0          | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0      |  |
| OLIGO-STOOL         | Control    | 0     | 0           | 0          | 0    | 1    | 0    | 0    | 1    | 0    | 0    | 0    | 1    | 2    | 1      |  |
|                     | 5000 ppm   | 0     | 0           | 0          | 1    | 2    | 2    | 2    | 1    | 1    | 1    | 1    | 2    | 1    | 2      |  |
|                     | 10000 ppm  | 0     | 0           | 0          | 1    | 0    | 0    | 0    | 1    | 2    | 1    | 1    | 1    | 1    | 0      |  |
|                     | 20000 ррт  | 1     | 2           | 1          | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    | 0    | 0    | 0      |  |
| SUBNORMAL TEMP      | Control    | . 0   | 0           | 0          | 0    | 0    | • 0  | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      |  |
|                     | 5000 ppm   | 0     | 0           | 0          | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      |  |
|                     | 10000 ppm  | 0     | 0           | 0          | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | . 0  | 0      |  |
|                     | 20000 ppm  | 0     | 0           | 0          | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0      |  |
| NON REMARKABLE      | Control    | 41    | 42          | 42         | 40   | 37   | 34   | 33   | 30   | 30   | 28   | 27   | 26   | 26   | 26     |  |
|                     | 5000 րթա   | 37    | 35          | 35         | 35   | 33   | 33   | 33   | 33   | 33   | 34   | 32   | 31   | 31   | 30     |  |
|                     | 10000 ppm  | 42    | 41          | 40         | 40   | 40   | 39   | 38   | 37   | 36   | 34   | 33   | 29   | 29   | 29     |  |
|                     | 20000 ppm  | 41    | 42          | 42         | 41   | 41   | 41   | 40   | 39   | 39   | 40   | 40   | 40   | 40   | 40     |  |
|                     |            |       |             |            |      |      |      |      |      |      |      |      |      |      |        |  |

(HAN190)

BAIS 4

.

# PAGE : 31

.

# CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

# SEX : MALE

PAGE : 32

| Clinical sign       | Group Name | Admin | istration ' | Veek-day _ |        |       |       |  |  |  |
|---------------------|------------|-------|-------------|------------|--------|-------|-------|--|--|--|
|                     |            | 99-7  | 100-7       | 101-7      | 102-7  | 103-7 | 104-7 |  |  |  |
|                     |            |       |             |            |        |       |       |  |  |  |
| IRREGULAR BREATHING | Control    | 1     | 0           | 0          | 0      | 0     | 0     |  |  |  |
|                     | 5000 ppm   | 1     | 1           | 1          | 0<br>2 | 2     | 2     |  |  |  |
|                     | 10000 ppm  | 0     | 0           | 0          | 0      | 0     | 0     |  |  |  |
|                     | 20000 ppm  | 0     | 0           | 1          | 1      | 2     | 2     |  |  |  |
| MALL STOOL          | Control    | 0     | 0           | 0          | 0      | 0     | 0     |  |  |  |
|                     | 5000 ppm   | 1     | 1           | 1          | 3      | 1     | 1     |  |  |  |
|                     | 10000 ppm  | 0     | 0           | 0          | 0      | 0     | 0     |  |  |  |
|                     | 20000 ppm  | 0     | 0           | 0          | 0      | 1     | 1     |  |  |  |
| LIGO-STOOL          | Control    | 1     | 0           | 1          | 1      | 1     | 0     |  |  |  |
|                     | 5000 ppm   | 2     | 2           | 4          | 4      | 1     | 1     |  |  |  |
|                     | 10000 ppm  | 0     | 0           | 0          | 0      | 0     | 0     |  |  |  |
|                     | 20000 ppm  | 0     | 0           | 4          | 3      | 3     | 3     |  |  |  |
| UBNORMAL TEMP       | Control    | 0     | 0           | 0          | 0      | 0     | 0     |  |  |  |
|                     | 5000 ppm   | 0     | 0           | 0          | 0      | 0     | 0     |  |  |  |
|                     | 10000 ppm  | 0     | 0           | 0          | 0      | 0     | 0     |  |  |  |
|                     | 20000 ppm  | 0     | 0           | 1          | 0      | 0     | 0     |  |  |  |
| ON REMARKABLE       | Control    | 26    | 25          | 24         | 23     | 22    | 21    |  |  |  |
|                     | 5000 ррш   | 30    | 28          | 26         | 27     | 26    | 25    |  |  |  |
|                     | 10000 ppm  | 29    | 29          | 27         | 27     | 24    | 25    |  |  |  |
|                     | 20000 ppm  | 40    | 39          | 36         | 33     | 31    | 32    |  |  |  |

(HAN190)

TABLE B 2

# CLINICAL OBSERVATION: FEMALE

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

-

SEX : FEMALE

| Clinical sign      | Group Name | Admini | stration We | eek-dav |        |        |        |     |     |     |      |        |        |        |        |
|--------------------|------------|--------|-------------|---------|--------|--------|--------|-----|-----|-----|------|--------|--------|--------|--------|
| origination origin |            | 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   |
|                    |            |        |             |         |        |        |        |     |     |     |      |        |        |        | ,      |
| EATH               | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0   | 0    | 0      | 0      | 0      | 0      |
|                    | 2500 ppm   | . 0    | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0   | 0    | 0      | 0      | 0      | 0      |
|                    | 5000 ppm   | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0   | õ    | Ő      | Ő      | Õ      | õ      |
|                    | 10000 ppm  | 0      | 0           | 0       | 0      | 0      | Ō      | Ő   | 0   | Ő   | Õ    | Õ      | ů<br>0 | 0      | 0      |
| ORIBUND SACRIFICE  | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0   | 0    | 0      | 0      | 0      | 0      |
|                    | 2500 ppm   | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0   | 0    | 0      | 0      | Ō      | Ō      |
|                    | 5000 ppm   | 0      | 0           | 0       | . 0    | 0<br>0 | 0      | Ő   | 0   | 0   | ů    | õ      | ŏ      | õ      | Ő      |
|                    | 10000 ppm  | 0      | 0           | 0       | 0      | 0<br>0 | ů<br>0 | ů   | 0   | 0   | ů    | Õ      | Õ      | Ő      | 0<br>0 |
| UNCHBACK POSITION  | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0   | 0    | 0      | 0      | 0      | 0      |
|                    | 2500 ppm   | ů      | ů           | 0       | ů      | 0      | 0      | 0   | 0   | 0   | 0    | · 0    | 0      | 0      | 0      |
|                    | 5000 ppm   | ů<br>0 | ů           | 0       | ů      | 0      | ů      | 0   | 0   | 0   | 0    | 0      | 0      | 0      | 0      |
|                    | 10000 ppm  | 0      | Ő           | 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      |
| AKALIIIC GAII      |            | -      |             | 0       | 0      | 0      | 0      | 0   | 0   | 0   | 0    | 0      | 0      | 0      | 0      |
|                    | 2500 ppm   | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0   | 0    | 0      | 0      | 0      | 0      |
|                    | 5000 ppm   | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0   | 0    | 0      | 0      | 0      | 0      |
|                    | 10000 ppm  | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0   | 0    | 0      | 0      | 0      | 0      |
| OLLING             | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0   | 0    | 0      | 0      | 0      | 0      |
|                    | 2500 ppm   | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0   | 0    | 0      | 0      | 0      | 0      |
|                    | 5000 ppm   | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0   | 0    | 0      | 0      | 0      | 0      |
|                    | 10000 ppm  | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0   | 0    | 0      | 0      | 0      | 0      |
| BNORMAL GAIT       | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0   | 0    | 0      | 0      | 0      | 0      |
|                    | 2500 ppm   | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0   | Ō    | 0      | 0      | 0      | Ō      |
|                    | 5000 ppm   | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | Ő   | õ    | · Õ    | õ      | ů<br>0 | ů<br>0 |
|                    | 10000 ppm  | 0      | 0           | 0       | 0      | 0      | 0      | 0   | õ   | Ő   | ů    | õ      | Ő      | 0      | ŏ      |
| DILED              | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0   | 0    | 0      | 0      | 0      | 0      |
|                    | 2500 ppm   | Ō      | ů<br>0      | 0<br>0  | ŏ      | ů      | õ      | ů   | Õ   | 0   | 0    | 0<br>0 | 0      | 0      | 0      |
|                    | 5000 ppm   | ů      | ů           | 0       | 0      | 0      | Õ      | 0   | 0   | 0   | 0    | 0      | 0      | 0      | 0      |
|                    | 10000 ppm  | 0      | 0           | 0       | 0<br>0 | 0      | 0<br>0 | õ   | 0   | 0   | 0    | 0      | 0      | 0      | 0      |
| LOERECTION         | Control    | 0      | 0           | 0       | 0      | 0      | · 0    | 0   | 0   | 0   | 0    | 0      | 0      | 0      | 0      |
|                    | 2500 ppm   | Ő      | ů<br>0      | 0       | 0      | 0      | Ő      | 0   | 0   | 0   | 0    | 0      | 0      | 0      | 0      |
|                    | 5000 ppm   | 0      | ů<br>0      | 0       | 0      | 0      | 0      | 0   | 0   | 0   | 0    | 0      | 0      | 0      | 0      |
|                    | 10000 ppm  | 0      | 0           | 0       | Ő      | 0      | 0      | 0   | 0   | 0   | 0    | 0      | 0      | 0      | 0      |
| SS OF HAIR         | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0   | ٥   | 0   |      | ٥      | 0      | 0      | 0      |
| 555 VI 1211N       | 2500 ppm   | 0      | 0           | 0       |        |        |        | -   | 0   | 0   | 0    | 0      | 0      | 0      | 0      |
|                    |            |        |             |         | 0      | 0      | 0      | 0   | 0   | 0   | 0    | 0      | 0      | 0      | 0      |
|                    | 5000 ppm   | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0   | 0    | 0      | 0      | 0      | 0      |
|                    | 10000 ppm  | 0      | 0           | 0       | 0      | 0      | 0      | 0   | 0   | 0   | 0    | 0      | 0      | 0      | 0      |

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

~~~

# SEX : FEMALE

| Clinical sign    | Group Name | Admini   | stration W | eek-dav |      |      |        |        |        |        |        |        |        |        |        |
|------------------|------------|----------|------------|---------|------|------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|                  |            | 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   |
|                  |            | <b>^</b> |            |         |      |      |        |        |        | _      |        | _      |        |        |        |
| ЕАТН             | Control    | 0        | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 2500 ppm   | 0        | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 5000 ppm   | 0        | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 10000 ррт  | 0        | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 1      | 1      |
| RIBUND SACRIFICE | Control    | 0        | 0          | 0       | 0    | 0    | 0      | 0      | 0.     | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 2500 ppm   | 0        | 0          | 0       | 0,   | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 5000 ррт   | 0        | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 10000 ppm  | 0        | 0          | 0       | 0    | 0    | 0      | 0      | · 0    | 0      | 0      | 0      | 0      | 0      | 0      |
| CHBACK POSITION  | Control    | 0        | 0          | 0       | 0    | 0    | 0      | • 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 2500 ppm   | 0        | 0          | 0       | 0    | 0    | 0      | 0      | 0      | Ō      | 0<br>0 | 0      | Ő      | Ő      | ů      |
|                  | 5000 ppm   | 0        | 0          | ů ů     | 0    | 0    | 0<br>0 | 0<br>0 | 0      | 0      | 0      | ů      | 0      | 0      | 0      |
|                  | 10000 ppm  | 0        | Õ          | õ       | Ő    | 0    | 0      | 0<br>0 | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  |            |          |            |         |      |      |        |        |        |        | -      | -      | Ŭ      | v      | Ŷ      |
| RALYTIC GAIT     | Control    | 0        | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 2500 ppm   | 0        | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 5000 ppm   | 0        | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 10000 ppm  | 0        | 0          | 0       | 0.   | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
| LING             | Control    | 0        | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 2500 ppm   | 0        | 0          | . 0     | 0    | 0    | 0      | 0<br>0 | 0<br>0 | Ő      | Õ      | Õ      | ů<br>0 | ů i    | Ő      |
|                  | 5000 ppm   | 0        | 0          | 0       | 0    | 0    | 0      | 0<br>0 | 0      | 0      | 0      | Õ      | ů<br>0 | ů      | ő      |
|                  | 10000 ppm  | 0        | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0      | ů<br>0 | 0      | 0<br>0 |
| NORMAL GAIT      | Control    | 0        | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 2500 ppm   | 0        | ů<br>0     | õ       | ů i  | 0    | 0<br>0 | 0      | 0      | 0      | 0      | 0      | 0      | ŏ      | 0      |
|                  | 5000 ppm   | ů        | 0          | 0<br>0  | õ    | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0<br>0 | 0      |
|                  | 10000 ppm  | 0<br>0   | 0          | 0       | õ    | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  |            |          |            | -       | -    | -    | ·      | •      | · ·    | Ū,     |        | Ū      | Ũ      | Ŭ      | v      |
| ILED             | Control    | 0        | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 2500 ppm   | 0        | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0.     | 0      |
|                  | 5000 ppm   | 0        | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 10000 ppm  | 0        | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
| OERECTION        | Control    | 0        | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 2500 ppm   | 0        | 0          | 0       | 0    | 0    | 0      | Ő      | 0      | 0      | 0<br>0 | Ő      | 0      | ů      | 0      |
|                  | 5000 ppm   | 0        | 0          | Ő       | õ    | Ő    | ů      | 0      | 0      | 0<br>0 | 0<br>0 | 0<br>0 | 0      | 0      | 0      |
|                  | 10000 ppm  | Ő        | ů          | 1       | 1    | 1    | 1      | 1      | 1      | 1      | 1      | 1      | . 1    | 0      | 0<br>0 |
| SS OF HAIR       | Control    | 0        | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      |        | ^      |        | 0      | 0      |
| SO OF HAIR       | 2500 ppm   | 1        |            | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  |            | 1        | 1          | 1       | 1    | 1    | 1      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 5000 ppm   | 0        | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |
|                  | 10000 ppm  | 0        | 0          | 0       | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      | 0      |

PAGE : 34

(HAN190)

# CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : FEMALE

| Clinical sign      | Group Name            | Admini | stration W | eek-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 |
|                    |                       |        |            |         |        |        |        |        |        |        |          |      |        |        |      |
| ЕАТН               | Control               | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0    | 0      | 0      | 0    |
|                    | 2500 ppm              | õ      | Ő          | 0       | Ő      | Õ      | ŏ      | ů      | ů<br>0 | 0<br>0 | 0<br>0   | 0    | Ő      | 0      | ő    |
|                    | 5000 ppm              | ŏ      | ů<br>0     | Õ       | 0<br>0 | ů<br>0 | ŏ      | ů      | 0      | 0      | 0        | 0    | 0      | 0      | ő    |
|                    | 10000 ppm             | 1      | ĩ          | 1       | 1      | 1      | 1      | ĩ      | 1      | 1      | 1        | 1    | 1      | 1      | 1    |
| ORIBUND SACRIFICE  | Control               | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0      | 0      | O        | 0    | 0      | 0      | 0    |
| INTERNE BROKTI TOL | 2500 ppm              | ŏ      | 0<br>0     | 0       | 0      | 0      | 0      | 0      | 0      | 0      | U<br>0   | 0    | 0      | 0      | 0    |
|                    | 5000 ppm              | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0    | -      |        | v    |
|                    |                       | 0      | 0          | 0       | 0      | 0      |        |        |        |        |          |      | 0      | 0      | 0    |
|                    | 10000 ppm             | U      | 0          | 0       | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0    | 0      | 0      | 0    |
| UNCHBACK POSITION  | Control               | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0    | 0      | 0      | 0    |
|                    | 2500 ppm              | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0    | 0      | 0      | 0    |
|                    | 5000 ppm              | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0    | 0      | 0      | 0    |
|                    | 10000 ppm             | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0    | 0      | 0      | 0    |
| ARALYTIC GAIT      | Control               | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0      | 0      | . 0      | 0    | 0      | 0      | 0    |
|                    | 2500 ppm              | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0    | 0      | 0      | 0    |
|                    | 5000 ppm              | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0    | 0      | 0      | 0    |
|                    | 10000 ppm             | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0    | 0      | 0      | 0    |
| DLLING             | Control               | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0    | 0      | 0      | 0    |
|                    | 2500 ppm              | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0      | Ó      | 0        | 0    | 0      | õ      | 0    |
|                    | 5000 ppm              | 0      | 0          | 0       | 0      | 0      | 0      | 0<br>0 | Ő      | õ      | Ő        | Ő    | Ő      | õ      | Ő    |
|                    | 10000 ppm             | 0      | 0          | 0       | Ő      | 0      | 0      | ů<br>0 | 0      | 0      | õ        | ů    | °<br>0 | ő      | 0    |
| BNORMAL GAIT       | Control               | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0      | 0      | .0       | 0    | 0      | 0      | 0    |
|                    | 2500 ppm              | Ő      | Ô          | Ő       | 0      | 0      | 0<br>0 | Ő      | 0      | 0<br>0 | 0        | 0    | 0      | 0      | 0    |
|                    | 5000 ppm              | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0    | 0      | 0      | 0    |
|                    | 10000 ppm             | 0      | 0          | 0       | 0      | 0.     | 0      | 0      | 0      | 0      | 0        | 0    | 0      | 0      | 0    |
| DILED              | Control               | . 0    | 0          | 0       | 0      | 0      | 0      | ^      | ^      | ^      | <u>^</u> | ~    | ^      | ^      | ~    |
| 1100               | 2500 ppm              | 0      | 0          | 0       | 0      | -      | 0      | 0      | 0      | 0      | 0        | 0    | 0      | 0      | 0    |
|                    |                       | 0      | 0          |         |        | 0      | 0      | 0      | 0      | 0.     | 0        | 0    | 0      | 0      | 0    |
|                    | 5000 ррт<br>10000 ррт | 0      | 0          | 0<br>0  | 0<br>0 | 0<br>0 | 0<br>0 | 0<br>0 | 0      | 0<br>0 | 0        | 0    | 0<br>0 | 0      | 0    |
|                    |                       |        |            |         |        | -      | -      |        |        | -      | -        | -    |        | -      | -    |
| ILOERECTION        | Control               | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0    | 0      | 0      | 0    |
|                    | 2500 ppm              | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0    | 0      | 0      | 0    |
|                    | 5000 ppm              | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0    | 0      | 0      | 0    |
|                    | 10000 ppm             | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0    | 0      | 0      | 0    |
| DSS OF HAIR        | Control               | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0    | 0      | 0      | 0    |
|                    | 2500 ppm              | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0    | 0      | 0      | 0    |
|                    | 5000 ppm              | 0      | 0          | 0       | 0      | Õ      | 0      | Ō      | Ő      | 0      | Ő        | · 0  | Õ      | ů<br>0 | ů    |
|                    | 10000 ppm             | 0      | Ő          | õ       | Ő      | ů      | õ      | ů      | ů<br>0 | Õ      | 0<br>0   | Õ    | 0      | 0      | ő    |

.

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

#### SEX : FEMALE

PILOERECTION

LOSS OF HAIR

Control

2500 ppm

5000 ppm

10000 ppm

Control

2500 ppm

5000 ppm

10000 ppm

| Clinical sign      | Group Name | Admini | stration | Week-dav |      |        |      |        |      |      |      |      |      |        |        |
|--------------------|------------|--------|----------|----------|------|--------|------|--------|------|------|------|------|------|--------|--------|
|                    |            | 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   |
| 155.4701           |            | 0      |          | 0        |      |        |      |        |      |      | _    | _    | _    | _      |        |
| DEATH              | Control    | 0      | 0        | 0        | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                    | 2500 ppm   | 0      | 0        | 0        | 0    | 1      | 1    | 1      | 1    | 1    | 2    | 2    | 2    | 3      | 3      |
|                    | 5000 ppm   | 0      | 0        | 0        | 0    | 0      | 0    | 0      | 0    | 1    | 1    | 1    | 1    | 1      | 1      |
|                    | 10000 ppm  | 1      | 1        | 1        | 1    | 1      | 1    | 1      | 1    | 1    | 1    | 1    | 1    | 1      | 1      |
| MORIBUND SACRIFICE | Control    | 0      | 0        | 0        | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                    | 2500 ppm   | 0      | 0        | 0        | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                    | 5000 ppm   | 0      | 0        | 0        | 0    | 0      | 1    | 1      | 1    | 1    | 1    | 1    | 1    | 1      | 1      |
|                    | 10000 ppm  | 0      | 0        | 0        | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
| HUNCHBACK POSITION | Control    | 0      | 0        | 0        | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                    | 2500 ppm   | 0      | 0        | 0        | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                    | 5000 ppm   | 0      | 0        | 0        | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                    | 10000 ppm  | 0      | 0        | 0        | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
| PARALYTIC GAIT     | Control    | 0      | 0        | 0        | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                    | 2500 ppm   | 0      | 0        | 0        | Õ    | 0      | õ    | 0<br>0 | Ô    | Ő    | õ    | Õ    | 1    | Õ      | Ő      |
|                    | 5000 ppm   | 0      | 0        | 0        | 0    | 0<br>0 | Ő    | 0      | 0    | õ    | ů    | ů    | ò    | ů      | ů      |
|                    | 10000 ppm  | 0      | 0        | 0        | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
| ROLLING            | Control    | 0      | 0        | 0        | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                    | 2500 ppm   | 0      | Õ        | Õ        | ŏ    | õ      | 1    | 1      | 1    | 1    | ĩ    | ů    | 1    | 0<br>0 | Ő      |
|                    | 5000 ppm   | 0<br>0 | 0        | 0        | ŏ    | ů      | Ô    | 0      | 0    | Ô    | 0    | 0    | 0    | ů<br>0 | 0<br>0 |
|                    | 10000 ppm  | 0      | 0        | 0        | 0    | 0      | 0    | 0      | 0    | 0    | 0    | Ő    | 0    | 0      | ŏ      |
| ABNORMAL GAIT      | Control    | 0      | 0        | 0        | 0    | . 0    | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                    | 2500 ppm   | ő      | Ő        | Ő        | 1    | 1      | 1    | 1      | 1    | 1    | 1    | 1    | 0    | 0      | 0      |
|                    | 5000 ppm   | ŏ      | Ő        | 0        | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                    | 10000 ppm  | Ŭ.     | ŏ        | õ        | õ    | 0      | ŏ    | 0      | 0    | 0    | 0    | 0    | 0    | . 0    | 0      |
|                    | viii bbu   | •      | č        | č        | v    | v      | v    | v      | v    | v    | v    | v    | v    | v      | v      |
| SOILED             | Control    | 1      | 0        | 0        | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
| · •                | 2500 ppm   | 0      | 0        | 0        | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                    | 5000 ppm   | 0      | 0        | 0        | 0    | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0      | 0      |
|                    | 10000 ppm  | 0      | 0        | 0        | . 0  | 0      | 0    | 0      | 0    | 0    | 0    | 0    | 0    | 0      | 0      |

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : FEMALE

PAGE : 37

| linical sign     | Group Name           | Admini | istration W | eek-dav |      |        |      |        |        |        |      |      |        |      |      |
|------------------|----------------------|--------|-------------|---------|------|--------|------|--------|--------|--------|------|------|--------|------|------|
|                  |                      | 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 |
| · · · · ·        |                      |        | _           |         | _    |        |      |        |        |        |      |      |        |      |      |
| ATH              | Control              | 0      | 0           | `0      | 0    | 0      | 0    | 0      | 0      | 1      | 1    | 1    | . 1    | . 1  | 1    |
|                  | 2500 ppm             | 3      | 3           | 3       | 3    | 3      | 4    | 4      | 4      | 4      | 5    | 5    | 6      | . 9  | 9    |
|                  | 5000 ppm             | 1      | 1           | 1       | 1    | 1      | 2    | 3      | 3      | 3      | 3    | 3    | 3      | 3    | 3    |
|                  | 10000 ppm            | 1      | 1           | 1       | 1    | 1      | 1    | 1      | 2      | 2      | 2    | 2    | 2      | 2    | 2    |
| RIBUND SACRIFICE | Control              | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0    | 0    |
|                  | 2500 ppm             | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0    | 0    |
|                  | 5000 ppm             | 1      | 1           | 1       | 1    | 1      | 1    | 1      | 1      | 1      | 1    | 1    | 1      | 1    | 1    |
|                  | 10000 ppm            | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0    | 0    |
| NCHBACK POSITION | Control              | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0    | 0    |
|                  | 2500 ppm             | 0      | 0           | · 0     | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | Ō      | 0    | 0    |
|                  | 5000 ppm             | 0      | 0           | 0       | 0    | 0      | 0    | 0      | Ő      | Ő      | 0    | ů    | ů<br>0 | 0    | Ő    |
|                  | 10000 ppm            | 0      | 0           | 0       | 0    | õ      | Ő    | Û      | ů<br>0 | ů<br>0 | ů    | ő    | 0      | ů    | 0    |
| RALYTIC GAIT     | Control              | - 1    | 1           | 1       | 1    | 1      | 1    | 1      | 1      | 1      | 1    | 1    | 1      | 1    | 1    |
|                  | 2500 ppm             | 0<br>0 | õ           | Ô       | Ô    | 0<br>0 | 0    | 0<br>0 | 0      | 0      | 0    | 0    | 0      | 0    | 0    |
|                  | 5000 ppm             | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0    | 0    |
|                  | 10000 ppm            | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0    | 0    |
| LLING            | Control              | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0    | 0    |
| LEING            | 2500 ppm             | ů<br>0 | 0           | 0       | 0    | 0      | 0    | 0      | 0      |        |      | 0    |        |      |      |
|                  |                      | 0      | 0           | 0       |      |        |      | •      |        | 0      | 0    | •    | 0      | 0    | 0    |
|                  | 5000 ppm             | -      | 0           |         | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0    | 0    |
|                  | 10000 ppm            | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0    | 0    |
| NORMAL GAIT      | Control              | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0    | 0    |
|                  | 2500 ррт             | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0    | 0    |
|                  | 5000 ppm             | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0    | 0    |
|                  | 10000 ррт            | 0      | 0           | 0.      | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0    | 0    |
| ILED             | Control              | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0    | 0    |
|                  | 2500 ppm             | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0    | 0    |
|                  | 5000 ppm             | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0      | Ō    | õ    |
|                  | 10000 ppm            | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0      | õ    | ů    |
| OERECTION        | Control              | 0      | 0           | 0       | 0    | 1      | 1    | 1      | 1      | 1      | 1    | 1    | 1      | 1    | 1    |
|                  | 2500 ppm             | 0      | 0           | 0       | 0    | 0      | 0    | ò      | 0      | 0      | 0    | 0    | 0      | 0    | 0    |
|                  | 5000 ppm             | ů<br>0 | 0           | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0    | 0    |
| ·                | 10000 ppm            | Ő      | Ő           | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0    | 0    |
| SS OF HAIR       | Control              | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0    | 0    |
|                  | 2500 ppm             | 0      | 0           | 0       | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0      |      |      |
|                  | 2000 ppm<br>5000 ppm | 0      | 0           | 0       | 0    |        |      |        |        |        |      |      | -      | 0    | 0    |
|                  |                      | 0      | 0           | 0       |      | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0    | 0    |
|                  | 10000 ppm            | U      | U           | U       | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0    | 0    |

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

· \_\_\_\_

#### SEX : FEMALE

| linical sign      | Group Name | Admini | stration W | eek-dav |        |      |        |        |      |        |        |        |      |      |      |
|-------------------|------------|--------|------------|---------|--------|------|--------|--------|------|--------|--------|--------|------|------|------|
|                   |            | 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 |
|                   |            |        |            |         |        |      |        |        |      |        |        |        |      |      |      |
| ЕАТН              | Control    | 2      | 3          | 3       | 3      | 4    | 5      | 5      | 6    | 6      | 6      | 6      | 6    | 6    | 8    |
|                   | 2500 ppm   | 9      | 9          | 9       | 10     | 10   | 10     | 10     | 11   | 11     | 13     | 13     | 14   | 14   | 16   |
|                   | 5000 ppm   | 3      | 3          | 4       | 5      | 5    | 5      | 5      | 5    | 7      | 7      | 7      | 8    | 8    | 8    |
|                   | 10000 ppm  | 2      | 2          | 2       | 2      | 3    | 3      | 4      | 4    | 6      | 6      | 6      | 8    | 8    | 8    |
| RIBUND SACRIFICE  | Control    | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0    |
|                   | 2500 ppm   | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0    |
|                   | 5000 ppm   | 1      | 1          | 1       | L      | 1    | 1      | 1      | 1    | 1      | 1      | 1      | 1    | 1    | 1    |
|                   | 10000 ppm  | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0    |
| INCHBACK POSITION | Control    | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0    |
|                   | 2500 ppm   | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0    |
|                   | 5000 ppm   | 0      | 0          | 0       | 0      | 0.   | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0    |
|                   | 10000 ppm  | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0    |
| ARALYTIC GAIT     | Control    | 1      | 1          | 1       | 1      | 1    | 1      | 1      | 0    | 0      | 0      | 0      | 0    | 0    | 0    |
|                   | 2500 ppm   | 0      | 0          | 0       | 0      | 1    | 1      | 1 .    | 0    | 0      | 0      | 0      | 0    | 0    | 0    |
|                   | 5000 ppm   | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0    |
|                   | 10000 ppm  | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0    |
| LLING             | Control    | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0    |
|                   | 2500 ppm   | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | Ō      | Ō      | 0      | Ő    | 0    | ŏ    |
|                   | 5000 ppm   | 0      | 0          | 0       | 0      | Õ    | 0      | õ      | Ő    | ů      | ů ···  | 0<br>0 | ů    | 0    | õ    |
|                   | 10000 ppm  | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | ů<br>0 | Ő    | 0    | 0    |
| NORMAL GAIT       | Control    | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0    |
|                   | 2500 ppm   | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0    |
|                   | 5000 ppm   | 0      | 0          | 0       | 0      | 0    | 0      | õ      | õ    | Õ      | ů      | õ      | õ    | 0    | Ő    |
|                   | 10000 ppm  | 0      | 0          | 0       | 0      | Ő    | õ      | Õ      | Ő    | 0      | 0<br>0 | ů      | 0    | 0    | 0    |
| ILED              | Control    | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0      | · 0  | 0    | 0    |
|                   | 2500 ppm   | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | õ      | õ      | Ő    | Ő    | Ő    |
|                   | 5000 ppm   | 0      | 0          | õ       | õ      | 0    | ů      | ů      | ů    | 0<br>0 | ů      | Ő      | 0    | 0    | 0    |
|                   | 10000 ppm  | 0      | 0          | 0<br>0  | Ő      | õ    | õ      | ů<br>0 | Ő    | · 0    | Ő      | 0      | 0    | 0    | 0    |
| LOERECTION        | Control    | 1      | 1          | 1       | 1      | 1    | 1      | 1      | 0    | 0      | 0      | 0      | 0    | 0    | 0    |
|                   | 2500 ppm   | 0      | 0          | õ       | 0      | Ô    | Ô      | ĩ      | 0    | Ő      | ů ů    | 1      | 1    | 1    | Ő    |
|                   | 5000 ppm   | 0      | ů.         | Ő       | ů<br>0 | ů    | ů<br>0 | 0      | Ő    | 0      | 0<br>0 | 0      | 0    | 0    | 0    |
|                   | 10000 ppm  | 0      | ů          | õ       | 1      | 1    | 1      | 1      | 1    | Ő      | 0      | 0      | 0    | 0    | 0    |
| SS OF HAIR        | Control    | 0      | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0    |
|                   | 2500 ppm   | ů      | ů          | õ       | Õ      | 0    | 0      | Ő      | 0    | 0      | 0      | 0      | 0    | 0    | 0    |
|                   | 5000 ppm   | 0<br>0 | 0          | 0       | 0      | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0    | 0    |
|                   | 0000 ppm   | v      | v          |         | · ·    | 0    | 0      | v      | 0    | U      | U      | v      | 0    | U    | U    |

.

# CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

<u>~</u>~

# SEX : FEMALE

| Clinical sign    | Group Name | Admini | stration W | /eek-dav |      |      |      |      |      |      |      |      |      |      |      |
|------------------|------------|--------|------------|----------|------|------|------|------|------|------|------|------|------|------|------|
| -                | •<br>•     | 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 |
|                  |            |        |            |          |      |      |      |      |      |      |      |      |      |      |      |
| EATH             | Control    | 9      | 9          | 9        | 9    | 10   | 10   | 10   | 10   | 11   | 11   | 12   | 12   | 16   | 16   |
|                  | 2500 ppm   | 16     | 16         | 16       | 16   | 16   | 16   | 16   | 16   | 17   | 17   | 19   | 19   | 20   | 20   |
|                  | 5000 ppm   | 8      | 9          | 9        | 9    | 9    | 10   | 10   | 11   | 12   | 12   | 12   | 13   | 13   | 13   |
|                  | 10000 ppm  | 10     | 11         | 13       | 13   | 13   | 13   | 13   | 16   | 16   | 17   | 17   | 17   | 18   | 19   |
| RIBUND SACRIFICE | Control    | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 2500 ppm   | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | . 0  |
|                  | 5000 ppm   | L      | 1          | 1        | 1    | 1    | 2    | 2    | 2    | 2    | 2    | 2    | 2    | 3    | 3    |
|                  | 10000 ppm  | 0      | 0          | 0        | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | L    | 1    | 1    |
| NCHBACK POSITION | Control    | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    |
|                  | 2500 ppm   | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 5000 ppm   | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 10000 ppm  | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| RALYTIC GAIT     | Control    | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 2500 ppm   | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 5000 ppm   | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 10000 ppm  | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LLING            | Control    | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 2500 ppm   | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 5000 թթա   | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 10000 ppm  | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| NORMAL GAIT      | Control    | 0      | 0          | 0        | 0    | 0.   | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 2500 ppm   | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 5000 ppm   | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | . 0  | 0    | 0    | 0    |
|                  | 10000 ppm  | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ILED             | Control    | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 2500 ppm   | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 5000 ppm   | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 10000 ppm  | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LOERECTION       | Control    | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 2    |
|                  | 2500 ppm   | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    | 0    | 0    |
|                  | 5000 ppm   | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 10000 ppm  | 1      | 1          | 0        | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    | 0    | 0    | 4    |
| SS OF HAIR       | Control    | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 2500 ppm   | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 5000 ppm   | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                  | 10000 ppm  | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |

BAIS 4

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

# SEX : FEMALE

PAGE : 40

| Clinical sign      | Group Name | Admin  | istration | Veek-dav |          |       |        |   |  |      |  |   |
|--------------------|------------|--------|-----------|----------|----------|-------|--------|---|--|------|--|---|
|                    | •          | 99-7   | 100-7     | 101-7    | 102-7    | 103-7 | 104-7  | • |  |      |  |   |
|                    |            |        |           |          |          |       |        |   |  | <br> |  |   |
| DEATH              | Control    | 16     | 16        | 18       | 18       | 19    | 20     |   |  |      |  |   |
|                    | 2500 ppm   | 20     | 20        | 21       | 22       | 24    | 24     |   |  |      |  |   |
|                    | 5000 ppm   | 13     | 13        | 14       | 15       | 15    | 16     |   |  |      |  |   |
|                    | 10000 ppm  | 21     | 23        | 25       | 15<br>25 |       | 29     |   |  |      |  |   |
|                    | 10000 ppm  | 21     | 23        | 25       | 25       | 26    | 29     |   |  |      |  |   |
| MORIBUND SACRIFICE | Control    | 0      | 0         | 0        | 0        | 1     | 1      |   |  |      |  |   |
|                    | 2500 ppm   | 0      | 0         | 0        | 0        | 0     | 0      |   |  |      |  |   |
|                    | 5000 ppm   | 3      | 3         | 3        | 3        | 3     | 3      |   |  |      |  |   |
|                    | 10000 ppm  | 1      | 1         | 1        | 1        | 1     | 1      |   |  |      |  |   |
| HUNCHBACK POSITION | Control    | 0      | 0         | 0        | 0        | 0     | 0      |   |  |      |  |   |
|                    | 2500 ppm   | 0      | 0         | 0        | 0        | 0     | 0      |   |  |      |  |   |
|                    | 5000 ppm   | 0      | 0         | 0        | 0        | 0     | 0      |   |  |      |  | • |
|                    | 10000 ppm  | 0      | ů         | · 0      | ů<br>0   | 0     | 0<br>0 |   |  |      |  |   |
| PARALYTIC GAIT     | Control    | 0      | 0         | 0        | 0        | 0     | 0      |   |  |      |  |   |
| I MINET I LO UNI I | 2500 ppm   |        |           |          |          |       |        |   |  |      |  |   |
|                    |            | 0      | 0         | 0        | 0        | 0     | 1      |   |  |      |  |   |
|                    | 5000 ppm   | 0      | 0         | 0        | 0        | 0     | 0      |   |  |      |  |   |
|                    | 10000 ppm  | 0      | 0         | 0        | 0        | 0     | 0      |   |  |      |  |   |
| ROLLING            | Control    | 0      | 0         | 0        | 0        | 0     | 0      |   |  |      |  | 7 |
|                    | 2500 ppm   | 0      | 0         | 0        | 0        | . 0   | 0      |   |  |      |  |   |
|                    | 5000 ppm   | 0      | 0         | 0        | 0        | 0     | 0      |   |  |      |  |   |
|                    | 10000 ppm  | 0      | 0         | 0        | 0        | 0     | 0      |   |  |      |  |   |
| ABNORMAL GAIT      | Control    | 0      | 0         | 0        | 0        | 0     | 0      |   |  |      |  |   |
|                    | 2500 ppm   | õ      | Õ         | Ő        | ů<br>0   | õ     | ő      |   |  |      |  |   |
|                    | 5000 ppm   | 0      | 0         | 0        | 0        | 0     | 0      |   |  |      |  |   |
|                    | 10000 ppm  | 0      | 0         | 0        | 0        | 0     | 0      |   |  |      |  |   |
|                    | TOOOO hhii | U      | U         | U        | U        | U     | U      |   |  |      |  |   |
| SOILED             | Control    | 0      | 0         | 0        | 0        | 0     | 0      |   |  |      |  |   |
|                    | 2500 ppm   | 0      | 0         | 0        | 0        | 0     | 0      |   |  |      |  |   |
|                    | 5000 ppm   | 0      | 0         | 0        | 0        | 0     | 0      |   |  |      |  |   |
|                    | 10000 ppm  | 0      | 0         | 0        | 0        | 0     | 0      |   |  |      |  |   |
| PILOERECTION       | Control    | 2      | 2         | 1        | 1        | 0     | 0      |   |  |      |  |   |
|                    | 2500 ppm   | 0      | 2         | 2        | 0        | 1     | 1      |   |  |      |  |   |
|                    | 5000 ppm   | 0<br>0 | 0         | 0        | 0        | 0     | 0      |   |  |      |  |   |
|                    | 10000 ppm  | 3      | 2         | 1        | 1        | , 1   | 0      |   |  |      |  |   |
| LOSS OF HAIR       | Control    | 0      | 0         | 0        | 0        | ^     | ^      |   |  |      |  |   |
| DODD OF HUTH       |            |        |           | 0        | 0        | 0     | 0      |   |  |      |  |   |
|                    | 2500 ppm   | 0      | 0         | 0        | 0        | 0     | 0      |   |  |      |  |   |
|                    | 5000 ppm   | 0 .    | 0         | 0        | 0        | 0     | 0      |   |  |      |  |   |
|                    | 10000 ppm  | 0      | 0         | 0        | 0        | 0     | 0      |   |  |      |  |   |

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : FEMALE

PAGE : 41

| linical sign            | Group Name | Adminis | stration We | eek-day |     |     |     |     |     |     |      |      |        |      |      |
|-------------------------|------------|---------|-------------|---------|-----|-----|-----|-----|-----|-----|------|------|--------|------|------|
|                         | -<br>      | 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 |
|                         |            |         |             |         |     |     |     |     |     |     |      |      |        |      |      |
| FROG BELLY              | Control    | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0      | 0    | 0    |
|                         | 2500 ppm   | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0      | 0    | 0    |
|                         | 5000 ppm   | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0      | 0    | 0    |
|                         | 10000 ppm  | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0      | 0    | 0    |
| OILED PERI-GENITALIA    | Control    | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0      | 0    | 0    |
|                         | 2500 ppm   | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0.   | 0    | 0      | 0    | 0    |
|                         | 5000 ppm   | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0      | 0    | 0    |
|                         | 10000 ppm  | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0      | 0    | 0    |
| XOPHTHALMOS             | Control    | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0      | 0    | 0    |
|                         | 2500 ppm   | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0      | 0    | 0    |
|                         | 5000 ppm   | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0      | 0    | 0    |
|                         | 10000 ppm  | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0      | 0    | 0    |
| ATARACT                 | Control    | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0      | 0    | 0    |
|                         | 2500 ррт   | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0      | 0    | 0    |
|                         | 5000 ppm   | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0      | 0    | 0    |
|                         | 10000 ppm  | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0      | 0    | 0    |
| ORNEAL OPACITY          | Control    | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0      | 0    | 0    |
|                         | 2500 ррт   | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0      | 0    | 0    |
|                         | 5000 րրտ   | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0      | 0    | 0    |
|                         | 10000 թթա  | 0       | 0           | 0       | 0.  | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0      | 0    | 0    |
| NTERIOR CHAMBER OPACITY | Control    | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0      | 0    | 0    |
|                         | 2500 ppm   | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0      | 0    | 0    |
|                         | 5000 ppm   | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0      | 0    | 0    |
|                         | 10000 ppm  | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0      | 0    | 0    |
| XTERNAL MASS            | Control    | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0      | 0    | 0    |
|                         | 2500 ppm   | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0      | 0    | 0    |
|                         | 5000 ppm   | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0      | 0    | 0    |
|                         | 10000 ppm  | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0      | 0    | Ő    |
| NTERNAL MASS            | Control    | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0      | 0    | 0    |
|                         | 2500 ppm   | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0      | Ō    | 0    |
|                         | 5000 ppm   | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0<br>0 | õ    | Ŏ    |
|                         | 10000 ppm  | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | Õ   | 0    | 0    | 0<br>0 | Õ    | 0    |
| EYE                     | Control    | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0      | 0    | 0    |
|                         | 2500 ppm   | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | Ō      | õ    | Ō    |
|                         | 5000 ppm   | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | Ō    | Õ    | 0      | Õ    | ŏ    |
|                         | 10000 ppm  | 0       | 0           | 0       | 0   | 0   | 0   | 0   | 0   | 0   | Õ    | Õ    | Õ      | õ    | õ    |

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : FEMALE

| Clinical sign           | Group Name             | Admini | istration W | leek-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   |
|                         |                        |        |             |            |        |        |        |        |        | 1 8 1 - 10 10 100 M |        |        |        |        |        |
| ROG BELLY               | Control                | 0      | 0           | 0          | 0      | 0      | 0      | 0      | 0      | 0                   | 0      | 0      | 0      | 0      | 0      |
|                         | 2500 ppm               | 0      | 0           | 0          | 0      | 0      | 0      | 0      | 0      | 0                   | 0      | 0      | 0      | 0      | 0      |
|                         | 5000 ppm               | 0      | 0           | 0          | 0      | 0      | 0      | 0      | 0      | 0                   | 0      | 0      | 0      | 0      | 0      |
|                         | 10000 ppm              | . 0    | 0           | 0          | 0      | 0      | 0      | 0      | 0      | 0                   | 0      | 0      | 0      | 0      | 0      |
| DILED PERI-GENITALIA    | Control                | 0      | 0           | 0          | 0      | 0      | 0      | 0      | 0      | 0                   | 0      | 0      | 0      | 0      | 0      |
|                         | 2500 ppm               | 0      | 0           | 0          | 0      | 0      | 0      | 0      | 0      | 0                   | 0      | 0      | 0      | 0      | 0      |
|                         | 5000 ppm               | 0      | · 0         | 0          | 0      | Õ      | Õ      | Õ      | ů<br>0 | õ                   | ů      | ů      | ů<br>0 | Ő      | Ő      |
|                         | 10000 ppm              | 0      | 0           | 0          | õ      | õ      | 0<br>0 | 0      | Ő      | õ                   | 0      | Ő      | 1      | 0      | 0      |
| XOPHTHALMOS             | Control                | 0      | 0           | 0          | 0      | 0      | 0      | 0      | 0      | 0                   | 0      | 0      | 0      | 0      | 0      |
|                         | 2500 ppm               | 0      | 0           | Õ          | Ő      | Õ      | ů<br>0 | ů<br>0 | 0      | õ                   | 0      | 0<br>0 | 0<br>0 | 0      | Ő      |
|                         | 5000 ppm               | ů      | ů<br>0      | 0          | 0      | 0      | 0.     | 0      | 0      | 0                   | 0      | 0      | 0      | 0      | 0      |
|                         | 10000 ppm              | õ      | ů           | 0          | õ      | Ő      | 0      | 0      | 0      | 0                   | 0      | 0      | 0      | 0      | 0      |
| ATARACT                 | Control                | 0      | 0           | 0          | 0      | 0      | 0      | 0      | 0      | 0                   | 0      | 0      | 0      | 0      | 0      |
| ATMAIOT                 | 2500 ppm               | 0      | 0           | 0          | 0<br>0 | 0      | 0      | 0      | 0      | 0                   | 0      | 0      | 0      | 0      | 0      |
|                         | 5000 ppm               | 0      | 0           | 0          | 0      | 0      | •      |        |        | -                   |        | •      | -      | •      | 0      |
|                         | 10000 ppm<br>10000 ppm | 0      | 0           | 0          | 0      | 0      | 0      | 0      | 0      | 0                   | 0      | 0      | 0      | 0      | 0      |
|                         | 10000 ppm              | U      | 0           | 0          | U      | U      | U      | 0      | 0      | 0                   | 0      | 0      | 0      | 0      | 0      |
| ORNEAL OPACITY          | Control                | 0      | . 0         | 0          | 0      | 0      | 0      | 0      | 0      | 0                   | 0      | 0      | 0      | 0      | 0      |
|                         | 2500 ppm               | 0      | 0           | 0          | 0      | 0      | 0      | 0      | 0      | 0                   | 0      | 0      | 0      | 0<br>0 | õ      |
| •                       | 5000 ppm               | 0      | 0           | 0          | 0      | 0      | 0      | 0      | 0      | 0                   | 0      | 0      | 0      | 0      | 0      |
|                         | 10000 ppm              | 0      | 0           | 0          | 0      | 0      | 0      | 0      | 0      | 0                   | 0      | 0      | Ő      | 0      | 0      |
| NTERIOR CHAMBER OPACITY | Control                | 0      | 0           | 0          | 0      | 0      | 0      | 0      | 0      | 0                   | 0      | 0      | 0      | 0      | 0      |
|                         | 2500 ppm               | 0      | 0           | 0          | Õ      | 0<br>0 | Õ      | õ      | Ő      | õ                   | 0<br>0 | 0<br>0 | 0      | 0      | Ő      |
|                         | 5000 ppm               | 0      | 0           | 0          | Õ      | Ő      | õ      | 0<br>0 | 0      | õ                   | 0      | 0<br>0 | Ő      | 0      | 0<br>0 |
|                         | 10000 ppm              | 0      | 0           | 0          | Õ      | 0      | 0      | õ      | 0      | 0                   | 0      | 0      | 0      | 0      | 0      |
| XTERNAL MASS            | Control                | 0      | 0           | 0          | 0      | 0      | 0      | 0      | 0      | 0                   | 0      | 0      | 0      | 0      | 0      |
|                         | 2500 ppm               | õ      | 0           | 0          | 0      | 0      | 0      | 0      | 0      | 0                   | 0      | 0      | 0      | 0      | 0      |
|                         | 5000 ppm               | õ      | 0           | 0          | 0      | 0      | 0      | 0      | 0      | 0                   | 0      | 0      | 0      | -      | •      |
|                         | 10000 ppm              | 0      | 0           | 0          | 0      | 0      | 0      | 0      | 0      | 0                   | 0      |        |        | 0      | 0      |
|                         | 10000 þþш              | v      | U           | U          | v      | U      | U      | U      | U      | U                   | U      | 0      | 0      | 0      | 0      |
| NTERNAL MASS            | Control                | 0      | 0           | 0          | 0      | 0      | 0      | 0      | 0      | 0                   | 0      | 0      | 1      | 0      | 0      |
|                         | 2500 ppm               | 0      | 0           | 0          | 0      | 0      | 0      | 0      | 0      | 0                   | 0      | 0      | 0<br>0 | 0      | Ő      |
|                         | 5000 ppm               | 0      | 0           | 0          | 0      | 0      | 0      | 0      | 0      | 0                   | 0      | 0<br>0 | 0<br>0 | 0      | õ      |
|                         | 10000 ppm              | 0      | 0           | <u>^</u> . | ^      | ^      |        |        |        |                     | -      | -      | -      | ~      | 5      |

PAGE : 42

----

(HAN190)

M. EYE

10000 ppm

Control

2500 ppm

5000 ppm

10000 ppm

0.

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

#### SEX : FEMALE

,

| Clinical sign          | Group Name           | Admini | stration W | /eek-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   |
| ROG BELLY              | Control              | 0      | 0          | 0        | 0      | . 0    | 0      | 0      | ٥    | 0    | 0    | ٥      | 0      | ٥    | 0      |
| OG BEEEI               | 2500 ppm             | 0      | 0          | 0        | 0      | 0      | 0      | 0<br>0 | 0    | 0    | 0    | 0      | 0      | 0    | 0      |
|                        | 2300 ppm<br>5000 ppm | 0      |            |          | -      |        | 0      |        | 0    | 0    | 0    | 0      | 0      | 1    | 1      |
|                        |                      | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0      | 0    | 0      |
|                        | 10000 ppm            | 0      | 0          | U        | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0      | 0    | 0      |
| ILED PERI-GENITALIA    | Control              | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0      | 0    | 0      |
|                        | 2500 ppm             | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0      | 0    | 0      |
|                        | 5000 ppm             | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0      | . 0    | 0    | 0      |
|                        | 10000 ppm            | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0      | 0    | 0      |
| OPHTHALMOS             | Control              | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0      | 0    | 0      |
|                        | 2500 ppm             | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0    | 0    | - 0  | 0      | 0      | 0    | Ő      |
|                        | 5000 ppm             | 0      | 0          | 0        | 0      | 0      | 0      | . 0    | 0    | 0    | 0    | 0      | 0<br>0 | 0    | Ő      |
|                        | 10000 ppm            | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0      | 0    | Ő      |
| TARACT                 | Control              | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0      | 0    | 0      |
|                        | 2500 ppm             | Ō      | 0          | 0        | Õ      | Ő      | Ő      | Ő      | Õ    | õ    | Ő    | õ      | 0      | Ő    | Ő      |
|                        | 5000 ppm             | Õ      | 0          | Õ        | 0      | ů<br>0 | ů      | õ      | 0    | 0    | Ő    | 0<br>0 | 0      | 0    | Ő      |
|                        | 10000 ppm            | 0      | 0          | 0        | 0      | Ő      | 0      | ů      | 0    | 0    | ő    | 0      | 0      | Ő    | õ      |
| RNEAL OPACITY          | Control              | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0      | 0    | 0      |
|                        | 2500 ppm             | õ      | ů ů        | 0<br>0   | 0<br>0 | 0      | ů<br>0 | 0      | 0    | 0    | 0    | 0      | 0      | . 0  | 0<br>0 |
|                        | 5000 ppm             | õ      | ů l        | Ő        | 0      | 0      | 0      | 0<br>0 | 0    | 0    | 0    | 0      | 0      | 0    | ő      |
|                        | 10000 ppm            | 0      | Ő          | 0        | 0      | 0      | Ő      | Ő      | 0    | 0    | 0    | 0      | 0      | 0    | 0      |
| TERIOR CHAMBER OPACITY | Control              | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0    | . 0  | 0    | 0      | 0      | 0    | 0      |
|                        | 2500 ppm             | Ō      | Õ          | õ        | õ      | 0<br>0 | ů<br>0 | Õ      | 0    | Ő    | 0    | õ      | Ő      | 0    | 0      |
|                        | 5000 ppm             | õ      | Õ          | 0<br>0   | 0      | 0      | 0      | 0<br>0 | 0    | 0    | 0    | 0      | 0      | 0    | 0      |
|                        | 10000 ppm            | õ      | Ő          | 0        | õ      | 0<br>0 | 0      | ů<br>0 | 0    | 0    | 0    | Ő      | 0      | 0    | 0.     |
|                        |                      | Ŷ      | v          | 0        | v      | v      | v      | v      | v    | 0    | U    | v      | v      | U    | U.     |
| FERNAL MASS            | Control              | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0      | 0    | 0      |
|                        | 2500 ppm             | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0      | 0    | 0      |
|                        | 5000 ppm             | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0      | 0    | 0      |
|                        | 10000 ppm            | 0      | 0          | 0        | 0      | 0      | 0      | 0      | 0    | 0    | 0    | 0      | 0      | 0    | 0      |

PAGE: 43

.

~~~~~

(HAN190)

M. EYE

INTERNAL MASS

Control

2500 ppm

5000 ppm

Control

2500 ppm

5000 ppm

10000 ppm

10000 ppm

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

 $\checkmark$ 

SEX : FEMALE

ALL ANIMALS

| Clinical sign           | Group Name | Adminis | stration W | eek-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 |
|                         |            |         |            |         |      |      |      |      |      |      |      |      |      |      | -    |
| FROG BELLY              | Control    | 0       | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2500 ppm   | 1       | 1          | 1       | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 5000 ppm   | 0       | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10000 ppm  | 0       | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SOILED PERI-GENITALIA   | Control    | 0       | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2500 ppm   | 0       | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 5000 ppm   | 0       | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10000 ppm  | 0       | 0          | 0       | 0    | 0    | 0    | 0    | 0    | . 0  | 0    | 0    | 0    | 0    | 0    |
| EXOPHTHALMOS            | Control    | 0       | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                         | 2500 ppm   | 0       | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | ` 0  | 0    | 0    |
|                         | 5000 ppm   | 0       | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10000 ppm  | 0       | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CATARACT                | Control    | 0       | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2500 ppm   | 0       | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 5000 ppm   | 0       | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10000 ppm  | 0       | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| CORNEAL OPACITY         | Control    | 0       | 0          | 0       | Ō    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2500 ppm   | 0       | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0 `  | 0    |
|                         | 5000 ррш   | 0       | . 0        | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10000 ppm  | 0       | 0          | 0       | 0    | 0    | 0    | 0    | 0 .  | 0    | 0    | 0    | 0    | 0    | 0    |
| NTERIOR CHAMBER OPACITY | Control    | 0       | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2500 ррт   | 0       | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 5000 ppm   | 0       | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10000 ppm  | 0       | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0,   | 0    | 0    | 0    | 0    |
| EXTERNAL MASS           | Control    | 0       | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2500 ppm   | 0       | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
|                         | 5000 ppm   | 0       | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | ō    |
|                         | 10000 ppm  | 0       | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| NTERNAL MASS            | Control    | 1       | 1          | 1       | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                         | 2500 ppm   | 1       | 2          | 2       | 2    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                         | 5000 ppm   | 0       | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 10000 ppm  | 0       | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| I. EYE                  | Control    | 0       | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                         | 2500 ppm   | 0       | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | Õ    |
|                         | 5000 ppm   | 0       | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | Õ    |
|                         | 10000 ppm  | 0       | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | Ő    | õ    |

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

#### SEX : FEMALE

| Clinical sign           | Group Name          |      |        |        |        |      |      |        |        |        |      |        |          |          |        |
|-------------------------|---------------------|------|--------|--------|--------|------|------|--------|--------|--------|------|--------|----------|----------|--------|
|                         |                     | 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   |
|                         | 0 1 1               | 0    | 0      | 0      | 0      | 0    | 0    | 0      |        |        |      |        |          |          | 0      |
| ROG BELLY               | Control<br>2500 ppm | 0    | 0      | 0<br>0 | 0      | 0    | . 0  | 0      | 0      | 0      | 0    | 0      | 0        | 0        | 0      |
|                         |                     | -    | -      |        | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0      | 0        | 0        | . 0    |
|                         | 5000 ppm            | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0      | 0        | 0        | 0      |
|                         | 10000 ppm           | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0      | 0        | 0        | 0      |
| OILED PERI-GENITALIA    | Control             | 1    | · 1    | 1      | 1      | 1    | 1    | 1      | 1      | 1      | 1    | 1      | 1        | 1        | 2      |
|                         | 2500 ррт            | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0      | 0        | 0        | 0      |
|                         | 5000 ppm            | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0      | 0        | 0        | 0      |
|                         | 10000 ppm           | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0      | 0        | 0        | 0      |
| XOPHITHALMOS            | Control             | 1    | 1      | 1      | 1      | 1    | 1    | 1      | 1      | 1      | 1    | 1      | 1        | 1        | 1      |
|                         | 2500 ppm            | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0      | Ô        | Ô        | 0      |
|                         | 5000 ppm            | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0      | 0        | 0        | 0      |
|                         | 10000 ppm           | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0      | 0        | 0        | 0      |
| ATARACT                 | Control             | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0      | 0        | 0        | 0      |
|                         | 2500 ppm            | ő    | ů<br>0 | õ      | õ      | Õ    | ° 0  | õ      | 0      | õ      | 0    | õ      | 0        | 0        | Ő      |
|                         | 5000 ppm            | 0    | 0      | 0      | 0      | 0    | 0    | 0<br>0 | 0      | 0      | 0    | 0      | 0        | 0        | 0      |
|                         | 10000 ppm           | 0    | 0<br>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    | ^      | <u>^</u> | <u>^</u> |        |
|                         | 2500 ppm            | 0    | 0      | . 0    | 0<br>0 | 0    | - 0  | 0      | 0      | 0      | 0    | 0      | 0        | 0        | 0      |
|                         |                     | •    | -      |        |        | 0    | 0    | -      | 0      | 0      | 0    | 0      | 0        | 0        | 0      |
|                         | 5000 ppm            | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0      | 0        | 0        | 0      |
|                         | 10000 ppm           | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0      | 0        | 0        | 0      |
| NTERIOR CHAMBER OPACITY | Control             | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0      | 0        | 0        | 0      |
|                         | 2500 ppm            | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0      | 0        | 0        | 0      |
|                         | 5000 ppm            | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0      | 0        | 0        | 0      |
|                         | 10000 ppm           | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0      | 0        | 0        | 0      |
| XTERNAL MASS            | Control             | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0      | 0        | 0        | 1      |
|                         | 2500 ppm            | 1    | 1      | 1      | 1      | 1    | 0    | 0      | 0      | 0      | 0    | 0      | 0        | 0        | 0      |
|                         | 5000 ppm            | . 0  | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0      | 0        | 0        | Ő      |
|                         | 10000 ppm           | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0      | õ        | õ        | ľ      |
| NTERNAL MASS            | Control             | 1    | 1      | 1      | 1      | 1    | 2    | 2      | 2      | 1      | 1    | 1      | 1        | 1        | 2      |
|                         | 2500 ppm            | 2    | 2      | 2      | 3      | 3    | 3    | 4      | 4      | 4      | 3    | 3      | 2        | 0        | 0      |
|                         | 5000 ppm            | 0    | 0      | 0      | 0      | 0    | 3    | 3      | 3      | 3      | 3    | 3      | 3        | 3        | 3      |
|                         | 10000 ppm           | 0    | 0      | 0      | 0      | 0    | 2    | 2      | 3<br>1 | 3<br>1 | 1    | 3<br>1 | 3<br>1   | 3<br>1   | 3<br>1 |
| . EYE                   | Control             | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0      | 0        | 0        | 0      |
|                         | 2500 ppm            | 0    | 0      | 0      |        |      |      | 0      | 0      | 0      | 0    | 0      | 0        | 0 .      | 0      |
|                         |                     | •    |        | -      | 0      | . 0  | 0    | 0      | 0      | 0      | 0    | 0      | 0        | 0        | 0      |
|                         | 5000 ppm            | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0      | 0        | 0        | 0      |
|                         | 10000 ppm           | 0    | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0      | 0        | 0        | 0      |

(HAN190)

BAIS 4

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

#### SEX : FEMALE

| 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   |
|                         |            |                         |      |            |      |        |      |      |      |      |        |        |        |      |        |
| FROG BELLY              | Control    | 0                       | 0    | 0          | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0      |
|                         | 2500 ppm   | 0                       | 0    | 0          | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0      |
|                         | 5000 ppm   | 0                       | 0    | 0          | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 1      | 0      | 0    | 0      |
|                         | 10000 ppm  | 0                       | 0    | 0          | 1    | 1      | 1    | 0    | 0    | 0    | 0      | 1      | 1      | 2    | 2      |
| OILED PERI-GENITALIA    | Control    | 1                       | 1    | 1          | 1    | 1      | 1    | 1    | 0    | 0    | 0      | 0      | 0      | 0    | 0      |
|                         | 2500 ppm   | 0                       | 0    | 0          | 0    | 1      | 1    | 1    | 0    | 0    | 0      | 0      | 0      | 0    | 0      |
|                         | 5000 ppm   | 0                       | 0    | 0          | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0      |
|                         | 10000 ppm  | 0                       | 0    | 0          | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0      |
| XOPHTHALMOS             | Control    | 1                       | 1    | 1          | 1    | 1      | 1    | 1    | 1    | 1    | 1      | 1      | 1      | 1    | 1      |
|                         | 2500 ppm   | 0                       | 0    | 0          | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0      |
|                         | 5000 ppm   | 0                       | 0    | 0          | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0      |
|                         | 10000 ppm  | 0                       | 0    | 0          | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      | 0    | ů<br>0 |
| ATARACT                 | Control    | 0                       | 0    | 0          | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0      |
|                         | 2500 ррт   | 0                       | 0    | 0          | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0      |
|                         | 5000 ppm   | 0                       | 1    | 0          | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | ů.     | 0    | Ō      |
|                         | 10000 ppm  | 0                       | 0    | 0          | 0    | 0      | 0    | 0    | 0    | 0    | 0      | Ō      | 0      | 0    | ů      |
| CORNEAL OPACITY         | Control    | 0                       | 0    | 0          | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0      |
|                         | 2500 ppm   | 0                       | 0    | 0          | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0      |
|                         | 5000 ppm   | 0                       | 0    | 0          | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0<br>0 | ů<br>0 | Õ    | Õ      |
|                         | 10000 ppm  | 0                       | 0    | 0          | 0    | 0      | 0    | . 0  | 0    | 0    | 0      | 0      | 0      | 0    | 0      |
| NTERIOR CHAMBER OPACITY | Control    | 0                       | 0    | 0          | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0      |
|                         | 2500 ppm   | 0                       | 0    | 0          | 0    | 0      | 0    | Ō    | 0    | Ō    | Ő      | 0      | Ő      | Õ    | õ      |
|                         | 5000 ppm   | ō                       | 0    | <b>0</b> . | Õ    | 0      | ů    | ů    | Ő    | Ő    | 0      | Ő      | 0<br>0 | 0    | 0      |
|                         | 10000 ppm  | 0                       | 0    | 0          | 0    | õ      | Õ    | 0    | 0    | Ő    | 0      | ů      | õ      | 0    | 0      |
| XTERNAL MASS            | Control    | 1                       | 0    | 0          | 0    | 2      | 3    | 3    | 3    | 3    | 3      | 3      | 3      | 3    | 3      |
|                         | 2500 ppm   | 0                       | 0    | 0          | 0    | 0      | õ    | ŏ    | Õ    | õ    | õ      | 0 O    | Ő      | Ő    | Ő      |
|                         | 5000 ppm   | 0                       | 0    | õ          | 0    | ů<br>0 | ů    | ů    | Ő    | Ő    | 0<br>0 | 0      | ů<br>0 | 0    | 0      |
|                         | 10000 ppm  | ĩ                       | 2    | 2          | 2    | 2      | 2    | 2    | 2    | 2    | 2      | 2      | 2      | 2    | 2      |
| TERNAL MASS             | Control    | 2                       | 1    | 1          | 2    | 4      | 3    | 3    | 4    | 4    | 4      | 4      | 4      | 5    | 4      |
|                         | 2500 ppm   | 0                       | ĩ    | 1          | 2    | 7      | 7    | 7    | 6    | 6    | 4      | 4      | 3      | 3    | 3      |
|                         | 5000 ppm   | 3<br>3                  | 3    | 3          | 2    | 2      | 2    | 2    | 3    | 1    | 1      | 3      | 2      | 3    | 3      |
|                         | 10000 ppm  | 1                       | 1    | 1          | 1    | 3      | 3    | 4    | 4    | 2    | 2      | 2      | 3      | 3    | 3      |
| . EYE                   | Control    | 0                       | 0    | 0          | 0    | 1      | 1    | 1    | 1    | 1    | 1      | 1      | 1      | 1    | 1      |
|                         | 2500 ppm   | Ő                       | õ    | Ő          | Õ    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0      |
|                         | 5000 ppm   | Ő                       | 0    | 0          | 0    | 0      | 0    | 0    | 0    | 0    | 0      | 0      | 0      | 0    | 0      |
|                         | 10000 ppm  | 0                       | 0    | 0          | 0    | 0      | 0    | v    | v    | v    | v      | U      | v      | U    | U      |

# (HAN190)

BAIS 4

#### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

#### SEX : FEMALE

PAGE : 47

| 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   |
|   |                                    |      |        |        |      |        |        |        |      |        |        |        |        |        |        |
| FROG BELLY  | Control                            | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
|   | 2500 ppm                           | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
|   | 5000 ppm                           | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
|   | 10000 ррт                          | 1    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
| OILED PERI-GENITALIA  | Control                            | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
|   | 2500 ppm                           | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
|   | 5000 ppm                           | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
|   | 10000 ppm                          | 0    | 0      | 0      | 0    | 0      | 0      | 1      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
| EXOPHTHALMOS  | Control                            | 1    | 1      | 1      | 1    | 1      | 1      | 1      | 1    | 1      | 1      | 1      | 1      | 0      | 0      |
|   | 2500 ppm                           | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
|   | 5000 ppm                           | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | Ő      |
|   | 10000 ppm                          | 0    | 0      | Ő      | Ŭ .  | ő      | 0      | Ő      | õ    | Ő      | 0      | 0      | 0      | 0      | 0      |
| CATARACT  | Control                            | 0    | 0.     | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
|   | 2500 ppm                           | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | Õ      | õ      |
|   | 5000 ppm                           | õ    | Ő      | ů<br>0 | ů    | 0      | 0      | ů<br>0 | 0    | 0<br>0 | 0      | 0      | 0      | 0      | 0      |
|   | 10000 ppm                          | Ő    | Õ      | 0      | õ    | 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      |
|   | 2500 ppm                           | 0    | 0      | 0      | Ō    | 0      | 0<br>0 | ŏ      | õ    | 0<br>0 | õ      | 0      | 0<br>0 | 0<br>0 | ŏ      |
|   | 5000 ppm                           | 0    | 0      | Õ      | õ    | 0<br>0 | ů      | õ      | ů    | 0      | ů      | ů      | 0      | 0      | 0      |
| ана стана стана<br>На стана с | 10000 ppm                          | 0    | 0      | 0      | õ    | 0      | 0      | 1      | 1    | 1      | 1      | - 1    | 1      | 1      | 1      |
| NTERIOR CHAMBER OPACITY   | Control                            | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
|   | 2500 ppm                           | 0    | 0      | 0      | 0    | 0      | 0<br>0 | õ      | ŏ    | 0      | Õ -    | Õ      | Ő      | 0      | ŏ      |
|   | 5000 ppm                           | 0    | 0<br>0 | 0      | õ    | 0      | 0<br>0 | ů      | Õ    | 0.     | 0      | 0      | 0      | 0      | 0<br>0 |
|   | 10000 ppm                          | Ő    | 0      | 0      | õ    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
| EXTERNAL MASS   | Control                            | 2    | 3      | 3      | 3    | 3      | 3      | 3      | 3    | 3      | 3      | 3      | 3      | 2      | 2      |
|   | 2500 ppm                           | 1    | ĩ      | 1      | ĩ    | 1      | 1      | 1      | 1    | 1      | 1      | 1      | 1      | 1      | 2      |
|   | 5000 ppm                           | 0    | 0      | 0      | 0    | 1      | 1      | 1      | 0    | 0      | 0      | 0      | 0      | 0      | 2      |
|   | 10000 ppm                          | 2    | 2      | 1      | 2    | 2      | 2      | 2      | 3    | 0<br>4 | 4      | 0<br>4 | 4      | 0<br>4 | 0<br>4 |
| NTERNAL MASS  | Control                            | 4    | 4      | 4      | 4    | 3      | 3      | 2      | 3    | 2      | 4      | 3      | 4      | 2      | 2      |
|   | 2500 ppm                           | 3    | 4      | 5      | 5    | 5      | 5      | 5      | 6    | 5      | 5      | 5      | 5      | 2<br>4 | 2<br>4 |
|   | 5000 ppm                           | . 3  | 2      | 3      | 3    | 3      | 3      | 3<br>2 | 3    | 2      | 5<br>2 |        |        |        |        |
|   | 10000 ppm                          | 3    | 2      | 3<br>1 |      |        |        |        |      |        |        | 4      | 3      | 3      | 3      |
|   | 10000 ppm                          | 3    | 4      | I      | 1    | 2      | 4      | 6      | 5    | 5      | 7      | 7      | 8      | 9      | 9      |
| . EYE   | Control                            | 1    | 2      | 2      | 2    | 2      | 2      | 2      | 2    | 2      | 2      | 2      | 2      | 1      | 1      |
|   | 2500 ppm                           | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
|   | 5000 ppm                           | 0    | 0      | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0      | 0      | 0      |
|   | 10000 ppm                          | 0    | 0      | 0      | 1    | 1      | 1      | 1      | 1    | 1      | 1      | 1      | 1      | 1      | 1      |

# CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

# SEX : FEMALE

PAGE: 48

~\_\_\_\_

|                          |            |       |           |            |       |       |       |       |  |  | 1105 - 4 |
|--------------------------|------------|-------|-----------|------------|-------|-------|-------|-------|--|--|----------|
| Clinical sign            | Group Name | Admin | istration | Week-day _ |       |       |       |       |  |  |          |
|                          |            | 99-7  | 100-7     | 101-7      | 102-7 | 103-7 | 104-7 | <br>- |  |  | ,        |
|                          |            |       |           |            |       |       |       |       |  |  |          |
| FROG BELLY               | Control    | 0     | 0         | 0          | 0     | 0     | 0     |       |  |  |          |
|                          | 2500 ppm   | 0     | 0         | 0          | 0     | • 0   | 0     |       |  |  |          |
|                          | 5000 ppm   | 0     | 0         | 0          | 0     | 1     | 0     |       |  |  |          |
|                          | 10000 ppm  | 0     | 1         | 0          | 0     | 0     | 0     |       |  |  |          |
| SOILED PERI-GENITALIA    | Control    | 0     | 0         | 0          | 0     | 0     | 0     |       |  |  |          |
|                          | 2500 ppm   | . 0   | 0         | 0          | 0     | 0     | 0     |       |  |  |          |
|                          | 5000 ppm   | 0     | 0         | 0          | 0     | 0     | 0     |       |  |  |          |
|                          | 10000 ppm  | 0     | 0         | 0          | 0     | 0     | 0     |       |  |  |          |
| EXOPHTHALMOS             | Control    | 0     | 0         | 0          | 0     | 0     | 0     |       |  |  |          |
|                          | 2500 ppm   | 0     | 0         | 0          | 0     | 0     | 0     |       |  |  |          |
|                          | 5000 ppm   | 0     | 0         | 0          | 0     | 0     | 0     |       |  |  |          |
|                          | 10000 ppm  | 0     | 0         | 0          | 0     | 0     | 1     |       |  |  |          |
| CATARACT                 | Control    | 0     | 0         | 0          | 0     | 0     | 0     |       |  |  |          |
|                          | 2500 ppm   | 0     | 0         | 0          | 0     | 0     | 0     |       |  |  |          |
|                          | 5000 ppm   | 0     | 0         | 0          | 0     | 0     | 0     |       |  |  |          |
|                          | 10000 ppm  | 0     | 0         | 0          | 0     | 0     | 0     |       |  |  |          |
| CORNEAL OPACITY          | Control    | 0     | 0         | 0          | 0     | 0     | 0     |       |  |  |          |
|                          | 2500 ppm   | 0     | 0         | 0          | 0     | 0     | 0     |       |  |  |          |
|                          | 5000 ppm   | 0     | 0         | 0          | 0     | 0     | 0     |       |  |  |          |
|                          | 10000 ppm  | 1     | 1         | 2          | 2     | 2     | 2     |       |  |  |          |
| ANTERIOR CHAMBER OPACITY | Control    | 0     | 0         | 0          | 0     | 0     | 0     |       |  |  |          |
|                          | 2500 ppm   | 0     | 0         | 0          | 0     | 0     | 0     |       |  |  |          |
|                          | 5000 ppm   | 0     | 0         | 0          | 0     | 0     | 0     |       |  |  |          |
|                          | 10000 ppm  | 0     | 1         | 0          | 0     | 0     | 0     |       |  |  |          |
| EXTERNAL MASS            | Control    | 2     | 2         | 2          | 2     | 1     | . 1   |       |  |  |          |
|                          | 2500 ррт   | 2     | 2         | 2          | 1     | 1     | 1     |       |  |  |          |
|                          | 5000 ppm   | 1     | 1         | 0          | 0     | 0     | 1     |       |  |  |          |
|                          | 10000 ppm  | 4     | 4         | 3          | 3     | 2     | 4     | -     |  |  |          |
| INTERNAL MASS            | Control    | 3     | 3         | 2          | 2     | 2     | 3     |       |  |  |          |
|                          | 2500 ppm   | 6     | 7         | 5          | 7     | 7     | 8     |       |  |  |          |
|                          | 5000 ppm   | 3     | 4         | 4          | 7     | 8     | 8     |       |  |  |          |
|                          | 10000 ppm  | 8     | 6         | 5          | 5     | 5     | 4     |       |  |  |          |
| M. EYE                   | Control    | 1     | 1         | 1          | 1     | 1     | 1     |       |  |  |          |
|                          | 2500 ppm   | 0     | 0         | 0          | 0     | 0     | 0     |       |  |  |          |
|                          | 5000 ppm   | 0     | 0         | 0          | 0     | 0     | 0     |       |  |  |          |
|                          | 10000 ppm  | 1     | 1         | 1          | 1     | 1     | 1     |       |  |  |          |

(HAN190)

### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : FEMALE

| Clinical sign      | Group Name | Admini | stration We | eek-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   |
|                    | ,          |        |             |         |        |        |        |        |     |        |        |                                       |        |        |        |
| A. EAR             | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0   | 0      | 0      | 0                                     | 0      | 0      | 0      |
|                    | 2500 ppm   | 0      | 0           | 0       | 0      | 0      | 0      | Ō      | 0   | Õ      | Ő      | 0                                     | õ      | õ      | õ      |
|                    | 5000 ppm   | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0   | 0      | 0      | Ő                                     | 0<br>0 | 0<br>0 | õ      |
|                    | 10000 ppm  | 0      | 0           | 0       | 0      | 0      | Ō      | 0      | 0   | 0      | Ő      | Ő                                     | Õ      | Ő      | Ő      |
| I. NECK            | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0   | 0      | 0      | 0                                     | 0      | 0      | 0      |
|                    | 2500 ppm   | ů      | ů           | 0<br>0  | . 0    | ů<br>0 | ŏ      | 0<br>0 | 0   | õ      | 0      | 0                                     | Ő      | 0      | Ő      |
|                    | 5000 ppm   | 0      | 0           | 0       | 0      | 0      | 0      | . 0    | 0   | 0      | 0      | 0                                     | 0      | 0      | 0      |
|                    | 10000 ppm  | 0      | . 0         | 0       | 0      | 0      | 0      | 0      | 0   | 0      | 0      | 0                                     | 0      | 0      | 0      |
|                    |            |        |             |         |        |        | -      |        |     | Ũ      |        | ,                                     | Ŭ      | Ũ      | 0      |
| . FORELIMB         | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0   | 0      | 0      | 0                                     | 0      | 0      | 0      |
|                    | 2500 ppm   | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0   | 0      | 0      | 0                                     | 0      | 0      | 0      |
|                    | 5000 ppm   | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0   | 0      | 0      | 0                                     | 0      | 0      | 0      |
|                    | 10000 ppm  | . 0    | 0           | 0       | 0      | 0      | 0      | 0      | 0   | 0      | 0      | 0                                     | 0      | 0      | 0      |
| . BREAST           | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0   | 0      | 0      | 0                                     | 0      | 0      | 0      |
|                    | 2500 ppm   | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0   | 0      | 0      | 0                                     | 0      | Õ      | õ      |
|                    | 5000 ppm   | 0      | 0           | 0       | 0      | 0      | 0      | õ      | Ő   | 0      | ů<br>0 | õ                                     | ŏ      | 0<br>0 | 0      |
|                    | 10000 ppm  | 0      | 0           | 0       | 0      | 0      | 0      | Ő      | Ő   | 0      | Ő      | ů                                     | ů      | ů      | 0<br>0 |
| . ABDOMEN          | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0   | 0      | 0      | 0                                     | 0      | 0      | 0      |
|                    | 2500 ppm   | õ      | õ           | 0       | 0<br>0 | 0      | 0      | 0      | 0   | 0      | 0      | 0                                     | 0      | 0      |        |
|                    | 5000 ppm   | 0      | 0           | 0       | 0      | 0      | 0      | 0      |     |        |        |                                       |        | -      | 0      |
|                    | 10000 ppm  | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0   | 0<br>0 | 0      | 0                                     | 0      | 0      | 0<br>0 |
|                    |            |        |             |         |        |        |        |        |     |        |        | -                                     | -      | 0      |        |
| ANTERIOR. DORSUM   | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0   | 0      | 0      | 0                                     | 0      | 0      | 0      |
|                    | 2500 ррт   | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0   | 0      | 0      | 0                                     | 0      | 0      | 0      |
|                    | 5000 ppm   | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0   | 0      | 0      | 0                                     | 0      | 0      | 0      |
|                    | 10000 ppm  | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0   | 0      | 0      | 0                                     | 0      | 0      | 0      |
| . POSTERIOR DORSUM | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0   | 0      | 0      | 0                                     | 0      | 0      | 0      |
|                    | 2500 ppm   | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0   | Õ      | Ő      | Ő                                     | Õ      | ů<br>0 | ŏ      |
|                    | 5000 ppm   | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0   | Õ      | ů      | õ                                     | ů      | 0      | 0<br>0 |
|                    | 10000 ppm  | 0      | 0           | 0       | Ő      | õ      | õ      | Õ      | 0   | 0      | ů<br>0 | 0                                     | õ      | 0      | Ő      |
| . HINDLIMB         | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0   | 0      | 0      | 0                                     | 0      | 0      | . 0    |
|                    | 2500 ppm   | ŏ      | Ő           | 0       | 0      | 0      | 0      | 0      | 0   | 0      | 0      | 0                                     | 0      | 0      |        |
|                    | 5000 ppm   | 0      | 0           | 0       | 0      |        |        |        |     |        |        |                                       |        |        | 0      |
|                    | 10000 ppm  | 0      | 0           | 0       | 0      | 0      | 0<br>0 | 0      | 0   | 0<br>0 | 0      | 0                                     | 0      | 0      | 0<br>0 |
|                    | 10000 ppm  | v      | Ū           | 0       | U U    | v      | U      | U      | U   | U      | U      | U                                     | U      | U      | U      |
| . GENITALIA        | Control    | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0   | 0      | 0      | 0                                     | 0      | 0      | 0      |
|                    | 2500 ррт   | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0   | 0      | 0      | 0                                     | 0      | 0      | 0      |
|                    | 5000 ppm   | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0   | 0      | 0      | 0                                     | 0      | 0      | 0      |
|                    | 10000 ppm  | 0      | 0           | 0       | 0      | 0      | 0      | 0      | 0   | 0      | 0      | 0                                     | 0      | 0      | 0      |
|                    |            |        |             |         |        |        |        |        |     |        |        |                                       |        |        |        |

### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

### SEX : FEMALE

\_\_\_\_\_

| Clinical sign      | Group Name          | Admini | stration 🛛 | leek-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   |
| . EAR              | 0 1                 | 0      | 0          | 0          | 0      | 0      | 0    | 0    | 0    | <u>^</u> |      |      |      |        |        |
| . CAK              | Control             | 0      | 0          | 0          | 0      | 0      | 0    | 0    | 0    | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 2500 ppm            | 0      | 0          | 0          | 0      | 0      | 0    | 0    | 0    | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 5000 ppm            | 0      | 0          | 0          | 0      | 0      | 0    | 0    | 0    | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 10000 ppm           | 0      | 0          | 0          | 0      | 0      | 0    | 0    | 0    | 0        | 0    | 0    | 0    | 0      | 0      |
| I. NECK            | Control             | 0      | 0          | 0          | 0      | 0      | 0    | 0    | 0    | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 2500 ppm            | 0      | 0          | 0          | 0      | 0      | 0    | 0    | 0    | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 5000 ppm            | 0      | 0          | 0          | 0      | 0      | 0    | 0    | 0    | 0        | .0   | 0    | 0    | 0      | 0      |
|                    | 10000 ppm           | 0      | 0          | 0          | 0      | 0      | 0    | 0    | 0    | 0        | 0    | 0    | 0    | 0      | 0      |
| I. FORELIMB        | Control             | 0      | 0          | 0          | 0      | 0      | 0    | 0    | 0    | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 2500 ppm            | 0      | 0          | 0          | 0      | 0      | 0    | 0    | 0    | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 5000 ppm            | 0      | 0          | 0          | 0      | 0      | 0    | 0    | 0    | . 0      | 0    | 0    | 0    | 0      | 0      |
|                    | 10000 ppm           | 0      | 0          | 0          | 0      | 0      | 0    | 0    | 0    | 0        | 0    | 0    | 0    | 0      | 0      |
| I. BREAST          | Control             | 0      | 0          | 0          | 0      | 0      | 0    | 0    | 0    | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 2500 ppm            | 0      | 0          | 0          | 0      | 0      | 0    | 0    | 0    | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 5000 ppm            | 0      | 0          | 0          | 0      | 0      | 0    | 0    | 0    | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 10000 ppm           | 0      | 0          | 0          | 0      | 0      | 0    | 0    | 0    | 0        | 0    | 0    | 0    | 0      | Ő      |
| I. ABDOMEN         | Control             | 0      | 0          | 0          | 0      | 0      | 0    | 0    | 0    | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 2500 ppm            | 0      | 0          | 0          | 0      | 0      | 0    | 0    | 0    | Ō        | 0    | 0    | õ    | 0      | Ő      |
|                    | 5000 ppm            | 0      | 0          | 0          | 0      | 0      | 0    | 0    | 0    | 0        | 0    | ů    | ů    | 0<br>0 | ů      |
|                    | 10000 ppm           | 0      | 0          | 0          | 0      | 0      | 0    | 0    | 0    | 0        | 0    | õ    | 0    | 0      | 0      |
| ANTERIOR. DORSUM   | Control             | 0      | 0          | 0          | 0      | 0      | 0    |      | 0    | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 2500 ppm            | 0      | 0          | 0          | 0      | 0      | 0    | 0    | 0    | Ō        | Õ    | õ    | õ    | Õ      | ŏ      |
|                    | 5000 ppm            | 0      | 0          | 0          | Ő      | Õ      | õ    | 0    | 0    | 0<br>0   | 0    | 0    | Ő    | 0      | 0      |
|                    | 10000 ppm           | 0      | õ          | Õ          | õ      | 0      | 0    | ő    | 0    | 0        | 0    | 0    | Ő    | 0      | 0      |
| . POSTERIOR DORSUM | Control             | 0      | 0          | 0          | 0      | 0      | 0    | 0    | 0    | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 2500 ppm            | õ      | ů          | 0<br>0     | Ő      | 0      | 0    | Ő    | 0    | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 5000 ppm            | Ő      | õ          | Ő          | 0      | 0<br>0 | 0    | 0    | 0    | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 10000 ppm           | 0      | ŏ          | 0          | 0      | Ő      | õ    | .0   | 0    | 0        | 0    | 0    | 0    | 0      | 0      |
| . HINDLIMB         | Control             | 0      | 0          | 0          | 0      | 0      | 0    | 0    | 0    | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 2500 ppm            | ő      | 0          | 0          | 0      | 0      | 0    | 0    | 0    | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 5000 ppm            | 0      | 0          | 0          | 0      | 0      | 0    | 0    | 0    | 0        | 0    | 0    | 0    | 0      |        |
|                    | 10000 ppm           | 0      | . 0        | 0          | 0      | 0      | 0    | 0    | 0    | 0        | 0    | 0    | 0    | 0      | 0<br>0 |
|                    |                     | Ŷ      | v          |            | v      | v      | v    | Ū    | v    | U        | v    | U    | v    | U      | U      |
| . GENITALIA        | Control<br>2500 ppm | 0      | 0<br>0     | 0<br>0     | 0<br>0 | 0      | 0    | 0    | 0    | 0        | 0    | 0    | 0    | 0      | 0      |
|                    |                     | e      | -          | -          |        | 0      | 0    | 0    | 0    | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 5000 ppm            | 0      | 0          | 0          | 0      | 0      | 0    | 0    | 0    | 0        | 0    | 0    | 0    | 0      | 0      |
|                    | 10000 ppm           | 0      | 0          | 0          | 0      | 0      | 0    | 0    | 0    | 0        | 0    | 0    | 0    | 0      | 0      |

(HAN190)

### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

### SEX : FEMALE

| Clinical sign      | Group Name            |        | stration W | eek-dav |        |        |          |        |      |          |      |      |        |        |        |
|--------------------|-----------------------|--------|------------|---------|--------|--------|----------|--------|------|----------|------|------|--------|--------|--------|
|                    |                       | 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   |
| EAR                | 0                     | 0      |            | 0       |        |        | <u>^</u> | 0      | 0    | <u>_</u> |      |      |        |        |        |
| LAR                | Control<br>2500 ppm   | 0<br>0 | 0<br>0     | 0<br>0  | 0<br>0 | 0      | 0        | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      |
|                    |                       | 0      |            | 0       |        | 0      | 0        | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      |
|                    | 5000 ррт<br>10000 ррт | 0      | 0<br>0     | 0       | 0<br>0 | 0      | 0        | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      |
|                    | 10000 ppm             | 0      | Ų          | U       | 0      | 0      | 0        | 0      | . 0  | 0        | 0    | 0    | 0      | 0      | 0      |
| . NECK             | Control               | 0      | 0          | 0       | 0      | 0      | 0        | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      |
|                    | 2500 ppm              | 0      | 0          | 0       | 0      | 0      | 0        | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      |
|                    | 5000 ppm              | 0      | 0          | 0       | 0      | 0      | 0        | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      |
|                    | 10000 ppm             | 0      | 0          | 0       | 0      | 0      | 0        | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      |
| . FORELIMB         | Control               | 0      | 0          | 0       | 0      | 0      | 0        | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      |
|                    | 2500 ppm              | õ      | ů          | õ       | ů      | 0      | 0        | Ő      | 0    | 0        | 0    | 0    | 0<br>0 | 0      | 0      |
|                    | 5000 ppm              | 0      | ů          | Ö       | ů<br>0 | 0      | 0        | ů<br>0 | 0    | 0        | 0    | 0    | 0      | 0      | 0      |
|                    | 10000 ppm             | Ő      | Õ          | 0       | õ      | 0<br>0 | 0<br>0   | 0<br>0 | 0    | 0        | 0    | 0    | 0      | 0      | 0      |
|                    | 0                     | 0      |            |         | •      |        |          |        |      |          |      |      |        |        |        |
| I. BREAST          | Control               | 0      | 0          | 0       | 0      | 0      | 0        | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      |
|                    | 2500 ppm              | 0      | 0          | 0       | 0      | 0      | 0        | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      |
|                    | 5000 ppm              | 0      | 0          | 0       | 0      | 0      | 0        | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      |
|                    | 10000 ppm             | 0      | 0          | 0       | 0      | 0      | 0        | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      |
| . ABDOMEN          | Control               | 0      | 0          | 0       | 0      | 0      | 0        | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      |
|                    | 2500 ppm              | 0      | 0          | 0       | 0      | 0      | 0        | 0      | 0    | 0        | 0    | 0    | 0      | 0      | õ      |
|                    | 5000 ppm              | 0      | 0          | 0       | 0      | 0      | 0        | 0      | 0    | 0        | 0    | 0    | 0      | 0<br>0 | õ      |
|                    | 10000 ppm             | 0      | 0          | 0       | 0      | 0      | 0        | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      |
| . ANTERIOR. DORSUM | Control               | 0      | 0          | 0       | 0      | 0      | 0        | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      |
|                    | 2500 ppm              | ő      | Ő          | 0       | õ      | 0<br>0 | õ        | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      |
|                    | 5000 ppm              | ŏ      | 0          | 0       | 0      | 0      | 0        | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      |
|                    | 10000 ppm             | Õ      | 0          | 0       | 0      | 0<br>0 | 0        | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      |
| . POSTERIOR DORSUM | (                     |        | 0          | 0       | 0      | 0      | <u>^</u> | 0      |      |          |      |      |        | _      | -      |
| L FUSTERIUR DURSUM | Control               | 0      | 0          | 0       | 0      | 0      | 0        | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      |
|                    | 2500 ppm              | 0      | 0          | 0       | 0      | 0      | 0        | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      |
|                    | 5000 ppm              | 0      | 0          | 0       | 0      | 0      | 0        | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      |
|                    | 10000 ppm             | 0      | 0          | 0       | 0      | 0      | 0        | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      |
| . HINDLIMB         | Control               | 0      | 0          | 0       | 0      | 0      | 0        | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      |
|                    | 2500 ppm              | 0      | 0          | 0       | 0      | 0      | 0        | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      |
|                    | 5000 ppm              | 0      | 0          | 0       | 0      | 0      | 0        | 0      | 0    | 0        | 0    | 0    | Ō      | Ő      | Ő      |
|                    | 10000 ppm             | 0      | 0          | 0       | 0      | 0      | 0        | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      |
| GENITALIA          | Control               | 0      | 0          | 0       | 0      | 0      | 0        | 0      | 0    | 0        | 0    | 0    | 0      | 0      | 0      |
|                    | 2500 ppm              | 0      | 0          | 0       | 0      | 0      | 0        | 0      | 0    | 0        | 0    | 0    | 0      |        | 0      |
|                    | 5000 ppm              | 0      | 0          | 0       | 0      | 0      | 0        | 0      |      |          |      |      | -      | 0      |        |
|                    | 10000 ppm             | 0      | 0          | 0       | 0      | 0      | 0        | 0      | 0    | 0<br>0   | 0    | 0    | 0      | 0      | 0<br>0 |

BAIS 4

PAGE : 51

.

### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 104

### SEX : FEMALE

| linical sign     | Group Name | Admini | stration W | eek-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   |
|                  | <i>a</i>   |        |            | _       | _      | _      | ·      |        | _    |      |        |        |      |      |        |
| EAR              | Control    | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0    | 0    | 0      |
|                  | 2500 ppm   | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0    | 0    | 0      |
|                  | 5000 ppm   | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0    | 0    | 0      |
|                  | 10000 ppm  | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0    | 0    | 0      |
| NECK             | Control    | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0    | 0    | 0      |
|                  | 2500 ppm   | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0    | 0    | 0      |
|                  | 5000 ppm   | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0    | 0    | 0      |
|                  | 10000 ppm  | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0    | 0    | 0      |
| FORELIMB         | Control    | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0    | 0    | 0      |
|                  | 2500 ppm   | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0.   | 0      | 0      | 0    | 0    | 0      |
|                  | 5000 ppm   | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0    | 0    | 0      |
|                  | 10000 ppm  | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | ů<br>0 | õ      | Ő    | õ    | 0<br>0 |
| BREAST           | Control    | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0    | 0    | 0      |
|                  | 2500 ppm   | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0    | 0    | Ō      |
|                  | 5000 ppm   | 0      | 0          | 0       | 0      | 0      | 0      | Ő      | õ    | Õ    | õ      | ů      | ů    | ů    | 0      |
|                  | 10000 ppm  | 0      | 0          | • 0     | 0      | 0      | 0      | 0      | 0    | 0    | ů      | Ő      | ů    | Õ    | ŏ      |
| ABDOMEN          | Control    | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0    | 0    | 0      |
|                  | 2500 ppm   | 0      | 0          | 0       | Ō      | 0      | 0      | õ      | ŏ    | õ    | õ      | õ      | Õ    | õ    | õ      |
|                  | 5000 ppm   | 0      | 0          | 0       | 0      | õ      | õ      | ů      | ů    | õ    | õ      | 0      | ŏ    | 0    | õ      |
|                  | 10000 ppm  | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0      | Ő      | 0    | Ő    | Ő      |
| ANTERIOR. DORSUM | Control    | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0    | 0    | 0      |
|                  | 2500 ppm   | 0      | 0          | 0       | Õ      | Õ      | õ      | ŏ      | ŏ    | Õ    | Õ      | 0<br>0 | ŏ    | Ő    | õ      |
|                  | 5000 ppm   | ŏ      | ŏ          | 0       | Ő      | 0      | ŏ      | 0      | 0    | 0    | 0      | 0      | 0    | 0    | 0      |
|                  | 10000 ppm  | Ő      | Õ          | 0       | Ő      | 0      | 0<br>0 | 0      | 0    | 0    | 0      | 0      | 0    | 0    | 0      |
| POSTERIOR DORSUM | Control    | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0    | 0    | 0      |
|                  | 2500 ppm   | 0      | Õ          | õ       | Õ      | õ      | Ő      | ŏ      | õ    | 0    | 0      | 0<br>0 | 0    | 1    | 1      |
|                  | 5000 ppm   | õ      | õ          | 0       | 0<br>0 | 0<br>0 | õ      | 0<br>0 | 0    | 0    | 0      | 0      | 0    | 0    | 0      |
|                  | 10000 ppm  | Ő      | ů<br>0     | 0       | õ      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0    | 0    | 0      |
| HINDLIMB         | Control    | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0    | 0    | 0      |
|                  | 2500 ppm   | ő      | Ő          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0    | 0    | 0      |
|                  | 5000 ppm   | ő      | Ő          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0    | 0    | 0      |
|                  | 10000 рры  | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0      | . 0    | 0    | 0    | 0      |
| GENITALIA        | Control    | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0    | 0    | 0      |
|                  | 2500 ppm   | ů      | Õ          | 0       | 0      | 0      | 0      | 0      | 0    | 0    | 0      | 0      | 0    | 0    | 0      |
|                  | 5000 ppm   | 0      | 0          | 0       | 0      | 0      | 0      | 0      | 0    |      | 0      |        |      |      | -      |
|                  | 10000 ppm  | 0      | v          | v       | v      | v      | v      | U      | v    | 0    | U      | 0      | 0    | 0    | 0      |

PAGE : 52

·-----

### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

~~

### SEX : FEMALE

| Clinical sign      | Group Name | Admini | stration W | Veek-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   |
|                    |            |        |            |          |        |      |      |          |        |        |        |        |      |        |        |
| I. EAR             | Control    | 0      | 0          | 0        | 0      | 0    | 0    | 0        | 0      | 0      | 0      | 0      | 0    | 0      | 0      |
|                    | 2500 ррт   | 0      | 0          | 0        | 0      | 0    | 0    | 0        | 0      | 0      | 0      | 0      | 0    | 0      | 0      |
|                    | 5000 ppm   | 0      | 0          | 0        | 0      | 0    | 0    | 0        | 0      | 0      | 0      | 0      | 0    | 0      | 0      |
|                    | 10000 ppm  | 0      | 0          | 0        | 0      | 0    | 0    | 0        | 0      | 0      | 0      | 0      | 0    | 0      | 0      |
| NECK               | Control    | 0      | 0          | 0        | 0      | 0    | 0    | 0        | 0      | 0      | 0      | 0      | 0    | 0      | 0      |
|                    | 2500 ppm   | 0      | 0          | 0        | 0      | 0    | 0    | 0        | 0      | 0      | 0      | 0      | 0    | 0      | 0      |
|                    | 5000 ppm   | 0      | 0          | 0        | 0      | 0    | 0    | 0        | 0      | 0      | 0      | 0      | 0    | 0      | 0      |
|                    | 10000 ppm  | 0      | 0          | 0        | 0      | 0    | 0    | 0        | 0      | 0      | 0      | 0      | 0    | 0      | 0      |
| . FORELIMB         | Control    | 0      | 0          | 0        | 0      | 0    | 0    | 0        | 0      | 0      | 0      | 0      | 0    | 0      | 1      |
|                    | 2500 ppm   | 0      | 0          | 0        | 0      | 0    | 0    | 0        | 0      | 0      | 0      | 0      | 0    | 0      | 0      |
|                    | 5000 ppm   | 0      | 0          | 0        | 0      | 0    | 0    | 0        | 0      | 0      | 0      | 0      | 0    | 0      | · 0    |
|                    | 10000 ppm  | 0      | 0          | 0        | 0      | 0    | 0    | 0        | 0      | 0      | 0      | 0      | õ    | 0      | 1      |
| . BREAST           | Control    | 0      | 0          | 0        | 0      | 0    | 0    | 0        | 0      | 0      | 0      | 0      | 0    | 0      | 0      |
|                    | 2500 ppm   | 0      | 0          | 0        | 0      | 0    | Õ    | Ő        | Õ      | Ő      | Ő      | õ      | Ő    | - 0    | õ      |
|                    | 5000 ppm   | 0      | 0          | 0        | 0      | 0    | 0    | 0<br>0   | 0      | 0<br>0 | Ő      | Õ      | Ő    | 0      | ů      |
|                    | 10000 ppm  | 0      | 0          | 0        | 0      | 0    | 0    | 0        | 0      | õ      | õ      | 0<br>0 | Ő    | 0      | Õ      |
| ABDOMEN            | Contro1    | 0      | 0          | 0        | 0      | 0    | 0    | 0        | 0      | 0      | 0      | 0      | 0    | 0      | 0      |
|                    | 2500 ppm   | 0      | 0          | 0        | 0      | Õ    | Õ    | õ        | 0<br>0 | 0<br>0 | ů<br>0 | 0<br>0 | 0    | 0<br>0 | Ő      |
|                    | 5000 ppm   | õ      | ů<br>0     | õ        | 0<br>0 | 0    | 0    | Ő        | 0      | 0      | 0      | 0      | 0    | 0      | 0      |
|                    | 10000 ppm  | 0      | 0          | 0        | 0      | 0    | 0    | 0        | 0      | 0      | 0      | 0      | 0    | 0      | 0      |
| . ANTERIOR. DORSUM | Control    | 0      | 0          | 0        | 0      | 0    | . 0  | 0        | 0      | 0      | 0      | 0      | 0    | 0      | 0      |
|                    | 2500 ppm   | 0      | 0          | 0        | 0      | 0    | . 0  | Ő        | õ      | 0<br>0 | Õ      | õ      | õ    | õ      | ő      |
|                    | 5000 ppm   | 0      | Õ          | õ        | õ      | Ő    | 0    | 0        | 0      | 0      | 0      | 0      | 0    | 0      | Ő      |
|                    | 10000 ppm  | 0      | õ          | 0        | 0      | 0    | 0    | 0        | 0      | 0      | 0<br>0 | 0      | 0    | 0      | 0      |
| POSTERIOR DORSUM   | Control    | 0      | 0          | 0        | 0      | 0    | 0    | 0        | 0      | 0      | 0      | 0      | 0    | 0      | 0      |
|                    | 2500 ppm   | ĩ      | 1          | 1        | 1      | 1    | 0    | 0        | 0      | 0      | 0      | . 0    | 0    | 0      | 0      |
|                    | 5000 ppm   | 0      | 0          | 0        | 0      | 0    | 0    | 0        | 0      | 0      | 0      | 0      | 0    | 0      | 0      |
|                    | 10000 ppm  | ů<br>0 | 0<br>0     | 0        | 0      | 0    | 0    | 0        | 0      | 0      | 0      | 0      | 0    | 0      | 0      |
| HINDLIMB           | Control    | 0      | 0          | 0        | 0      | 0    | 0    | 0        | 0      | 0      | 0      | 0      | 0    | 0      | 0      |
|                    | 2500 ppm   | ů<br>0 | 0          | 0        | 0      | 0    | 0    | 0        | 0      | 0      | 0      | 0      | 0    | 0      | 0      |
|                    | 5000 ppm - | 0      | 0          | 0        | 0      | 0    | 0    | 0        | 0      | 0      | 0      |        |      |        |        |
|                    | 10000 ppm  | 0      | 0          | 0        | 0      | 0    | 0    | 0        | 0      | 0      | 0      | 0<br>0 | 0    | 0<br>0 | 0<br>0 |
| CENITRAL TA        |            | 0      | 0          | 0        | 0      | 0    |      | <u>^</u> |        |        |        |        |      |        |        |
| . GENITALIA        | Control    | 0      | 0          | 0        | 0      | 0    | 0    | 0        | 0      | 0      | 0      | 0      | 0    | 0      | 0      |
|                    | 2500 ppm   | 0      | 0          | 0        | 0      | 0    | 0    | 0        | 0      | 0      | 0      | 0      | 0    | 0      | 0      |
|                    | 5000 ppm   | 0      | 0          | 0        | 0      | 0    | 0    | 0        | 0      | 0      | 0      | 0      | 0    | 0      | 0      |
|                    | 10000 ppm  | 0      | 0          | 0        | 0      | 0    | 0    | 0        | 0      | 0      | 0      | 0      | 0    | 0      | 0      |

(HAN190)

U.

PAGE : 53

.

### CLINICAL.OBSERVATION (SUMMARY) ALL ANIMALS

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1] REPORT TYPE : A1 104

### SEX : FEMALE

| 75-7 | 76-7 | 77-7 | 78-7 | 79-7 | 80-7 | 81-7 | 82-7 | 8 |
|------|------|------|------|------|------|------|------|---|

-

|                     |           | 71-7   | 72-7   | 70 7 | <b></b> |        |      |      |        |        |        |        |        |      |        |
|---------------------|-----------|--------|--------|------|---------|--------|------|------|--------|--------|--------|--------|--------|------|--------|
|                     |           |        | 14-1   | 73-7 | 74-7    | 75-7   | 76-7 | 77-7 | 78-7   | 79-7   | 80-7   | 81-7   | 82-7   | 83-7 | 84-7   |
| I. EAR              | Create 1  | 0      | 0      | 0    | 0       | 0      |      |      |        |        |        |        |        |      |        |
| A. LAK              | Control   | 0      | 0      | 0    | 0       | 0      | 1    | 1    | 1      | 1      | 1      | 1      | 1      | 1    | 1      |
|                     | 2500 ppm  | 0      | Ũ      | 0    | 0       | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      |
|                     | 5000 ppm  | 0      | 0      | 0    | 0       | 0      | 0    | 0    | 0      | 0      | 0 -    | 0      | 0      | 0    | 0      |
|                     | 10000 ppm | 0      | 0      | 0    | 0       | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      |
| I. NECK             | Control   | 0      | 0      | 0    | 0       | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      |
|                     | 2500 ррт  | 0      | 0      | 0    | 0       | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      |
|                     | 5000 ppm  | 0      | 0      | 0    | 0       | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      |
|                     | 10000 ppm | 0      | 0      | 0    | 0       | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      |
| I. FORELIMB         | Control   | ĺ      | 0      | 0    | 0       | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      |
|                     | 2500 ppm  | 0      | 0      | 0    | 0       | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      |
|                     | 5000 ppm  | 0      | . 0    | 0    | 0       | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      |
|                     | 10000 ppm | 1      | 1      | 1    | 1       | 1      | 1    | 1    | 1      | 1      | 1      | 1      | 1      | 1    | 1      |
| I. BREAST           | Control   | 0      | 0      | 0    | 0       | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      |
|                     | 2500 ppm  | 0      | 0      | 0    | 0       | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | . 0    |
|                     | 5000 ppm  | 0      | 0      | 0    | Õ       | õ      | õ    | ů    | ů<br>0 | ů<br>0 | ů<br>0 | . 0    | õ      | 0    | Ő      |
|                     | 10000 ppm | 0      | 0      | 0    | 0       | Ő      | 0    | 0    | õ      | ő      | ő      | 0      | õ      | ő    | 0      |
| A. ABDOMEN          | Control   | 0      | 0      | 0    | 0       | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      |
|                     | 2500 ppm  | 0      | 0      | 0    | 0       | 0      | 0    | 0    | 0      | 0      | Õ      | Õ      | 0      | Õ    | Ő      |
|                     | 5000 ppm  | 0      | 0      | 0    | 0       | Õ      | 0    | Ő    | 0<br>0 | Ő      | ů<br>0 | õ      | ů<br>0 | 0    | 0<br>0 |
|                     | 10000 ppm | 0      | ů      | õ    | ů       | 0<br>0 | 0    | 0    | 0      | 0      | 0      | 0      | 0<br>0 | 0    | 0      |
| AMPEDIAL DODGIN     |           | 0      | 0      |      |         | 0      |      |      | _      | 2      | _      |        |        |      |        |
| L ANTERIOR. DORSUM  | Control   | 0      | 0      | 0    | 0       | 0      | 0    | 0    | 0      | 0      | 0      | . 0    | 0      | 0    | 0      |
|                     | 2500 ppm  | 0      | 0      | 0    | 0       | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      |
|                     | 5000 ppm  | 0      | 0      | 0    | 0       | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      |
|                     | 10000 ppm | 0      | 0      | 0    | 0       | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      |
| I. POSTERIOR DORSUM | Control   | 0      | 0      | 0    | 0       | 0      | 0    | 0    | 1      | 1      | 1      | 1      | . 1    | 1    | 1      |
|                     | 2500 ppm  | 0      | 0      | 0    | 0       | 0      | 0    | 0.   | 0      | 0      | 0      | 0      | 0      | 0    | 0      |
|                     | 5000 ppm  | 0      | 0      | 0    | 0       | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      |
|                     | 10000 ppm | 0      | 0      | 0    | 0       | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      |
| A. HINDLIMB         | Control   | 0      | 0      | 0    | 0       | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      |
|                     | 2500 ppm  | 0      | 0      | 0    | 0       | 0      | 0    | 0    | 0      | 0      | 0      | 0      | 0      | 0    | 0      |
|                     | 5000 ppm  | 0      | 0      | 0    | 0       | 0      | 0    | 0    | 0      | 0      | Ő      | ů<br>0 | ů      | 0    | ů      |
|                     | 10000 ppm | 0      | 0      | 0    | 0       | 0      | Õ    | 0    | Ő      | Ő      | õ      | Ő      | Ő      | ő    | Ő      |
| I. GENITALIA        | Control   | 0      | 0      | . 0  | 0       | 1      | 1    | 1    | 0      | 0      | 0      | 0      | 0      | 0    | 0      |
|                     | 2500 ppm  | õ      | Õ      | 0    | õ       | 0      | 0    | Ō    | õ      | 0      | 0      | õ      | 0<br>0 | 0    | 0      |
|                     | 5000 ppm  | ů<br>0 | 0<br>0 | 0    | 0       | 0      | 0    | 0    | 0<br>0 | 0      | 0      | 0      | 0      | 0    | 0      |
|                     |           | 0      | 1      |      |         |        |      |      |        |        |        |        |        |      |        |
|                     | 10000 ppm | 0      | 1      | 1    | 1       | 1      | 1    | 1    | 1      | 1      | 1      | 1      | 1      | 1    | 1      |

### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

~~~

### SEX : FEMALE

| SEX : FEMALE        |                        |      |           |        |        |          |        |        |        |        | 2      |        |          |        | PAGE : 55 |
|---------------------|------------------------|------|-----------|--------|--------|----------|--------|--------|--------|--------|--------|--------|----------|--------|-----------|
| Clinical sign       | Group Name             |      | istration |        |        |          |        |        |        |        |        |        |          |        |           |
|                     |                        | 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      |
| 1. EAR              | Control                | 1    |           | 1      | 1      |          |        |        |        | 1      |        |        |          | 0      | 0         |
| A. EAK              | 2500 ppm               | 1    | 1<br>0    | 0      | 1<br>0 | · 1<br>0 | 1<br>0 | 1      | 1<br>0 | 1      | 1<br>0 | 1      | 1        | 0<br>0 | 0         |
|                     | 2000 ppm<br>5000 ppm   | 0    | 0         | 0      |        | 0        |        |        |        | 0      |        | 0      | 0        |        | 0         |
|                     |                        | 0    | 0         | 0      | 0<br>0 | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0      | 0         |
|                     | 10000 ррт              | U    | 0         | 0      | U      | U        | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0      | 0         |
| I. NECK             | Control                | 0    | 0         | 0      | 0      | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0      | 0         |
|                     | 2500 ppm               | 0    | 0         | 0      | 0      | 0        | 0      | . 0    | 0      | 0      | 0      | 0      | 0        | 0      | 0         |
|                     | 5000 ppm               | 0    | 0         | 0      | 0      | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0      | 0         |
|                     | 10000 ppm              | 0    | 0         | 0      | 0      | 0        | 0      | 0      | 1      | 2      | 2      | 2      | 2        | 2      | 2         |
| A. FORELIMB         | Control                | 0    | 0         | 0      | 0      | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0        |        | 0         |
| L FORELIMD          |                        | 0    | 0         | 0      | 0      | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0      | 0         |
|                     | 2500 ppm               | -    | 0         | 0      | 0      | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0        | . 0    | 0         |
|                     | 5000 ppm               | 0    | 0         | 0      | 0      | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0      | 0         |
|                     | 10000 ppm              | 1    | 1         | 1      | 1      | 1        | 1      | 1      | 1      | 1      | 1      | 1      | 1        | 1      | 1         |
| M. BREAST           | Control                | 0    | 0         | 0      | 0      | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0      | 0         |
|                     | 2500 ppm               | 0    | 0         | 0      | 0      | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0      | 0         |
|                     | 5000 ppm               | 0    | 0         | 0      | 0      | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0      | ů         |
|                     | 10000 ppm              | 0    | 0         | 0      | 0      | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0        | Ō      | Õ         |
| M. ABDOMEN          | Control                | 0    | 0         | 0      | 0      | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0      | 0         |
|                     | 2500 ppm               | ů    | ů         | ů      | ŏ      | 0<br>0   | ů<br>0 | 0      | õ      | Ő      | 0      | 0      | 0        | 0      | 0         |
|                     | 5000 ppm               | ů    | ů<br>0    | 0      | 0<br>0 | 1        | 1      | Ŭ      | 0      | 0      | 0      | 0      | 0        | 0      | 0         |
|                     | 10000 ppm              | ů    | 0         | 0      | 0      | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0      | 0         |
| 4                   |                        |      |           |        |        |          |        |        |        |        |        |        |          |        |           |
| A. ANTERIOR. DORSUM | Control                | 0    | 0         | 0      | 0      | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0      | 0         |
|                     | 2500 ppm               | 0    | 0         | 0      | 0      | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0      | 1         |
|                     | 5000 ррт               | 0    | 0         | 0      | 0      | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0      | 0         |
|                     | 10000 ppm              | 0    | 0         | 0      | 0      | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0      | 0         |
| 1. POSTERIOR DORSUM | Control                | 0    | 0         | 0      | 0      | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0      | 0         |
|                     | 2500 ppm               | 0    | 0         | 0      | 0      | 0        | Ő      | Õ      | õ      | õ      | õ      | õ      | 0        | 0      | ů<br>0    |
|                     | 5000 ppm               | 0    | 0         | 0      | 0      | 0        | 0      | 0      | 0      | Õ      | ů      | õ      | ů<br>0   | 0      | Ő         |
|                     | 10000 ppm              | 0    | 0         | 0      | 0      | 0        | 0      | 0      | ů<br>0 | õ      | 0      | õ      | ő        | 0      | õ         |
| 1. HINDLIMB         | Control                | 0    | 1         | 1      | 1      |          | 1      |        |        |        |        |        | <b>.</b> |        |           |
| 0+ 11114/0/1/1837   | 2500 ppm               | 0    | 1<br>0    | 1<br>0 | 1<br>0 | 1        | 1      | 1      | 1      | 1      | 1      | 1      | 1        | 1      | 1         |
|                     | 2500 ppm<br>5000 ppm   | 0    | 0         | 0      | 0      | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0      | 0         |
|                     | 10000 ppm<br>10000 ppm | 0    | 0         | 0      | 0      | 0        | 0<br>0 | 0<br>0 | 0      | 0<br>0 | 0      | 0<br>0 | 0<br>0   | 0<br>0 | 0<br>0    |
|                     |                        |      |           |        |        |          |        | -      | -      | -      | -      | ·      | ÷        | ÷      | Ť         |
| M. GENITALIA        | Control                | 0    | 0         | 0      | 0      | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0      | 0         |
|                     | 2500 ppm               | 0    | 0         | 0      | 0      | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0      | 0         |
|                     | 5000 ppm               | 0    | 0         | 0      | 0      | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0      | 0         |
|                     | 10000 ppm              | 1    | 1         | 0      | 0      | 0        | 0      | 0      | 0      | 0      | 0      | 0      | 0        | 0      | 0         |

### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

### SEX : FEMALE

PAGE : 56

| Clinical sign       | Group Name | Admini | stration | Week-day |       |       |       | <br> | <br> |  | <br> |
|---------------------|------------|--------|----------|----------|-------|-------|-------|------|------|--|------|
|                     |            | 99-7   | 100-7    | 101-7    | 102-7 | 103-7 | 104-7 |      |      |  |      |
|                     |            |        |          |          |       |       |       |      |      |  |      |
| M. EAR              | Control    | 0      | 0        | 0        | 0     | 0     | 0     |      |      |  |      |
|                     | 2500 ppm   | 0      | 0        | 0        | 0     | 0     | 0     |      |      |  |      |
|                     | 5000 ppm   | 0      | 0        | 0        | 0     | 0     | 0     |      |      |  |      |
|                     | 10000 ppm  | 0      | 0        | 0        | 0     | 0     | 0     |      |      |  |      |
| M. NECK             | Control    | 0      | 0        | 0        | 0     | 0     | 0     |      |      |  |      |
|                     | 2500 ppm   | 0      | 0        | 0        | 0     | 0     | 0     |      |      |  |      |
|                     | 5000 ppm   | 0      | 0        | 0        | 0     | 0     | 0     |      |      |  |      |
|                     | 10000 ppm  | 2      | 2        | 1        | 1     | 0     | 1     |      |      |  |      |
| M. FORELIMB         | Control    | 0      | 0        | 0        | 0     | 0     | 0     |      |      |  |      |
|                     | 2500 ppm   | 0      | 0        | 0        | 0     | 0     | 0     |      |      |  |      |
|                     | 5000 ppm   | 0      | 0        | 0        | 0     | 0     | 0     |      |      |  |      |
|                     | 10000 ppm  | 1      | 1        | 1        | 1     | 1     | 0     |      |      |  |      |
| M. BREAST           | Control    | 0      | 0        | 0        | 0     | 0     | 0     |      |      |  |      |
| •                   | 2500 ppm   | 0      | 0        | . 0      | 0     | 0     | 0     |      |      |  |      |
|                     | 5000 ppm   | 0      | 0        | 0        | 0     | 0     | 0     |      |      |  |      |
| _                   | 10000 ppm  | 0      | 0        | 0        | 0     | 0     | 1     |      |      |  |      |
| M. ABDOMEN          | Control    | 0      | 0        | 0        | 0     | 0     | 0     |      |      |  |      |
|                     | 2500 ppm   | 0      | 0        | 0        | 0     | 0     | 0     |      |      |  |      |
|                     | 5000 թթո   | 0      | 0        | 0        | 0     | 0     | 0     |      |      |  |      |
|                     | 10000 ppm  | 0      | 0        | 0        | 0     | 0     | 1     |      |      |  |      |
| M. ANTERIOR. DORSUM | Control    | 0      | 0        | 0        | 0     | 0     | 0     |      |      |  |      |
|                     | 2500 ppm   | 1      | 1        | 1        | 0     | 0     | 0     |      |      |  |      |
|                     | 5000 ppm   | 1      | 1        | 0        | 0     | 0     | 0     |      |      |  |      |
|                     | 10000 ppm  | 0      | 0        | 0        | 0     | 0     | 0     |      |      |  | •    |
|                     | •          |        |          |          |       |       |       |      |      |  |      |
| M. POSTERIOR DORSUM | Control    | 0      | 0        | 0        | 0     | 0     | 0     |      |      |  |      |
|                     | 2500 ppm   | 0      | 0        | 0        | 0     | 0     | 0     |      |      |  |      |
|                     | 5000 ppm   | 0      | 0        | 0        | 0     | 0     | 1     |      |      |  |      |
|                     | 10000 ppm  | 0      | 0        | 0        | 0     | 0     | · 0   |      |      |  |      |
| A. HINDLIMB         | Control    | 1      | 1        | 1        | 1     | 0     | 0     |      |      |  |      |
|                     | 2500 ppm   | 0      | 0        | 0        | 0     | 0     | 0     |      |      |  |      |
|                     | 5000 ppm   | 0      | 0        | 0        | 0     | 0     | 0     |      |      |  |      |
|                     | 10000 ppm  | 0      | 0        | 0        | 0     | 0     | 0     |      |      |  |      |
| M. GENITALIA        | Control    | 0      | 0        | 0        | 0     | 0     | 0     |      |      |  |      |
|                     | 2500 ppm   | 0      | 0        | 0        | 0     | 0     | 1     |      |      |  |      |
|                     | 5000 ppm   | 0      | 0        | 0        | 0     | 0     | Ō     |      |      |  |      |
|                     | 10000 ppm  | 0      | 0        | 0        | 0     | 0     | 0     |      |      |  |      |

### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : FEMALE

|  | e |  |  |  |
|--|---|--|--|--|
|  |   |  |  |  |

| Clinical sign     | Group Name | Admini | stration W | ek-dav |     |        |        |        |        |        |      |        |        |        |      |
|-------------------|------------|--------|------------|--------|-----|--------|--------|--------|--------|--------|------|--------|--------|--------|------|
|                   | -          | 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 |
|                   |            |        |            |        |     |        |        |        |        |        |      |        |        |        |      |
| . TAIL            | Control    | 0      | 0          | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0    |
|                   | 2500 ppm   | 0      | 0          | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0    |
|                   | 5000 ppm   | 0      | 0          | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0    |
|                   | 10000 ppm  | 0      | 0          | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0    |
| ЕМА               | Control    | 0      | 0          | 0      | 0   | 0      | 0      | 0      | 0      | 0      | ο.   | 0      | 0      | 0      | 0    |
|                   | 2500 ppm   | 0      | 0          | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0      | . 0    | 0    |
|                   | 5000 ppm   | 0      | 0          | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0    |
|                   | 10000 ppm  | 0      | 0          | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0    |
| IEMIA             | Control    | 0      | 0          | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0    |
|                   | 2500 ppm   | 0      | 0          | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0    |
|                   | 5000 ppm   | 0      | 0          | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0    |
|                   | 10000 ppm  | 0      | 0          | 0      | 0   | 0      | 0      | 0      | 0      | 0      | Õ    | 0      | Ő      | Õ      | Ő    |
| CER               | Control    | 0      | 0          | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0    |
|                   | 2500 ppm   | 0      | 0          | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0    |
|                   | 5000 ppm   | 0      | 0          | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0    |
|                   | 10000 ppm  | 0      | 0          | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0    |
| OSION             | Control    | 0      | 0          | 0.     | 0   | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0    |
|                   | 2500 ppm   | 0      | 0          | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0    |
|                   | 5000 ppm   | 0      | 0          | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0    | 0<br>0 | 0      | 0<br>0 | 0    |
|                   | 10000 ppm  | 0      | 0          | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0    | õ      | 0      | Ö      | 0    |
| USTA              | Control    | 0      | 0          | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0    |
|                   | 2500 ppm   | 0      | 0          | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0      | Ō      | 0    |
|                   | 5000 ppm   | 0      | 0          | 0      | 0   | 0      | 0      | Õ      | õ      | 0<br>0 | õ    | ů      | Õ      | 0      | Ő    |
|                   | 10000 ppm  | 0      | 0          | 0      | Ő   | Õ      | 0<br>0 | 0<br>0 | õ      | Ő      | õ    | . 0    | 0      | 0      | 0    |
| ELLING            | Control    | 0      | 0          | 0      | 0   | 0      | 0      | 0      | Ó      | 0      | 0    | 0      | 0      | 0      | 0    |
|                   | 2500 ppm   | 0      | 0          | 0      | 0   | 0      | 0      | 0      | 0      | 0      | Ō    | Ő      | Õ      | Õ      | Ő    |
|                   | 5000 ppm   | 0      | 0          | 0      | Õ   | Ő      | õ      | Õ      | õ      | 0      | ů    | ů      | Ő      | 0      | ŏ    |
|                   | 10000 ppm  | 0      | õ          | 0      | Õ   | ů<br>0 | 0      | 0      | 0 O    | 0      | õ    | 0<br>0 | Ŏ      | 0      | 0    |
| RTICOLLIS         | Control    | 0      | 0          | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0    |
| •                 | 2500 ppm   | 0      | 0          | 0      | 0   | 0      | 0      | Õ      | 0<br>0 | 0      | ů    | 0      | ů      | Õ      | ŏ    |
|                   | 5000 ppm   | ů<br>0 | 0          | 0      | õ   | ů      | õ      | 0<br>0 | 0      | 0      | 0    | 0      | 0<br>0 | 0      | 0    |
|                   | 10000 ppm  | 0      | Õ          | 0      | Ő   | Ő      | 0      | 0      | ő      | Ő      | õ    | 0      | Ő      | Ő      | 0    |
| REGULAR BREATHING | Control    | 0      | 0          | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0    |
|                   | 2500 ppm   | 0      | 0          | 0<br>0 | Õ   | ů      | õ      | Õ      | ů      | Õ      | ů    | 0      | õ      | 0      | õ    |
|                   | 5000 ppm   | ů      | ů ů        | Ő      | 0   | 0      | Õ      | 0      | 0      | 0      | 0    | 0      | 0      | 0      | 0    |
|                   | 10000 ppm  | 0      | 0          | 0      | 0   | 0      | 0      | 0      | 0      | 0      | 0    | 0      |        |        |      |
|                   | 10000 ppm  | v      | v          | 0      | U   | U      | U      | v      | 0      | U      | U    | U      | 0      | 0      | 0    |

.

(HAN190)

.

### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

### SEX : FEMALE

| Clinical sign       | Group Name          | Admin | istration W | eek-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. TAIL             | Control             | 0     | 0           | 0       | 0    | 0      | 0        | 0        | 0    |        |        | 0      | <u>,</u> | 0        | 0                                     |
| M. IAIL             | Control<br>2500 ppm | 0     | 0<br>0      | 0       | 0    | 0      | 0        | 0        | 0    | 0      | 0      | 0      | 0        | 0        | 0                                     |
|                     |                     | 0     |             | 0       | 0    | 0      | 0        | 0        | 0    | 0      | 0      | . 0    | 0        | 0        | 0                                     |
|                     | 5000 ppm            | 0     | 0           | 0       | 0    | 0      | 0        | 0        | 0    | 0      | 0      | 0      | 0        | 0        | 0                                     |
|                     | 10000 ppm           | U     | 0           | 0       | 0    | 0      | 0        | 0        | 0    | 0      | 0      | 0      | 0        | 0        | 0                                     |
| EDEMA               | Control             | 0     | 0           | 0       | 0    | 0      | 0        | 0        | 0    | 0      | 0      | 0      | 0        | 0        | 0                                     |
|                     | 2500 ppm            | 0     | 0           | 0       | 0    | 0      | 0        | 0        | 0    | 0      | 0      | 0      | 0        | 0        | 0                                     |
|                     | 5000 ppm            | 0     | 0           | 0       | 0    | 0      | 0        | 0        | 0    | 0      | 0      | 0      | 0        | 0        | 0                                     |
|                     | 10000 ppm           | 0     | 0           | 0       | 0    | 0      | 0        | 0        | 0    | 0      | 0      | 0      | 0        | 0        | 0                                     |
| ANEMIA              | Control             | 0     | 0           | 0       | 0    | 0      | 0        | 0        | 0    | 0      | 0      | 0      | 0        | 0        | 0                                     |
|                     | 2500 ppm            | 0     | 0           | 0       | 0    | 0      | Õ        | 0        | Ő    | 0<br>0 | 0      | Ő      | 0        | 0        | 0                                     |
|                     | 5000 ppm            | ů     | 0           | 0       | 0    | 0      | Ö        | 0        | 0    | 0      | 0      | 0      | 0        | 0        | 0                                     |
|                     | 10000 ppm           | 0     | 0           | 0       | ő    | Ő      | 0        | 0        | 0    | 0      | 0      | 0      | . 0      | Ő        | 0                                     |
| ULCER               | Control             | 0     | 0           | 0       | 0    | 0      | 0        | 0        | 0    | 0      | 0      | 0      | 0        |          | 0                                     |
| JECER               | 2500 ppm            | 0     | 0           | 0       | 0    |        | 0        | 0        | 0    | 0      | 0      | 0      | 0        | 0        | 0                                     |
|                     | 2000 ppm            | 0     | 0           | 0<br>Ò  | 0    | 0      | 0        | 0        | 0    | 0      | 0      | 0      | 0        | 0        | 0                                     |
|                     | 10000 ppm           | 0     | 0           | 0       | 0    | 0<br>0 | 0<br>0   | 0<br>0   | 0    | 0      | 0<br>0 | 0      | 0        | · 0<br>0 | 0                                     |
|                     | recee ppm           | Ŷ     | Ū           | Ŷ       | Ū    | v      | v        | v        | U    | 0      | U      | v      | v        | Ū        | 0                                     |
| EROSION             | Control             | 0     | 0           | 0       | 0    | 0      | 0        | 0        | 0    | 0      | 0      | 0      | 0        | 0        | 0                                     |
|                     | 2500 րթա            | 0     | 0           | 0       | 0    | 0      | 0        | 0        | 0    | 0      | 0      | 0      | 0        | 0        | 0                                     |
|                     | 5000 ppm            | 0     | 0           | 0       | 0    | 0      | 0        | 0        | 0    | 0      | 0      | 0      | 0        | 0        | 0                                     |
|                     | 10000 ppm           | 0     | 0           | 0       | 0    | 0      | 0        | 0        | 0    | 0      | 0      | 0      | 0        | 0        | 0                                     |
| CRUSTA              | Control             | 0     | 0           | 0       | 0    | 0      | 0        | 0        | 0    | 0      | 0      | 0      | 0        | 0        | 0                                     |
|                     | 2500 ppm            | 0     | 0           | 0       | 0    | 0      | 0        | 0        | 0    | 0      | 0      | 0<br>0 | 0        | Õ        | 0                                     |
|                     | 5000 ppm            | 0     | 0           | 0       | 0    | 0      | 0        | 0        | 0    | 0      | 0      | 0<br>0 | 0<br>0   | Õ        | õ                                     |
|                     | 10000 ppm           | 0     | 0           | 0       | 0    | 0      | 0        | 0        | 0    | 0      | 0      | 0      | 0        | Õ        | õ                                     |
| SWELLING            | Control             | 0     | 0           | 0       | 0    | 0      | 0        | 0        | 0    | 0      | 0      | 0      | 0        | 0        | 0                                     |
|                     | 2500 ppm            | Ő     | 0           | 0       | 0    | 0      | 0        | 0<br>0   | 0    | 0      | 0      | 0      | 0        | 0        | 0                                     |
|                     | 5000 ppm            | 0     | 0           | 0       | 0    | 0      | 0        | 0        | 0    | 0      | 0      | 0      | 0        | 0        | 0                                     |
|                     | 10000 ppm           | ů     | 0           | õ       | · Õ  | õ      | Ő        | 0        | 0    | 0      | 0      | 0      | 0        | 0        | 0                                     |
| TORTICOLLIS         | Control             | 0     | 0           | 0       | ^    | 0      | <u>^</u> | <u>^</u> | ^    | ^      | ~      |        | -        |          | a a a a a a a a a a a a a a a a a a a |
| TOWTTOOPPTS         | Control             | 0     | 0           | 0       | 0    | 0      | 0        | 0        | 0    | 0      | 0      | 0      | 0        | 0        | 0                                     |
|                     | 2500 ppm            | -     | 0           | 0       | 0    | 0      | 0        | 0        | 0    | 0      | 0      | 0      | 0        | 0        | 0                                     |
|                     | 5000 ppm            | 0     | 0           | 0       | 0    | 0      | 0        | 0        | 0    | 0      | 0      | 0      | 0        | 0        | 0                                     |
|                     | 10000 ppm           | 0     | 0           | 0       | 0    | 0      | 0        | 0        | 0    | 0      | 0      | 0      | 0        | 0        | 0                                     |
| IRREGULAR BREATHING | Control             | 0     | 0           | 0       | 0    | 0      | 0        | 0        | 0    | 0      | 0      | 0      | 0        | 0        | 0                                     |
|                     | 2500 ppm            | 0     | 0           | 0       | 0    | 0      | 0        | 0        | 0    | 0      | 0      | 0      | 0        | 0        | 0                                     |
|                     | 5000 ppm            | 0     | 0           | 0       | 0    | 0      | 0        | 0        | 0    | 0      | 0      | 0      | 0        | 0        | 0                                     |
|                     | 10000 ppm           | 0     | 0           | 0       | 0    | 0      | 0        | 0        | 0    | 1      | 1      | 1      | 1        | 0        | 0                                     |

PAGE : 58

(HAN190)

### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : FEMALE

| Clinical sign     | Group Name | Admini | istration W | eek-dav |      |      |      |        |      |      |        |        |        |      |      |
|-------------------|------------|--------|-------------|---------|------|------|------|--------|------|------|--------|--------|--------|------|------|
|                   |            | 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 |
|                   |            |        |             |         |      |      |      |        |      |      |        |        |        |      |      |
| TAIL              | Control    | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                   | 2500 ppm   | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                   | 5000 ppm   | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                   | 10000 ppm  | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
| ЕМА               | Control    | 0      | 0           | 0       | 0    | 0    | 0    | 0      | . 0  | 0    | 0      | 0      | 0      | 0    | 0    |
|                   | 2500 ppm   | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                   | 5000 ppm   | 0      | . 0         | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                   | 10000 ppm  | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
| EMIA              | Control    | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                   | 2500 ppm   | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                   | 5000 ppm   | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                   | 10000 ppm  | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
| CER               | Control    | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                   | 2500 ppm   | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                   | 5000 ppm   | 0      | 0           | 0       | 0    | 0    | · 0  | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                   | 10000 ppm  | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
| OSION             | Control    | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                   | 2500 ppm   | 0      | 0           | . 0     | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | · 0  | 0    |
|                   | 5000 ррт   | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                   | 10000 ppm  | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
| USTA              | Control    | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                   | 2500 ppm   | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                   | 5000 ppm   | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                   | 10000 ppm  | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
| ELLING            | Control    | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                   | 2500 ppm   | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                   | 5000 ppm   | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | ů<br>0 | õ    | õ    |
|                   | 10000 ppm  | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0    | ů<br>0 | ů<br>0 | ů      | õ    | Ő    |
| RTICOLLIS         | Contro1    | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                   | 2500 ppm   | 0      | 0           | 0       | 0    | 0    | 0    | õ      | 0    | Ő    | õ      | ů      | ů      | ů .  | Ő    |
|                   | 5000 ppm   | 0      | 0           | 0       | õ    | Ő    | ů    | ŏ      | ů    | Ő    | 0      | Ő      | 0      | 0    | 0    |
|                   | 10000 ppm  | 0      | 0           | 0       | õ    | ů    | 0    | 0      | 0    | Ő    | Ő      | Ő      | 0      | 0    | 0    |
| REGULAR BREATHING | Control    | 0      | 0           | 0       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                   | 2500 ppm   | 0      | Ő           | 0       | 0    | Ū.   | õ    | ů      | 0    | 0    | 0<br>0 | õ      | ŏ      | Ő    | 0    |
|                   | 5000 ppm   | ŏ      | ů           | 0       | 0    | 0    | õ    | 0<br>0 | 0    | 0    | 0      | 0      | 0      | 0    | 0    |
|                   | 10000 ppm  | ŏ      | 0           | Ő       | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    | 0    |

### : FEMALE

### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : FEMALE

| Clinical sign     | Group Name | Admini | stration W | eek-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 |
|                   |            |        |            |         |      |      |      |      |        |      |      |        |        |        |      |
| TAIL              | Control    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    |
|                   | 2500 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    |
|                   | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    |
|                   | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0      | 0    | 0    | · 0    | 0      | 0      | 0    |
| EMA               | Control -  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    |
|                   | 2500 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    |
|                   | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    |
|                   | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    |
| EMIA              | Control    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    |
|                   | 2500 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    |
|                   | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    |
|                   | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    |
| CER               | Control    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    |
|                   | 2500 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 1      | 1      | 1    |
|                   | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    |
|                   | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    |
| OSION             | Control    | 0      | 0          | 0       | 0    | 0.0  | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    |
|                   | 2500 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    |
|                   | 5000 թթա   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    |
|                   | 10000 թթա  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    |
| RUSTA             | Control    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    |
|                   | 2500 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    |
|                   | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    |
|                   | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    |
| ELLING            | Control    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    |
|                   | 2500 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    |
|                   | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | Ő    |
| **                | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | 0      | 0    |
| RTICOLLIS         | Control    | 1      | 1          | · 1     | 1    | 1    | 1    | 1    | 1      | 1    | 2    | 2      | 2      | 2      | 2    |
|                   | 2500 ppm   | 0      | 0          | 0       | 0    | 0    | 1    | 1    | 1      | 1    | 1    | 1      | 1      | 0      | 0    |
|                   | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 1    | l    | 1      | 1    | 1    | 1      | ĩ      | 1      | ĩ    |
|                   | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0      | 0    | 0    | 0      | 0      | õ      | Ō    |
| REGULAR BREATHING | Control    | 1      | 1          | 1       | 1    | 1    | 1    | 1    | 1      | 1    | 1    | 1      | 1      | 1      | 1    |
|                   | 2500 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0      | 0    | Ō    | 0      | 0      | 0      | ō    |
|                   | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0<br>0 | ů.   | Ő    | 0<br>0 | ů<br>0 | ů<br>0 | Ő    |
|                   | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0      | 0    | õ    | Õ      | 0<br>0 | 0<br>0 | õ    |

### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

### SEX : FEMALE

PAGE : 61

| Clinical sign     | Group Name | Admini | stration W | eek-dav |        |        |        |      |        |      |      |        |      |      |        |
|-------------------|------------|--------|------------|---------|--------|--------|--------|------|--------|------|------|--------|------|------|--------|
| -                 | -          | 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   |
| . TAIL            | Control    | 0      | 0          | 0       | 0      | 0      | 0      | 0    | ٥      | 0    | 0    | 0      | 0    | 0    | 0      |
| I. IALL           | 2500 ppm   | 0      | 0          | 0       | 0<br>0 | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0      |
|                   |            |        |            |         |        | . 0    | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0      |
|                   | 5000 ppm   | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0      |
|                   | 10000 ppm  | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0      |
| DEMA              | Control    | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0      |
|                   | 2500 ppm   | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0      |
|                   | 5000 ppm   | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0      |
|                   | 10000 ppm  | 0      | 0          | 0       | 0      | 0      | 0      | 1    | 0      | 0    | 0    | 0      | 0    | 0    | 0      |
| NEMIA             | Control    | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0      |
|                   | 2500 ppm   | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0      |
|                   | 5000 ppm   | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | Ő      |
|                   | 10000 ppm  | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0      |
| LCER              | Control    | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0      |
|                   | 2500 ppm   | 1      | 1          | 1       | 1      | 1      | 0      | Ō    | Õ      | õ    | 0    | Õ      | Ő    | Ő    | Ő      |
|                   | 5000 ppm   | 0      | Ō          | 0       | Ô      | 0      | 0      | ů    | • 0    | ŏ    | 0    | 0<br>0 | 0    | 0    | ů<br>0 |
|                   | 10000 ppm  | 0      | 0          | 0       | 0      | 0      | ů<br>0 | 0    | ů<br>0 | ů    | ů    | ů<br>0 | 0    | 0    | 0      |
| ROSION            | Control    | 0      | 0          | 0       | 0      | 0      | 0      | 1    | 1      | 1    | 1    | 1      | 1    | 1    | 1      |
|                   | 2500 ppm   | ů      | Õ          | 0<br>0  | õ      | õ      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0      |
|                   | 5000 ppm   | ů      | Õ          | 0<br>0  | ů      | ů      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0      |
|                   | 10000 ppm  | Ő      | 0<br>0     | 0       | õ      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0      |
|                   | 10000 ppm  | v      | 0          | v       | U      | U      | U      | U    | U      | U    | U    | U      | U    | 0    | 0      |
| RUSTA             | Control    | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0      |
|                   | 2500 ppm   | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0      |
|                   | 5000 ppm   | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0      |
|                   | 10000 ppm  | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0      |
| WELLING           | Control    | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0      |
|                   | 2500 ppm   | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | . 0  | 0    | 0      |
|                   | 5000 ppm   | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | . 0  | 0    | 0      |
|                   | 10000 ppm  | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0      |
| RTICOLLIS         | Control    | 2      | 2          | 2       | 2      | 2      | 2      | 2    | 2      | 1    | 1    | 1      | 1    | 1    | 1      |
|                   | 2500 ppm   | 0      | 0          | 0       | ō      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0      |
|                   | 5000 ppm   | ĩ      | ĩ          | Î       | ĩ      | 1      | 1      | 1    | 1      | 1    | 1    | 1      | 1    | 1    | 1      |
|                   | 10000 ppm  | 0      | 0          | Ô       | 0      | 0      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0      |
| REGULAR BREATHING | Control    | 2      | 2          | 2       | 2      | 2      | 2      | 2    | 2      | 1    | 1    | 1      | 1    | 1    | 1      |
| Sector Pharman    | 2500 ppm   | 0      | 0          | 0       | 0      | 0      | 0      | 0    | 0      | 0    | 0    | -      | -    | 1    |        |
|                   | 5000 ppm   | 0      | 0          | 0       | 0      |        | 0      |      |        |      |      | 0      | 0    | 0    | 0      |
|                   | 10000 ppm  | 0      | 0          | 0       | 0      | 0<br>0 |        | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0      |
|                   | 10000 hbm  | U      | U          | U       | U      | U      | 0      | 0    | 0      | 0    | 0    | 0      | 0    | 0    | 0      |

### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

~~~~

### SEX : FEMALE

|                    |            |        |            |         |      |      |        |        |      |        |      |      |      |        | THOL . 0 |
|--------------------|------------|--------|------------|---------|------|------|--------|--------|------|--------|------|------|------|--------|----------|
| Clinical sign      | Group Name | Admini | stration W | eek-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     |
|                    |            |        |            |         |      |      |        |        |      |        |      |      |      |        |          |
| . TAIL             | Control    | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0    | 0    | 0    | 0      | 0        |
|                    | 2500 ppm   | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0    | 0    | 0    | 0      | 0        |
|                    | 5000 ррт   | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0    | 0    | 0    | 0      | 0        |
|                    | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0    | 0    | 0    | 0      | 0        |
| DEMA               | Control    | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0    | 0    | 0    | 0      | 0        |
|                    | 2500 ррт   | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0    | 0    | 0    | 0      | 0        |
|                    | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0    | 0    | 0    | 0      | 0        |
|                    | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0    | 0    | 0    | 0      | 1        |
| NEMIA              | Control    | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0    | 0    | 0    | 0      | 0        |
|                    | 2500 ppm   | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0    | 0    | 0    | 0      | 0        |
|                    | 5000 ppm   | 0      | 0          | 0       | · 0  | 0    | 0      | 0      | 0    | 0      | 0    | 0    | 0    | 0      | 0        |
|                    | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0    | 0    | 0    | 0      | 0        |
| ILCER              | Control    | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0    | 0    | 0    | 0      | 0        |
|                    | 2500 ppm   | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0    | 0    | 0    | 0      | 0        |
|                    | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0 .  | . 0    | 0    | 0    | 0    | 0      | 0        |
|                    | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0    | 0    | 0    | 0      | 0        |
| ROSION             | Control    | 1      | 1          | 1       | 1    | 1    | 1      | 1      | 0    | 0      | 0    | 1    | 1    | 1      | 1        |
|                    | 2500 ppm   | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0    | 0    | 0    | 0      | 0        |
|                    | 5000 րրտ   | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0    | 0    | 0    | 0      | 0        |
|                    | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0    | 1    | 1    | 1      | 1        |
| RUSTA              | Control    | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0    | 0    | 0    | 0      | 0        |
|                    | 2500 ppm   | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0    | 0    | 0    | 1      | 0        |
|                    | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0    | 0    | 0    | 0      | 0        |
|                    | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0    | 0    | 0    | 0      | 0        |
| WELLING            | Control    | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0.   | 0    | 0    | 0      | 0        |
|                    | 2500 ppm   | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0    | 0    | 0    | 0      | 0        |
|                    | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0    | 0    | 0    | 0      | 0        |
|                    | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | 0    | 0    | 0    | 0      | 0        |
| ORTICOLLIS         | Control    | 1      | 1          | 1       | 1    | 1    | 1      | 1      | 0    | 0      | 0    | 0    | 0    | 0      | 0        |
|                    | 2500 ppm   | 0      | 0          | 0       | 0    | 0    | 0      | 0      | 0    | 0      | õ    | 0    | Ő    | 0<br>0 | Ő        |
|                    | 5000 ppm   | 1      | 1          | 0       | 0    | 0    | 0      | 0      | 0    | Ō      | õ    | Õ    | ů    | 0      | ů<br>0   |
|                    | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0      | 1      | 1    | 0      | 0    | 0    | 0    | 0      | 0        |
| RREGULAR BREATHING | Control    | 1      | 1          | 1       | 1    | 1    | 1      | 1      | 0    | 0      | 0    | 0    | 0    | 0      | 0        |
|                    | 2500 ppm   | 0      | 0          | Ō       | 0    | Ō    | Ō      | 0      | Ő    | õ      | Õ    | 1    | 1    | 1      | 0        |
|                    | 5000 ppm   | 0      | 0          | 0       | Ō    | Õ    | 0      | 0<br>0 | ů    | 0      | 0    | Ô    | 0    | 0      | õ        |
|                    | 10000 ppm  | 0      | 0          | 0       | 0    | Õ    | ů<br>0 | Ő      | õ    | ů<br>0 | 1    | 1    | õ    | 0      | ŏ        |

(HAN190)

### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

~\_\_\_\_

### SEX : FEMALE

PAGE : 63

~~

| Clinical sign  | Group Name           | Admini | istration W                              | eek-dav |        |      |        |      |        |        |        |      |        |        |        |
|--|----------------------|--------|--|---------|--------|------|--------|------|--------|--------|--------|------|--------|--------|--------|
|  |                      | 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   |
|  |                      |        | 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1 |         |        |      |        |      |        |        |        |      |        |        |        |
| I. TAIL  | Control              | 0      | 0  | 0       | 0      | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      |
|  | 2500 ppm             | 1      | - 1                                      | 1       | 1      | 1    | 1      | 1    | 1      | 1      | 1      | 1    | 1      | 1      | 1      |
|  | 5000 ppm             | 0      | 0  | 0       | 0      | ō    | 0      | Ō    | ō      | Ō      | 0      | 0    | 0      | õ      | Ô      |
|  | 10000 ppm            | 0      | 0  | 0       | 0      | Ō    | 0<br>0 | Ő    | 0      | ů      | 0<br>0 | Ő    | õ      | 0      | Ő      |
| DEMA   | Control              | 0      | 0  | 0       | 0      | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      |
|  | 2500 ppm             | ů<br>0 | 0  | 0       | 0<br>0 | 0    | Ő      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      |
|  | 5000 ppm             | 0      | 0  | 0       | 0      | 0    | 0      | 0    | 0      | 0      | 0      | -    | 0      | 0      |        |
|  |                      | 0      | 0  | 0       |        |      |        |      |        |        |        | 0    |        | -      | 0      |
|  | 10000 ppm            | U      | 0  | 0       | 0      | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      |
| <b>VEMIA</b>   | Control              | 0      | 0  | 0       | 0      | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      |
|  | 2500 ppm             | 0      | 0  | 0       | 0      | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      |
|  | 5000 ppm             | 0      | 0  | 0       | 0      | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      |
|  | 10000 ppm            | 0      | 1  | 0       | 0      | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      |
| CER  | Control              | 0      | 0  | 0       | 0      | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      |
|  | 2500 ppm             | 0      | 0  | 0       | 0      | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | Ő      |
|  | 5000 ppm             | 0      | 0  | 0       | 0      | õ    | 0      | ŏ    | 0      | õ      | õ      | õ    | Õ      | 0<br>0 | ů<br>0 |
|  | 10000 ppm            | 0      | ů  | 0       | Ő      | Ő    | ů      | Õ    | 0      | 0      | 0      | 0    | 0      | · 0    | 0      |
| ROSION   | Control              | 1      | 1  | 1       | 0      | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      |
|  | 2500 ppm             | õ      | 0  | 0       | Ő      | Ő    | ů<br>0 | ů    | 0<br>0 | 0      | 0      | Ő    | 0<br>0 | 0      | Ő      |
|  | 5000 ppm             | ů      | 0  | 0       | 0      | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      |        |
|  | 10000 ppm            | 0      | 0  | 0       | 0      | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0<br>0 |
|  | roooo ppm            | v      | U  | 0       | 0      | U    | U      | U    | U      | U      | U      | U    | U      | 0      | 0      |
| RUSTA.   | Control              | 0      | 0  | 0       | 0      | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      |
| 4 .  | 2500 ppm             | 0      | 0  | 0       | . 0    | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      |
|  | 5000 ppm             | 0 .    | 0  | 0       | 0      | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      |
|  | 10000 ppm            | 0      | 0  | 0       | . 0    | .0   | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      |
| ELLING   | Control              | 0      | 0  | 0       | 0      | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      |
|  | 2500 ppm             | 0      | 0  | 0       | 0      | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      |
|  | 5000 ppm             | 0      | 0  | 0       | 1      | 1    | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      |
|  | 10000 ppm            | 0      | 0  | 0       | 0      | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      |
| RTICOLLIS  | Control              | 0      | 0  | 0       | 0      | 0    | 0      | 0    | 0      | 0      | 0      | 0    | 0      | 0      | 0      |
|  | 2500 ppm             | 0      | 0  | 0       | 0      | õ    | 0      | 0    | 0      | ů      | 0      | 0    | 0      | 0      | 0      |
|  | 5000 ppm             | ů      | 0  | 0       | ů<br>0 | Ő    | 0      | 0    | 1      | 1      | 1      | 1    | 1      | 1      | 1      |
|  | 10000 ppm            | õ      | 0  | 0       | õ      | 0    | 0      | 0    | 0      | 1<br>0 | 0      | 0    | 1<br>0 | 0      | 0      |
| REGULAR BREATHING  | Control              | 0      | 0  | 0       | 0      | 0    | 0      | 0    | 1      | 0      | 0      | 1    | 1      | 0      | 0      |
| and the second s | 2500 ppm             | 0      | 0  | 0       | 0      | 0    | 0      |      |        |        |        | 1    | 1      |        | 0      |
|  | 2300 ppm<br>5000 ppm | -      | •  |         |        |      |        | 0    | 1      | 1      | 1      | 0    | 0      | 0      | 0      |
|  |                      | 0      | 0  | 0       | 0      | 1    | 0      | 1    | 0      | 0      | 0      | 0    | 0      | 0      | 0      |
|  | 10000 ppm            | 1      | 2  | 0       | . 0    | 0    | 0      | 0 .  | 1      | 1      | 0      | 0    | 0      | 0      | 1      |

### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

### SEX : FEMALE

| Clinical sign      | Group Name | Admin | istration W | eek-day _ |        |       |       | <br> |  | <br> |       |
|--------------------|------------|-------|-------------|-----------|--------|-------|-------|------|--|------|-------|
|                    |            | 99-7  | 100-7       | 101-7     | 102-7  | 103-7 | 104-7 |      |  |      |       |
|                    |            |       | •           |           |        |       |       | <br> |  | <br> | · · · |
| m / 21             |            | -     |             | ·         | _      | _     |       |      |  |      |       |
| TAIL               | Control    | 0     | 0           | 0         | 0      | 0     | 0     |      |  |      |       |
|                    | 2500 ppm   | 1     | 1           | 1         | 1      | 1     | 1     |      |  |      |       |
|                    | 5000 ppm   | 0     | 0           | 0         | 0      | 0     | 0     |      |  |      |       |
|                    | 10000 ppm  | 0     | 0           | 0         | 0      | 0     | 0     |      |  |      |       |
| EMA                | Control    | 0     | 0           | 0         | 0      | 0     | 0     |      |  |      |       |
|                    | 2500 ppm   | 0     | 0           | 0         | 0      | 0     | 0     |      |  |      |       |
|                    | 5000 ppm   | 0     | 0           | 0         | 0      | 0     | 0     |      |  |      |       |
|                    | 10000 ppm  | 2     | 1           | 1         | 1      | 0     | 0     |      |  |      |       |
| NEMIA              | Control    | 0     | 0           | 0         | 0      | 0     | 0     |      |  |      |       |
|                    | 2500 ppm   | 0     | 0           | Ö         | 0      | 0     | 0     |      |  |      |       |
|                    | 5000 ppm   | 0     | 0           | 0         | 0      | 0     | 0     |      |  |      |       |
|                    | 10000 ppm  | 0     | 0           | 0         | 0      | 0     | 0     |      |  |      |       |
| I OPP              |            |       | -           |           |        |       |       |      |  |      |       |
| LCER               | Control    | 0     | 0           | 0         | 0      | 0     | 0     |      |  |      |       |
|                    | 2500 ppm   | 0     | 0           | 0         | 0      | 0     | 0     |      |  |      |       |
|                    | 5000 ppm   | 0     | 0           | 0         | 0      | 0     | 0     |      |  |      |       |
|                    | 10000 ppm  | 0     | 0           | 0         | 0      | 0     | 0     |      |  |      |       |
| ROSION             | Control    | 0     | 0           | 0         | 0      | 0     | 0     |      |  |      |       |
|                    | 2500 ppm   | 0     | 0           | 0         | 0      | 0     | 0     |      |  |      |       |
|                    | 5000 թթա   | 0     | 0           | 0         | 0      | 0     | 0     |      |  |      |       |
|                    | 10000 ppm  | 0     | 0           | 0         | 0      | 0     | 0     |      |  |      |       |
| RUSTA              | Control    | 0     | 0           | 0         | 0      | 0     | 0     |      |  |      |       |
|                    | 2500 ppm   | 0     | 0           | 0         | 0      | 0     | 0     |      |  |      |       |
|                    | 5000 ppm   | 0     | 0           | 0         | 0      | 0     | 0     |      |  |      |       |
|                    | 10000 ppm  | 0     | 0           | 0         | 0      | 0     | 0     |      |  |      |       |
| WELL THO           | 0 1        | •     | <u>^</u>    |           |        |       |       |      |  |      |       |
| WELLING            | Control    | 0     | 0           | 0         | 0      | 0     | 0     |      |  |      |       |
|                    | 2500 ppm   | 0     | 0           | 0         | 0      | 0     | 0     |      |  |      |       |
|                    | 5000 ppm   | 0     | 0           | 0         | 0      | 0     | 0     |      |  |      |       |
|                    | 10000 ppm  | 0     | 0           | 0         | 0      | 0     | 0     |      |  |      |       |
| ORTICOLLIS         | Control    | 0     | 0           | 0         | 0      | 0     | 0     |      |  |      |       |
|                    | 2500 ppm   | 0     | 0           | 0         | 0      | 0     | 0     |      |  |      |       |
|                    | 5000 ppm   | 1     | L           | 1         | 1      | 1     | 1     |      |  |      |       |
|                    | 10000 ppm  | 0     | 0           | 0         | 0      | 0     | 0     |      |  |      |       |
| RREGULAR BREATHING | Control    | 0     | 0           | 0         | 0      | 0     | 0     |      |  |      |       |
|                    | 2500 ppm   | 0     | 3           | 2         | 3      | 2     | - 3   |      |  |      |       |
|                    | 5000 ppm   | 0     |             | 0         | о<br>0 | 0     |       |      |  |      |       |
|                    |            |       | 2           |           |        |       | 0     |      |  |      |       |
|                    | 10000 ppm  | 2     | 1           | 0         | 1      | 2     | · 1   |      |  |      |       |

### CLINICAL OBSERVATION (SUMMARY)

 $\sim \sim$ 

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 104

### SEX : FEMALE

| 0011110110 | obobit militon, | (Dought Hitt) |  |
|------------|-----------------|---------------|--|
| ALL ANIM/  | ALS             |               |  |
|            |                 |               |  |
|            |                 |               |  |

| Clinical sign  | Group Name | Admini | stration W | eek-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 |
|                |            |        |            |         |     |     |     |     |     |     |      |      |      |      |      |
| DEEP BREATHING | Control    | 0      | 0          | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                | 2500 ppm   | 0      | 0          | 0       | 0 . | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                | 5000 ppm   | 0      | 0          | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                | 10000 ppm  | 0      | 0          | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| MALL STOOL     | Control    | 0      | 0          | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                | 2500 ppm   | 0      | 0          | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                | 5000 ppm   | 0      | 0          | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | . 0  |
|                | 10000 ppm  | 0      | 0          | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| LIGO-STOOL     | Control    | 0      | 0          | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                | 2500 ppm   | 1      | 0          | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                | 5000 ppm   | 0      | 0          | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
|                | 10000 ppm  | 0      | 0          | 0       | 0   | 0   | 0   | 0   | 0   | 0   | 0    | 0    | 0    | 0    | 0    |
| ION REMARKABLE | Control    | 50     | 50         | 50      | 50  | 50  | 50  | 50  | 50  | 50  | 50   | 50   | 50   | 50   | 50   |
|                | 2500 ppm   | 49     | 50         | 50      | 50  | 50  | 50  | 50  | 50  | 50  | 50   | 50   | 50   | 50   | 50   |
|                | 5000 ppm   | 50     | 50         | 50      | 50  | 50  | 50  | 50  | 50  | 50  | 50   | 50   | 50   | 50   | 50   |
|                | 10000 ppm  | 50     | 50         | 50      | 50  | 50  | 50  | 50  | 50  | 50  | 50   | 50   | 50   | 50   | 50   |

(HAN190)

BAIS 4

### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

### SEX : FEMALE

PAGE : 66

-----

| inical sign    | Group Name                            | Admini | stration W | leek-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 |
|                | · · · · · · · · · · · · · · · · · · · |        |            | -        |      |      |      |      |      |      |      |      |      |      |      |
| DEEP BREATHING | Control                               | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 2500 ppm                              | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 5000 ppm                              | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 10000 ppm                             | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| MALL STOOL     | Control                               | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 2500 ppm                              | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 5000 ppm                              | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 10000 ppm                             | 0      | 0          | 0        | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LIGO-STOOL     | Control                               | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 2500 ppm                              | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 5000 ppm                              | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 10000 ppm                             | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ION REMARKABLE | Control                               | 50     | 50         | 50       | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 49   | 50   | 50   |
|                | 2500 ppm                              | 49     | 49         | 49       | 49   | 49   | 49   | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 50   |
|                | 5000 ppm                              | 50     | 50         | 50       | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 50   |
|                | 10000 ppm                             | 50     | 50         | 49       | 49   | 49   | 49   | 49   | 49   | 49   | 49   | 49   | 49   | 49   | 49   |

(HAN190)

### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

.

### SEX : FEMALE

| PAGE |  |
|------|--|
|      |  |

~\_~

| Clinical sign  | Group Name | Admini | stration W | /eek-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 |
|                |            |        |            |            |      |      |      |      |      |      |      |      |      |      |      |
| DEEP BREATHING | Control    | 0      | 0          | 0          | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 2500 ppm   | 0      | 0          | 0          | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 5000 ppm   | 0      | 0          | 0          | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 10000 ppm  | 0      | 0          | 0          | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SMALL STOOL    | Contro1    | 0      | 0          | 0          | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 2500 ppm   | 0      | 0          | 0          | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 5000 ppm   | 0      | 0          | 0          | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 10000 ppm  | 0      | 0          | 0          | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| DLIGO-STOOL    | Control    | 0      | 0          | 0          | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 0    |
|                | 2500 ppm   | 0      | 0          | 0          | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 5000 ppm   | 0      | 0          | 0          | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 10000 ppm  | 0      | 0          | 0          | 0    | 0    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| NON REMARKABLE | Control    | 50     | 50         | 50         | 49   | 49   | 49   | 49   | 49   | 49   | 49   | 49   | 48   | 48   | 49   |
|                | 2500 ppm   | 50     | 50         | 50         | 50   | 50   | 49   | 49   | 49   | 49   | 49   | 49   | 49   | 49   | 49   |
|                | 5000 ppm   | 50     | 50         | 50         | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 50   | 50   |
|                | 10000 ppm  | 49     | 49         | 49         | 49   | 49   | 48   | 48   | 49   | 49   | 49   | 49   | 49   | 49   | 49   |

(HAN190)

### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

### SEX : FEMALE

| GE | 68 |
|----|----|
|    |    |
|    |    |

| Clinical sign  | Group Name | Admini | stration W | leek-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 |
|                |            |        |            |          |      |      |      |      |      |      |      |      |      |      |      |
| DEEP BREATHING | Control    | 0      | . 0        | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 2500 ppm   | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 5000 ppm   | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 10000 ppm  | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| MALL STOOL     | Control    | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 2500 ppm   | 0      | 0          | 0        | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 5000 ppm   | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 10000 ppm  | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| LIGO-STOOL     | Control    | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    |
|                | 2500 ppm   | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    | 0    | 0    | 0    |
|                | 5000 ppm   | 0      | 0          | 0        | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | i    |
|                | 10000 ppm  | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ON REMARKABLE  | Control    | 49     | 49         | 49       | 49   | 49   | 49   | 49   | 49   | 49   | 48   | 48   | 48   | 48   | 47   |
|                | 2500 ppm   | 49     | 48         | 48       | 47   | 47   | 47   | 47   | 46   | 46   | 46   | 46   | 45   | 45   | 45   |
|                | 5000 ppm   | 50     | 50         | 50       | 50   | 50   | 48   | 48   | 48   | 47   | 47   | 47   | 47   | 47   | 47   |
|                | 10000 ppm  | 49     | 49         | 49       | 49   | 49   | 49   | 49   | 49   | 49   | 49   | 49   | 49   | 49   | 49   |

(HAN190)

### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

~

SEX : FEMALE

| PAGE | 69 |
|------|----|
|      |    |

| Clinical sign  | Group Name | Admini | stration W | eek-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 |
|                |            |        |            |         |      |      |      |      |      |      |      |      |      |      |      |
| DEEP BREATHING | Control    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 2500 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SMALL STOOL    | Control    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 2500 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    |
|                | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | - 0  | 0    | 0    | 0    | 0    |
|                | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| DLIGO-STOOL    | Control    | 1      | 1          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    |
|                | 2500 ppm   | 0      | 0          | 0       | 0    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 1    | 0    | 0    |
|                | 5000 ppm   | 1      | 1          | 1       | 1    | 1    | 1    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 1    |
|                | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| ION REMARKABLE | Control    | 47     | 47         | 47      | 47   | 47   | 46   | 46   | 46   | 46   | 46   | 46   | 46   | 45   | 44   |
|                | 2500 ppm   | 44     | 44         | 44      | 43   | 42   | 42   | 42   | 42   | 42   | 42   | 42   | 41   | 41   | 41   |
|                | 5000 ppm   | 47     | 47         | 47      | 47   | 47   | 43   | 42   | 42   | 42   | 42   | 42   | 42   | 42   | 42   |
|                | 10000 ppm  | 49     | 49         | 49      | 49   | 49   | 47   | 47   | 47   | 47   | 47   | 47   | 47   | 47   | 46   |

(HAN190)

### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

### SEX : FEMALE

| Clinical sign  | Group Name | Admini | stration W | Veek-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 |
|                |            |        |            |          |      |      |      |      |      |      |      |      |      |      |      |
| DEEP BREATHING | Control    | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 2500 ppm   | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 5000 ppm   | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 10000 ppm  | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SMALL STOOL    | Control    | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 2500 ppm   | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 5000 ppm   | 0      | 0          | 1        | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 10000 ppm  | 0      | 0          | 0        | 0    | 0    | 0    | 0    | 0    | 0    | 1    | 1    | 0    | 0    | 0    |
| OLIGO-STOOL    | Control    | 0      | 0          | 0        | 0    | 0    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    |
|                | 2500 ppm   | 0      | 0          | 0        | 0    | 0    | 1    | 0    | 0    | 1    | 0    | 0    | 0    | 0    | 0    |
|                | 5000 ppm   | 1      | 1          | 1        | 0    | 0    | 0    | 1    | 3    | 1    | 1    | 1    | 1    | 1    | 1    |
|                | 10000 ppm  | 0      | . 0        | 1        | 1    | 1    | 1    | 0    | 1    | 1    | . 1  | 1    | 0    | 0    | 0    |
| NON REMARKABLE | Control    | 44     | 44         | 44       | 43   | 39   | 39   | 39   | -37  | 37   | 37   | 36   | 36   | 35   | 34   |
|                | 2500 ppm   | 41     | 40         | 40       | 38   | 33   | 33   | 33   | 33   | 33   | 33   | 32   | 32   | 32   | 31   |
|                | 5000 ppm   | 42     | 42         | 42       | 42   | 42   | 42   | 40   | 40   | 40   | 40   | 38   | 38   | 37   | 37   |
|                | 10000 ppm  | 46     | 45         | 44       | 43   | 40   | 40   | 40   | 39   | 39   | 39   | 39   | 37   | 37   | 37   |

(HAN190)

BAIS 4

PAGE : 70

\_\_\_\_

~~~

### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

 $\sim$ 

### SEX : FEMALE

PAGE : 71

1......

| Clinical sign  | Group Name | Admini | stration W | eek-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 |
|                |            |        |            |         |      |      |      |      |      |      |      |      |      |      |      |
| DEEP BREATHING | Control    | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 2500 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | . 0  |
|                | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
|                | 10000 ppm  | 0      | 0          | 0       | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| SMALL STOOL    | Control    | 0      | 0          | 0       | 1    | 0    | 0    | 0    | 1    | 0    | 0    | 1    | 1    | 0    | 1    |
|                | 2500 ppm   | 0      | 0          | 0       | 1    | 1    | 1    | 0    | 1    | 1    | 1    | 0    | 0    | 0    | 0    |
|                | 5000 ppm   | 0      | 0          | 0       | 0    | 0    | 1    | L    | 0    | 0    | 0    | 1    | 1    | 0    | 0    |
|                | 10000 ppm  | 0      | 1          | 0       | 0    | 0    | 2    | 2    | 0    | 0    | 0    | 1    | L    | 2    | 3    |
| OLIGO-STOOL    | Control    | 1      | 1          | 1       | 1    | 1    | 1    | 0    | 1    | 0    | 4    | 2    | 2    | 1    | 2    |
|                | 2500 ppm   | 0      | 3          | 1       | 1    | 1    | 0 -  | 0    | 0    | 2    | 2    | 1    | 1    | 1    | 1    |
|                | 5000 ppm   | 1      | 1          | 0       | 0    | 1    | 1    | 1    | 0    | 1    | 2    | 3    | 2    | 0    | 0    |
|                | 10000 ppm  | 1      | 2          | 1       | 1    | 0    | 1    | 1    | 1    | 1    | 0    | 2    | 2    | 4    | 5    |
| NON REMARKABLE | Control    | 34     | 33         | 33      | 34   | 34   | 34   | 35   | 34   | 34   | 30   | 31   | 30   | 29   | 27   |
|                | 2500 ppm   | 30     | 27         | 27      | 27   | 27   | 27   | 28   | 26   | 26   | 26   | 25   | 25   | 24   | 23   |
|                | 5000 ppm   | 37     | 37         | 37      | 36   | 35   | 34   | 35   | 33   | 32   | 31   | 28   | 29   | 30   | 30   |
|                | 10000 ppm  | 35     | 34         | 34      | 33   | 32   | 29   | 27   | 25   | 24   | 22   | 22   | 21   | 19   | 18   |

(HAN190)

### CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

 $\sim \sim$ 

### SEX : FEMALE

PAGE : 72

~\_\_\_\_

•

| Clinical sign  | Group Name | Admin | istration | Week-day _ |       |       |       |  |   |  |
|----------------|------------|-------|-----------|------------|-------|-------|-------|--|---|--|
| <u>.</u>       |            | 99-7  | 100-7     | 101-7      | 102-7 | 103–7 | 104-7 |  |   |  |
|                |            |       |           |            |       |       |       |  |   |  |
| DEEP BREATHING | Control    | 0     | 0         | 0          | 0     | 0     | 0     |  |   |  |
|                | 2500 ppm   | 0     | 0         | 0          | 0     | 0     | 0     |  |   |  |
|                | 5000 ppm   | 0     | 0         | 0          | 0     | 0     | 0     |  |   |  |
|                | 10000 ppm  | 1     | 1         | 0          | 0     | 0     | 0     |  |   |  |
| SMALL STOOL    | Control    | 1     | 1         | 0          | 0     | 0     | 1     |  |   |  |
|                | 2500 ppm   | 0     | 3         | 2          | 1     | 1     | 4     |  |   |  |
|                | 5000 ppm   | 0     | 1         | 0          | 0     | 2     | 1     |  | • |  |
|                | 10000 ppm  | 3     | 1         | 0          | 1     | 1     | 0     |  |   |  |
| OLIGO-STOOL    | Control    | 2     | 2         | 2          | 1     | 0     | 1     |  |   |  |
|                | 2500 ppm   | 1     | 3         | 4          | 1     | 0     | 0     |  |   |  |
|                | 5000 ppm   | 0     | 1         | - 1        | 2     | 2     | 2     |  |   |  |
|                | 10000 ppm  | 4     | 3         | 0          | 1     | 3     | 0     |  |   |  |
| NON REMARKABLE | Control    | 27    | 27        | 27         | 27    | 27    | 25    |  |   |  |
|                | 2500 ppm   | 22    | 20        | 20         | 19    | 18    | 15    |  |   |  |
|                | 5000 ppm   | 30    | 29        | 28         | 23    | 22    | 21    |  |   |  |
|                | 10000 ppm  | 17    | 17        | 17         | 16    | 15    | 12    |  |   |  |

(HAN190)

# TABLE C 1

# BODY WEIGHT CHANGES AND

# SURVIVAL ANIMAL NUMBERS: MALE

### MEAN BODY WEIGHTS AND SURVIVAL

S. 2

~~~

### STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : MALE

|                      | Control   |                          | 5000      | ppm                   |                   | 10000     | ppm                   |                  | 20000     | ppm                   |                   |  |
|----------------------|-----------|--------------------------|-----------|-----------------------|-------------------|-----------|-----------------------|------------------|-----------|-----------------------|-------------------|--|
| Week-Day<br>on Study |           | 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. |  |
| 0-0                  | 23.9 (50) | 50/50                    | 23.9 (50) | 100                   | 50/50             | 23.9 (50) | 100                   | 50/50            | 23.9 (50) | 100                   | 50/50             |  |
| 1-7                  | 24.5 (50) |                          | 24.3 (50) | 99                    | 50/50             | 24.5 (50) | 100                   | 50/50            | 24.4 (50) | 100                   | 50/50             |  |
| 2-7                  | 25.4 (50) |                          | 25.2 (50) | 99                    | 50/50             | 25.4 (50) | 100                   | 50/50            | 25.3 (50) | 100                   | 50/50             |  |
| 3-7                  | 26.4 (50) |                          | 26.2 (50) | 99                    | 50/50             | 26.4 (50) | 100                   | 50/50            | 26.2 (50) | 99                    | 50/50             |  |
| 4-7                  | 27.0 (50) |                          | 26.8 (50) | 99                    | 50/50             | 27.2 (50) | 101                   | 50/50            | 26.9 (50) | 100                   | 50/50             |  |
| 5-7                  | 27.4 (50) |                          | 27.7 (50) | 101                   | 50/50             | 27.8 (50) | 101                   | 50/50            | 27.6 (50) | 101                   | 50/50             |  |
| 6-7                  | 28.0 (50) | 50/50                    | 28.3 (50) | 101                   | 50/50             | 28.4 (50) | 101                   | 50/50            | 28.1 (50) | 100                   | 50/50             |  |
| 7-7                  | 28.5 (50) | 50/50                    | 28.7 (50) | 101                   | 50/50             | 28.9 (50) | 101                   | 50/50            | 28.4 (50) | 100                   | 50/50             |  |
| 8-7                  | 29.0 (50) | 50/50                    | 29.3 (50) | 101                   | 50/50             | 29.5 (50) | 102                   | 50/50            | 29.1 (50) | 100                   | 50/50             |  |
| 9-7                  | 30.0 (50) |                          | 30.3 (50) | 101                   | 50/50             | 30.6 (50) | 102                   | 50/50            | 30.0 (50) | 100                   | 50/50             |  |
| 10-7                 | 30.6 (50) |                          | 31.0 (50) | 101                   | 50/50             | 31.2 (50) | 102                   | 50/50            | 30.5 (50) | 100                   | 50/50             |  |
| 11-7                 | 30.9 (50) | 50/50                    | 31.4 (50) | 102                   | 50/50             | 31.7 (50) | 103                   | 50/50            | 31.0 (50) | 100                   | 50/50             |  |
| 12-7                 | 31.9 (50) |                          | 32.4 (50) | 102                   | 50/50             | 32.5 (50) | 102                   | 50/50            | 31.8 (50) | 100                   | 50/50             |  |
| 13-7                 | 32.9 (50) | 50/50                    | 33.2 (50) | 101                   | 50/50             | 33.3 (50) | 101                   | 50/50            | 32.5 (50) | 99                    | 50/50             |  |
| 14-7                 | 32.9 (50) |                          | 33.6 (50) | 102                   | 50/50             | 33.8 (50) | 103                   | 50/50            | 33.0 (50) | 100                   | 50/50             |  |
| 18-7                 | 35.2 (50) |                          | 35.8 (50) | 102                   | 50/50             | 36.0 (50) | 102                   | 50/50            | 34.9 (50) | 99                    | 50/50             |  |
| 22-7                 | 37.2 (50) |                          | 37.9 (50) | 102                   | 50/50             | 37.8 (50) | 102                   | 50/50            | 36.6 (50) | 98                    | 50/50             |  |
| 26-7                 | 39.2 (50) |                          | 39.6 (50) | 101                   | 50/50             | 39.6 (50) | 101                   | 50/50            | 38.0 (50) | 97                    | 50/50             |  |
| 30-7                 | 41.3 (50) |                          | 41.6 (49) | 101                   | 49/50             | 41.5 (50) | 100                   | 50/50            | 39.9 (50) | 97                    | 50/50             |  |
| 34 - 7               | 42.4 (50) |                          | 42.8 (49) | 101                   | 49/50             | 42.6 (50) | 100                   | 50/50            | 40.9 (50) | 96                    | 50/50             |  |
| 38-7                 | 43.9 (50) |                          | 44.2 (49) | 101                   | 49/50             | 43.9 (50) | 100                   | 50/50            | 42.1 (50) | 96                    | 50/50             |  |
| 42-7                 | 44.9 (50) |                          | 45.2 (49) | 101                   | 49/50             | 44.7 (50) | 100                   | 50/50            | 43.1 (50) | 96                    | 50/50             |  |
| 46-7                 | 46.3 (50) |                          | 46.3 (49) | 100                   | 49/50             | 45.8 (50) | 99                    | 50/50            | 44.2 (50) | 95                    | 50/50             |  |
| 50-7                 | 47.5 (50) | 50/50                    | 47.6 (49) | 100                   | 49/50             | 47.1 (50) | 99                    | 50/50            | 45.4 (50) | 96                    | 50/50             |  |
| 54-7                 | 48.6 (50) |                          | 48.5 (49) | 100                   | 49/50             | 48.1 (50) | 99                    | 50/50            | 46.4 (50) | 95                    | 50/50             |  |
| 58-7                 | 49.2 (50) |                          | 49.1 (49) | 100                   | 49/50             | 48.6 (49) | 99                    | 49/50            | 47.1 (49) | 96                    | 49/50             |  |
| 62-7                 | 49.6 (50) |                          | 49.1 (49) | 99                    | 49/50             | 48.9 (49) | 99                    | 49/50            | 47.5 (49) | 96                    | 49/50             |  |
| 66-7                 | 49.3 (50) |                          | 49.3 (49) | 100                   | 49/50             | 49.4 (49) | 100                   | 49/50            | 47.9 (49) | 97                    | 49/50             |  |
| 70-7                 | 49.9 (49) |                          | 50.2 (47) | 101                   | 47/50             | 49.8 (49) | 100                   | 49/50            | 48.4 (49) | 97                    | 49/50             |  |
| 74-7                 | 50.6 (47) | 47/50                    | 50.4 (47) | 100                   | 47/50             | 50.0 (48) | 99                    | 48/50            | 48.6 (49) | 96                    | 49/50             |  |
| 78-7                 | 50.2 (47) |                          | 49.4 (46) | 98                    | 46/50             | 49.3 (48) | 98                    | 48/50            | 47.9 (49) | 95                    | 49/50             |  |
| 82-7                 | 50.5 (46) | 46/50                    | 50.1 (43) | 99                    | 43/50             | 49.6 (46) | 98                    | 46/50            | 48.4 (48) | 96                    | 48/50             |  |
| 86-7                 | 51.1 (44) | 44/50                    | 49.9 (41) | 98                    | 41/50             | 49.8 (45) | 97                    | 45/50            | 48.1 (48) | 94                    | 48/50             |  |
| 90-7                 | 49.6 (41) |                          | 49.4 (40) | 100                   | 40/50             | 50.1 (43) | 101                   | 43/50            | 49.5 (45) | 100                   | 45/50             |  |
| 94-7                 | 48.0 (40) | 40/50                    | 49.1 (38) | 102                   | 38/50             | 49.0 (41) | 102                   | 41/50            | 48.9 (45) | 102                   | 45/50             |  |
| 98-7                 | 47.8 (38) |                          | 49.1 (36) | 103                   | 36/50             | 49.6 (36) | 104                   | 36/50            | 48.6 (45) | 102                   | 45/50             |  |
| 102-7                | 46.2 (35) |                          | 47.5 (35) | 103                   | 35/50             | 48.2 (36) | 104                   | 36/50            | 47.5 (41) | 103                   | 41/50             |  |
| 104-7                | 45.5 (35) | 35/50                    | 47.8 (33) | 105                   | 33/50             | 47.5 (36) | 104                   | 36/50            | 46.8 (41) | 103                   | 41/50             |  |
|                      |           |                          |           |                       | No.of measur      |           |                       |                  |           |                       |                   |  |

PAGE : 1

(BI0040)

TABLE C 2

# BODY WEIGHT CHANGES AND

# SURVIVAL ANIMAL NUMBERS: FEMALE

### MEAN BODY WEIGHTS AND SURVIVAL

~

 $\sim$ 

### STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : FEMALE

\_\_\_\_\_

|                      | Contro1  |                          | 2500      | ppm                   |                   | 5000      | ppm                   |                  | 10000     | ppm                   |                  |  |
|----------------------|----------|--------------------------|-----------|-----------------------|-------------------|-----------|-----------------------|------------------|-----------|-----------------------|------------------|--|
| Week-Day<br>on Study | Av. Wt.  | No.of<br>Surviv.<br><50> | Λv.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. |  |
| 0-0                  | 19.5 (50 | ) 50/50                  | 19.5 (50) | 100                   | 50/50             | 19.5 (50) | 100                   | 50/50            | 19.5 (50) | 100                   | 50/50            |  |
| 1-7                  | 19.8 (50 |                          | 19.5 (50) | 98                    | 50/50             | 19.8 (50) | 100                   | 50/50            | 19.7 (50) | 99                    | 50/50            |  |
| 2-7                  | 20.4 (50 |                          | 20.3 (50) | 100                   | 50/50             | 20.3 (50) | 100                   | 50/50            | 20.4 (50) | 100                   | 50/50            |  |
| 3-7                  | 21.0 (50 |                          | 21.0 (50) | 100                   | 50/50             | 21.0 (50) | 100                   | 50/50            | 21.1 (50) | 100                   | 50/50            |  |
| 4-7                  | 21.5 (50 |                          | 21.5 (50) | 100                   | 50/50             | 21.4 (50) | 100                   | 50/50            | 21.6 (50) | 100                   | 50/50            |  |
| 5-7                  | 22.1 (50 |                          | 22.0 (50) | 100                   | 50/50             | 22.0 (50) | 100                   | 50/50            | 22.0 (50) | 100                   | 50/50            |  |
| 6-7                  | 22.4 (50 |                          | 22.4 (50) | 100                   | 50/50             | 22.3 (50) | 100                   | 50/50            | 22.4 (50) | 100                   | 50/50            |  |
| 7-7                  | 22.8 (50 |                          | 22.8 (50) | 100                   | 50/50             | 22.8 (50) | 100                   | 50/50            | 22.7 (50) | 100                   | 50/50            |  |
| 8-7                  | 23.2 (50 |                          | 23.5 (50) | 101                   | 50/50             | 23.1 (50) | 100                   | 50/50            | 23.3 (50) | 100                   | 50/50            |  |
| 9-7                  | 23.6 (50 |                          | 23.8 (50) | 101                   | 50/50             | 23.4 (50) | 99                    | 50/50            | 23.7 (50) | 100                   | 50/50            |  |
| 10-7                 | 24.2 (50 |                          | 24.0 (50) | 99                    | 50/50             | 23.9 (50) | 99                    | 50/50            | 23.9 (50) | 99                    | 50/50            |  |
| 11-7                 | 24.0 (50 |                          | 24.2 (50) | 101                   | 50/50             | 23.8 (50) | 99                    | 50/50            | 23.9 (50) | 100                   | 50/50            |  |
| 12-7                 | 24.6 (50 |                          | 24.3 (50) | 99                    | 50/50             | 24.2 (50) | 98                    | 50/50            | 24.3 (50) | 99                    | 50/50            |  |
| 13-7                 | 24.8 (50 |                          | 24.8 (50) | 100                   | 50/50             | 24.3 (50) | 98                    | 50/50            | 24.5 (50) | 99                    | 50/50            |  |
| 14-7                 | 25.0 (50 |                          | 25.1 (50) | 100                   | 50/50             | 24.8 (50) | 99                    | 50/50            | 24.6 (50) | 98                    | 50/50            |  |
| 18-7                 | 26.0 (50 |                          | 26.3 (50) | 101                   | 50/50             | 25.6 (50) | 98                    | 50/50            | 26.1 (50) | 100                   | 50/50            |  |
| 22-7                 | 27.0 (50 |                          | 27.3 (50) | 101                   | 50/50             | 26.6 (50) | 99                    | 50/50            | 26.8 (50) | 99                    | 50/50            |  |
| 26-7                 | 27.6 (50 |                          | 27.9 (50) | 101                   | 50/50             | 27.3 (50) | 99                    | 50/50            | 27.9 (50) | 101                   | 50/50            |  |
| 30-7                 | 29.0 (50 |                          | 28.9 (50) | 100                   | 50/50             | 28.0 (50) | 97                    | 50/50            | 28.7 (49) | 99                    | 49/50            |  |
| 34-7                 | 29.5 (50 |                          | 29.5 (50) | 100                   | 50/50             | 28.8 (50) | 98                    | 50/50            | 29.1 (49) | 99                    | 49/50            |  |
| 38-7                 | 30.8 (50 |                          | 30.6 (50) | 99                    | 50/50             | 30.2 (50) | 98                    | 50/50            | 30.1 (49) | 98                    | 49/50            |  |
| 42-7                 | 31.1 (50 |                          | 31.0 (50) | 100                   | 50/50             | 30.1 (50) | 97                    | 50/50            | 30.3 (49) | 97                    | 49/50            |  |
| 46-7                 | 32.2 (50 |                          | 31.8 (50) | 99                    | 50/50             | 31.2 (50) | 97                    | 50/50            | 31.3 (49) | 97                    | 49/50            |  |
| 50-7                 | 33.2 (50 |                          | 32.7 (49) | 98                    | 49/50             | 32.1 (49) | 97                    | 49/50            | 32.3 (49) | 97                    | 49/50            |  |
| 54-7                 | 33.9 (50 |                          | 33.3 (48) | 98                    | 48/50             | 32.6 (48) | 96                    | 48/50            | 33.0 (49) | 97                    | 49/50            |  |
| 58-7<br>69-7         | 34.3 (50 |                          | 34.4 (47) | 100                   | 47/50             | 32.7 (48) | 95                    | 48/50            | 33.2 (49) | 97                    | 49/50            |  |
| 62-7<br>66 7         | 34.8 (50 |                          | 34.6 (46) | 99                    | 46/50             | 32.7 (47) | 94                    | 47/50            | 33.3 (49) | 96                    | 49/50            |  |
| 66-7                 | 35.5 (49 |                          | 34.7 (45) | 98                    | 45/50             | 33.3 (46) | 94                    | 46/50            | 33.7 (48) | 95                    | 48/50            |  |
| 70-7                 | 35.7 (49 |                          | 34.9 (41) | 98                    | 41/50             | 33.5 (46) | 94                    | 46/50            | 34.2 (48) | 96                    | 48/50            |  |
| 74-7                 | 35.9 (47 |                          | 34.7 (40) | 97                    | 40/50             | 34.0 (44) | 95                    | 44/50            | 33.7 (48) | 94                    | 48/50            |  |
| 78-7                 | 35.4 (44 |                          | 34.7 (39) | 98                    | 39/50             | 33.9 (44) | 96                    | 44/50            | 33.4 (46) | 94                    | 46/50            |  |
| 82-7                 | 36.2 (44 |                          | 35.4 (36) | 98                    | 36/50             | 34.1 (41) | 94                    | 41/50            | 34.3 (42) | 95                    | 42/50            |  |
| 86-7                 | 36.9 (41 |                          | 35.5 (34) | 96                    | 34/50             | 34.1 (40) | 92                    | 40/50            | 34.5 (39) | 93                    | 39/50            |  |
| 90-7<br>04 7         | 36.8 (40 |                          | 35.9 (34) | 98<br>97              | 34/50             | 34.5 (38) | 94                    | 38/50            | 33.7 (36) | 92                    | 36/50            |  |
| 94-7<br>08 7         | 36.3 (39 |                          | 35.3 (33) | . 97                  | 33/50             | 34.3 (36) | 94                    | 36/50            | 33.6 (32) | 93                    | 32/50            |  |
| 98-7                 | 36.2 (34 |                          | 35.9 (30) | 99<br>97              | 30/50             | 34.5 (34) | 95                    | 34/50            | 33.2 (30) | 92                    | 30/50            |  |
| 102-7                | 35.8 (32 |                          | 34.8 (28) | 97                    | 28/50             | 34.5 (32) | 96<br>96              | 32/50            | 33.8 (24) | 94                    | 24/50            |  |
| 104-7                | 35.6 (29 | ) 29/50                  | 33.4 (26) | 94                    | 26/50             | 34.2 (31) | 96                    | 31/50            | 31.4 (20) | 88                    | 20/50            |  |

(BI0040)

BAIS 4

TABLE C 3

# BODY WEIGHT CHANGES: MALE

### BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS

Same 2

 $\sim -$ 

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1,j[Cr,j:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : MALE

PAGE : 1

| Group Name                            | Administration | week-day      |           |                 |           |           |                |
|---------------------------------------|----------------|---------------|-----------|-----------------|-----------|-----------|----------------|
| · · · · · · · · · · · · · · · · · · · | 0-0            | 1–7           | 2–7       | 3–7             | 4-7       | 5-7       | 6-7            |
| Control                               | 23.9± 0.9      | 24.5± 0.9     | 25.4± 1.0 | 26.4± 1.1       | 27.0± 1.2 | 27.4± 1.3 | 28.0± 1.4      |
| 5000 ppm                              | $23.9 \pm 0.9$ | 24.3± 1.6     | 25.2± 1.4 | 26.2± 1.1       | 26.8± 1.2 | 27.7± 1.4 | 28.3± 1.3      |
| 10000 ppm                             | $23.9\pm 0.9$  | 24.5± 1.0     | 25.4± 1.2 | 26.4± 1.2       | 27.2± 1.2 | 27.8± 1.3 | $28.4 \pm 1.5$ |
| 20000 ppm                             | 23.9± 0.9      | 24.4± 0.8     | 25.3± 0.8 | 26.2± 0.9       | 26.9± 1.1 | 27.6± 1.2 | 28.1± 1.4      |
|                                       |                |               | ·         |                 | ·         |           |                |
| Significant difference                | ; *:P≦ 0.05    | ** : P ≤ 0.01 |           | Test of Dunnett |           |           |                |

(HAN260)

### BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS

 $\sim$ 

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : MALE

PAGE : 2

| Administration                        | week-day  |   |  |  |   |   |
|---------------------------------------|---|---|--|--|---|---|
| 7-7                                   | 8-7   | 9-7   | 10-7   | 11-7   | 12-7  | 13-7  |
| · · · · · · · · · · · · · · · · · · · | `   |   |  |  |   |   |
| 28.5± 1.5                             | 29.0± 1.6   | 30.0± 1.9   | 30.6± 2.0  | 30.9± 2.1  | 31.9± 2.2   | 32.9± 2.3   |
|                                       |   |   |  |  |   |   |
| 28.7± 1.6                             | 29.3± 1.6   | 30.3± 1.9   | 31.0± 2.0  | 31.4± 2.2  | 32.4± 2.2   | $33.2\pm 2.3$   |
| $28.9 \pm 1.5$                        | 29.5± 1.8   | 30.6± 2.0   | 31.2± 2.1  | 31.7± 2.2  | 32.5± 2.4   | 33.3± 2.6   |
|                                       |   |   |  |  |   | 20 5 1 0 0  |
| 28.4 1.5                              | 29.1± 1.5   | 30.0± 1.8   | 30.5± 2.3  | 31.0± 2.1  | 31.8± 2.3   | 32.5± 2.3   |
|                                       |   |   |  |  |   |   |
| * : P ≦ 0.05                          | <b>**</b> : P ≤ 0.01  |   | Test of Dunnett  |  |   |   |
|                                       | 7-7<br>28.5 $\pm$ 1.5<br>28.7 $\pm$ 1.6<br>28.9 $\pm$ 1.5<br>28.4 $\pm$ 1.5 | $28.5 \pm$ $1.5$ $29.0 \pm$ $1.6$ $28.7 \pm$ $1.6$ $29.3 \pm$ $1.6$ $28.9 \pm$ $1.5$ $29.5 \pm$ $1.8$ $28.4 \pm$ $1.5$ $29.1 \pm$ $1.5$ | $7-7$ $8-7$ $9-7$ $28.5 \pm$ $1.5$ $29.0 \pm$ $1.6$ $30.0 \pm$ $1.9$ $28.7 \pm$ $1.6$ $29.3 \pm$ $1.6$ $30.3 \pm$ $1.9$ $28.7 \pm$ $1.6$ $29.3 \pm$ $1.6$ $30.3 \pm$ $1.9$ $28.9 \pm$ $1.5$ $29.5 \pm$ $1.8$ $30.6 \pm$ $2.0$ $28.4 \pm$ $1.5$ $29.1 \pm$ $1.5$ $30.0 \pm$ $1.8$ | $7-7$ $8-7$ $9-7$ $10-7$ $28.5 \pm$ $1.5$ $29.0 \pm$ $1.6$ $30.0 \pm$ $1.9$ $30.6 \pm$ $2.0$ $28.7 \pm$ $1.6$ $29.3 \pm$ $1.6$ $30.3 \pm$ $1.9$ $31.0 \pm$ $2.0$ $28.7 \pm$ $1.6$ $29.3 \pm$ $1.6$ $30.3 \pm$ $1.9$ $31.0 \pm$ $2.0$ $28.9 \pm$ $1.5$ $29.5 \pm$ $1.8$ $30.6 \pm$ $2.0$ $31.2 \pm$ $2.1$ $28.4 \pm$ $1.5$ $29.1 \pm$ $1.5$ $30.0 \pm$ $1.8$ $30.5 \pm$ $2.3$ | $7-7$ $8-7$ $9-7$ $10-7$ $11-7$ $28.5 \pm 1.5$ $29.0 \pm 1.6$ $30.0 \pm 1.9$ $30.6 \pm 2.0$ $30.9 \pm 2.1$ $28.7 \pm 1.6$ $29.3 \pm 1.6$ $30.3 \pm 1.9$ $31.0 \pm 2.0$ $31.4 \pm 2.2$ $28.9 \pm 1.5$ $29.5 \pm 1.8$ $30.6 \pm 2.0$ $31.2 \pm 2.1$ $31.7 \pm 2.2$ $28.4 \pm 1.5$ $29.1 \pm 1.5$ $30.0 \pm 1.8$ $30.5 \pm 2.3$ $31.0 \pm 2.1$ | $7-7$ $8-7$ $9-7$ $10-7$ $11-7$ $11-7$ $12-7$ $28.5 \pm 1.5$ $29.0 \pm 1.6$ $30.0 \pm 1.9$ $30.6 \pm 2.0$ $30.9 \pm 2.1$ $31.9 \pm 2.2$ $28.7 \pm 1.6$ $29.3 \pm 1.6$ $30.3 \pm 1.9$ $31.0 \pm 2.0$ $31.4 \pm 2.2$ $32.4 \pm 2.2$ $28.9 \pm 1.5$ $29.5 \pm 1.8$ $30.6 \pm 2.0$ $31.2 \pm 2.1$ $31.7 \pm 2.2$ $32.5 \pm 2.4$ $28.4 \pm 1.5$ $29.1 \pm 1.5$ $30.0 \pm 1.8$ $30.5 \pm 2.3$ $31.0 \pm 2.1$ $31.8 \pm 2.3$ |

BAIS 4

.

### BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1;[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : MALE

PAGE : 3

| Administration | week-day  |   |  |   |  |   |
|----------------|---|---|--|---|--|---|
| 14-7           | 18-7  | 22-7  | 26-7   | 30-7  | 34-7   | 38-7  |
| 22.0+ 2.4      |   |   |  | 41.0.1 4.0  |  |   |
| 32.9± 2.4      | 35. 2 ± 2. 9  | 31.2 ± 3.2  | 39.2± 3.9  | 41.3工 4.2   | 42.4 ± 4.5   | 43.9± 4.7   |
| 33.6 $\pm$ 2.4 | 35.8± 2.8   | 37.9± 3.1   | 39.6± 3.5  | 41.6± 3.7   | 42.8± 3.7  | 44.2± 4.1   |
| 33.8± 2.7      | 36. 0± 3. 0   | 37.8± 3.3   | 39.6± 3.7  | 41.5± 4.0   | 42.6± 4.2  | 43.9± 4.3   |
| 33.0± 2.4      | 34.9± 2.7   | 36.6± 3.2   | 38.0± 3.5  | <b>39.</b> 9± <b>3.</b> 9   | <b>40.</b> 9± <b>4.</b> 1  | 42.1± 4.3   |
|                |   |   |  |   |  |   |
|                | $14-7$ 32.9 $\pm$ 2.4 33.6 $\pm$ 2.4 33.8 $\pm$ 2.7 | $32.9 \pm 2.4$ $35.2 \pm 2.9$ $33.6 \pm 2.4$ $35.8 \pm 2.8$ $33.8 \pm 2.7$ $36.0 \pm 3.0$ | $14-7$ $18-7$ $22-7$ $32.9 \pm 2.4$ $35.2 \pm 2.9$ $37.2 \pm 3.2$ $33.6 \pm 2.4$ $35.8 \pm 2.8$ $37.9 \pm 3.1$ $33.8 \pm 2.7$ $36.0 \pm 3.0$ $37.8 \pm 3.3$ $33.0 \pm 2.4$ $34.9 \pm 2.7$ $36.6 \pm 3.2$ | $14-7$ $18-7$ $22-7$ $26-7$ $32.9 \pm 2.4$ $35.2 \pm 2.9$ $37.2 \pm 3.2$ $39.2 \pm 3.9$ $33.6 \pm 2.4$ $35.8 \pm 2.8$ $37.9 \pm 3.1$ $39.6 \pm 3.5$ $33.8 \pm 2.7$ $36.0 \pm 3.0$ $37.8 \pm 3.3$ $39.6 \pm 3.7$ $33.0 \pm 2.4$ $34.9 \pm 2.7$ $36.6 \pm 3.2$ $38.0 \pm 3.5$ | $14-7$ $18-7$ $22-7$ $26-7$ $30-7$ $32.9 \pm 2.4$ $35.2 \pm 2.9$ $37.2 \pm 3.2$ $39.2 \pm 3.9$ $41.3 \pm 4.2$ $33.6 \pm 2.4$ $35.8 \pm 2.8$ $37.9 \pm 3.1$ $39.6 \pm 3.5$ $41.6 \pm 3.7$ $33.8 \pm 2.7$ $36.0 \pm 3.0$ $37.8 \pm 3.3$ $39.6 \pm 3.7$ $41.5 \pm 4.0$ $33.0 \pm 2.4$ $34.9 \pm 2.7$ $36.6 \pm 3.2$ $38.0 \pm 3.5$ $39.9 \pm 3.9$ | $14-7$ $18-7$ $22-7$ $26-7$ $30-7$ $34-7$ $32.9 \pm 2.4$ $35.2 \pm 2.9$ $37.2 \pm 3.2$ $39.2 \pm 3.9$ $41.3 \pm 4.2$ $42.4 \pm 4.5$ $33.6 \pm 2.4$ $35.8 \pm 2.8$ $37.9 \pm 3.1$ $39.6 \pm 3.5$ $41.6 \pm 3.7$ $42.8 \pm 3.7$ $33.8 \pm 2.7$ $36.0 \pm 3.0$ $37.8 \pm 3.3$ $39.6 \pm 3.7$ $41.5 \pm 4.0$ $42.6 \pm 4.2$ $33.0 \pm 2.4$ $34.9 \pm 2.7$ $36.6 \pm 3.2$ $38.0 \pm 3.5$ $39.9 \pm 3.9$ $40.9 \pm 4.1$ |

(HAN260)

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

Test of Dunnett

# STUDY NO. : 0613 BODY WEIGHT CHANGES (SUMMARY) ANIMAL : MOUSE B6D2F1/Cr1;[Cr;:BDF1] ALL ANIMALS UNIT : g REPORT TYPE : A1 104 SEX : MALE

BAIS 4

| Group Name          | Administration  | week-day      |                           |                 |            |           |                                 |  |
|---------------------|-----------------|---------------|---------------------------|-----------------|------------|-----------|---------------------------------|--|
|                     | 42-7            | 46-7          | 50-7                      | 54-7            | 58-7       | 62-7      | 66-7                            |  |
|                     |                 |               |                           |                 |            |           |                                 |  |
| Control             | 44.9± 4.7       | 46.3± 4.7     | 47.5± 4.6                 | 48.6± 4.5       | 49.2± 4.4  | 49.6± 4.3 | 49.3± 4.6                       |  |
| 5000 ppm            | 45.2± 4.0       | 46.3± 3.8     | 47.6± 3.8                 | 48.5± 3.7       | 49.1± 3.7  | 49.1± 3.9 | 49.3± 4.9                       |  |
| 10000 թթա           | 44.7± 4.5       | 45.8± 4.5     | 47.1± 4.6                 | 48.1± 4.5       | 48.6± 3.9  | 48.9± 4.1 | 49.4± 4.2                       |  |
| 20000 ppm           | 43.1± 4.2       | 44.2± 4.3*    | <b>45.</b> 4± <b>4.</b> 5 | 46.4± 4.6*      | 47.1± 4.4* | 47.5± 4.5 | <b>47.9</b> <u>+</u> <b>4.4</b> |  |
|                     |                 |               |                           |                 |            |           |                                 |  |
| Significant differe | ence; *:P≦ 0.05 | ** : P ≦ 0.01 |                           | Test of Dunnett |            |           |                                 |  |

(HAN260)

-----

### STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : MALE

\_

### BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS

 $\sim$ 

| Group Name            | Administration     | week-day      |           |                 |           |                   |                |  |
|-----------------------|--------------------|---------------|-----------|-----------------|-----------|-------------------|----------------|--|
|                       | 70–7               | 74-7          | 78-7      | 82-7            | 86-7      | 90-7              | 94-7           |  |
| Control               | 49.9± 5.7          | 50.6± 5.2     | 50.2± 6.1 | 50.5± 5.9       | 51.1± 6.0 | 49.6± 6.6         | 48.0± 7.6      |  |
| 5000 ppm              | 50.2± 4.6          | 50.4± 4.9     | 49.4± 6.2 | 50.1± 6.0       | 49.9± 5.4 | 49.4± 6.9         | 49.1± 5.9      |  |
| 10000 ppm             | 49.8± 4.4          | 50.0± 4.8     | 49.3± 5.1 | 49.6± 5.1       | 49.8± 5.5 | 50.1± 6.0         | 49.0 $\pm$ 5.6 |  |
| 20000 ppm             | <b>48.</b> 4± 4. 5 | 48.6± 5.1     | 47.9± 5.2 | 48.4± 5.6       | 48.1± 6.9 | <b>49</b> .5± 6.1 | 48.9± 6.4      |  |
|                       |                    |               |           |                 |           |                   |                |  |
| Significant differenc | xe; ∗:P≦0.05       | ** : P ≦ 0.01 |           | Test of Dunnett |           |                   |                |  |
| (HAN260)              |                    |               |           |                 |           |                   |                |  |

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : MALE

### BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS

`**~~**~

PAGE : 6

-----

.

| Group Name         | Administration week-day               |               |           |                 | <br>- |  |
|--------------------|---------------------------------------|---------------|-----------|-----------------|-------|--|
|                    | 98-7                                  | 102-7         | 104-7     |                 |       |  |
|                    |                                       |               |           |                 | <br>  |  |
| Control            | 47.8± 7.5                             | 46.2± 7.3     | 45.5± 7.6 |                 |       |  |
|                    |                                       |               |           |                 |       |  |
| 5000 ppm           | <b>49.</b> 1 ± 6. 0                   | 47.5± 7.6     | 47.8± 7.3 |                 |       |  |
|                    |                                       |               |           |                 |       |  |
| 10000 թթա          | $49.6\pm5.3$                          | 48.2± 5.3     | 47.5± 5.1 |                 |       |  |
|                    |                                       |               |           |                 |       |  |
| 20000 ppm          | $48.6 \pm 6.7$                        | 47.5± 7.1     | 46.8± 7.7 |                 |       |  |
|                    |                                       |               |           |                 |       |  |
|                    |                                       |               |           |                 |       |  |
|                    | · · · · · · · · · · · · · · · · · · · |               |           |                 | <br>  |  |
| Significant differ | rence; $*: P \leq 0.05$               | ** : P ≦ 0.01 |           | Test of Dunnett |       |  |

(HAN260)

TABLE C 4

BODY WEIGHT CHANGES: FEMALE

#### BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1,j[Cr,j:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : FEMALE

PAGE : 7

~~~~

| Group Name             | Administration | Administration week-day |           |                 |           |           |           |     |  |  |  |
|------------------------|----------------|-------------------------|-----------|-----------------|-----------|-----------|-----------|-----|--|--|--|
|                        | 0-0            | 1-7                     | 2-7       | 3-7             | 4-7       | 5-7       | 6-7       |     |  |  |  |
| Control                | 19.5± 0.9      | 19.8± 1.0               | 20.4± 0.9 | 21.0± 1.1       | 21.5± 1.1 | 22.1± 1.1 | 22.4± 1.0 |     |  |  |  |
| 2500 ppm               | 19.5± 0.9      | 19.5± 1.2               | 20.3± 1.0 | 21.0± 1.0       | 21.5± 1.1 | 22.0± 1.0 | 22.4± 1.1 |     |  |  |  |
| 5000 ppm               | 19.5± 0.9      | 19.8± 0.9               | 20.3± 0.8 | 21.0± 0.9       | 21.4± 0.9 | 22.0± 1.1 | 22.3± 1.2 |     |  |  |  |
| 10000 ppm              | 19.5± 0.9      | 19.7± 0.9               | 20.4± 1.0 | 21.1± 1.0       | 21.6± 1.1 | 22.0± 1.1 | 22.4± 1.1 |     |  |  |  |
|                        |                | -                       |           |                 |           |           |           |     |  |  |  |
| Significant difference | ; *:P≦0.05     | ** : P ≦ 0.01           |           | Test of Dunnett |           |           |           |     |  |  |  |
| (HAN260)               |                |                         | ·         |                 |           |           |           | DAT |  |  |  |

(HAN260)

BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS

| Control              | 22.8± 1.1      | 23.2± 1.2     | 23.6± 1.2 | 24.2± 1.6       | 24. 0± 1. 2 | 24.6± 1.4      | 24.8± 1.5 |
|----------------------|----------------|---------------|-----------|-----------------|-------------|----------------|-----------|
| 2500 ppm             | 22.8± 1.2      | 23.5± 1.1     | 23.8± 1.3 | 24.0± 1.4       | 24.2± 1.6   | 24.3± 1.4      | 24.8± 1.6 |
| 5000 ppm             | 22.8± 1.1      | • 23.1± 1.3   | 23.4± 1.4 | $23.9 \pm 1.5$  | 23.8± 1.5   | 24.2 $\pm$ 1.6 | 24.3± 1.7 |
| 10000 ppm            | 22.7± 1.2      | 23.3± 1.2     | 23.7± 1.3 | 23.9± 1.3       | 23.9± 1.5   | 24.3± 1.5      | 24.5± 1.6 |
|                      |                |               |           |                 |             |                |           |
| Significant differen | nce; *:P≦ 0.05 | ** : P ≦ 0.01 |           | Test of Dunnett |             |                |           |

(HAN260)

Group Name

BAIS 4

PAGE : 8

13-7

12-7

#### BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS

.

STUDY NO. : 0613 ANIMAL · : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : FEMALE

PAGE : 9

~~~

| Group Name            | Administration      | Administration week-day |                                       |                 |                |           |           |      |  |  |
|-----------------------|---------------------|-------------------------|---------------------------------------|-----------------|----------------|-----------|-----------|------|--|--|
|                       | 14-7                | 18-7                    | 22-7                                  | 26-7            | 30-7           | 34-7      | 38-7      |      |  |  |
| Control               | 25.0± 1.4           | 26.0± 1.6               | 27.0± 1.7                             | 27.6± 2.0       | 29.0± 2.5      | 29.5± 2.9 | 30.8± 2.9 |      |  |  |
| 2500 ppm              | $25.1 \pm 1.5$      | 26.3± 1.7               | 27.3± 2.3                             | 27.9± 2.6       | 28.9± 3.0      | 29.5± 2.8 | 30.6± 3.3 |      |  |  |
| 5000 թթա              | 24.8± 1.7           | $25.6 \pm 1.8$          | 26.6± 1.9                             | 27.3± 2.2       | 28.0± 2.8      | 28.8± 2.6 | 30.2± 3.3 |      |  |  |
| 10000 ppm             | <b>24.</b> 6 ± 1. 6 | 26.1± 2.3               | 26.8± 2.1                             | 27.9± 2.4       | $28.7 \pm 2.6$ | 29.1± 3.0 | 30.1± 3.4 |      |  |  |
|                       |                     |                         |                                       |                 |                |           |           |      |  |  |
| Significant differenc | e; *:P≦0.05         | ** : P ≦ 0.01           |                                       | Test of Dunnett |                |           |           |      |  |  |
| (HAN260)              |                     |                         | · · · · · · · · · · · · · · · · · · · |                 | ······         |           |           | BAIS |  |  |

#### BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS

~~~~

 $\sim$ 

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : FEMALE

PAGE : 10

| Group Name         | Administration          | week-day       |                |                 |                |                |           |  |
|--------------------|-------------------------|----------------|----------------|-----------------|----------------|----------------|-----------|--|
|                    | 42-7                    | 46-7           | 50-7           | 54-7            | 58-7           | 62-7           | 66-7      |  |
|                    |                         |                | -              |                 |                |                |           |  |
| Control            | 31.1± 2.9               | $32.2\pm 3.3$  | $33.2\pm 3.5$  | 33.9± 4.4       | 34.3± 4.6      | 34.8± 4.3      | 35.5± 4.1 |  |
|                    |                         |                |                | ч.              |                |                |           |  |
| 2500 ppm           | $31.0\pm 3.3$           | 31.8± 3.9      | 32.7± 3.9      | 33.3± 4.5       | 34.4± 4.5      | $34.6 \pm 4.4$ | 34.7± 4.3 |  |
| F000               |                         |                |                |                 |                |                |           |  |
| 5000 ppm           | $30.1\pm 3.5$           | $31.2 \pm 4.0$ | 32.1± 4.3      | $32.6 \pm 4.6$  | $32.7 \pm 4.8$ | $32.7 \pm 4.8$ | 33.3± 4.8 |  |
| 10000 ppm          | $30.3 \pm 3.6$          | 31.3± 3.9      | $32.3 \pm 4.2$ | 33.0± 4.0       | 33.2± 4.6      | 33.3± 4.5      | 33.7± 4.4 |  |
|                    |                         |                |                |                 |                |                |           |  |
|                    |                         |                |                |                 |                |                |           |  |
|                    |                         |                |                |                 |                |                |           |  |
| Significant differ | rence; $*: P \leq 0.05$ | ** : P ≦ 0.01  |                | Test of Dunnett |                |                |           |  |

(HAN260)

#### BODÝ WEIGHT CHANGES (SUMMARY) ALL ANIMALS

 $\sim \sim$ 

PAGE : 11

`~~~~`

| Group Name             | Administration      | week-day             |                                         |                 |               |            |               |  |
|------------------------|---------------------|----------------------|-----------------------------------------|-----------------|---------------|------------|---------------|--|
|                        | 70-7                | 74-7                 | 78-7                                    | 82-7            | 86-7          | 90-7       | 94-7          |  |
|                        |                     |                      |                                         | ······          |               |            |               |  |
| Control                | 35.7± 4.7           | 35.9± 4.9            | $35.4 \pm 4.5$                          | 36.2± 4.7       | $36.9\pm 5.2$ | 36.8± 5.1  | $36.3\pm 6.1$ |  |
| 2500 ppm               | $34.9\pm 4.0$       | 34.7± 4.0            | 34.7± 4.1                               | 35.4± 4.5       | 35.5± 4.6     | 35.9± 5.0  | 35.3± 4.6     |  |
| <b>F</b> Fm            |                     | •***=                |                                         |                 | 00.0_ 1.0     | 00.7- 0.0  | 00.0-1.0      |  |
| 5000 ppm               | 33.5± 4.9           | $34.0 \pm 4.3$       | 33.9± 4.3                               | 34.1± 4.5       | 34.1± 4.5*    | 34.5± 4.7  | 34.3± 4.7     |  |
| 10000 ppm              | 34.2± 4.2           | 33.7± 4.7            | 33.4± 4.4                               | 34.3± 4.4       | 34.5± 4.2     | 33.7± 4.1* | 33.6± 3.8     |  |
|                        |                     |                      |                                         |                 |               |            |               |  |
|                        |                     |                      |                                         |                 |               |            |               |  |
| Significant difference | ; * : P $\leq$ 0.05 | <b>**</b> : P ≤ 0.01 |                                         | Test of Dunnett |               |            |               |  |
| (11)(0/0)              |                     |                      | 10 - 10 - 10 - 10 - 11 - 11 - 11 - 11 - |                 |               |            |               |  |

(HAN260)

BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS

Sec. -

PAGE : 12

| Group Name | Administration             | week-day                              |             |  |  |
|------------|----------------------------|---------------------------------------|-------------|--|--|
|            | 98-7                       | 102-7                                 | 104-7       |  |  |
|            |                            | · · · · · · · · · · · · · · · · · · · |             |  |  |
| ontrol     | $36.2 \pm 5.8$             | 35.8± 6.1                             | 35.6± 6.3   |  |  |
| 500 ppm    | 35.9± 4.8                  | 34.8± 3.8                             | 33.4± 4.0   |  |  |
| 000 ppm    | <b>34.</b> 5 ± <b>4.</b> 6 | · 34.5± 4.9                           | 34.2± 5.0   |  |  |
| 0000 ppm   | 33.2± 4.9                  | 33.8± 6.3                             | 31.4± 3.8** |  |  |
|            |                            |                                       |             |  |  |
|            |                            |                                       |             |  |  |

Significant difference ; ★ : P ≤ 0.05 ★★ : P ≤ 0.01

Test of Dunnett

(HAN260)

### TABLE D 1

# FOOD CONSUMPTION CHANGES AND

### SURVIVAL ANIMAL NUMBERS: MALE

#### MEAN FOOD CONSUMPTION (FC) AND SURVIVAL

 $\sim$ 

 $\sim \sim$ 

#### STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : MALE

|                      | Control  |                          | 5000     | ppm                   |                  | 10000    | ppm                   |                  | 20000    | ) ppm                   |                   |   |   |  |
|----------------------|----------|--------------------------|----------|-----------------------|------------------|----------|-----------------------|------------------|----------|-------------------------|-------------------|---|---|--|
| Yeek-Day<br>on Study | 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                  | 3.8 (50) |                          | 3.8 (49) | 100                   | 50/50            | 3.8 (50) | 100                   | 50/50            | 3.6 (50) | 95                      | 50/50             |   |   |  |
| 2-7                  | 3.8 (50  |                          | 3.7 (50) | 97                    | 50/50            | 3.7 (50) | 97                    | 50/50            | 3.7 (49) | 97                      | 50/50             |   |   |  |
| 3-7                  | 3.8 (50  |                          | 3.7 (50) | 97                    | 50/50            | 3.7 (50) | 97                    | 50/50            | 3.7 (50) | 97                      | 50/50             | , |   |  |
| 4-7                  | 3.9 (50) |                          | 3.8 (50) | 97                    | 50/50            | 3.8 (50) | 97                    | 50/50            | 3.8 (50) | 97                      | 50/50             |   |   |  |
| 5-7                  | 3.9 (50  |                          | 3.9 (50) | 100                   | 50/50            | 3.8 (50) | 97                    | 50/50            | 3.7 (50) | 95                      | 50/50             |   |   |  |
| 6-7                  | 3.9 (50) |                          | 3.8 (50) | 97                    | 50/50            | 3.8 (50) | 97                    | 50/50            | 3.8 (50) | 97                      | 50/50             |   |   |  |
| 7-7                  | 4.0 (50) |                          | 3.9 (50) | 98                    | 50/50            | 3.9 (50) | 98                    | 50/50            | 3.8 (50) | 95                      | 50/50             |   |   |  |
| 8-7                  | 4.1 (50) |                          | 4.0 (50) | 98                    | 50/50            | 4.0 (50) | 98                    | 50/50            | 4.0 (50) | 98                      | 50/50             |   |   |  |
| 9-7                  | 4.2 (50) |                          | 4.2 (50) | 100                   | 50/50            | 4.1 (50) | 98                    | 50/50            | 4.1 (50) | 98                      | 50/50             |   |   |  |
| 10-7                 | 4.2 (50) |                          | 4.1 (50) | 98                    | 50/50            | 4.1 (50) | 98                    | 50/50            | 4.0 (50) | 95                      | 50/50             |   |   |  |
| 11-7                 | 4.2 (50) |                          | 4.1 (50) | 98                    | 50/50            | 4.1 (50) | 98                    | 50/50            | 4.0 (50) | 95                      | 50/50             |   |   |  |
| 12-7                 | 4.2 (50) |                          | 4.0 (50) | 95                    | 50/50            | 4.0 (50) | 95                    | 50/50            | 4.0 (50) | 95                      | 50/50             |   |   |  |
| 13-7                 | 4.3 (50) |                          | 4.1 (50) | 95                    | 50/50            | 4.1 (50) | 95                    | 50/50            | 4.0 (50) | 93                      | 50/50             |   |   |  |
| 14-7                 | 3.9 (50  |                          | 3.9 (50) | 100                   | 50/50            | 3.9 (50) | 100                   | 50/50            | 3.9 (50) | 100                     | 50/50             |   |   |  |
| 18-7                 | 4.1 (50) |                          | 4.0 (50) | 98                    | 50/50            | 3.9 (50) | 95                    | 50/50            | 3.9 (50) | 95                      | 50/50             |   |   |  |
| 22-7                 | 4.2 (50) |                          | 4.1 (50) | 98                    | 50/50            | 4.0 (49) | 95                    | 50/50            | 4.0 (50) | 95                      | 50/50             |   |   |  |
| 26-7                 | 4.4 (50) |                          | 4.2 (50) | 95                    | 50/50            | 4.2 (50) | 95                    | 50/50            | 4.1 (50) | 93                      | 50/50             |   |   |  |
| 30-7                 | 4.3 (50) |                          | 4.2 (49) | 98                    | 49/50            | 4.1 (50) | 95                    | 50/50            | 4.2 (50) | 98                      | 50/50             |   |   |  |
| 34-7                 | 4.3 (50) |                          | 4.2 (49) | 98                    | 49/50 ·          | 4.2 (50) | 98                    | 50/50            | 4.1 (50) | 95                      | 50/50             |   |   |  |
| 38-7                 | 4.4 (50) |                          | 4.3 (49) | 98                    | 49/50            | 4.2 (50) | 95                    | 50/50            | 4.2 (50) | 95                      | 50/50             |   |   |  |
| 42-7                 | 4.5 (50) |                          | 4.4 (49) | 98                    | 49/50            | 4.3 (50) | 96                    | 50/50            | 4.3 (50) | 96                      | 50/50             |   |   |  |
| 46-7                 | 4.4 (50) |                          | 4.3 (49) | 98                    | 49/50            | 4.2 (50) | 95                    | 50/50            | 4.2 (50) | 95                      | 50/50             |   |   |  |
| 50-7                 | 4.4 (50) |                          | 4.3 (49) | 98                    | 49/50            | 4.2 (50) | 95                    | 50/50            | 4.2 (50) | 95                      | 50/50             |   |   |  |
| 54-7                 | 4.4 (50) |                          | 4.2 (49) | 95                    | 49/50            | 4.1 (50) | 93                    | 50/50            | 4.0 (50) | 91                      | 50/50             |   |   |  |
| 58-7                 | 4.4 (50) |                          | 4.2 (49) | 95                    | 49/50            | 4.1 (49) | 93                    | 49/50            | 4.2 (49) | 95                      | 49/50             |   |   |  |
| 62-7                 | 4.7 (50) |                          | 4.5 (49) | 96                    | 49/50            | 4.3 (49) | 91                    | 49/50            | 4.3 (49) | 91                      | 49/50             |   |   |  |
| 66-7                 | 4.6 (50) |                          | 4.6 (49) | 100                   | 49/50            | 4.5 (49) | 98                    | 49/50            | 4.3 (49) | 93                      | 49/50             |   |   |  |
| 70-7                 | 4.8 (49) |                          | 4.8 (47) | 100                   | 47/50            | 4.6 (49) | 96                    | 49/50            | 4.5 (49) | 94                      | 49/50             |   |   |  |
| 74-7                 | 5.0 (47) |                          | 4.8 (47) | 96<br>06              | 47/50            | 4.7 (48) | 94                    | 48/50            | 4.6 (49) | 92                      | 49/50             |   |   |  |
| 78-7                 | 4.9 (47) |                          | 4.7 (46) | 96                    | 46/50            | 4.6 (48) | 94                    | 48/50            | 4.6 (49) | 94                      | 49/50             |   |   |  |
| 82-7                 | 4.9 (46) |                          | 4.9 (43) | 100                   | 43/50            | 4.8 (46) | 98                    | 46/50            | 4.6 (48) | 94                      | 48/50             |   |   |  |
| 86-7                 | 5.1 (44) |                          | 4.9 (41) | 96                    | 41/50            | 4.9 (45) | 96                    | 45/50            | 4.6 (48) | 90                      | 48/50             |   |   |  |
| 90-7                 | 4.8 (41) |                          | 4.8 (40) | 100                   | 40/50            | 4.8 (43) | 100                   | 43/50            | 4.7 (45) | 98                      | 45/50             |   |   |  |
| 94-7                 | 4.8 (40) |                          | 4.8 (38) | 100                   | 38/50            | 4.7 (41) | 98                    | 41/50            | 4.5 (45) | 94                      | 45/50             |   |   |  |
| 98-7                 | 5.2 (38) |                          | 5.0 (36) | 96                    | 36/50            | 4.9 (36) | 94                    | 36/50            | 4.6 (45) | 88                      | 45/50             |   |   |  |
| 102-7                | 5.0 (35) |                          | 4.8 (35) | 96                    | 35/50            | 4.6 (36) | 92                    | 36/50            | 4.5 (41) | 90                      | 41/50             |   |   |  |
| 104-7                | 4.9 (35) | 35/50                    | 4.8 (33) | 98                    | 33/50            | 4.6 (36) | 94                    | 36/50            | 4.4 (41) | 90                      | 41/50             |   |   |  |

(B10040)

BAIS 4

•

PAGE : 1

TABLE D 2

# FOOD CONSUMPTION CHANGES AND

# SURVIVAL ANIMAL NUMBERS: FEMALE

#### MEAN FOOD CONSUMPTION(FC) AND SURVIVAL

~~

 $\sim \sim$ 

#### STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : FEMALE

\_

|                      | Control  |                         | 2500     | ppm                   |                   | 5000     | ppm                   |                  | 10000    | ppm                   |                  |                                       |   |       |  |
|----------------------|----------|-------------------------|----------|-----------------------|-------------------|----------|-----------------------|------------------|----------|-----------------------|------------------|---------------------------------------|---|-------|--|
| feek-Day<br>on Study |          | 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                  | 3.4 (50) |                         | 3.3 (50) | 97                    | 50/50             | 3.4 (50) | 100                   | 50/50            | 3.4 (50) | 100                   | 50/50            | · · · · · · · · · · · · · · · · · · · |   | · · · |  |
| 2-7                  | 3.4 (50) |                         | 3.3 (50) | 97                    | 50/50             | 3.3 (50) | 97                    | 50/50            | 3.3 (50) | 97                    | 50/50            |                                       |   |       |  |
| 3-7                  | 3.5 (50) |                         | 3.4 (50) | 97                    | 50/50             | 3.3 (50) | 94                    | 50/50            | 3.4 (50) | 97                    | 50/50            |                                       |   |       |  |
| 4-7                  | 3.4 (50) |                         | 3.4 (50) | 100                   | 50/50             | 3.3 (50) | 97                    | 50/50            | 3.3 (50) | 97                    | 50/50            |                                       |   |       |  |
| 5-7                  | 3.5 (50) |                         | 3.5 (50) | 100                   | 50/50             | 3.5 (50) | 100                   | 50/50            | 3.4 (50) | 97                    | 50/50            |                                       |   |       |  |
| 6-7                  | 3.6 (50) |                         | 3.5 (50) | 97                    | 50/50             | 3.4 (50) | 94                    | 50/50            | 3.4 (50) | 94                    | 50/50            |                                       |   |       |  |
| 7-7                  | 3.7 (50) |                         | 3.7 (50) | 100                   | 50/50             | 3.6 (50) | 97                    | 50/50            | 3.5 (50) | 95                    | 50/50            |                                       |   |       |  |
| 8-7                  | 3.8 (50) |                         | 3.8 (50) | 100                   | 50/50             | 3.7 (50) | 97                    | 50/50            | 3.8 (50) | 100                   | 50/50            |                                       |   |       |  |
| 9-7                  | 3.8 (50) |                         | 3.8 (50) | 100                   | 50/50             | 3.7 (50) | 97                    | 50/50            | 3.8 (50) | 100                   | 50/50            |                                       |   |       |  |
| 10-7                 | 3.9 (50) |                         | 3.8 (50) | 97                    | 50/50             | 3.7 (50) | 95                    | 50/50            | 3.7 (50) | 95                    | 50/50            |                                       |   |       |  |
| 11-7                 | 3.8 (50) |                         | 3.8 (50) | 100                   | 50/50             | 3.7 (50) | 97                    | 50/50            | 3.8 (50) | 100                   | 50/50            |                                       |   |       |  |
| 12-7                 | 3.8 (50) |                         | 3.7 (50) | 97                    | 50/50             | 3.7 (50) | 97                    | 50/50            | 3.7 (50) | 97                    | 50/50            |                                       |   |       |  |
| 13-7                 | 3.8 (50) |                         | 3.8 (50) | 100                   | 50/50             | 3.7 (50) | 97                    | 50/50            | 3.7 (50) | 97                    | 50/50            |                                       |   |       |  |
| 14-7                 | 3.6 (50) | 50/50                   | 3.7 (50) | 103                   | 50/50             | 3.6 (50) | 100                   | 50/50            | 3.5 (49) | 97                    | 50/50            |                                       |   |       |  |
| 18-7                 | 3.6 (50) | 50/50                   | 3.7 (50) | 103                   | 50/50             | 3.5 (50) | 97                    | 50/50            | 3.6 (50) | 100                   | 50/50            |                                       |   |       |  |
| 22-7                 | 3.8 (50) | 50/50                   | 3.8 (50) | 100                   | 50/50             | 3.7 (50) | 97                    | 50/50            | 3.7 (50) | 97                    | 50/50            |                                       |   |       |  |
| 26 - 7               | 3.9 (50) | 50/50                   | 4.0 (50) | 103                   | 50/50             | 3.9 (50) | 100                   | 50/50            | 4.0 (50) | 103                   | 50/50            |                                       |   |       |  |
| 30-7                 | 3.8 (50) | 50/50                   | 3.8 (50) | 100                   | 50/50             | 3.7 (50) | . 97                  | 50/50            | 3.9 (49) | 103                   | 49/50            |                                       | - |       |  |
| 34-7                 | 3.8 (50) | 50/50                   | 3.8 (50) | 100                   | 50/50             | 3.7 (50) | 97                    | 50/50            | 3.8 (49) | 100                   | 49/50            |                                       |   |       |  |
| 38-7                 | 4.0 (50) | 50/50                   | 3.9 (50) | 98                    | 50/50             | 3.9 (50) | 98                    | 50/50            | 3.8 (49) | 95                    | 49/50            |                                       |   |       |  |
| 42-7                 | 4.1 (50) | 50/50                   | 4.0 (50) | 98                    | 50/50             | 3.9 (50) | 95                    | 50/50            | 3.8 (49) | 93                    | 49/50            |                                       |   |       |  |
| 46-7                 | 3.9 (50) | 50/50                   | 3.9 (50) | 100                   | 50/50             | 3.9 (50) | 100                   | 50/50            | 3.8 (49) | 97                    | 49/50            |                                       |   |       |  |
| 50-7                 | 4.1 (50) | 50/50                   | 3.9 (49) | 95                    | 49/50             | 3.9 (49) | 95                    | 49/50            | 3.9 (49) | 95                    | 49/50            |                                       |   |       |  |
| 54-7                 | 4.0 (50) | 50/50                   | 3.8 (48) | 95                    | 48/50             | 3.8 (48) | 95                    | 48/50            | 3.9 (49) | 98                    | 49/50            |                                       |   |       |  |
| 58-7                 | 3.8 (50) | 50/50                   | 3.9 (47) | 103                   | 47/50             | 3.6 (48) | 95                    | 48/50            | 3.7 (49) | 97                    | 49/50            |                                       |   |       |  |
| 62-7                 | 4.1 (50) | 50/50                   | 4.0 (46) | 98                    | 46/50             | 3.8 (47) | 93                    | 47/50            | 3.9 (49) | 95                    | 49/50            |                                       |   |       |  |
| 66-7                 | 4.2 (49) | 49/50                   | 4.0 (45) | 95                    | 45/50             | 4.0 (46) | 95                    | 46/50            | 3.9 (48) | 93                    | 48/50            |                                       |   |       |  |
| 70-7                 | 4.1 (49) | 49/50                   | 4.1 (41) | 100                   | 41/50             | 4.0 (46) | 98                    | 46/50            | 4.0 (48) | 98                    | 48/50            |                                       |   |       |  |
| 74-7                 | 4.0 (47) | 47/50                   | 4.1 (40) | 103                   | 40/50             | 3.9 (44) | 98                    | 44/50            | 3.7 (48) | 93                    | 48/50            |                                       |   |       |  |
| 78-7                 | 4.0 (44) | 44/50                   | 4.0 (39) | 100                   | 39/50             | 3.8 (44) | 95                    | 44/50            | 3.8 (46) | 95                    | 46/50            |                                       |   |       |  |
| 82-7                 | 4.1 (44) | 44/50                   | 4.3 (36) | 105                   | 36/50             | 4.1 (41) | 100                   | 41/50            | 4.0 (42) | 98                    | 42/50            |                                       |   |       |  |
| 86-7                 | 4.4 (41) | 41/50                   | 4.2 (34) | 95                    | 34/50             | 4.3 (40) | 98                    | 40/50            | 4.1 (39) | 93                    | 39/50            |                                       |   |       |  |
| 90-7                 | 4.5 (40) | 40/50                   | 4.2 (34) | 93                    | 34/50             | 4.1 (38) | 91                    | 38/50            | 4.0 (36) | 89                    | 36/50            |                                       |   |       |  |
| 94-7                 | 4.3 (39) | 39/50                   | 4.4 (33) | 102                   | 33/50             | 4.3 (36) | 100                   | 36/50            | 3.8 (32) | 88                    | 32/50            |                                       |   |       |  |
| 98-7                 | 4.6 (34) |                         | 4.4 (30) | 96                    | 30/50             | 4.4 (34) | 96                    | 34/50            | 3.9 (30) | 85                    | 30/50            |                                       |   |       |  |
| 102-7                | 4.2 (32) |                         | 4.2 (28) | 100                   | 28/50             | 4.2 (32) | 100                   | 32/50            | 4.0 (24) | 95                    | 24/50            |                                       |   |       |  |
| 104-7                | 4.3 (29) |                         | 4.2 (26) | 98                    | 26/50             | 4.2 (31) | 98                    | 31/50            | 3.9 (20) | 91                    | 20/50            |                                       |   |       |  |

PAGE : 2

(B10040)

TABLE D 3

FOOD CONSUMPTION CHANGES: MALE

#### FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

 $\sim$ 

PAGE : 1

| Group Name               | Administration w    | veek-day(effective) |             |                   |              |            |                     |
|--------------------------|---------------------|---------------------|-------------|-------------------|--------------|------------|---------------------|
|                          | 1-7(7)              | 2–7 (7)             | 3–7 (7)     | 4–7 (7)           | 5-7(7)       | 6-7(7)     | 7-7(7)              |
| ontrol                   | 3.8± 0.3            | 3.8± 0.3            | 3.8± 0.3    | 3.9± 0.2          | $3.9\pm 0.3$ | 3.9± 0.3   | 4.0± 0.3            |
|                          | 0.0 - 0.0           | 0.0 - 0.0           | J. 0 - 0. J | 3.9 - 0.2         | J. 7 U. J    | 3.9- 0.3   | 4.0 - 0.3           |
| 000 ppm                  | 3.8± 0.4            | 3.7± 0.3            | 3.7± 0.3    | 3.8± 0.3          | 3.9± 0.3     | 3.8± 0.2   | $3.9\pm 0.3$        |
| 0000 ppm                 | $3.8\pm 0.3$        | 3.7± 0.2            | 3.7± 0.2    | 3.8± 0.2*         | 3.8± 0.3     | 3.8± 0.2   | 3.9± 0.3 <b>*</b> ≭ |
| 0000 ppm                 | 3.6± 0.2 <b>*</b> * | 3.7± 0.2**          | 3.7± 0.2**  | 3.8± 0.2 <b>≭</b> | 3.7± 0.2*    | 3.8± 0.4** | 3.8± 0.2**          |
|                          |                     |                     |             |                   |              |            |                     |
| Significant difference ; | *:P≦0.05 **         | • : P ≤ 0.01        |             | Test of Dunnett   |              |            |                     |
| HAN260)                  |                     |                     |             |                   |              |            | BA                  |

#### FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : MALE

PAGE : 2

| Group Name | Administration w | eek-day(effective) |                     |                     |                     |            |          |
|------------|------------------|--------------------|---------------------|---------------------|---------------------|------------|----------|
|            | 8-7(7)           | 9-7(7)             | 10-7(7)             | 11-7 (7)            | 12-7(7)             | 13-7 (7)   | 14-7(7)  |
|            |                  |                    |                     |                     |                     |            |          |
| Control    | 4.1± 0.3         | 4.2± 0.3           | 4.2± 0.3            | 4.2± 0.3            | 4.2± 0.3            | 4.3± 0.3   | 3.9± 0.3 |
| 5000 ppm   | 4.0± 0.2         | 4.2± 0.3           | 4.1± 0.3            | 4.1± 0.2            | 4.0± 0.2            | 4.1± 0.3*  | 3.9± 0.3 |
| 10000 ppm  | 4.0± 0.2**       | 4.1± 0.3           | 4.1± 0.2*           | 4.1± 0.3            | 4.0± 0.3*           | 4.1± 0.3** | 3.9± 0.3 |
| 20000 ppm  | 4.0± 0.3*        | 4.1± 0.3 <b>∗</b>  | 4.0± 0.3 <b>*</b> * | 4.0± 0.3 <b>*</b> * | 4.0± 0.3 <b>*</b> ∗ | 4.0± 0.2** | 3.9± 0.2 |

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

(HAN260)

### FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

 $\sim \sim$ 

PAGE : 3

| Group Name | Administration we | ek-day(effective) |            |                     |           |            |                              |
|------------|-------------------|-------------------|------------|---------------------|-----------|------------|------------------------------|
|            | 18-7(7)           | 22–7 (7)          | 26-7(7)    | 30-7 (7)            | 34-7(7)   | 38-7(7)    | 42-7(7)                      |
|            |                   |                   |            |                     |           |            |                              |
| Control    | 4.1 $\pm$ 0.3     | 4.2± 0.2          | 4.4± 0.3   | 4.3± 0.3            | 4.3± 0.3  | 4.4± 0.3   | 4.5± 0.3                     |
|            |                   |                   |            |                     |           |            |                              |
| 5000 ppm   | 4.0± 0.2*         | 4.1± 0.3          | 4.2± 0.3*  | 4.2± 0.3            | 4.2± 0.3  | 4.3± 0.3*  | 4.4± 0.3                     |
| 10000 ppm  | 3.9± 0.3**        | 4.0± 0.3**        | 4.2± 0.3*  | 4.1± 0.3 <b>*</b> * | 4.2± 0.3  | 4.2± 0.3** | 4.3± 0.3**                   |
|            |                   |                   |            |                     |           |            |                              |
| 20000 ppm  | 3.9± 0.3**        | 4.0± 0.3**        | 4.1± 0.3** | 4.2 $\pm$ 0.3       | 4.1± 0.3* | 4.2± 0.3** | <b>4.</b> 3 ± 0. 3 <b>**</b> |
|            |                   |                   |            |                     |           |            |                              |
|            | •                 |                   |            |                     |           |            |                              |

Significant difference ; ★: P ≤ 0.05 ★★ : P ≤ 0.01 Test of Dunnett

(HAN260)

#### FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

 $\sim$ 

PAGE: 4

| Group Name               |                     | week-day(effective) |            |                 |                     |            |             |
|--------------------------|---------------------|---------------------|------------|-----------------|---------------------|------------|-------------|
|                          | 46-7 (7)            | 50-7(7)             | 54-7(7)    | 58-7(7)         | 62-7(7)             | 66-7(7)    | 70-7(7)     |
|                          |                     |                     |            |                 |                     |            |             |
| Control                  | 4.4± 0.3            | 4.4± 0.3            | 4.4± 0.3   | 4.4± 0.3        | 4.7± 0.3            | 4.6± 0.6   | 4.8± 0.5    |
|                          |                     |                     |            |                 |                     |            |             |
| 5000 ррт                 | 4.3± 0.3            | 4.3± 0.3            | 4.2± 0.3** | 4.2± 0.3**      | 4.5 ± 0.3**         | 4.6± 0.5   | 4.8± 0.3    |
| 10000 ppm                | 4.2± 0.3*           | 4.2± 0.3            | 4.1± 0.3** | 4.1± 0.3**      | 4.3± 0.3 <b>*</b> * | 4.5± 0.3** | 4.6± 0.4**  |
| 10000 ppm                | 1.2                 | 1.2_ 0.0            | 1.1_ 0.000 | 7.1± 0.000      | 1.0 - 0.0           | 1.0± 0.0   | 4.0 - 0.4** |
| 20000 ppm                | 4.2± 0.3 <b>*</b> * | 4.2± 0.3**          | 4.0± 0.3** | 4.2± 0.3**      | 4.3± 0.3**          | 4.3± 0.3** | 4.5± 0.3**  |
|                          |                     |                     |            |                 |                     | • · · ·    |             |
|                          |                     |                     |            |                 |                     |            |             |
| Significant difference ; | *:P≤0.05 *          | * : P ≦ 0.01        |            | Test of Dunnett |                     |            |             |
| (HAN260)                 |                     |                     |            |                 |                     |            |             |
| (TAN200)                 |                     |                     |            |                 |                     |            |             |

### FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

PAGE : 5

| 74-7 (7)          | 78-7 (7)                                 | 82-7 (7)                                                          | 86-7 (7)                                                                                                                  | 90-7(7)                                                                                                                                                              | 94-7 (7)                                                                                                                                                                                                       | 98-7(7)                                                                                                                                                                                                                                                  |
|-------------------|------------------------------------------|-------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                   |                                          |                                                                   |                                                                                                                           |                                                                                                                                                                      |                                                                                                                                                                                                                |                                                                                                                                                                                                                                                          |
| 0± 0.4            | 4.9± 0.4                                 | 4.9± 0.8                                                          | 5.1± 0.4                                                                                                                  | 4.8± 0.6                                                                                                                                                             | 4.8± 0.6                                                                                                                                                                                                       | 5.2± 0.7                                                                                                                                                                                                                                                 |
| 8± 0.4            | 4.7± 0.8                                 | 4.9± 0.5                                                          | 4.9± 0.7                                                                                                                  | 4.8± 0.5                                                                                                                                                             | 4.8± 0.4                                                                                                                                                                                                       | 5.0± 0.6                                                                                                                                                                                                                                                 |
|                   | 4.6± 0.4**                               | 4.8± 0.3                                                          | 4.9± 0.3*                                                                                                                 | 4.8± 0.4                                                                                                                                                             | 4.7± 0.5                                                                                                                                                                                                       | 4.9± 0.3*                                                                                                                                                                                                                                                |
| 5± 0.3 <b>*</b> * | 4.6± 0.3 <b>*</b> *                      | 4.6± 0.4**                                                        | 4.6± 0.5 <b>*</b> *                                                                                                       | 4.7± 0.4                                                                                                                                                             | 4.5± 0.4*                                                                                                                                                                                                      | 4.6± 0.4**                                                                                                                                                                                                                                               |
|                   | 0± 0.4<br>8± 0.4<br>7± 0.5**<br>6± 0.3** | 8±     0.4     4.7±     0.8       7±     0.5**     4.6±     0.4** | 8±       0.4       4.7±       0.8       4.9±       0.5         7±       0.5**       4.6±       0.4**       4.8±       0.3 | 8±       0.4       4.7±       0.8       4.9±       0.5       4.9±       0.7         7±       0.5**       4.6±       0.4**       4.8±       0.3       4.9±       0.3* | 8±       0.4       4.7±       0.8       4.9±       0.5       4.9±       0.7       4.8±       0.5         7±       0.5**       4.6±       0.4**       4.8±       0.3       4.9±       0.3*       4.8±       0.4 | 8±       0.4       4.7±       0.8       4.9±       0.5       4.9±       0.7       4.8±       0.5       4.8±       0.4         7±       0.5**       4.6±       0.4**       4.8±       0.3       4.9±       0.3*       4.8±       0.4       4.7±       0.5 |

(HAN260)

.

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

Test of Dunnett

~

| STUDY NO. : 0613<br>ANIMAL : MOUSE B6D2F1/Cr1.j[C<br>UNIT : g | rj:BDF1]                   |                                 | FOOD CONSUMPTION CHANGE<br>ALL ANIMALS | ES (SUMMARY)    |                                        |   |          |
|---------------------------------------------------------------|----------------------------|---------------------------------|----------------------------------------|-----------------|----------------------------------------|---|----------|
| REPORT TYPE : A1 104<br>SEX : MALE                            |                            |                                 |                                        |                 |                                        | • | PAGE : 6 |
| Group Name                                                    | Administration<br>102-7(7) | week-day(effective)<br>104-7(7) |                                        |                 | ······································ |   |          |
| Control                                                       | 5.0± 0.5                   | 4.9± 0.5                        |                                        |                 |                                        |   |          |
| 5000 ppm                                                      | 4.8± 0.8                   | 4.8± 0.7                        |                                        |                 |                                        |   |          |
| 10000 ppm                                                     | 4.6± 0.4 <b>*</b> *        | 4.6± 0.4*                       |                                        |                 |                                        |   |          |
| 20000 ppm                                                     | 4.5± 0.6**                 | 4.4± 0.5**                      |                                        |                 |                                        |   |          |
|                                                               |                            |                                 |                                        |                 |                                        |   |          |
| Significant difference ;                                      | * : P ≦ 0.05 *             | * : P ≦ 0.01                    |                                        | Test of Dunnett |                                        |   |          |

BAIS 4

(HAN260)

TABLE D 4

FOOD CONSUMPTION CHANGES: FEMALE

#### FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

-----

PAGE : 7

| Administration<br>1-7(7) | week-day(effective)<br>2-7(7)                                                                                          | 3-7(7)                                                                                    | 4-7 (7)                                                                                                                                         | 5-7(7)                                                                                                                                                                                                                                              | 6-7(7)                                                                                                                                                                                                                                                                                 | 7-7(7)                                                                                                                                                                                                                                                                                           |
|--------------------------|------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                          |                                                                                                                        |                                                                                           |                                                                                                                                                 |                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                  |
| 3.4± 0.3                 | $3.4\pm$ 0.2                                                                                                           | 3.5± 0.2                                                                                  | $3.4\pm 0.2$                                                                                                                                    | 3.5± 0.2                                                                                                                                                                                                                                            | 3.6± 0.2                                                                                                                                                                                                                                                                               | 3.7± 0.2                                                                                                                                                                                                                                                                                         |
| 3.3± 0.3                 | 3.3± 0.2                                                                                                               | 3.4± 0.2                                                                                  | 3.4± 0.2                                                                                                                                        | 3.5± 0.2                                                                                                                                                                                                                                            | $3.5\pm 0.2$                                                                                                                                                                                                                                                                           | 3.7± 0.2                                                                                                                                                                                                                                                                                         |
| 3.4± 0.3                 | 3.3± 0.2                                                                                                               | 3.3± 0.2                                                                                  | 3.3± 0.2*                                                                                                                                       | 3.5± 0.2                                                                                                                                                                                                                                            | 3.4± 0.2**                                                                                                                                                                                                                                                                             | 3.6± 0.2*                                                                                                                                                                                                                                                                                        |
| 3.4± 0.3                 | 3.3± 0.2                                                                                                               | 3.4± 0.2                                                                                  | 3.3± 0.2*                                                                                                                                       | 3.4 生 0.2**                                                                                                                                                                                                                                         | 3.4± 0.2*                                                                                                                                                                                                                                                                              | 3.5± 0.2**                                                                                                                                                                                                                                                                                       |
|                          |                                                                                                                        |                                                                                           |                                                                                                                                                 |                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                                                                                                  |
|                          | $\begin{array}{rrrr} 1-7(7) \\ \hline & 3.4 \pm & 0.3 \\ \hline & 3.3 \pm & 0.3 \\ \hline & 3.4 \pm & 0.3 \end{array}$ | $3.4\pm$ $0.3$ $3.4\pm$ $0.2$ $3.3\pm$ $0.3$ $3.3\pm$ $0.2$ $3.4\pm$ $0.3$ $3.3\pm$ $0.2$ | $1-7(7)$ $2-7(7)$ $3-7(7)$ $3.4\pm 0.3$ $3.4\pm 0.2$ $3.5\pm 0.2$ $3.3\pm 0.3$ $3.3\pm 0.2$ $3.4\pm 0.2$ $3.4\pm 0.3$ $3.3\pm 0.2$ $3.3\pm 0.2$ | $1-7(7)$ $2-7(7)$ $3-7(7)$ $4-7(7)$ $3.4\pm 0.3$ $3.4\pm 0.2$ $3.5\pm 0.2$ $3.4\pm 0.2$ $3.3\pm 0.3$ $3.3\pm 0.2$ $3.4\pm 0.2$ $3.4\pm 0.2$ $3.4\pm 0.3$ $3.3\pm 0.2$ $3.4\pm 0.2$ $3.4\pm 0.2$ $3.4\pm 0.3$ $3.3\pm 0.2$ $3.3\pm 0.2$ $3.3\pm 0.2$ | $1-7(7)$ $2-7(7)$ $3-7(7)$ $4-7(7)$ $5-7(7)$ $3.4\pm 0.3$ $3.4\pm 0.2$ $3.5\pm 0.2$ $3.4\pm 0.2$ $3.5\pm 0.2$ $3.3\pm 0.3$ $3.3\pm 0.2$ $3.4\pm 0.2$ $3.4\pm 0.2$ $3.5\pm 0.2$ $3.4\pm 0.3$ $3.3\pm 0.2$ $3.4\pm 0.2$ $3.5\pm 0.2$ $3.4\pm 0.3$ $3.3\pm 0.2$ $3.3\pm 0.2$ $3.3\pm 0.2$ | $1-7(7)$ $2-7(7)$ $3-7(7)$ $4-7(7)$ $5-7(7)$ $6-7(7)$ $3.4\pm 0.3$ $3.4\pm 0.2$ $3.5\pm 0.2$ $3.4\pm 0.2$ $3.5\pm 0.2$ $3.6\pm 0.2$ $3.3\pm 0.3$ $3.3\pm 0.2$ $3.4\pm 0.2$ $3.4\pm 0.2$ $3.5\pm 0.2$ $3.5\pm 0.2$ $3.4\pm 0.3$ $3.3\pm 0.2$ $3.3\pm 0.2$ $3.3\pm 0.2$ $3.3\pm 0.2*$ $3.5\pm 0.2$ |

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

(HAN260)

•

#### FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

 $\overline{}$ 

PAGE : 8

·-----

| Froup Name           | Administration  | week-day(effective)                      |                     |                 |          |              |               |
|----------------------|-----------------|------------------------------------------|---------------------|-----------------|----------|--------------|---------------|
|                      | 8–7 (7)         | 9–7 (7)                                  | 10-7(7)             | 11-7(7)         | 12-7(7)  | 13-7(7)      | 14-7(7)       |
|                      |                 | (, ) ) ( ) ( ) ( ) ( ) ( ) ( ) ( ) ( ) ( |                     |                 |          |              |               |
| ntrol                | 3.8± 0.2        | 3.8± 0.2                                 | 3.9±. 0.3           | 3.8± 0.3        | 3.8± 0.2 | 3.8± 0.3     | $3.6 \pm 0.2$ |
| 500 ppm              | 3.8± 0.2        | 3.8± 0.2                                 | 3.8± 0.2            | 3.8± 0.3        | 3.7± 0.2 | 3.8± 0.2     | 3.7± 0.3      |
| 100 mgg 000          | $3.7 \pm 0.3$   | 3.7± 0.2                                 | 3.7± 0.3**          | 3.7± 0.2        | 3.7± 0.3 | 3.7± 0.2     | 3.6± 0.3      |
| 0000 ppm             | 3.8± 0.3        | 3.8± 0.2                                 | 3.7± 0.3 <b>*</b> * | 3.8± 0.2        | 3.7± 0.3 | $3.7\pm 0.3$ | 3.5± 0.2      |
|                      |                 |                                          |                     |                 | _        |              |               |
| Significant differen | ce; *:P≦0.05 ** | * : P ≦ 0.01                             |                     | Test of Dunnett |          |              |               |
| HAN260)              |                 |                                          |                     |                 |          |              | В             |

### FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

 $\sim$ 

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                               | 3.6± 0.6                  | 3.8± 0.3                       | 3.9± 0.4 | 3.8± 0.4        | 3.8± 0.4 | 4.0± 0.4 | 4.1± 0.4     |
| 2500 ppm                              | 3.7± 0.3                  | 3.8± 0.3                       | 4.0± 0.3 | 3.8± 0.3        | 3.8± 0.4 | 3.9± 0.5 | 4.0± 0.4     |
| 5000 ppm                              | 3.5± 0.3                  | 3.7± 0.3                       | 3.9± 0.3 | 3.7± 0.4        | 3.7± 0.3 | 3.9± 0.4 | $3.9\pm$ 0.4 |
| 10000 ppm                             | 3.6± 0.4                  | 3.7± 0.3                       | 4.0± 0.3 | 3.9± 0.4        | 3.8± 0.4 | 3.8± 0.4 | 3.8± 0.4**   |
| · · · · · · · · · · · · · · · · · · · |                           |                                |          |                 |          |          |              |
| Significant difference                | ; * : P $\leq$ 0.05       | ** : P ≦ 0.01                  |          | Test of Dunnett |          |          |              |
| (HAN960)                              |                           |                                |          |                 |          |          |              |

(HAN260)

.

BAIS 4

.

#### FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

 $\cdot$   $\smile$ 

PAGE : 10

~~~~

| Group Name           | Administration        | week-day(effective) |          |                 |           |            |          |     |
|----------------------|-----------------------|---------------------|----------|-----------------|-----------|------------|----------|-----|
|                      | 46-7(7)               | 50-7(7)             | 54-7(7)  | 58-7(7)         | 62-7(7)   | 66-7(7)    | 70-7(7)  |     |
| Control              | 3.9± 0.4              | 4.1± 0.6            | 4.0± 0.5 | 3.8± 0.5        | 4.1± 0.6  | 4.2± 0.5   | 4.1± 0.6 |     |
| 500 ppm              | 3.9± 0.4              | $3.9\pm 0.5$        | 3.8± 0.4 | 3.9± 0.4        | 4.0± 0.5  | 4.0± 0.7*  | 4.1± 0.4 |     |
| ազգ 000              | 3.9± 0.4              | 3.9± 0.4            | 3.8± 0.4 | $3.6\pm 0.4$    | 3.8± 0.5∗ | 4.0± 0.4*  | 4.0± 0.4 |     |
| 10000 ppm            | 3.8± 0.4              | 3.9± 0.4            | 3.9± 0.4 | 3.7± 0.5        | 3.9± 0.5  | 3.9± 0.4** | 4.0± 0.5 |     |
|                      |                       |                     |          |                 |           |            |          |     |
| Significant differen | nce; $*: P \leq 0.05$ | ** : P ≦ 0.01       |          | Test of Dunnett |           |            |          |     |
| (HAN260)             |                       |                     |          |                 |           | ····       |          | BAI |

#### 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)             | 94-7(7)    | 98–7 (7)   |
| ontrol              | 4.0± 0.6         | 4.0± 0.5            | 4.1± 0.6   | 4.4± 0.5          | 4.5± 0.6            | 4.3± 0.9   | 4.6± 0.7   |
| 2500 ppm            | 4.1± 0.5         | 4.0± 0.6            | 4.3± 0.6   | 4.2± 0.7          | 4.2± 0.6            | 4.4± 0.9   | 4.4± 0.7   |
| 5000 թթա            | $3.9\pm$ 0.5     | 3.8± 0.5            | 4.1± 0.5   | 4.3± 0.9          | 4.1± 0.5*           | 4.3± 0.5   | 4.4± 0.4   |
| 10000 ppm           | 3.7± 0.4         | 3.8± 0.4            | 4.0± 0.5   | 4.1± 0.5 <b>≭</b> | 4.0± 0.8 <b>*</b> * | 3.8± 0.5** | 3.9± 0.7** |
|                     |                  |                     |            |                   |                     |            |            |
| Significant differe | ence; *:P≦0.05 ≉ | o∗ : P ≦ 0.01       |            | Test of Dunnett   |                     |            |            |
| (HAN260)            |                  |                     |            | n my = = = + :    |                     |            |            |

.

#### FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

 $\sim$ 

PAGE : 12

| Group Name |          | eek-day(effective) |  | <br> | <br> |
|------------|----------|--------------------|--|------|------|
|            | 102-7(7) | 104-7(7)           |  |      |      |
| -          |          |                    |  |      |      |
| Control    | 4.2± 0.6 | 4.3± 0.8           |  |      |      |
|            |          |                    |  |      |      |
| 2500 ppm   | 4.2± 0.7 | 4.2± 0.7           |  |      |      |
|            |          |                    |  |      |      |
| 5000 ppm   | 4.2± 0.6 | 4.2± 0.6           |  |      |      |
|            |          |                    |  |      |      |
| 10000 ppm  | 4.0± 0.5 | 3.9± 0.5           |  |      |      |
|            |          |                    |  |      |      |
|            |          |                    |  |      |      |

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

Test of Dunnett

~~~~~

(HAN260)

### TABLE E 1

### WATER CONSUMPTION CHANGES AND

# SURVIVAL ANIMAL NUMBERS: MALE

#### MEAN WATER CONSUMPTION(WC) AND SURVIVAL

~

 $\sim$ 

#### STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : MALE

\_\_\_\_

|          | Control |                   | 5000     | ppm           |                  | 10000    | ppm             |                   | 20000    | ppm           |                  |   |      |  |
|----------|---------|-------------------|----------|---------------|------------------|----------|-----------------|-------------------|----------|---------------|------------------|---|------|--|
| leek-Day | Av. WC. | No. of<br>Surviv. | Av. WC.  | % of<br>cont. | No.of<br>Surviv. | Av. WC.  | % of<br>cont.   | No. of<br>Surviv. | Av. WC.  | % of<br>cont. | No.of<br>Surviv. | _ |      |  |
| ı Study  |         | <50>              |          | <50>          |                  |          | <50>            |                   |          | <50>          |                  |   |      |  |
| 1-7      | 4.5 (5  |                   | 4.0 (50) | 89            | 50/50            | 4.0 (49) | 89              | 50/50             | 3.7 (49) | 82            | 50/50            |   | <br> |  |
| 2-7      | 4.3 (4  |                   | 4.0 (50) | 93            | 50/50            | 3.9 (50) | 91              | 50/50             | 3.7 (50) | 86            | 50/50            |   |      |  |
| 3-7      | 4.3 (4  |                   | 4.0 (50) | 93            | 50/50            | 3.8 (49) | 88              | 50/50             | 3.6 (49) | 84            | 50/50            |   |      |  |
| 4-7      | 4.2 (4  |                   | 3.8 (50) | 90            | 50/50            | 3.7 (50) | 88              | 50/50             | 3.4 (50) | 81            | 50/50            |   |      |  |
| 5-7      | 4.5 (5  |                   | 3.8 (50) | 84            | 50/50            | 3.6 (49) | <sup>-</sup> 80 | 50/50             | 3.5 (50) | 78            | 50/50            |   |      |  |
| 6-7      | 4.2 (5  |                   | 3.7 (50) | 88            | 50/50            | 3.5 (49) | 83              | 50/50             | 3.3 (50) | 79            | 50/50            |   |      |  |
| 7-7      | 4.3 (5  |                   | 3.8 (50) | 88            | 50/50            | 3.6 (50) | 84              | 50/50             | 3.3 (50) | 77            | 50/50            |   |      |  |
| 8-7      | 4.2 (5  |                   | 3.7 (50) | 88            | 50/50            | 3.5 (50) | 83              | 50/50             | 3.2 (50) | 76            | 50/50            |   |      |  |
| 9-7      | 4.1 (5  |                   | 3.6 (50) | 88            | 50/50            | 3.3 (50) | 80              | 50/50             | 3.1 (50) | 76            | 50/50            |   |      |  |
| 10-7     | 4.0 (5  |                   | 3.4 (50) | 85            | 50/50            | 3.2 (50) | 80              | 50/50             | 3.0 (49) | 75            | 50/50            |   |      |  |
| 11-7     | 3.8 (5  |                   | 3.4 (50) | 89            | 50/50            | 3.2 (50) | 84              | 50/50             | 3.0 (50) | 79            | 50/50            |   |      |  |
| 12-7     | 3.9 (5  |                   | 3.4 (50) | 87            | 50/50            | 3.2 (50) | 82              | 50/50             | 3.0 (50) | 77            | 50/50            |   |      |  |
| 13-7     | 3.8 (5  |                   | 3.3 (50) | 87            | 50/50            | 3.1 (50) | 82              | 50/50             | 2.9 (50) | 76            | 50/50            |   |      |  |
| 14-7     | 3.9 (5  |                   | 3.4 (50) | 87            | 50/50            | 3.2 (50) | 82              | 50/50             | 3.1 (50) | 79            | 50/50            |   |      |  |
| 18-7     | 3.8 (5  |                   | 3.3 (49) | 87            | 50/50            | 3.3 (50) | 87              | 50/50             | 2.9 (49) | 76            | 50/50            |   |      |  |
| 22-7     | 3.8 (5  |                   | 3.3 (50) | 87            | 50/50            | 3.1 (49) | 82              | 50/50             | 2.8 (50) | 74            | 50/50            |   |      |  |
| 26-7     | 3.7 (4  |                   | 3.3 (50) | 89            | 50/50            | 3.2 (49) | 86              | 50/50             | 3.0 (48) | 81            | 50/50            |   |      |  |
| 30-7     | 3.7 (5  |                   | 3.3 (49) | 89            | 49/50            | 3.1 (50) | 84              | 50/50             | 2.9 (50) | 78            | 50/50            |   |      |  |
| 34-7     | 3.8 (5  |                   | 3.3 (49) | 87            | 49/50            | 3.1 (50) | 82              | 50/50             | 2.9 (50) | 76            | 50/50            |   |      |  |
| 38-7     | 3.8 (5  | 0) 50/50          | 3.3 (49) | 87            | 49/50            | 3.2 (50) | 84              | 50/50             | 3.0 (50) | 79            | 50/50            |   |      |  |
| 42-7     | 3.8 (4  | 9) 50/50          | 3.4 (49) | 89            | 49/50            | 3.2 (50) | 84              | 50/50             | 3.0 (50) | 79            | 50/50            |   |      |  |
| 46-7     | 3.9 (5  |                   | 3.3 (49) | 85            | 49/50            | 3.2 (50) | 82              | 50/50             | 3.0 (50) | 77            | 50/50            |   |      |  |
| 50-7     | 3.8 (5  |                   | 3.3 (49) | 87            | 49/50            | 3.3 (50) | 87              | 50/50             | 2.9 (50) | 76            | 50/50            |   |      |  |
| 54-7     | 3.9 (5  | 0) 50/50          | 3.3 (49) | 85            | 49/50            | 3.3 (50) | 85              | 50/50             | 3.1 (50) | 79            | 50/50            |   |      |  |
| 58-7     | 3.8 (4  | 9) 50/50          | 3.3 (49) | 87            | 49/50            | 3.2 (49) | 84              | 49/50             | 3.1 (49) | 82            | 49/50            |   |      |  |
| 62-7     | 4.1 (5  | 0) 50/50          | 3.5 (49) | 85            | 49/50            | 3.5 (49) | 85              | 49/50             | 3.3 (49) | 80            | 49/50            |   |      |  |
| 66-7     | 4.2 (5  | 0) 50/50          | 3.7 (49) | 88            | 49/50            | 3.6 (49) | 86              | 49/50             | 3.3 (49) | 79            | 49/50            |   |      |  |
| 70-7     | 4.3 (4  | 9) 49/50          | 3.7 (47) | 86            | 47/50            | 3.6 (49) | 84              | 49/50             | 3.4 (49) | 79            | 49/50            |   |      |  |
| 74-7     | 4.3 (4  | 6) 47/50          | 3.8 (47) | 88            | 47/50            | 3.7 (48) | 86              | 48/50             | 3.5 (49) | 81            | 49/50            |   |      |  |
| 78-7     | 4.6 (4  | 6) 47/50          | 3.9 (45) | 85            | 46/50            | 3.9 (48) | 85              | 48/50             | 3.7 (49) | 80            | 49/50            |   |      |  |
| 82-7     | 4.4 (4  | 5) 46/50          | 4.0 (43) | 91            | 43/50            | 3.9 (46) | 89              | 46/50             | 3.6 (48) | 82            | 48/50            |   |      |  |
| 86-7     | 4.4 (4  | 3) 44/50          | 3.7 (41) | 84            | 41/50            | 3.9 (44) | 89              | 45/50             | 3.4 (48) | 77            | 48/50            |   |      |  |
| 90-7     | 4.5 (3  |                   | 4.0 (40) | 89            | 40/50            | 3.8 (42) | 84              | 43/50             | 3.7 (45) | 82            | 45/50            |   |      |  |
| 94-7     | 4.7 (3  |                   | 4.1 (38) | 87            | 38/50            | 4.0 (40) | 85              | 41/50             | 3.8 (45) | 81            | 45/50            |   |      |  |
| 98-7     | 4.9 (3  |                   | 4.4 (36) | 90            | 36/50            | 4.2 (36) | 86              | 36/50             | 3.8 (45) | 78            | 45/50            |   |      |  |
| 102-7    | 4.9 (3  |                   | 4.1 (34) | 84            | 35/50            | 4.2 (36) | 86              | 36/50             | 3.9 (41) | 80            | 41/50            |   |      |  |
| 104-7    | 4.9 (2  |                   | 4.1 (32) | 84            | 33/50            | 4.1 (35) | 84              | 36/50             | 3.9 (40) | 80            | 41/50            |   |      |  |

(B10040)

BAIS 4

PAGE : 1

TABLE E 2

# WATER CONSUMPTION CHANGES AND

# SURVIVAL ANIMAL NUMBERS: FEMALE

#### MEAN WATER CONSUMPTION (WC) AND SURVIVAL

 $\sim -$ 

 $\sim$ 

#### STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : FEMALE

|                      | Control 2500 ppm |                          |          |                       | 5000 ppm 10000 ppm |          |                       |                  |          |                       |                   |  |
|----------------------|------------------|--------------------------|----------|-----------------------|--------------------|----------|-----------------------|------------------|----------|-----------------------|-------------------|--|
| ∛eek-Day<br>on Study | Av. WC.          | No.of<br>Surviv.<br><50> | Av. WC.  | % of<br>cont.<br><50> | No. of<br>Surviv.  | Av. WC.  | % of<br>cont.<br><50> | No.of<br>Surviv. | Av. WC.  | % of<br>cont.<br><50> | No. of<br>Surviv. |  |
| 1-7                  | 4.3 (50          | ) 50/50                  | 3.8 (50) | 88                    | 50/50              | 3.8 (50) | 88                    | 50/50            | 3.8 (50) | 88                    | 50/50             |  |
| 2-7                  | 4.1 (50          | ) 50/50                  | 3.9 (50) | 95                    | 50/50              | 3.7 (50) | 90                    | 50/50            | 3.7 (50) | 90                    | 50/50             |  |
| 3-7                  | 4.1 (50          | ) 50/50                  | 3.9 (50) | 95                    | 50/50              | 3.8 (50) | 93                    | 50/50            | 3.8 (50) | 93                    | 50/50             |  |
| 4-7                  | 4.0 (50          | ) 50/50                  | 3.9 (50) | 98                    | 50/50              | 3.7 (50) | 93                    | 50/50            | 3.6 (50) | 90                    | 50/50             |  |
| 5-7                  | 4.1 (50          | ) 50/50                  | 3.8 (49) | 93                    | 50/50              | 3.7 (50) | 90                    | 50/50            | 3.6 (50) | 88                    | 50/50             |  |
| 6-7                  | 4.1 (50          | ) 50/50                  | 3.9 (50) | 95                    | 50/50              | 3.6 (50) | 88                    | 50/50            | 3.7 (50) | 90                    | 50/50             |  |
| 7-7                  | 4.3 (50          | ) 50/50                  | 4.2 (50) | 98                    | 50/50              | 4.0 (50) | 93                    | 50/50            | 3.9 (50) | 91                    | 50/50             |  |
| 8-7                  | 4.0 (50          | ) 50/50                  | 3.9 (49) | 98                    | 50/50              | 3.9 (50) | 98                    | 50/50            | 3.8 (50) | 95                    | 50/50             |  |
| 9-7                  | 4.0 (50          | ) 50/50                  | 3.9 (50) | 98                    | 50/50              | 3.7 (50) | 93                    | 50/50            | 3.6 (50) | 90                    | 50/50             |  |
| 10-7                 | 4.0 (50          | ) 50/50                  | 3.8 (50) | 95                    | 50/50              | 3.6 (50) | 90                    | 50/50            | 3.7 (50) | 93                    | 50/50             |  |
| 11-7                 | 3.8 (50          | ) 50/50                  | 3.8 (50) | 100                   | 50/50              | 3.5 (50) | 92                    | 50/50            | 3.7 (50) | 97                    | 50/50             |  |
| 12-7                 | 3.8 (50          | ) 50/50                  | 3.7 (50) | 97                    | 50/50              | 3.7 (50) | 97                    | 50/50            | 3.6 (50) | 95                    | 50/50             |  |
| 13-7                 | 3.9 (50          | ) 50/50                  | 3.7 (50) | 95                    | 50/50              | 3.5 (50) | 90                    | 50/50            | 3.5 (50) | 90                    | 50/50             |  |
| 14-7                 | 3.8 (50          | ) 50/50                  | 3.7 (50) | 97                    | 50/50              | 3.6 (50) | 95                    | 50/50            | 3.4 (50) | 89                    | 50/50             |  |
| 18-7                 | 4.2 (50          | ) 50/50                  | 3.8 (48) | 90                    | 50/50              | 3.6 (50) | 86                    | 50/50            | 3.6 (50) | 86                    | 50/50             |  |
| 22-7                 | 4.1 (49          | ) 50/50                  | 3.7 (49) | 90                    | 50/50              | 3.7 (50) | 90                    | 50/50            | 3.5 (50) | 85                    | 50/50             |  |
| 26-7                 | 4.0 (50          |                          | 3.7 (49) | 93                    | 50/50              | 3.6 (50) | 90                    | 50/50            | 3.7 (50) | 93                    | 50/50             |  |
| 30-7                 | 4.0 (50          | ) 50/50                  | 3.6 (48) | 90                    | 50/50              | 3.4 (50) | 85                    | 50/50            | 3.4 (49) | 85                    | 49/50             |  |
| 34-7                 | 4.0 (49          | ) 50/50                  | 3.6 (49) | 90                    | 50/50              | 3.6 (49) | 90                    | 50/50            | 3.4 (48) | 85                    | 49/50             |  |
| 38-7                 | 3.8 (49          | ) 50/50                  | 3.6 (49) | 95                    | 50/50              | 3.7 (50) | 97                    | 50/50            | 3.4 (48) | 89                    | 49/50             |  |
| 42-7                 | 3.9 (50          | ) 50/50                  | 3.5 (49) | 90                    | 50/50              | 3.6 (50) | 92                    | 50/50            | 3.3 (49) | 85                    | 49/50             |  |
| 46-7                 | 3.9 (50          |                          | 3.5 (50) | 90                    | 50/50              | 3.4 (49) | 87                    | 50/50            | 3.3 (49) | 85                    | 49/50             |  |
| 50-7                 | 3.9 (50          | ) 50/50                  | 3.4 (48) | 87                    | 49/50              | 3.4 (49) | 87                    | 49/50            | 3.2 (49) | 82                    | 49/50             |  |
| 54-7                 | 3.8 (50          | ) 50/50                  | 3.5 (48) | 92                    | 48/50              | 3.4 (48) | 89                    | 48/50            | 3.4 (49) | 89                    | 49/50             |  |
| 58-7                 | 3.7 (50          | ) 50/50                  | 3.5 (47) | 95                    | 47/50              | 3.2 (48) | 86                    | 48/50            | 3.2 (49) | 86                    | 49/50             |  |
| 62-7                 | 3.9 (49          | ) 50/50                  | 3.6 (46) | 92                    | 46/50              | 3.5 (47) | 90                    | 47/50            | 3.3 (49) | 85                    | 49/50             |  |
| 66-7                 | 4.1 (48          | ) 49/50                  | 3.7 (43) | 90                    | 45/50              | 3.4 (46) | 83                    | 46/50            | 3.3 (48) | 80                    | 48/50             |  |
| 70-7                 | 4.0 (47          | ) 49/50                  | 3.7 (40) | 93                    | 41/50              | 3.5 (46) | 88                    | 46/50            | 3.1 (48) | 78                    | 48/50             |  |
| 74-7                 | 4.3 (46          |                          | 3.9 (40) | 91                    | 40/50              | 3.5 (44) | 81                    | 44/50            | 3.3 (48) | 77                    | 48/50             |  |
| 78-7                 | 4.2 (44          |                          | 3.8 (37) | 90                    | 39/50              | 3.5 (44) | 83                    | 44/50            | 3.4 (46) | 81                    | 46/50             |  |
| 82-7                 | 4.1 (43          | ) 44/50                  | 3.9 (35) | 95                    | 36/50              | 3.6 (41) | 88                    | 41/50            | 3.4 (42) | 83                    | 42/50             |  |
| 86-7                 | 4.2 (40          |                          | 3.5 (34) | 83                    | 34/50              | 3.5 (40) | 83                    | 40/50            | 3.4 (39) | 81                    | 39/50             |  |
| 90-7                 | 4.3 (39          |                          | 3.7 (34) | 86                    | 34/50              | 3.6 (38) | 84                    | 38/50            | 3.3 (35) | 77                    | 36/50             |  |
| 94-7                 | 4.3 (38          |                          | 3.9 (33) | 91                    | 33/50              | 3.7 (36) | 86                    | 36/50            | 3.5 (32) | 81                    | 32/50             |  |
| 98-7                 | 4.3 (32          |                          | 4.1 (30) | 95                    | 30/50              | 3.8 (34) | 88                    | 34/50            | 3.5 (30) | 81                    | 30/50             |  |
| 102-7                | 4.3 (32          |                          | 3.9 (28) | 91                    | 28/50              | 3.7 (32) | 86                    | 32/50            | 3.8 (24) | 88                    | 24/50             |  |
| 104-7                | 4.2 (29          |                          | 3.7 (26) | 88                    | 26/50              | 3.7 (31) | 88                    | 31/50            | 3.8 (20) | 90                    | 24/50             |  |

(B10040)

BAIS 4

PAGE : 2

TABLE E 3

WATER CONSUMPTION CHANGES: MALE

.

#### WATER CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

~~~~

PAGE : 1

| Group Name          | Administration<br>1-7(3) | week-day(effective)<br>2-7(3)           | 3-7 (3)    | 4-7 (3)             | 5-7(3)              | 6-7(3)     | 7-7(3)              |
|---------------------|--------------------------|-----------------------------------------|------------|---------------------|---------------------|------------|---------------------|
| Control             | 4.5± 0.7                 | 4.3± 0.8                                | 4.3± 0.8   | 4.2± 0.7            | 4.5± 0.9            | 4.2± 0.9   | 4.3± 0.7            |
| 000 ppm             | 4.0± 0.9**               | 4.0± 0.7                                | 4.0± 0.7   | 3.8± 0.7*           | 3.8± 0.6**          | 3.7± 0.7** | 3.8± 0.7**          |
| 0000 ppm            | 4.0± 0.8 <b>*</b> *      | 3.9± 0.8*                               | 3.8± 0.6** | 3.7± 0.8 <b>*</b> * | 3.6± 0.6**          | 3.5± 0.5** | 3.6± 0.7**          |
| 0000 ppm            | 3.7± 0.5 <b>*</b> *      | 3.7± 0.8**                              | 3.6± 0.4** | 3.4± 0.6 <b>*</b> * | 3.5± 0.5 <b>*</b> * | 3.3± 0.5** | 3.3± 0.4 <b>*</b> * |
|                     |                          |                                         |            |                     |                     |            |                     |
| Significant differe | ence; *:P≦0.05 **        | * : P ≦ 0.01                            |            | Test of Dunnett     |                     |            |                     |
| (HAN260)            |                          | 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - |            |                     |                     |            | B                   |

#### WATER CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

~~

PAGE : 2

| Group Name          | Administration<br>8-7(3) | week-day(effective)<br>9-7(3) | 10-7(3)             | 11-7(3)         | 12-7(3)             | 13-7(3)    | 14-7(3)             |
|---------------------|--------------------------|-------------------------------|---------------------|-----------------|---------------------|------------|---------------------|
|                     |                          |                               |                     |                 |                     | 10 1 (0)   |                     |
| Control             | 4.2± 0.7                 | 4.1± 0.6                      | 4.0± 0.7            | 3.8± 0.6        | 3.9± 0.6            | 3.8± 0.5   | 3.9± 0.5            |
| 000 ppm             | 3.7± 0.7₩*               | 3.6± 0.6**                    | 3.4± 0.6 <b>*</b> * | 3.4± 0.5**      | 3.4± 0.5**          | 3.3± 0.5** | 3.4± 0.5 <b>*</b> * |
| 10000 ppm           | 3.5± 0.6**               | 3.3± 0.5**                    | 3.2± 0.5₩           | 3.2± 0.4**      | 3.2± 0.4**          | 3.1± 0.4** | 3.2± 0.4**          |
| 20000 ppm           | 3.2± 0.6**               | 3.1± 0.4**                    | 3.0± 0.4**          | 3.0± 0.4**      | 3.0± 0.5 <b>*</b> * | 2.9± 0.4** | 3.1± 0.4**          |
|                     |                          |                               |                     |                 |                     |            |                     |
| Significant differe | ence; $*: P \leq 0.05$ * | * : P ≦ 0.01                  |                     | Test of Dunnett |                     |            |                     |
| (HAN260)            |                          |                               |                     |                 |                     |            |                     |

#### WATER CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

~~~

~~

PAGE : 3

| Group Name               | Administration v<br>18-7(3) | week-day(effective)<br>22-7(3)        | 26-7 (3)            | 30-7 (3)        | 34-7 (3)            | 38-7 (3)   | 42–7 (3)            |
|--------------------------|-----------------------------|---------------------------------------|---------------------|-----------------|---------------------|------------|---------------------|
| Control                  | 3.8± 0.5                    | 3.8± 0.4                              | 3.7± 0.3            | 3.7± 0.3        | 3.8± 0.5            | 3.8± 0.4   | 3.8± 0.4            |
| 5000 ppm                 | 3.3± 0.4**                  | 3.3± 0.3**                            | 3.3± 0.3**          | 3.3± 0.5**      | 3.3± 0.3**          | 3.3± 0.3** | 3.4± 0.3**          |
| 10000 ppm                | 3.3± 0.6**                  | 3.1± 0.4**                            | 3.2± 0.6 <b>*</b> ∗ | 3.1± 0.4**      | 3.1± 0.4**          | 3.2± 0.4** | 3.2± 0.4**          |
| 20000 ppm                | 2.9± 0.4**                  | 2.8± 0.3**                            | 3.0± 0.5 <b>*</b> * | 2.9± 0.3**      | 2.9± 0.3 <b>*</b> * | 3.0± 0.3** | 3.0± 0.3 <b>*</b> ≉ |
|                          |                             | · · · · · · · · · · · · · · · · · · · |                     |                 |                     |            |                     |
| Significant difference ; | * : P ≦ 0.05 *              | ⊧ : P ≦ 0.01                          |                     | Test of Dunnett |                     |            |                     |
| (HAN260)                 |                             |                                       |                     |                 |                     |            | BAIS                |

#### WATER CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

PAGE: 4

| Group Name | Administration w<br>46-7(3) | eek-day(effective)<br>50-7(3) | 54-7 (3)            | 58-7(3)    | 62-7(3)    | 66-7(3)    | 70-7(3)             |
|------------|-----------------------------|-------------------------------|---------------------|------------|------------|------------|---------------------|
|            |                             |                               |                     |            |            |            |                     |
| Control    | 3.9± 0.6                    | $3.8\pm 0.5$                  | 3.9± 0.4            | 3.8± 0.5   | 4.1± 0.4   | 4.2± 0.8   | 4.3± 0.8            |
| 5000 ppm   | 3.3± 0.3**                  | 3.3± 0.3**                    | 3.3± 0.3**          | 3.3± 0.3** | 3.5± 0.3** | 3.7± 0.4** | 3.7± 0.4**          |
| 10000 ppm  | 3.2± 0.4**                  | 3.3± 0.4 <b>*</b> *           | 3.3± 0.4 <b>*</b> ∗ | 3.2± 0.3** | 3.5± 0.3** | 3.6± 0.4** | 3.6± 0.5**          |
| 20000 ppm  | 3.0± 0.3**                  | 2.9± 0.3**                    | 3.1± 0.3 <b>*</b> * | 3.1± 0.3** | 3.3± 0.3** | 3.3± 0.3** | 3.4± 0.3 <b>*</b> ≭ |
|            |                             |                               |                     |            |            |            |                     |

(HAN260)

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

.

Test of Dunnett

.

#### WATER CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1;[Cr;]:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : MALE

PAGE : 5

| Group Name               | Administration<br>74-7(3) | week-day(effective)<br>78-7(3) | 82-7(3)    | 86-7(3)         | 90-7(3)             | 94-7(3)    | 98-7(3)    |
|--------------------------|---------------------------|--------------------------------|------------|-----------------|---------------------|------------|------------|
|                          |                           |                                |            |                 |                     |            |            |
| Control                  | 4.3± 0.5                  | 4.6± 0.5                       | 4.4± 0.7   | 4.4± 0.7        | 4.5± 1.0            | 4.7± 0.6   | 4.9± 0.8   |
| 000 ppm                  | 3.8± 0.5**                | 3.9± 0.7**                     | 4.0± 0.5** | 3.7± 0.7**      | 4.0± 0.6 <b>*</b> * | 4.1± 0.7** | 4.4± 0.8*  |
| 0000 թթա                 | 3.7± 0.7 <b>*</b> ∗       | 3.9± 0.6**                     | 3.9± 0.5** | 3.9± 0.7**      | 3.8± 0.5 <b>*</b> ∗ | 4.0± 0.7** | 4.2± 0.6** |
| 0000 ppm                 | 3.5± 0.3 <b>*</b> *       | 3.7± 0.3**                     | 3.6± 0.4** | 3.4± 0.6**      | 3.7± 0.3 <b>*</b> * | 3.8± 0.6** | 3.8± 0.5** |
|                          |                           |                                |            |                 |                     |            |            |
| Significant difference ; | * : P ≦ 0.05 *            | * : P ≦ 0.01                   |            | Test of Dunnett |                     |            |            |
| (HAN260)                 |                           |                                |            |                 |                     |            | B          |

#### WATER CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

PAGE : 6

BAIS 4

| Group Name | Administration w<br>102-7(3) | k-day(effective)<br>104-7(3) |  |
|------------|------------------------------|------------------------------|--|
| Control    | 4.9± 1.0                     | 4.9± 0.8                     |  |
| 5000 ppm   | 4.1± 0.8**                   | 4.1± 0.8**                   |  |
| 10000 ppm  | 4.2± 0.8**                   | 4.1± 0.5**                   |  |
| 20000 ppm  | 3.9± 0.6**                   | 3.9± 0.8** ·                 |  |

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

Test of Dunnett

(HAN260)

TABLE E 4

# WATER CONSUMPTION CHANGES: FEMALE

### STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : FEMALE

### WATER CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

 $\sim$ 

PAGE : 7

| week-day(effective)<br>2-7(3) | 3-7 (3)             | 4-7 (3)             | 5-7 (3)                     | 6-7 (3)                     | 7-7 (3)                     |
|-------------------------------|---------------------|---------------------|-----------------------------|-----------------------------|-----------------------------|
| 4.1± 0.4                      | 4.1± 0.4            | 4.0± 0.3            | 4.1± 0.4                    | 4.1± 0.4                    | 4.3± 0.4                    |
| 3.9± 0.5**                    | 3.9± 0.4            | 3.9± 0.4            | 3.8± 0.3**                  | 3.9± 0.4                    | 4.2± 0.6                    |
| 3.7± 0.3 <b>*</b> *           | 3.8± 0.3 <b>*</b> * | 3.7± 0.4 <b>*</b> * | 3.7± 0.3 <b>*</b> *         | 3.6± 0.4**                  | 4.0± 0.4**                  |
| 3.7± 0.5**                    | 3.8± 0.5**          | 3.6± 0.4**          | 3.6± 0.4**                  | 3.7± 0.4**                  | 3.9± 0.4**                  |
|                               |                     |                     |                             |                             |                             |
| * : P ≦ 0.01                  |                     | Test of Dunnett     |                             |                             |                             |
| *                             | : P ≦ 0.01          | : P ≤ 0.01          | a: P ≤ 0.01 Test of Dunnett | a: P ≤ 0.01 Test of Dunnett | a: P ≤ 0.01 Test of Dunnett |

(HAN260)

### STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : FEMALE

### WATER CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

PAGE : 8

`~\_\_\_~

|           |           |                     |                     | 11-7 (3)   | 12-7(3)   | 13-7 (3)   | 14-7 (3)            |
|-----------|-----------|---------------------|---------------------|------------|-----------|------------|---------------------|
| Control   | 4.0± 0.4  | 4.0± 0.4            | 4.0± 0.4            | 3.8± 0.4   | 3.8± 0.4  | 3.9± 0.5   | 3.8± 0.4            |
| 2500 ppm  | 3.9± 0.4  | 3.9± 0.6*           | 3.8± 0.4*           | 3.8± 0.4   | 3.7± 0.6  | 3.7± 0.4*  | 3.7± 0.5            |
| 5000 ppm  | 3.9± 0.5  | 3.7± 0.6 <b>*</b> * | 3.6± 0.3 <b>*</b> ≉ | 3.5± 0.4** | 3.7± 0.4  | 3.5± 0.4** | 3.6± 0.5*           |
| 10000 ppm | 3.8± 0.4* | 3.6± 0.4**          | 3.7± 0.4**          | 3.7± 0.4   | 3.6± 0.3* | 3.5土 0.4** | 3.4± 0.3 <b>*</b> * |

| Significant difference ; | * : P ≦ 0.05 | ** : P ≦ 0.01 | Test of Dunnett |  |  |
|--------------------------|--------------|---------------|-----------------|--|--|
|                          |              |               |                 |  |  |
| (HANOCO)                 |              |               |                 |  |  |

(HAN260)

### STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : FEMALE

### WATER CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

~\_\_\_\_

 $\sim$ 

PAGE : 9

| Group Name | Administration w                      | eek-day(effective) |                     |            |                    |               |                     |
|------------|---------------------------------------|--------------------|---------------------|------------|--------------------|---------------|---------------------|
|            | 18-7 (3)                              | 22-7(3)            | 26-7(3)             | 30-7(3)    | 34-7(3)            | 38-7 (3)      | 42-7 (3)            |
|            | · · · · · · · · · · · · · · · · · · · |                    |                     |            |                    |               |                     |
| Control    | 4.2± 0.7                              | 4.1± 0.7           | 4.0± 0.8            | 4.0± 0.8   | 4.0 $\pm$ 0.8      | 3.8± 0.7      | 3.9± 0.6            |
| 2500 ppm   | 3.8± 0.5**                            | 3.7土 0.3**         | 3.7± 0.5            | 3.6± 0.4   | 3.6± 0.7**         | 3.6± 0.4      | 3.5± 0.5**          |
| 2000 ppm   | 0.0                                   | 0.12 0.0           | 0. Finite 0. 0      | 3.0 - 0.4  | J. U.L U. 177      | 5.01 0.4      | 3.9 - 0.9**         |
| 5000 ppm   | 3.6± 0.5**                            | 3.7± 0.4**         | 3.6± 0.4            | 3.4± 0.5** | 3.6± 0.4*          | $3.7 \pm 0.4$ | 3.6± 0.8**          |
| 10000 ppm  | 3.6± 0.3**                            |                    |                     |            |                    |               |                     |
|            | <b>3.</b> 0 ⊥ 0, 3≁≁                  | 3.5± 0.4**         | 3.7± 0.9 <b>*</b> * | 3.4± 0.5** | 3.4± 0.6 <b>**</b> | 3.4土 0.5**    | 3.3± 0.4 <b>*</b> * |
|            |                                       |                    |                     |            |                    |               |                     |

| Significant difference ; | * : P $\leq$ 0.05 | <b>**</b> : P ≤ 0.01 | Test of Dunnett |  |
|--------------------------|-------------------|----------------------|-----------------|--|
| (114N9c9)                |                   |                      |                 |  |

(HAN260)

### WATER CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1;[Cr;:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : FEMALE

PAGE : 10

| · · · ·  |            |                     |                                |  |  |  |
|----------|------------|---------------------|--------------------------------|--|--|--|
| 9± 0.7   | 3.9± 0.5   | 3.8± 0.6            | 3.7± 0.4                       | 3.9± 0.6   | 4.1± 0.5   | 4.0± 0.7   |
| 5± 0.6** | 3.4± 0.7** | 3.5± 0.6*           | 3.5± 0.8 <b>*</b> *            | 3.6± 0.7 <b>*</b> ≉  | 3.7± 0.8**   | 3.7± 0.6   |
| 4± 0.8** | 3.4± 0.4** | 3.4± 0.5 <b>*</b> * | 3.2± 0.5 <b>*</b> *            | 3.5± 0.5**   | 3.4± 0.5**   | 3.5± 0.7 <b>*</b> *  |
| 3± 0.5** | 3.2± 0.5** | 3.4± 0.4**          | 3.2± 0.4 <b>*</b> *            | 3.3± 0.5**   | 3.3± 0.5**   | 3.1± 0.4**   |
|          | 4± 0.8**   | 4± 0.8** 3.4± 0.4** | 4± 0.8** 3.4± 0.4** 3.4± 0.5** | 5± 0.6**       3.4± 0.7**       3.5± 0.6*       3.5± 0.8**         4± 0.8**       3.4± 0.4**       3.4± 0.5**       3.2± 0.5** | 5± 0.6**       3.4± 0.7**       3.5± 0.6*       3.5± 0.8**       3.6± 0.7**         4± 0.8**       3.4± 0.4**       3.4± 0.5**       3.2± 0.5**       3.5± 0.5** | 5± 0.6**       3.4± 0.7**       3.5± 0.6*       3.5± 0.8**       3.6± 0.7**       3.7± 0.8**         4± 0.8**       3.4± 0.4**       3.4± 0.5**       3.2± 0.5**       3.5± 0.5**       3.4± 0.5** |

(HAN260)

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

Test of Dunnett

~~~

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1;[Cr;:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : FEMALE

### WATER CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

PAGE : 11

| Group Name             | Administration         | week-day(effective)     |                     |                     |               |            |                    |
|------------------------|------------------------|-------------------------|---------------------|---------------------|---------------|------------|--------------------|
|                        | 74-7 (3)               | 78-7 (3)                | 82-7 (3)            | 86-7 (3)            | 90-7(3)       | 94–7 (3)   | 98–7 (3)           |
|                        |                        |                         |                     |                     |               |            |                    |
| Control                | 4.3± 0.7               | 4.2± 0.8                | 4.1± 0.7            | 4.2± 0.6            | 4.3± 0.6      | 4.3± 1.0   | 4.3± 0.7           |
| 2500 ppm               | 3.9± 1.0**             | 3.8± 1.1**              | 3.9± 0.9            | 3.5± 0.8**          | 3.7± 0.8**    | 3.9± 1.0   | 4.1± 0.7           |
| Jooo ppm               | 0.0 - 1.000            | <b>0.</b> 0 ± 1. 1 ···· | 3.9± 0.9            | 3.0 - 0.0**         | J. 1 - U. Omm | 3.9- 1.0   | 4.1 - 0.7          |
| 5000 ppm               | 3.5± 0.5**             | 3.5± 0.6**              | 3.6± 0.6 <b>*</b> ∗ | 3.5± 0.6**          | 3.6± 0.9**    | 3.7± 0.7** | 3.8± 0.7*          |
| 10000 ppm              | 3.3± 0.6 <b>*</b> ∗    | 3.4± 0.7**              | 3.4± 0.5 <b>*</b> * |                     |               |            |                    |
|                        | J. J_ U. UTT           | 3.41 U. (**             | 3.4 0.5**           | 3.4± 0.8 <b>*</b> * | 3.3± 0.9**    | 3.5土 0.7** | 3.5± 0.9 <b>**</b> |
|                        |                        |                         |                     |                     |               |            |                    |
| Significant difference |                        | <b>*</b> : P ≦ 0.01     |                     | *<br>               |               |            |                    |
| Significant difference | $* \cdot r \ge 0.00$ * | $* \cdot P \ge 0.01$    |                     | Test of Dunnett     |               |            |                    |

(HAN260)

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : g REPORT TYPE : A1 104 SEX : FEMALE

### WATER CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

PAGE : 12

-----

| Group Name | Administration w<br>102-7(3) | eek-day(effective)<br>104-7(3) |   |  |  |  |
|------------|------------------------------|--------------------------------|---|--|--|--|
| Control    | 4.3± 0.7                     | 4.2± 0.8                       |   |  |  |  |
| 2500 ppm   | 3.9± 0.8                     | 3.7± 1.1                       |   |  |  |  |
| 5000 ppm   | 3.7± 0.8 <b>*</b> *          | 3.7± 1.0                       |   |  |  |  |
| 10000 ppm  | 3.8± 0.8*                    | 3.8± 0.8                       | • |  |  |  |
|            |                              |                                |   |  |  |  |

| Significant difference ; | * : P ≦ 0.05 | ** : P ≤ 0.01 | Test of Dunnett |        |
|--------------------------|--------------|---------------|-----------------|--------|
| (HAN260)                 |              |               |                 | RATS A |

(HAN260)

## TABLE F 1

# CHEMICAL INTAKE CHANGES: MALE

~~~~

.

 $\sim$ 

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1] UNIT : mg/kg/day REPORT TYPE : A1 104 SEX : MALE

PAGE : 1

| Adminis   | tration                              | (weeks)               |   |   |  |  |   |   |  |  |  |   |  |
|-----------|--------------------------------------|-----------------------|---|---|--|--|---|---|--|--|--|---|--|
| 1         |                                      | 2                     |   | 3   |  | 4  |   | 5   |  | 6  |  | 7   |  |
| 0±        | 0                                    | $0\pm$                | 0   | 0±  | 0  | 0±   | 0   | 0±  | 0  | 0±   | 0  | 0±  | 0  |
| $809\pm$  | 165                                  | $800\pm$              | 124   | 767±  | 131  | 716±   | 134   | 683±  | 105  | 648±   | 124  | 660±  | 141  |
| 1621±     | 322                                  | $1554\pm$             | 328   | $1452\pm$   | 224  | $1362\pm$  | 325   | 1300±   | 218  | $1241\pm$  | 179  | $1267\pm$   | 282  |
| $3077\pm$ | 482                                  | $2970\pm$             | 670   | 2716±   | 347  | $2537\pm$  | 474   | 2525土   | 384  | $2376\pm$  | 415  | $2361\pm$   | 354  |
|           | 1<br>$0\pm$<br>$809\pm$<br>$1621\pm$ | 809± 165<br>1621± 322 | 1         2 $0 \pm$ $0 \pm$ $809 \pm$ $165$ $800 \pm$ $1621 \pm$ $322$ $1554 \pm$ | 1     2 $0 \pm$ $0 \pm$ $0$ $809 \pm$ $165$ $800 \pm$ $124$ $1621 \pm$ $322$ $1554 \pm$ $328$ | 1         2         3 $0 \pm$ $0$ $0 \pm$ $0 \pm$ $809 \pm$ $165$ $800 \pm$ $124$ $767 \pm$ $1621 \pm$ $322$ $1554 \pm$ $328$ $1452 \pm$ | 1       2       3 $0 \pm$ 0 $0 \pm$ 0 $0 \pm$ 0 $809 \pm$ 165 $800 \pm$ 124 $767 \pm$ 131 $1621 \pm$ 322 $1554 \pm$ 328 $1452 \pm$ 224 | 1       2       3       4 $0 \pm$ 0 $0 \pm$ 0 $0 \pm$ 0 $0 \pm$ $809 \pm$ 165 $800 \pm$ 124 $767 \pm$ 131 $716 \pm$ $1621 \pm$ 322 $1554 \pm$ 328 $1452 \pm$ 224 $1362 \pm$ | 1       2       3       4 $0 \pm$ | 1       2       3       4       5 $0 \pm$ 0 $0 \pm$ 0 $0 \pm$ 0 $0 \pm$ 0 $0 \pm$ $0 \pm$ 0 $0 \pm$ 0 $0 \pm$ 0 $0 \pm$ 0 $0 \pm$ $809 \pm$ 165 $800 \pm$ 124 $767 \pm$ 131 $716 \pm$ 134 $683 \pm$ $1621 \pm$ 322 $1554 \pm$ 328 $1452 \pm$ 224 $1362 \pm$ $325$ $1300 \pm$ | 1       2       3       4       5 $0 \pm$ 0 $809 \pm$ 165 $800 \pm$ 124 $767 \pm$ 131 $716 \pm$ 134 $683 \pm$ 105 $1621 \pm$ 322 $1554 \pm$ 328 $1452 \pm$ 224 $1362 \pm$ $325$ $1300 \pm$ 218 | 1       2       3       4       5       6 $0 \pm$ 0       0 $0 \pm$ 0       0       0 $0 \pm$ 0       0< | 1       2       3       4       5       6 $0 \pm$ 0 $809 \pm$ 165 $800 \pm$ 124       767 \pm       131       716 \pm       134 $683 \pm$ 105 $648 \pm$ 124 $1621 \pm$ 322       1554 \pm       328       1452 \pm       224       1362 \pm       325       1300 \pm       218       1241 \pm       179 | 1       2       3       4       5       6       7 $0 \pm$ </td |

(HAN300)

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : mg∕kg∕day REPORT TYPE : A1 104 SEX : MALE

PAGE : 2

~

| Adminis   |                          |  |   |   |   |   |   | ·   |  |  |   |   |  |
|-----------|--------------------------|--|---|---|---|---|---|---|--|--|---|---|--|
| 8         |                          | 9  |   | 10  |   | 11  |   | 12  |  | 13   |   | 14  |  |
| 0±        | 0                        | 0±   | 0   | 0±  | 0   | 0±  | 0   | 0±  | 0  | 0±   | 0   | 0±  | 0  |
| $636\pm$  | 128                      | $590\pm$   | 112   | 559±  | 116   | $538\pm$  | 100   | 526±  | 106  | $505\pm$   | 95  | $514\pm$  | 97   |
| 1181±     | 238                      | 1100±  | 191   | $1045\pm$   | 198   | 1007±   | 179   | $999\pm$  | 158  | $934\pm$   | 149   | $968\pm$  | 171  |
| $2227\pm$ | 411                      | $2101\pm$  | 341   | 1982±   | 324   | $1944\pm$   | 360   | $1897\pm$   | 352  | 1776±  | 289   | $1898\pm$   | 326  |
|           | 8<br>0±<br>636±<br>1181± | $\begin{array}{cccc} 8 & & & & & & \\ 0 \pm & 0 & & & & & \\ 636 \pm & 128 & & & & \\ 1181 \pm & 238 & & & \\ \end{array}$ | 8         9 $0 \pm$ $0 \pm$ $636 \pm$ $128$ $590 \pm$ $1181 \pm$ $238$ $1100 \pm$ | 8         9 $0 \pm$ $0 \pm$ $0$ $636 \pm$ $128$ $590 \pm$ $112$ $1181 \pm$ $238$ $1100 \pm$ $191$ | 8         9         10 $0 \pm$ $0$ $0 \pm$ $0 \pm$ $636 \pm$ $128$ $590 \pm$ $112$ $559 \pm$ $1181 \pm$ $238$ $1100 \pm$ $191$ $1045 \pm$ | 8         9         10 $0 \pm$ $0$ $0 \pm$ $0$ $636 \pm$ $128$ $590 \pm$ $112$ $559 \pm$ $116$ $1181 \pm$ $238$ $1100 \pm$ $191$ $1045 \pm$ $198$ | 8         9         10         11 $0 \pm$ $0$ $0 \pm$ $0$ $0 \pm$ $0 \pm$ $636 \pm$ $128$ $590 \pm$ $112$ $559 \pm$ $116$ $538 \pm$ $1181 \pm$ $238$ $1100 \pm$ $191$ $1045 \pm$ $198$ $1007 \pm$ | 8         9         10         11 $0 \pm$ $0$ $0 \pm$ $0$ $0 \pm$ $0$ $636 \pm$ $128$ $590 \pm$ $112$ $559 \pm$ $116$ $538 \pm$ $100$ $1181 \pm$ $238$ $1100 \pm$ $191$ $1045 \pm$ $198$ $1007 \pm$ $179$ | 8         9         10         11         12 $0 \pm$ $0$ $0 \pm$ $0$ $0 \pm$ $0$ $0 \pm$ $0 \pm$ $0$ $0 \pm$ $0$ $0 \pm$ $0$ $0 \pm$ $636 \pm$ $128$ $590 \pm$ $112$ $559 \pm$ $116$ $538 \pm$ $100$ $526 \pm$ $1181 \pm$ $238$ $1100 \pm$ $191$ $1045 \pm$ $198$ $1007 \pm$ $179$ $999 \pm$ | 8         9         10         11         12 $0 \pm$ $0$ $0 \pm$ $0$ $0 \pm$ $0$ $0 \pm$ $0$ $636 \pm$ 128 $590 \pm$ 112 $559 \pm$ $116$ $538 \pm$ $100$ $526 \pm$ $106$ $1181 \pm$ $238$ $1100 \pm$ $191$ $1045 \pm$ $198$ $1007 \pm$ $179$ $999 \pm$ $158$ | 8         9         10         11         12         13 $0 \pm$ $0$ | 8         9         10         11         12         13 $0 \pm$ 0 $0 \pm$ < | 8         9         10         11         12         13         14 $0 \pm$ 0         0 $0 \pm$ 0 $0 \pm$ 0         0 <th< td=""></th<> |

~~~~

(HAN300)

÷

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : mg/kg/day REPORT TYPE : A1 104 SEX : MALE

PAGE : 3

| Administration (weeks) |                          |                                   |                                                                              |                                                                                         |                                                                                                                  |                                                                                                                                       |                                                                                                                                                                |                                                                                                                                                                                               |                                                                                                                                                                                                                                    |                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|------------------------|--------------------------|-----------------------------------|------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 18                     |                          | 22                                |                                                                              | 26                                                                                      |                                                                                                                  | 30                                                                                                                                    |                                                                                                                                                                | 34                                                                                                                                                                                            |                                                                                                                                                                                                                                    | 38                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 42                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|                        |                          |                                   |                                                                              |                                                                                         |                                                                                                                  |                                                                                                                                       |                                                                                                                                                                |                                                                                                                                                                                               |                                                                                                                                                                                                                                    |                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| 0±                     | 0                        | 0±                                | 0                                                                            | 0±                                                                                      | 0                                                                                                                | 0±                                                                                                                                    | 0                                                                                                                                                              | 0±                                                                                                                                                                                            | 0                                                                                                                                                                                                                                  | 0±                                                                                                                                                                                                                            | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 0±                                                                                                                                                                                                                                                                            | 0                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| $469\pm$               | 86                       | $434\pm$                          | 60                                                                           | 421±                                                                                    | 57                                                                                                               | 401±                                                                                                                                  | 73                                                                                                                                                             | 386±                                                                                                                                                                                          | 57                                                                                                                                                                                                                                 | 371±                                                                                                                                                                                                                          | 50                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 376±                                                                                                                                                                                                                                                                          | 49                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| 911±                   | 198                      | $816\pm$                          | 138                                                                          | $809\pm$                                                                                | 198                                                                                                              | 764±                                                                                                                                  | 121                                                                                                                                                            | 723±                                                                                                                                                                                          | 117                                                                                                                                                                                                                                | 735±                                                                                                                                                                                                                          | 125                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 729±                                                                                                                                                                                                                                                                          | 98                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| 1703土                  | 292                      | $1565\pm$                         | 204                                                                          | 1576±                                                                                   | 318                                                                                                              | $1481\pm$                                                                                                                             | 195                                                                                                                                                            | 1449±                                                                                                                                                                                         | 172                                                                                                                                                                                                                                | $1421\pm$                                                                                                                                                                                                                     | 187                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | $1424\pm$                                                                                                                                                                                                                                                                     | 177                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
|                        | 18<br>0±<br>469±<br>911± | 18<br>0± 0<br>469± 86<br>911± 198 | 18     22 $0 \pm$ $0 \pm$ $469 \pm$ $86$ $434 \pm$ $911 \pm$ $198$ $816 \pm$ | 18     22 $0 \pm$ $0 \pm$ $469 \pm$ $86$ $434 \pm$ $60$ $911 \pm$ $198$ $816 \pm$ $138$ | 18     22     26 $0 \pm$ $0 \pm$ $0 \pm$ $469 \pm$ $86$ $434 \pm$ $60$ $411 \pm$ $911 \pm$ $198$ $816 \pm$ $138$ | 18     22     26 $0 \pm$ $0$ $0 \pm$ $0$ $469 \pm$ $86$ $434 \pm$ $60$ $421 \pm$ $57$ $911 \pm$ $198$ $816 \pm$ $138$ $809 \pm$ $198$ | 18     22     26     30 $0 \pm$ $0$ $0 \pm$ $0$ $0 \pm$ $469 \pm$ $86$ $434 \pm$ $60$ $421 \pm$ $57$ $911 \pm$ $198$ $816 \pm$ $138$ $809 \pm$ $198$ $764 \pm$ | 18       22       26       30 $0 \pm$ $0$ $0 \pm$ $0$ $0 \pm$ $0$ $469 \pm$ $86$ $434 \pm$ $60$ $421 \pm$ $57$ $401 \pm$ $73$ $911 \pm$ $198$ $816 \pm$ $138$ $809 \pm$ $198$ $764 \pm$ $121$ | 18       22       26       30       34 $0 \pm$ $0$ $0 \pm$ $0$ $0 \pm$ $0$ $0 \pm$ $469 \pm$ $86$ $434 \pm$ $60$ $421 \pm$ $57$ $401 \pm$ $73$ $386 \pm$ $911 \pm$ $198$ $816 \pm$ $138$ $809 \pm$ $198$ $764 \pm$ $121$ $723 \pm$ | 18       22       26       30       34 $0 \pm$ $0$ $0 \pm$ $0$ $0 \pm$ $0$ $0 \pm$ $0$ $469 \pm$ 86 $434 \pm$ 60 $421 \pm$ 57 $401 \pm$ 73 $386 \pm$ 57 $911 \pm$ 198 $816 \pm$ 138 $809 \pm$ 198 $764 \pm$ 121 $723 \pm$ 117 | 18       22       26       30       34       38 $0 \pm 0$ | 18       22       26       30       34       38 $0 \pm 0$ $469 \pm 86$ $434 \pm 60$ $421 \pm 57$ $401 \pm 73$ $386 \pm 57$ $371 \pm 50$ $911 \pm 198$ $816 \pm 138$ $809 \pm 198$ $764 \pm 121$ $723 \pm 117$ $735 \pm 125$ | 18       22       26       30       34       38       42 $0 \pm$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ $0$ |

(HAN300)

 $\sim$ 

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1,j[Cr,j:BDF1] UNIT : mg/kg/day REPORT TYPE : A1 104 SEX : MALE

PAGE: 4

| roup Name                             | Adminis   | stration | (weeks)   |     |           |     |           |     |           |     |           |     |           |     |
|---------------------------------------|-----------|----------|-----------|-----|-----------|-----|-----------|-----|-----------|-----|-----------|-----|-----------|-----|
|                                       | 46        |          | 50        |     | 54        |     | 58        |     | 62        |     | 66        |     | 70        |     |
| · · · · · · · · · · · · · · · · · · · |           |          |           |     |           |     |           |     |           |     |           |     |           |     |
| Control                               | 0±        | 0        | $0\pm$    | 0   | 0±        | 0   | 0±        | 0   | 0±        | 0   | 0±        | 0   | 0±        | 0   |
| 5000 ppm                              | $361\pm$  | 48       | $345\pm$  | 46  | $339\pm$  | 39  | $342\pm$  | 37  | 360±      | 44  | 375±      | 50  | 375±      | 53  |
| 10000 ppm                             | 707±      | 104      | $696\pm$  | 103 | 686±      | 122 | $662\pm$  | 79  | 709±      | 81  | 728±      | 97  | 725±      | 105 |
| 20000 ppm                             | $1358\pm$ | 167      | $1298\pm$ | 151 | $1348\pm$ | 153 | $1327\pm$ | 156 | $1403\pm$ | 152 | $1388\pm$ | 171 | $1422\pm$ | 163 |

(HAN300)

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1] UNIT : mg/kg/day REPORT TYPE : A1 104 SEX : MALE

### CHEMICAL INTAKE CHANGES (SUMMARY) ALL ANIMALS

~\_\_\_\_

 $\overline{\phantom{a}}$ 

PAGE : 5

| Group Name | Adminis   | stration | (weeks)  |     |       |     |           |     |          |     |           |     |           |     |
|------------|-----------|----------|----------|-----|-------|-----|-----------|-----|----------|-----|-----------|-----|-----------|-----|
|            | 74        |          | 78       |     | 82    |     | 86        |     | 90       |     | 94        |     | - 98      |     |
| Control    | 0±        | 0        | 0±       | 0   | 0±    | 0   | 0±        | 0   | 0±       | 0   | 0±        | 0   | 0±        | 0   |
| 5000 ppm   | $381\pm$  | 64       | $401\pm$ | 80  | 406±  | 72  | · 374±    | 90  | 413±     | 94  | 430±      | 107 | 454±      | 123 |
| 10000 ppm  | 733±      | 147      | 793±     | 129 | 796±  | 143 | 793±      | 174 | $768\pm$ | 125 | 814±      | 133 | $864\pm$  | 148 |
| 20000 ppm  | $1446\pm$ | 158      | 1544±    | 210 | 1507± | 205 | $1410\pm$ | 239 | 1512±    | 231 | $1596\pm$ | 400 | $1589\pm$ | 293 |

(HAN300)

BAIS 4

.

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1] UNIT : mg/kg/day REPORT TYPE : A1 104 SEX : MALE

### CHEMICAL INTAKE CHANGES (SUMMARY) ALL ANIMALS

~

PAGE : 6

| Group Name | Administ  | tration | (weeks)   |     |
|------------|-----------|---------|-----------|-----|
| •          | 102       |         | 104       |     |
|            |           |         |           |     |
| Control    | $0\pm$    | 0       | 0±        | 0   |
| 5000 ppm   | $432\pm$  | 111     | $434\pm$  | 123 |
| 10000 ppm  | 872±      | 175     | 874±      | 173 |
| 20000 ppm  | $1654\pm$ | 342     | $1665\pm$ | 388 |

(HAN300)

TABLE F 2

## CHEMICAL INTAKE CHANGES: FEMALE

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:EDF1] UNIT : mg/kg/day REPORT TYPE : A1 104 SEX : FEMALE

PAGE : 7

1

| Group Name | Adminis   | stration | (weeks)  |     |           | •   |          |     |           |     |           |     |           |     |
|------------|-----------|----------|----------|-----|-----------|-----|----------|-----|-----------|-----|-----------|-----|-----------|-----|
|            | 1         |          | 2        |     | 3         |     | 4        |     | 5         |     | 6         |     | 7         |     |
|            |           |          |          |     |           |     |          |     |           |     |           |     |           |     |
| Control    | 0±        | 0        | 0±       | 0   | 0±        | 0   | 0±       | 0   | 0±        | 0   | 0±        | 0   | 0±        | 0   |
| 2500 ppm   | 484±      | 70       | 487±     | 69  | 471±      | 37  | 451±     | 47  | 436±      | 39  | 441±      | 48  | 459±      | 73  |
| 5000 թթա   | $948\pm$  | 97       | $917\pm$ | 90  | 909±      | 83  | $865\pm$ | 70  | $833\pm$  | 68  | 815±      | 79  | 879±      | 87  |
| 10000 ppm  | $1925\pm$ | 207      | 1830±    | 236 | $1809\pm$ | 225 | 1679±    | 216 | $1635\pm$ | 182 | $1639\pm$ | 181 | $1718\pm$ | 200 |
|            |           |          |          |     |           |     |          |     |           |     |           |     |           |     |

(HAN300)

 $\sim$ 

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : mg∕kg⁄day REPORT TYPE : A1 104 SEX : FEMALE

.

PAGE : 8

| Group Name | Adminis   | stration | (weeks)   |     |           |     |           |     |          |     |       |     |           |     |
|------------|-----------|----------|-----------|-----|-----------|-----|-----------|-----|----------|-----|-------|-----|-----------|-----|
|            | 8         |          | 9         |     | 10        |     | 11        |     | 12       |     | 13    |     | 14        |     |
| Control    | 0±        | 0        | 0±        | 0   | 0±        | 0   | 0±        | 0   | 0±       | 0   | .0±   | 0   | 0±        | 0   |
| 2500 ppm   | 419±      | 41       | 408±      | 70  | 395±      | 50  | 394±      | 45  | 387±     | 69  | 374±  | 56  | 368±      | 64  |
| 5000 ppm   | $835\pm$  | 98       | $785\pm$  | 140 | 763±      | 75  | 746±      | 77  | $763\pm$ | 81  | 713±  | 83  | 732±      | 105 |
| 10000 ppm  | $1649\pm$ | 173      | $1538\pm$ | 187 | $1561\pm$ | 193 | $1540\pm$ | 187 | 1494±    | 162 | 1444± | 194 | $1399\pm$ | 155 |
|            |           |          |           |     |           |     |           |     |          |     |       |     |           |     |

(HAN300)

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : mg/kg/day REPORT TYPE : A1 104 SEX : FEMALE

PAGE : 9

| Group Name | Admini    | stration | (weeks)   |     |           |     |           |     |          |     |           |     |           |     |
|------------|-----------|----------|-----------|-----|-----------|-----|-----------|-----|----------|-----|-----------|-----|-----------|-----|
|            | 18        |          | 22        |     | 26        |     | 30        |     | 34       |     | 38        |     | 42        |     |
| Control    | 0±        | 0        | 0±        | 0   | 0±        | 0   | 0±        | 0   | 0±       | 0   | 0±        | 0   | 0±        | 0   |
| 2500 ppm   | $360\pm$  | 57       | 341±      | 42  | 335±      | 60  | $316\pm$  | 48  | 308±     | 74  | 300±      | 48  | 288±      | 57  |
| 5000 yym   | $697\pm$  | 88       | $697\pm$  | 87  | 672±      | 85  | $606\pm$  | 93  | $629\pm$ | 97  | 611±      | 88  | 610±      | 143 |
| 10000 ppm  | $1386\pm$ | 154      | $1311\pm$ | 174 | $1332\pm$ | 365 | $1183\pm$ | 222 | 1191±    | 265 | $1135\pm$ | 195 | $1121\pm$ | 213 |

(HAN300)

 $\sim -$ 

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1,j[Cr,j:BDF1] UNIT : mg/kg/day REPORT TYPE : A1 104 SEX : FEMALE

PAGE : 10

| Group Name | Adminis | stration | (weeks)   |     |       |     |          |     |          |     |           |     |          |     |
|------------|---------|----------|-----------|-----|-------|-----|----------|-----|----------|-----|-----------|-----|----------|-----|
|            | 46      |          | 50        |     | 54    |     | 58       |     | 62       |     | 66        |     | 70       |     |
| Control    | 0±      | 0        | 0±        | 0   | 0±    | 0   | 0±       | 0   | 0±       | 0   | 0±        | 0   | 0±       | 0   |
| 2500 ppm   | 283±    | 61       | 269±      | 78  | 271±  | 79  | 261±     | 67  | $265\pm$ | 61  | 269±      | 75  | $267\pm$ | 47  |
| 5000 ppm   | 551±    | 122      | $535\pm$  | 95  | 532±  | 99  | $504\pm$ | 89  | $536\pm$ | 93  | $516\pm$  | 99  | $534\pm$ | 150 |
| 10000 ppm  | 1060土   | 210      | $1020\pm$ | 213 | 1041± | 192 | 994±     | 176 | $997\pm$ | 189 | $1006\pm$ | 200 | $936\pm$ | 176 |

(HAN300)

BAIS 4

-

### STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : mg/kg/day REPORT TYPE : A1 104 SEX : FEMALE

### CHEMICAL INTAKE CHANGES (SUMMARY) ALL ANIMALS

PAGE : 11

| Group Name | Admini | stration | (weeks)   |     |       |     |           |     |          |     |           |     |          |     |
|------------|--------|----------|-----------|-----|-------|-----|-----------|-----|----------|-----|-----------|-----|----------|-----|
|            | 74     |          | 78        |     | 82    |     | 86        |     | 90       |     | 94        |     | 98       |     |
|            |        |          |           |     |       |     |           |     |          |     |           |     |          |     |
| Control    | 0±     | 0        | 0±        | 0   | 0±    | 0   | 0±        | 0   | 0±       | 0   | 0±        | 0   | 0±       | 0   |
| 2500 ppm   | 286±   | 73       | 275±      | 78  | 276±  | 78  | 247±      | 53  | $259\pm$ | 61  | 275±      | 64  | 288±     | 58  |
| 5000 ppm   | 523±   | 104      | 520±      | 117 | 543±  | 117 | $524\pm$  | 126 | 526±     | 151 | $545\pm$  | 128 | $561\pm$ | 133 |
| 10000 ppm  | 1008±  | 200      | $1048\pm$ | 259 | 1004± | 177 | $1006\pm$ | 248 | $978\pm$ | 286 | $1046\pm$ | 196 | 1049±    | 242 |

(HAN300)

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : mg/kg/day REPORT TYPE : A1 104 SEX : FEMALE

### CHEMICAL INTAKE CHANGES (SUMMARY) ALL ANIMALS

PAGE : 12

•

| Group Name | Admin<br>102 | nistration | (weeks)<br>104 |     |  | <br> |  | <br> |  |
|------------|--------------|------------|----------------|-----|--|------|--|------|--|
| Control    | 0±           | 0          | 0±             | 0   |  | <br> |  |      |  |
| 2500 ppm   | 281±         | 64         | 281±           | 104 |  |      |  |      |  |
| 5000 ppm   | 548±         | 131        | $548\pm$       | 152 |  |      |  |      |  |
| 10000 ppm  | 1145±        | 225        | $1220\pm$      | 353 |  |      |  |      |  |

(HAN300)

BAIS 4

.

## TABLE G 1

### HEMATOLOGY: MALE

| STUDY NO. : 0613<br>ANIMAL : MOUSE<br>MEASURE. TIME : 1 | B6D2F1/Cr1,j[Cr,j:BDF1] | HEMATOLOGY (SUMMARY)<br>ALL ANIMALS (105W) |
|---------------------------------------------------------|-------------------------|--------------------------------------------|
| SEX : MALE                                              | REPORT TYPE : AI        |                                            |

PAGE : 1 )

| Group Name | NO. of<br>Animals | RED BLOOD CELL<br>1 0 <sup>6</sup> /µl | HEMOGLOBIN<br>g∕dl | HEMATOCRIT<br>% | MCV<br>f <b>l</b> | MCH<br>pg | MCHC<br>g∕dℓ | PLATELET<br>1 O³/µl |
|------------|-------------------|----------------------------------------|--------------------|-----------------|-------------------|-----------|--------------|---------------------|
| Control    | 35                | 9.25± 1.98                             | 13.5± 2.7          | 42.2± 7.2       | 46.4± 4.9         | 14.6± 0.8 | 31.7± 1.8    | $1653 \pm 373$      |
| 5000 ppm   | 32                | 9.06± 1.71                             | 13. $3\pm$ 2. 4    | 41.6± 6.6       | 46.6± 3.7         | 14.7± 0.6 | 31.7± 1.7    | 1577± 416           |
| 10000 ppm  | 36                | 9.45± 1.03                             | 13.8± 1.4          | 43.1± 3.8       | 45.8± 2.3         | 14.7± 0.8 | 32.0± 0.7    | 1579± 391           |
| 20000 ррт  | 39                | $9.56 \pm 0.54$                        | 14.1± 0.9          | 43.9± 2.4       | 46.0土 1.1         | 14.8± 0.4 | 32.2土 0.7    | $1548 \pm 334$      |

(HCL070)

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj;BDF1] MEASURE. TIME : 1 SEX : MALE REPORT TYPE : A1

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

**\*\*** : P ≦ 0.01

HEMATOLOGY (SUMMARY) ALL ANIMALS (105W)

SEX : MALE PAGE : 2 NO. of RETICULOCYTE Group Name Animals % 35  $3.5 \pm 3.7$ Control 3.6± 3.9 5000 ppm 32 10000 ppm 36 2.7± 1.0 20000 ppm 39 2.5 ± 0.9

.

Test of Dunnett

(HCL070)

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] MEASURE. TIME : 1 SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY) ALL ANIMALS (105W)

PAGE : 3

| NO. of<br>Animals | WBC<br>1 O <sup>3</sup> /µl | Dif<br>N-BAND                                                                                                                                      | ferential                                                                                                                                                                                                  | WBC (%<br>N-SEG                                                                                                                                                                                    | <b>6</b> )                                                                                                                                                                                                                                                                        | EOSINO                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                   | BASO                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                            | MONO                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                          | LYMPHO                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                  | OTHER                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|-------------------|-----------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 35                | . 4.62± 2.54                | $2\pm$                                                                                                                                             | 5                                                                                                                                                                                                          | 29±                                                                                                                                                                                                | 13                                                                                                                                                                                                                                                                                | 2土                                                                                                                                                                                                                                                                                                                  | 1                                                                                                                                                                                                                                                                                                                                                                                 | 0±                                                                                                                                                                                                                                                                                                                                                                                             | 0                                                                                                                                                                                                                                                                                                                                                                          | 4±                                                                                                                                                                                                                                                                                                                                                                                             | 2                                                                                                                                                                                                                                                                                                                                                                                                                                        | 62±                                                                                                                                                                                                                                                                                                                                                                  | 17                                                                                                                                                                                                                                                                                                                                                                                                                               | 1±                                                                                                                                                                                                                                                                                                                                                                                                                        | 4                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| 32                | 4.31± 2.26                  | 1±                                                                                                                                                 | 3                                                                                                                                                                                                          | 25±                                                                                                                                                                                                | 12                                                                                                                                                                                                                                                                                | 2±                                                                                                                                                                                                                                                                                                                  | 1                                                                                                                                                                                                                                                                                                                                                                                 | 0±                                                                                                                                                                                                                                                                                                                                                                                             | 0                                                                                                                                                                                                                                                                                                                                                                          | 4±                                                                                                                                                                                                                                                                                                                                                                                             | 2                                                                                                                                                                                                                                                                                                                                                                                                                                        | 68±                                                                                                                                                                                                                                                                                                                                                                  | 14                                                                                                                                                                                                                                                                                                                                                                                                                               | 1±                                                                                                                                                                                                                                                                                                                                                                                                                        | 2                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| 36                | 4.60± 2.66                  | 1±                                                                                                                                                 | 1                                                                                                                                                                                                          | 24±                                                                                                                                                                                                | 10                                                                                                                                                                                                                                                                                | 3±                                                                                                                                                                                                                                                                                                                  | 3                                                                                                                                                                                                                                                                                                                                                                                 | 0±                                                                                                                                                                                                                                                                                                                                                                                             | 0                                                                                                                                                                                                                                                                                                                                                                          | $5\pm$                                                                                                                                                                                                                                                                                                                                                                                         | 2                                                                                                                                                                                                                                                                                                                                                                                                                                        | 66±                                                                                                                                                                                                                                                                                                                                                                  | 11                                                                                                                                                                                                                                                                                                                                                                                                                               | 1±                                                                                                                                                                                                                                                                                                                                                                                                                        | 4                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| 39                | 4.07± 2.05                  | 1±                                                                                                                                                 | 1                                                                                                                                                                                                          | 28±                                                                                                                                                                                                | 16                                                                                                                                                                                                                                                                                | 2土                                                                                                                                                                                                                                                                                                                  | 1                                                                                                                                                                                                                                                                                                                                                                                 | 0±                                                                                                                                                                                                                                                                                                                                                                                             | 0                                                                                                                                                                                                                                                                                                                                                                          | 4土                                                                                                                                                                                                                                                                                                                                                                                             | 2                                                                                                                                                                                                                                                                                                                                                                                                                                        | $65\pm$                                                                                                                                                                                                                                                                                                                                                              | 16                                                                                                                                                                                                                                                                                                                                                                                                                               | 0土                                                                                                                                                                                                                                                                                                                                                                                                                        | 1                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|                   | Animals<br>35<br>32<br>36   | Animals         1 $0^3 / \mu \ell$ 35         . 4.62±         2.54           32         4.31±         2.26           36         4.60±         2.66 | Animals         1 $O^3 / \mu \ell$ N-BAND           35         . 4.62 ±         2.54         2 ±           32         4.31 ±         2.26         1 ±           36         4.60 ±         2.66         1 ± | Animals       1 $O^3 / \mu \ell$ N-BAND         35       . 4.62±       2.54       2±       5         32       4.31±       2.26       1±       3         36       4.60±       2.66       1±       1 | Animals         1 $0^3 / \mu^2$ N-BAND         N-SEG           35         . 4.62±         2.54         2±         5         29±           32         4.31±         2.26         1±         3         25±           36         4.60±         2.66         1±         1         24± | Animals         1 $0^3 / \mu \ell$ N-BAND         N-SEG           35         4.62±         2.54         2±         5         29±         13           32         4.31±         2.26         1±         3         25±         12           36         4.60±         2.66         1±         1         24±         10 | Animals         1 $0^3 / \mu \ell$ N-BAND         N-SEG         EOSINO           35         . 4.62 ±         2.54         2 ±         5         29 ±         13         2 ±           32         4.31 ±         2.26         1 ±         3         25 ±         12         2 ±           36         4.60 ±         2.66         1 ±         1         24 ±         10         3 ± | Animals         1 $0^3 / \mu^2$ N-BAND         N-SEG         EOSINO           35         4.62±         2.54         2±         5         29±         13         2±         1           32         4.31±         2.26         1±         3         25±         12         2±         1           36         4.60±         2.66         1±         1         24±         10         3±         3 | Animals       1 $0^3 / \mu^2$ N-BAND       N-SEG       EOSINO       BASO         35       . 4.62±       2.54       2±       5       29±       13       2±       1       0±         32       4.31±       2.26       1±       3       25±       12       2±       1       0±         36       4.60±       2.66       1±       1       24±       10       3±       3       0± | Animals       1 $0^3 / u^2$ N-BAND       N-SEG       EOSINO       BASO         35       4.62±       2.54       2±       5       29±       13       2±       1       0±       0         32       4.31±       2.26       1±       3       25±       12       2±       1       0±       0         36       4.60±       2.66       1±       1       24±       10       3±       3       0±       0 | Animals       1 $0^3 / \mu^2$ N-BAND       N-SEG       EOSINO       BASO       MONO         35       . 4.62±       2.54       2±       5       29±       13       2±       1       0±       0       4±         32       4.31±       2.26       1±       3       25±       12       2±       1       0±       0       4±         36       4.60±       2.66       1±       1       24±       10       3±       3       0±       0       5± | Animals     1 $0^3 / u^2$ N-BAND     N-SEG     EOSINO     BASO     MONO       35     4.62±     2.54     2±     5     29±     13     2±     1     0±     0     4±     2       32     4.31±     2.26     1±     3     25±     12     2±     1     0±     0     4±     2       36     4.60±     2.66     1±     1     24±     10     3±     3     0±     0     5±     2 | Animals $1 0^3 / u^2$ N-BAND       N-SEG       EOSINO       BASO       MONO       LYMPHO         35 $4.62 \pm 2.54$ $2 \pm 5$ $29 \pm 13$ $2 \pm 1$ $0 \pm 0$ $4 \pm 2$ $62 \pm$ 32 $4.31 \pm 2.26$ $1 \pm 3$ $25 \pm 12$ $2 \pm 1$ $0 \pm 0$ $4 \pm 2$ $68 \pm$ 36 $4.60 \pm 2.66$ $1 \pm 1$ $24 \pm 10$ $3 \pm 3$ $0 \pm 0$ $5 \pm 2$ $66 \pm$ 39 $4.07 \pm 2.05$ $1 \pm 1$ $28 \pm 16$ $2 \pm 1$ $0 \pm 0$ $4 \pm 2$ $65 \pm$ | Animals $1 \ 0^3 / \mu^2$ N-BAND       N-SEG       EOSINO       BASO       MONO       LYMPHO         35 $4.62 \pm 2.54$ $2\pm 5$ $29 \pm 13$ $2\pm 1$ $0\pm 0$ $4\pm 2$ $62\pm 17$ 32 $4.31 \pm 2.26$ $1\pm 3$ $25\pm 12$ $2\pm 1$ $0\pm 0$ $4\pm 2$ $68\pm 14$ 36 $4.60 \pm 2.66$ $1\pm 1$ $24\pm 10$ $3\pm 3$ $0\pm 0$ $5\pm 2$ $66\pm 11$ 39 $4.07 \pm 2.05$ $1\pm 1$ $28\pm 16$ $2\pm 1$ $0\pm 0$ $4\pm 2$ $65\pm 16$ | Animals $1 \ 0^3 / \mu \ell$ N-BAND       N-SEG       EOSINO       BASO       MONO       LYMPHO       OTHER         35 $4.62 \pm 2.54$ $2\pm 5$ $29\pm 13$ $2\pm 1$ $0\pm 0$ $4\pm 2$ $62\pm 17$ $1\pm$ 32 $4.31 \pm 2.26$ $1\pm 3$ $25\pm 12$ $2\pm 1$ $0\pm 0$ $4\pm 2$ $68\pm 14$ $1\pm$ 36 $4.60 \pm 2.66$ $1\pm 1$ $24\pm 10$ $3\pm 3$ $0\pm 0$ $5\pm 2$ $66\pm 11$ $1\pm 3$ 39 $4.07 \pm 2.05$ $1\pm 1$ $28\pm 16$ $2\pm 1$ $0\pm 0$ $4\pm 2$ $65\pm 16$ $0\pm$ |

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

(HCL070)

### TABLE G 2

## HEMATOLOGY: FEMALE

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1;[Cr;:BDF1] MEASURE. TIME : 1 SEX : FEMALE REPORT TYPE : A1

### HEMATOLOGY (SUMMARY) ALL ANIMALS (105W)

#### Group Name NO. of RED BLOOD CELL HEMOGLOBIN HEMATOCRIT MCV MCH MCHC PLATELET Animals 1 0<sup>6</sup>∕µl g∕dl % f L g∕dℓ $10^3/\mu\ell$ рg Control 27 9.44± 1.16 14.0± 1.8 43.8± 4.9 46.5 $\pm$ 1.5 14.8± 0.5 32.0± 1.1 967± 313 2500 ppm 258.76± 1.67 $13.2 \pm$ 2.241.8± 5.2 $48.8 \pm$ 6.8 15.2± 0.9 31.4± 2.1 $1012\pm$ 423 5000 ррт 30 9.46± 0.93 13.9± 1.5 43.3± 3.8 $45.9\pm$ 1.8 14.7± 0.6 32.1± 1.0 $980\pm$ 339 10000 ppm 18 9.25± 1.07 13.7± 1.9 42.5± 4.6 46.1± 2.2 14.8土 0.8 $32.2 \pm 1.1$ $1049\pm$ 250

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

Test of Dunnett

(HCL070)

BAIS 4

#### PAGE : 4

| STUDY NO. : 06<br>ANIMAL : MO<br>MEASURE. TIME | USE B6D2F1/Cr1j   | [Crj:BDF1]      |     | GY (SUMMARY)<br>Als (105W) |      |          |
|------------------------------------------------|-------------------|-----------------|-----|----------------------------|------|----------|
| SEX : FEMALE                                   | REPORT 7          | ГҮРЕ : АІ       |     |                            |      | PAGE : 5 |
| Group Name                                     | NO. of<br>Animals | RETICULOCY<br>% | re  |                            |      |          |
| Control                                        | 27                | 3.6± 2.         | 6   |                            |      |          |
| 2500 ppm                                       | 25                | 6.7± 10.        | 8   |                            |      |          |
| 5000 ppm                                       | 30                | 4.1± 4.         | . 2 |                            |      |          |
| 10000 ppm                                      | 18                | 4.0± 3.         | 8   |                            |      |          |
|                                                |                   |                 |     | <br>                       | <br> | <br>     |

Test of Dunnett

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

(HCL070)

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] MEASURE. TIME : 1 SEX : FEMALE REPORT TYPE : A1

ALL ANIMALS (105W)

 $\sim \sim$ 

#### NO. of WBC Differential WBC (%) Group Name Animals $10^3/\mu\ell$ N-SEG EOSINO BASO N-BAND Control 27 11.42± 36.08 $1\pm$ 1 $19\pm$ 8 $3\pm$ 4 $0\pm$

2500 ppm 2522.16± 96.11  $2\pm$  $28\pm$ 3 14  $3\pm$ 4 0± 0  $4\pm$ 2  $56\pm$ 20  $6\pm$ 5000 ppm 30 4.17± 2.97  $1\pm$  $21\pm$ 1 10  $1\pm$ 1  $0\pm$ 0  $4\pm$ 2  $68\pm$ 13  $5\pm$ 10000 ppm 18 3.46± 2.90  $1\pm$ 1  $27\pm$ 16  $2\pm$ 1  $0\pm$ 0  $5\pm$  $62\pm$ 18  $4\pm$ 2 **\*\*** : P ≦ 0.01 Test of Dunnett

Significant difference ;  $*: P \leq 0.05$ 

(HCL070)

BAIS 4



21

19

9

6

OTHER

 $7\pm$ 

.

MONO

 $4\pm$ 

2

0

LYMPHO

 $67\pm$ 

17

HEMATOLOGY (SUMMARY)

## TABLE H 1

# BIOCHEMISTRY: MALE

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] MEASURE. TIME : 1 SEX : MALE REPORT TYPE : A1

### BIOCHEMISTRY (SUMMARY) ALL ANIMALS (105W)

| SEX : MALE | REPORT 1          | YPE : A1              |                 |           |                      |                    |                        | PAGE :                |
|------------|-------------------|-----------------------|-----------------|-----------|----------------------|--------------------|------------------------|-----------------------|
| 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    | 35                | 5.0± 0.8              | 2.3± 0.4        | 0.9± 0.1  | 0.13± 0.03           | $156 \pm 52$       | 112± 41                | 46± 27                |
| 000 ppm    | 32                | 5.0 $\pm$ 0.8         | 2.4± 0.4        | 1.0± 0.2  | 0.13± 0.03           | 175± 38            | 110± 45                | 45± 22                |
| 0000 ppm   | 36                | 5.4± 0.9              | 2.6± 0.4        | 0.9± 0.1  | 0.13± 0.02           | 194± 26 <b>**</b>  | 127± 52                | 45± 18                |
| 20000 ppm  | 40                | 5.0 $\pm$ 0.5         | 2.4± 0.3        | 1.0± 0.1* | 0.13± 0.03           | 190± 41 <b>*</b> ≉ | $105 \pm 30$           | 44± 24                |

`~\_\_\_\_`

(HCL074)

BAIS 4

,

| SEX : MALE | REPORT 1          | TYPE : Al             |                      |             |             |              |               | PAGE : :            |
|------------|-------------------|-----------------------|----------------------|-------------|-------------|--------------|---------------|---------------------|
| Group Name | NO. of<br>Animals | PHOSPHOLIPID<br>mg∕dℓ | AST<br>I U∕ <b>£</b> | ALT<br>IU⁄£ | LDH<br>IU∕¢ | ALP<br>IU∕ℓ  | G-GTP<br>IU∕ℓ | CK<br>I U∕ <b>£</b> |
| Control    | 35                | 186± 61               | 174± 292             | 97± 169     | 571± 667    | 136± 48      | 1± 1          | 91± 115             |
| 5000 ppm   | 32                | 194± 72               | 74± 47               | 44± 73      | 424± 393    | 139± 131     | 1± 1          | 60± 33              |
| 10000 ppm  | 36                | 219± 67               | 98± 140              | 73± 132     | 452± 277    | 133± 43      | 1± 1          | $55\pm$ 23          |
| 20000 ppm  | 40                | 185± 40               | $79 \pm 103$         | 32± 44*     | 409± 192    | $135 \pm 35$ | 1± 1          | $59\pm$ 30          |

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

(HCL074)

Test of Dunnett

BAIS 4

# BIOCHEMISTRY (SUMMARY) ALL ANIMALS (105W)

 $\sim$  .

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] MEASURE. TIME : 1 SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (105W)

 $\sim$ 

|            |                   |                        |                         |   |                 |      | •                 |   |                  |     |                  |                |  |
|------------|-------------------|------------------------|-------------------------|---|-----------------|------|-------------------|---|------------------|-----|------------------|----------------|--|
| Group Name | NO. of<br>Animals | UREA NITROGEN<br>mg∕d£ | SODIUM<br>mEq⁄ <b>L</b> |   | POTASSI<br>mEq/ |      | CHLORIDE<br>mEq⁄£ |   | CALCIUN<br>mg∕dℓ | [   | INORGAN<br>mg∕dl | VIC PHOSPHORUS |  |
| Control    | 35                | 28.6± 21.1             | 154土                    | 2 | 4.6±            | 0.9  | $122\pm$          | 5 | 8.7±             | 0.5 | 6.1±             | 0.9            |  |
| 000 ppm    | 32                | 24.4± 9.9              | $153\pm$                | 3 | 4.2±            | 0.3* | $121\pm$          | 4 | 8.7±             | 0.4 | 5.8±             | 0.8            |  |
| mqq 0000   | 36                | 22.5± 3.4              | $153\pm$                | 2 | 4.2±            | 0.3  | 120±              | 3 | 8.9±             | 0.6 | 5.7±             | 0.6            |  |
| 0000 ppm   | 40                | 22.7± 10.1*            | $153\pm$                | 2 | 4.3±            | 0.3  | $121\pm$          | 2 | $8.6\pm$         | 0.3 | 5.8±             | 0.8            |  |

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

Test of Dunnett

~~

(HCL074)

### TABLE H 2

# BIOCHEMISTRY: FEMALE

STUDY NO. : 0613 BIOCHEMISTRY (SUMMARY) ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] ALL ANIMALS (105W) MEASURE. TIME : 1 SEX : FEMALE REPORT TYPE : A1

.

PAGE: 4

| Group Name | NO. of<br>Animals | TOTAL H<br>g∕dl | PROTEIN | ALBUMIN<br>g∕dl | I    | A/G RAT | 10  | T-BILI<br>mg∕dℓ |       | GLUCOSE<br>mg∕dl |    | T−CHOLE<br>mg∕dℓ | STEROL | TRIGLYC<br>mg∕d£ | ERIDE |
|------------|-------------------|-----------------|---------|-----------------|------|---------|-----|-----------------|-------|------------------|----|------------------|--------|------------------|-------|
| ontrol     | 28                | 5.0土            | 0. 6    | 2.5±            | 0. 3 | 1.0土    | 0.2 | 0.14±           | 0.05  | 134±             | 31 | 82土              | 28     | 52±              | 38    |
| 2500 ppm   | 25                | 5.2±            | 0.9     | 2.5±            | 0.3  | 1.0±    | 0.3 | 0.18±           | 0.17  | $136\pm$         | 30 | 86±              | 36     | 37±              | 21    |
| 5000 ppm   | 31                | 4.9±            | 0.4     | 2.5±            | 0.2  | 1.0±    | 0.2 | 0.14±           | 0.05  | 138±             | 37 | 74±              | 25     | 36±              | 20    |
| 10000 ppm  | 19                | 5.1±            | 0.5     | $2.5\pm$        | 0.2  | 1.0±    | 0.2 | 0.13±           | 0. 03 | 147±             | 20 | $82\pm$          | 24     | $38\pm$          | 25    |

### 

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] MEASURE. TIME : 1 DEDODT TYDE

### BIOCHEMISTRY (SUMMARY) ALL ANIMALS (105W)

----

| SEX : FEMALE | REPORT 1          | ГҮРЕ : АІ             |              |        |          |             |               | PAGE : 5            |
|--------------|-------------------|-----------------------|--------------|--------|----------|-------------|---------------|---------------------|
| Group Name   | NO. of<br>Animals | PHOSPHOLIPID<br>mg∕dl | AST<br>IU∕₽  |        |          | ALP<br>IU∕₽ | G−GTP<br>IU∕£ | ск<br>I U∕ <b>£</b> |
| Control      | 28                | $145 \pm 42$          | $141\pm$ 156 | 53± 40 | 467± 266 | $234\pm159$ | 1± 1          | 82± 45              |
| 2500 ppm     | 25                | 151± 65               | 127± 99      | 60± 63 | 719± 872 | 173± 70     | 1± 1          | $118 \pm 153$       |
| 5000 ppm     | 31                | 138± 39               | 142± 142     | 52± 60 | 602± 648 | 194± 79     | 1± 1          | 97± 91              |
| 10000 ppm    | 19                | 149± 36               | 100± 45      | 29± 9  | 573± 631 | 170± 67     | 1± 0          | 104土 60             |
|              |                   |                       |              |        |          |             |               |                     |

Test of Dunnett

 $\sim \sim$ 

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

(HCL074)

 STUDY NO. : 0613

 ANIMAL
 : MOUSE B6D2F1/Cr1j[Cr.j:BDF1]

 MEASURE. TIME : 1

 SEX : FEMALE
 REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (105W)

 $\sim \sim$ 

#### NO. of UREA NITROGEN SODIUM Group Name POTASSIUM CHLORIDE CALCIUM INORGANIC PHOSPHORUS Animals mg∕dℓ mEq∕ℓ mEq∕**ℓ** mEq∕ℓ mg∕dl mg∕dℓ Control 2816.8± 5.9 $152\pm$ 2 4.2± 0.4 $121\pm$ 3 9.0± 0.4 6.1± 1.1 2500 ppm 2520.7± 11.6 $152\pm$ 2 4.3± 0.5 $121\pm$ 3 $9.0\pm$ 0.5 6.3± 1.5 5000 ppm 31 19.0± 10.0 $152\pm$ 2 4.3± 0.6 $121\pm$ 2 $8.9\pm$ 0.4 6.3± 1.3 10000 ppm 19 18.0± 4.4 $151\pm$ 2 4.1± 0.4 $120\pm$ 3 8.8± 0.5 5.9± 1.0

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

Test of Dunnett

(HCL074)

BAIS 4

#### PAGE : 6

# TABLE I 1

# URINALYSIS: MALE

| roup Name  | NO. of  | pH_ |   |     |     |     |     |     |     | Protein       |     | <u>(1)</u>                                                                              | Katana ka ka                        | 0 1 1 1 1                           |
|------------|---------|-----|---|-----|-----|-----|-----|-----|-----|---------------|-----|-----------------------------------------------------------------------------------------|-------------------------------------|-------------------------------------|
| noup walle | Animals |     |   | 6.5 | 7.0 | 7.5 | 8.0 | 8.5 | CHI | $-\pm+2+3+4+$ | CHI | $\begin{array}{rrrr} \text{Glucose}_{-} \\ - \pm + 2 + 3 + 4 + \end{array}  \text{CHI}$ | Ketone body $ \pm$ $+$ 2+ 3+ 4+ CHI | Occult blood<br>$- \pm + 2+ 3+$ CHI |
|            |         |     |   |     |     |     |     |     |     |               |     |                                                                                         |                                     |                                     |
| ontrol     | 33      | 0   | 3 | 9   | 8   | 12  | 1   | 0   |     | 0 17 14 1 1 0 |     | 33 0 0 0 0 0                                                                            | 15 9 9 0 0 0                        | 27 0 1 1 4                          |
| 000 ppm    | 33      | 0   | 1 | 11  | 17  | 4   | 0   | 0   |     | 0 10 16 6 1 0 |     | 33 0 0 0 0 0                                                                            | 8 12 12 1 0 0                       | 29 0 0.0 4                          |
| 0000 ppm   | 36      | 0   | 3 | 16  | 15  | 2   | 0   | 0   | *   | 0 4 18 14 0 0 | **  | 36 0 0 0 0 0                                                                            | 8 12 14 2 0 0                       | 32 0 0 0 4                          |
| 000 ppm    | 40      | 0   | 4 | 25  | 9   | 2   | 0   | 0   | **  | 0 10 26 4 0 0 |     | 40 0 0 0 0 0                                                                            | 12 12 16 0 0 0                      | 38 0 0 0 2                          |

(HCL101)

| Group Name | NO. of<br>Animals | Urobilinogen<br>± + 2+ 3+ 4+ CHI      |      |     |                                       |  |
|------------|-------------------|---------------------------------------|------|-----|---------------------------------------|--|
|            |                   | · · · · · · · · · · · · · · · · · · · | <br> | *** | · · · · · · · · · · · · · · · · · · · |  |
| Control    | 33                | 33 0 0 0 0                            |      |     |                                       |  |
| 5000 ppm   | 33                | 33 0 0 0 0                            |      |     |                                       |  |
| 10000 ppm  | 36                | 36 0 0 0 0                            |      |     |                                       |  |
| 20000 ppm  | 40                | 40 0 0 0 0                            |      |     |                                       |  |

 $\sim$ 

# TABLE I 2

# URINALYSIS: FEMALE

| roup Name | NO. of  | pH_  |     |     |     |     |     |     |     | Protein            | Glucose          | Ketone body        | Occult blood       |
|-----------|---------|------|-----|-----|-----|-----|-----|-----|-----|--------------------|------------------|--------------------|--------------------|
|           | Animals | 5. 0 | 6.0 | 6.5 | 7.0 | 7.5 | 8.0 | 8.5 | CHI | - ± + 2+ 3+ 4+ CHI | ± + 2+ 3+ 4+ CHI | - ± + 2+ 3+ 4+ CHI | $-\pm$ + 2+ 3+ CHI |
| ontrol    | 30      | 0    | 2   | 4   | 0   | 9   | 11  | 4   |     | 0 4 15 9 2 0       | 30 0 0 0 0 0     | 6 18 3 3 0 0       | 25 0 0 4 1         |
| 500 ppm   | 26      | 0    | 3   | 6   | 6   | 5   | 5   | 1   | *   | 0 1 7 17 1 0       | 26 0 0 0 0 0     | 1 15 6 4 0 0       | 17 1 4 1 3         |
| 000 ppm   | 32      | 0    | 2   | 4   | 5   | 11  | 9   | 1   |     | 0 1 18 12 1 0      | 32 0 0 0 0 0     | 0 18 10 4 0 0 *    | 28 0 1 0 3         |
| 0000 ppm  | 21      | 0    | 1   | 2   | 6   | 10  | 1   | 1   | **  | 0 1 10 8 2 0       | 21 0 0 0 0 0     | 2 12 4 3 0 0       | 20 0 0 0 1         |

~~

(HCL101)

|                               | DUSE B6D2F1/Cr1   | j[Crj:BDF1]                      | URINALYSIS | S |                                       |      |            |
|-------------------------------|-------------------|----------------------------------|------------|---|---------------------------------------|------|------------|
| MEASURE. TIME<br>SEX : FEMALE |                   | TYPE : AI                        |            |   |                                       |      | PAGE : 4   |
| Group Name                    | NO. of<br>Animals | Urobilinogen<br>± + 2+ 3+ 4+ CHI |            |   |                                       |      |            |
|                               |                   |                                  |            |   |                                       |      | <br>·      |
| Control                       | 30                | 30 0 0 0 0                       |            |   |                                       |      |            |
| 2500 ppm                      | 26                | 26 0 0 0 0                       |            |   |                                       |      |            |
| 5000 ppm                      | 32                | 32 0 0 0 0                       |            |   |                                       |      |            |
| 10000 ppm                     | 21                | 21 0 0 0 0                       |            |   |                                       |      |            |
|                               |                   |                                  |            |   |                                       | <br> |            |
| Significar                    | nt difference     | $* : P \leq 0.05$ ** : P         | ≦ 0.01     |   | Test of CHI SQUARE                    |      |            |
| (HCL101)                      |                   |                                  |            |   | · · · · · · · · · · · · · · · · · · · | <br> | <br>BAIS 4 |

 $\sim$ 

TABLE J 1

# GROSS FINDINGS: MALE: ALL ANIMALS

## STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 SEX : MALE

# GROSS FINDINGS (SUMMARY)

ALL ANIMALS (0-105W)

| EX :       | MALE                       |                              |                   |                    |                      | PAGE :              |
|------------|----------------------------|------------------------------|-------------------|--------------------|----------------------|---------------------|
| rgan       | Findings                   | Group Name<br>NO. of Animals | Control<br>50 (%) | 5000 ppm<br>50 (%) | 10000 ppm<br>·50 (%) | 20000 ppm<br>50 (%) |
| lin (ann   | -                          |                              | D ( 1)            |                    |                      |                     |
| kin/app    | erosion                    |                              | 2 (4)             | 0 ( 0)             | 0 ( 0)               | 0 ( 0)              |
|            | scab                       |                              | 1 ( 2)            | 3 (6)              | 1 ( 2)               | 1 (2)               |
| ubcutis    | edema                      |                              | 0 ( 0)            | 0 ( 0)             | 0 ( 0)               | 1 (2)               |
|            | mass                       |                              | 4 (8)             | 2 ( 4)             | 1 (2)                | 0 ( 0)              |
| ung        | red                        |                              | 0 ( 0)            | 1 ( 2)             | 0 ( 0)               | 1 ( 2)              |
|            | white zone                 |                              | 0 ( 0)            | 0 ( 0)             | 1 ( 2)               | 0 ( 0)              |
|            | red zone                   |                              | 0 ( 0)            | 1 ( 2)             | 0 ( 0)               | 0 ( 0)              |
|            | nodule                     |                              | 9 (18)            | 12 (24)            | 9 (18)               | 9 (18)              |
|            | adhesion                   |                              | 1 (2)             | 0 ( 0)             | 0 ( 0)               | 0 ( 0)              |
| ymph node  | enlarged                   |                              | 13 (26)           | 6 (12)             | 3 (6)                | 5 (10)              |
| •          | nodule                     |                              | 0 ( 0)            | 1 ( 2)             | 0 ( 0)               | 0 ( 0)              |
| pleen      | enlarged                   |                              | 8 (16)            | 1 (2)              | 1 (2)                | 2 (4)               |
|            | white zone                 |                              | 0 ( 0)            | 0 ( 0)             | 0 ( 0)               | 1 ( 2)              |
|            | red zone                   |                              | 1 (2)             | 0 ( 0)             | 0 ( 0)               | 0 ( 0)              |
|            | black zone                 |                              | 1 (2)             | 0 ( 0)             | 0 ( 0)               | 2 ( 4)              |
|            | nodule                     |                              | 2 (4)             | 0 ( 0)             | 3 (6)                | 2 (4)               |
|            | deformed                   |                              | 0 ( 0)            | 1 (2)              | 1 (2)                | 0 ( 0)              |
|            | accentuation of white pulp |                              | 0 ( 0)            | 1 ( 2)             | 0 ( 0)               | 1 (2)               |
| eart       | white zone                 |                              | 0 ( 0)            | 0 ( 0)             | 0 ( 0)               | 1 (2)               |
| alivary gl | nodule                     |                              | 0 ( 0)            | 1 ( 2)             | 0 ( 0)               | 0 ( 0)              |
| orestomach | nodule                     |                              | 0 ( 0)            | 0 ( 0)             | 0 ( 0)               | 1 (2)               |
|            | thick                      |                              | 1 (2)             | 0 ( 0)             | 0 ( 0)               | 0 ( 0)              |

(HPT080)

#### STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 SEX : MALE

# GROSS FINDINGS (SUMMARY)

# ALL ANIMALS (0-105W)

| SEX :       | MALE                   | <br>                             |                   |                    |                     | PAGE : 2            |
|-------------|------------------------|----------------------------------|-------------------|--------------------|---------------------|---------------------|
| Organ       | Findings               | <br>Group Name<br>NO. of Animals | Control<br>50 (%) | 5000 ppm<br>50 (%) | 10000 ppm<br>50 (%) | 20000 ppm<br>50 (%) |
| gl stomach  | thick                  |                                  | 1 (2)             | 2 (4)              | 2 (4)               | 0 ( 0)              |
| duodenum    | nodule                 |                                  | 1 (2)             | 0 ( 0)             | 0 ( 0)              | 0 ( 0)              |
| small intes | nodule                 |                                  | 0 ( 0)            | 0 ( 0)             | 2 ( 4)              | 0 ( 0)              |
|             | dilated                |                                  | 0 ( 0)            | 1 ( 2)             | 0 ( 0)              | 0 ( 0)              |
|             | thick                  |                                  | 1 (2)             | 0 ( 0)             | 0 ( 0)              | 0 ( 0)              |
| liver       | enlarged               | Ŷ                                | 1 (2)             | 1 ( 2)             | 0 ( 0)              | 2 ( 4)              |
|             | white zone             |                                  | 7 (14)            | 4 ( 8)             | 1 (2)               | 1 (2)               |
|             | red zone               |                                  | 2 (4)             | 2 ( 4)             | 2 (4)               | 4 ( 8)              |
|             | yellow zone            |                                  | 1 (2)             | 0 ( 0)             | 0 ( 0)              | 0 ( 0)              |
|             | nodule                 |                                  | 17 (34)           | 18 (36)            | 19 (38)             | 11 (22)             |
|             | cyst .                 |                                  | 0 ( 0)            | 1 ( 2)             | 0 ( 0)              | 0 ( 0)              |
| pancreas    | nodule                 |                                  | 0 ( 0)            | 1 ( 2)             | 0 ( 0)              | 1 (2)               |
| kidney      | enlarged               |                                  | 0 ( 0)            | 1 ( 2)             | 0 ( 0)              | 0 ( 0)              |
|             | white zone             |                                  | 0 ( 0)            | 0 ( 0)             | 0 ( 0)              | 1 (2)               |
|             | hydronephrosis         |                                  | 1 (2)             | 3 ( 6)             | 4 ( 8)              | 0 ( 0)              |
| urin bladd  | nodule                 |                                  | 1 (2)             | 0 ( 0)             | 1 ( 2)              | 0 ( 0)              |
|             | urine:marked retention |                                  | 3 (6)             | 1 ( 2)             | 1 (2)               | 0 ( 0)              |
| pituitary   | enlarged               |                                  | 0 ( 0)            | 1 ( 2)             | 0 ( 0)              | 0 ( 0)              |
| thyroid     | enlarged               |                                  | 1 (2)             | 0 ( 0)             | 0 ( 0)              | 0 ( 0)              |
| testis      | enlarged               |                                  | 1 (2)             | 0 ( 0)             | 0 ( 0)              | 0 ( 0)              |
|             | small                  |                                  | 0 ( 0)            | 0 ( 0)             | 2 ( 4)              | 1 ( 2)              |
| epididymis  | nodule                 |                                  | 2 (4)             | 1 ( 2)             | 1 ( 2)              | 0 ( 0)              |

-

# GROSS FINDINGS (SUMMARY)

## STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1] REPORT TYPE : A1 SEX : MALE

# ALL ANIMALS (0-105W)

| gah       | Findings      | Group Name Control<br>NO. of Animals 50 (%) | 5000 ppm<br>50 (%) | 10000 ppm<br>50 (%) | 20000 ppm<br>50 (%) |
|-----------|---------------|---------------------------------------------|--------------------|---------------------|---------------------|
| min ves   | red           | 0 ( 0)                                      | 1 (2)              | 0 ( 0)              | 0 ( 0)              |
| ep/cli gl | nodule        | 0 ( 0)                                      | 1 ( 2)             | 1 ( 2)              | 0 ( 0)              |
| in        | enlarged      | 0 ( 0)                                      | 1 ( 2)             | 0 ( 0)              | 0 ( 0)              |
| riph nerv | nodule        | 0 ( 0)                                      | 0 ( 0)             | 1 ( 2)              | 0 ( 0)              |
| der gl    | enlarged      | 0 ( 0)                                      | 0 ( 0)             | 1 (2)               | 1 ( 2)              |
|           | nodule        | 2 (4)                                       | 2 ( 4)             | 1 ( 2)              | 0 ( 0)              |
| cle       | nodule        | 0 ( 0)                                      | 1 ( 2)             | 0 ( 0)              | 0 ( 0)              |
| э         | nodule        | 1 ( 2)                                      | 0 ( 0)             | 0 ( 0)              | 0 ( 0)              |
| ıra       | nodule        | 0 ( 0)                                      | 1 ( 2)             | 0 ( 0)              | 0 ( 0)              |
| iastinum  | mass          | 1 (2)                                       | 0 ( 0)             | 1 ( 2)              | 0 ( 0)              |
| itoneum   | nodule        | 1 (2)                                       | 0 ( 0)             | 1 ( 2)              | 1 (2)               |
| roperit   | mass          | 0 ( 0)                                      | 1 ( 2)             | 0 ( 0)              | 0 ( 0)              |
| ominal c  | ascites       | 1 (2)                                       | 2 ( 4)             | 1 (2)               | 0 ( 0)              |
| racic ca  | hemorrhage    | 0 ( 0)                                      | 2 ( 4)             | 1 ( 2)              | 1 ( 2)              |
| ·         | pleural fluid | 3 (6)                                       | 3 ( 6)             | 1 ( 2)              | 2 ( 4)              |
| er        | ulcer         | 0 ( 0)                                      | 1 ( 2)             | 0 ( 0)              | 0 ( 0)              |
|           | tail:nodule   | 1 (2)                                       | 2 ( 4)             | 1 ( 2)              | 0 ( 0)              |
|           | ear:nodule    | 1 (2)                                       | 0 ( 0)             | 0 ( 0)              | 1 ( 2)              |
|           | nose:elevated | 0 ( 0)                                      | 1 ( 2)             | 0 ( 0)              | 0 ( 0)              |
| le body   | anemic        | 0 ( 0)                                      | 1 (2)              | 0 ( 0)              | 0 ( 0)              |

(HPT080)

TABLE J 2

# GROSS FINDINGS: MALE: DEAD AND MORIBUND ANIMALS

#### STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1

# GROSS FINDINGS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

| SEX :       | MALE       |                                       |                              |                   |                    |                     | PAGE : 1           |
|-------------|------------|---------------------------------------|------------------------------|-------------------|--------------------|---------------------|--------------------|
| Organ       | Findings   | · · · · · · · · · · · · · · · · · · · | Group Name<br>NO. of Animals | Control<br>15 (%) | 5000 ppm<br>17 (%) | 10000 ppm<br>14 (%) | 20000 ppm<br>9 (%) |
|             |            |                                       |                              |                   |                    |                     |                    |
| skin/app    | scab       |                                       |                              | 0 ( 0)            | 1 ( 6)             | 0 ( 0)              | 0 ( 0)             |
| subcutis    | edema      |                                       |                              | 0 ( 0)            | 0 ( 0)             | 0 ( 0)              | 1 (11)             |
|             | mass       |                                       |                              | 2 (13)            | 0 ( 0)             | 1 (7)               | 0 ( 0)             |
| lung        | red        |                                       |                              | 0 ( 0)            | 1 ( 6)             | 0 ( 0)              | 1 (11)             |
|             | white zone |                                       |                              | 0 ( 0)            | 0 ( 0)             | 1 (7)               | 0 ( 0)             |
|             | red zone   |                                       |                              | 0 ( 0)            | 1 (6)              | 0 ( 0)              | 0 ( 0)             |
|             | nodule     |                                       |                              | 2 (13)            | 4 (24)             | 3 (21)              | 3 (33)             |
|             | adhesion   |                                       |                              | 1 (7)             | 0 ( 0)             | 0 ( 0)              | 0 ( 0)             |
| lymph node  | enlarged   |                                       |                              | 6 (40)            | 4 (24)             | 2 (14)              | 0 ( 0)             |
| spleen      | enlarged   |                                       |                              | 5 (33)            | 0 ( 0)             | 0 ( 0)              | 2 (22)             |
|             | white zone |                                       |                              | 0 ( 0)            | 0 ( 0)             | 0 ( 0)              | 1 (11)             |
|             | nodule     |                                       |                              | 1 (7)             | 0 ( 0)             | 2 (14)              | 0 ( 0)             |
| heart       | white zone |                                       |                              | 0 ( 0)            | 0 ( 0)             | 0 ( 0)              | 1 (11)             |
| forestomach | thick      |                                       |                              | 1 (7)             | 0 ( 0)             | 0 ( 0)              | 0 ( 0)             |
| gl stomach  | thick      |                                       |                              | 1 (7)             | 1 (6)              | 0 ( 0)              | 0 ( 0)             |
| duodenum    | nodule     |                                       |                              | 1 (7)             | 0 ( 0)             | 0 ( 0)              | 0 ( 0)             |
| small intes | nodule     |                                       |                              | 0 ( 0)            | 0 ( 0)             | 1 (7)               | 0 ( 0)             |
|             | thick      |                                       |                              | 1 (7)             | 0 ( 0)             | 0 ( 0)              | 0 ( 0)             |
| liver       | enlarged   |                                       |                              | 1 (7)             | 0 ( 0)             | 0 ( 0)              | 2 (22)             |
|             | -          |                                       |                              |                   |                    | ,                   | u ( 55,            |

3 (20)

1 (7)

8 (53)

2 (12)

1 ( 6)

7 (41)

0 ( 0)

0 ( 0)

6 (43)

white zone

red zone

nodule

1 (11)

2 (22)

7 (78)

#### STUDY NO. : 0613 : MOUSE B6D2F1/Cr1j[Crj:BDF1] ANIMAL REPORT TYPE : A1

## GROSS FINDINGS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

SEX : MALE

| Organ       | Findings               | Group Name Control<br>NO. of Animals 15 (%) | 5000 ppm<br>17 (%) | 10000 ppm<br>14 (%) | 20000 ppm<br>9 (%) |
|-------------|------------------------|---------------------------------------------|--------------------|---------------------|--------------------|
| kidney      | enlarged               | 0 ( 0)                                      | 1 (6)              | 0 ( 0)              | 0 ( 0)             |
|             | white zone             | 0 ( 0)                                      | 0 ( 0)             | 0 ( 0)              | 1 (11)             |
|             | hydronephrosis         | 1 (7)                                       | 0 ( 0)             | 0 ( 0)              | 0 ( 0)             |
| urin bladd  | nodule                 | 1 ( 7)                                      | 0 ( 0)             | 1 (7)               | 0 ( 0)             |
|             | urine:marked retention | 3 (20)                                      | 1 (6)              | 1 (7)               | 0 ( 0)             |
| pituitary   | enlarged               | 0 ( 0)                                      | 1 (6)              | 0 ( 0)              | 0 ( 0)             |
| thyroid     | enlarged               | 1 (7)                                       | 0 ( 0)             | 0 ( 0)              | 0 ( 0)             |
| testis      | enlarged               | 1 (7)                                       | 0 ( 0)             | 0 ( 0)              | 0 ( 0)             |
|             | small                  | 0 ( 0)                                      | 0 ( 0)             | 1 (7)               | 0 ( 0)             |
| epididymis  | nodule                 | 1 (7)                                       | 1 ( 6)             | 1 (7)               | 0 ( 0)             |
| semin ves   | red                    | 0 ( 0)                                      | 1 (6)              | 0 ( 0)              | 0 ( 0)             |
| prep/cli gl | nodule                 | 0 ( 0)                                      | 1 (6)              | 0 ( 0)              | 0 ( 0)             |
| brain       | enlarged               | 0 ( 0)                                      | 1 (6)              | 0 ( 0)              | 0 ( 0)             |
| periph nerv | nodule                 | 0 ( 0)                                      | 0 ( 0)             | 1 (7)               | 0 ( 0)             |
| Harder gl   | enlarged               | 0 ( 0)                                      | 0 ( 0)             | 1 (7)               | 0 ( 0)             |
|             | nodule                 | 1 (7)                                       | 0 ( 0)             | 0 ( 0)              | 0 ( 0)             |
| muscle      | nodule                 | 0 ( 0)                                      | 1 (6)              | 0 ( 0)              | 0 ( 0)             |
| pleura      | nodule                 | 0 ( 0)                                      | 1 (6)              | 0 ( 0)              | 0 ( 0)             |
| mediastinum | mass                   | 1 ( 7)                                      | 0 ( 0)             | 1 (7)               | 0 ( 0)             |
| retroperit  | mass                   | 0 ( 0)                                      | 1 (6)              | 0 ( 0)              | 0 ( 0)             |
| abdominal c | ascites                | 1 (7)                                       | 1 ( 6)             | 1 (7)               | 0 ( 0)             |
| thoracic ca | hemorrhage             | 0 ( 0)                                      | 2 (12)             | 1 (7)               | 1 (11)             |

PAGE : 2

## STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1] REPORT TYPE : A1

## SEX : MALE

## GROSS FINDINGS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

5

| rgan       | Findings      | Group Name<br>NO. of Animals | Control<br>15 (%) | 5000 ppm<br>17 (%) | 10000 ppm<br>14 (%) | 20000 ppm<br>9 (%) |
|------------|---------------|------------------------------|-------------------|--------------------|---------------------|--------------------|
|            |               |                              |                   |                    | · · · · · ·         |                    |
| noracic ca | pleural fluid |                              | 3 (20)            | 3 (18)             | 1 (7)               | 0 ( 0)             |
| her        | tail:nodule   |                              | 0 ( 0)            | 1 ( 6)             | 0 ( 0)              | 0 ( 0)             |
|            | ear:nodule    |                              | 0 ( 0)            | 0 ( 0)             | 0 ( 0)              | 1 (11)             |
|            | nose:elevated |                              | 0 ( 0)            | 1 (6)              | 0 ( 0)              | 0 ( 0)             |
| ole body   | anemic        |                              | 0 ( 0)            | 1 (6)              | 0 ( 0)              | 0 ( 0)             |

(HPT080)

BAIS 4

e

PAGE : 3

TABLE J 3

# GROSS FINDINGS: MALE: SACRIFICED ANIMALS

# STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1

# GROSS FINDINGS (SUMMARY)

# SACRIFICED ANIMALS (105W)

· \_\_\_\_

SEX : MALE

|             |                            |                              |                   |                    |                     | 1100 1              |
|-------------|----------------------------|------------------------------|-------------------|--------------------|---------------------|---------------------|
| Organ       | Findings                   | Group Name<br>NO. of Animals | Control<br>35 (%) | 5000 ррш<br>33 (%) | 10000 ppm<br>36 (%) | 20000 ppm<br>41 (%) |
| skin/app    | erosion                    |                              | 2 (6)             | 0 ( 0)             | 0 ( 0)              | 0 ( 0)              |
|             | scab                       |                              | 1 (3)             | 2 ( 6)             | 1 ( 3)              | 1 ( 2)              |
| subcutis    | mass                       |                              | 2 ( 6)            | 2 ( 6)             | 0 ( 0)              | 0 ( 0)              |
| lung        | nodule                     |                              | 7 (20)            | 8 (24)             | 6 (17)              | 6 (15)              |
| lymph node  | enlarged                   |                              | 7 (20)            | 2 ( 6)             | 1 ( 3)              | 5 (12)              |
|             | nodule                     |                              | 0 ( 0)            | 1 ( 3)             | 0 ( 0)              | 0 ( 0)              |
| spleen      | enlarged                   |                              | 3 (9)             | 1 ( 3)             | 1 (3)               | 0 ( 0)              |
|             | red zone                   |                              | 1 (3)             | 0 ( 0)             | 0 ( 0)              | 0 ( 0)              |
|             | black zone                 |                              | 1 (3)             | 0 ( 0)             | 0 ( 0)              | 2 ( 5)              |
|             | nodule                     |                              | 1 (3)             | 0 ( 0)             | 1 ( 3)              | 2 ( 5)              |
|             | deformed                   |                              | 0 ( 0)            | 1 ( 3)             | 1 ( 3)              | 0 ( 0)              |
|             | accentuation of white pulp |                              | 0 ( 0)            | 1 (3)              | 0 ( 0)              | 1 ( 2)              |
| salivary gl | nodule                     |                              | 0 ( 0)            | 1 ( 3)             | 0 ( 0)              | 0 ( 0)              |
| forestomach | nodule                     |                              | 0 ( 0)            | 0 ( 0)             | 0 ( 0)              | 1 ( 2)              |
| gl stomach  | thick                      |                              | 0 ( 0)            | 1 ( 3)             | 2 ( 6)              | 0 ( 0)              |
| small intes | nodule                     |                              | 0 ( 0)            | 0 ( 0)             | 1 ( 3)              | 0 ( 0)              |
|             | dilated                    |                              | 0 ( 0)            | 1 ( 3)             | 0 ( 0)              | 0 ( 0)              |
| liver       | enlarged                   |                              | 0 ( 0)            | 1 (3)              | 0 ( 0)              | 0 ( 0)              |
|             | white zone                 |                              | 4 (11)            | 2 ( 6)             | 1 ( 3)              | 0 ( 0)              |
|             | red zone                   |                              | 1 (3)             | 1 ( 3)             | 2 ( 6)              | 2 ( 5)              |
|             | yellow zone                |                              | 1 (3)             | 0 ( 0)             | 0 ( 0)              | 0 ( 0)              |
|             | nodule                     |                              | 9 (26)            | 11 ( 33)           | 13 (36)             | 4 (10)              |
|             |                            |                              |                   |                    |                     |                     |

BAIS 4

PAGE : 1

# GROSS FINDINGS (SUMMARY)

# SACRIFICED ANIMALS (105W)

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 SEX : MALE

-

| Organ       | Findings       | Group Name<br>NO. of Animals | Control<br>35 (%) | 5000 ppm<br>33 (%) | 10000 ppm<br>36 (%) | 20000 ppm<br>41 (%) |
|-------------|----------------|------------------------------|-------------------|--------------------|---------------------|---------------------|
| liver       | cyst           |                              | 0 ( 0)            | 1 (3)              | 0 (* 0)             | 0 ( 0)              |
| pancreas    | nodule         |                              | 0 ( 0)            | 1 ( 3)             | 0 ( 0)              | 1 (2)               |
| kidney      | hydronephrosis |                              | 0 ( 0)            | 3 (9)              | 4 (11)              | 0 ( 0)              |
| testis      | small          |                              | 0 ( 0)            | 0 ( 0)             | 1 ( 3)              | 1 (2)               |
| epididymis  | nodule         |                              | 1 (3)             | 0 ( 0)             | 0 ( 0)              | 0 ( 0)              |
| prep/cli gl | nodule         |                              | 0 ( 0)            | 0 ( 0)             | 1 (3)               | 0 ( 0)              |
| Harder gl   | enlarged       |                              | 0 ( 0)            | 0 ( 0)             | 0 ( 0)              | 1 (2)               |
|             | nodule         |                              | 1 (3)             | 2 ( 6)             | 1 ( 3)              | 0 ( 0)              |
| oone        | nodule         |                              | 1 ( 3)            | 0 ( 0)             | 0 ( 0)              | 0 ( 0)              |
| peritoneum  | nodule         |                              | 1 (3)             | 0 ( 0)             | 1 ( 3)              | 1 ( 2)              |
| abdominal c | ascites        |                              | 0 ( 0)            | 1 ( 3)             | 0 ( 0)              | 0 ( 0)              |
| thoracic ca | pleural fluid  |                              | 0 ( 0)            | 0 ( 0)             | 0 ( 0)              | 2 (5)               |
| other       | ulcer          |                              | 0 ( 0)            | 1 ( 3)             | 0 (0)               | 0 ( 0)              |
|             | tail:nodule    |                              | 1 (3)             | 1 ( 3)             | 1 (3)               | 0 ( 0)              |
|             | ear:nodule     |                              | 1 (3)             | 0 ( 0)             | 0 ( 0)              | 0 ( 0)              |

(HPT080)

BAIS 4

PAGE : 2

TABLE J 4

# GROSS FINDINGS: FEMALE: ALL ANIMALS

# STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1] REPORT TYPE : A1 SEX : FEMALE

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

-----

#### Group Name Control 2500 ppm 5000 ppm 10000 ppm Findings\_ NO. of Animals 50 (%) Organ\_ 50 (%) 50 (%) 50 (%) skin/app nodule 1 (2) 0 ( 0) 1 (2) 0 ( 0) erosion 1 (2) 0 (0) 0 ( 0) 0 ( 0) subcutis edema 4 (8) 3 (6) 5 (10) 7 (14) mass 3 (6) 5 (10) 1 (2) 3 (6) lung white zone 0 ( 0) 1 (2) 0 ( 0) 0 ( 0) red zone 1 (2) 0 ( 0) 1 (2) 1 (2) nodule 2 (4) 3 (6) 0 ( 0) 3 (6) lymph node enlarged 7 (14) 13 (26) 13 (26) 14 (28) spleen enlarged 10 (20) 9 (18) 10 (20) 12 (24) white zone 0 ( 0) 0 ( 0) 0 ( 0) 1 (2) nodule 1 (2) 0 ( 0) 0 ( 0) 1 (2) deformed 0 ( 0) 0 ( 0) 1 (2) 0 ( 0) accentuation of white pulp 1 (2) 0 ( 0) 0 ( 0) 0 ( 0) salivary gl nodule 1 (2) 0 ( 0) 0 ( 0) 0 ( 0) forestomach nodule 0 ( 0) 1 (2) 0 ( 0) 0 ( 0) gl stomach ulcer 1 (2) 0 ( 0) 0 ( 0) 0 ( 0) liver enlarged 4 (8) 4 (8) 0 ( 0) 2 (4) white zone 7 (14) 9 (18) 4 (8) 7 (14) red zone 6 (12) 4 (8) 3 (6) 1 (2) nodule 5 (10) 4 (8) 9 (18) 4 (8) pancreas red 0 ( 0) 0 ( 0) 0 ( 0) 1 (2)

1 (2)

0 ( 0)

0 ( 0)

PAGE : 4

(HPT080)

kidney

pale

0 ( 0)

## STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 SEX : FEMALE

# GROSS FINDINGS (SUMMARY)

# ALL ANIMALS (0-105W)

~

| Organ      | Findings               | Group Name Control<br>NO. of Animals 50 (%) | 2500 ppm<br>50 (%) | 5000 ppm<br>50 (%) | 10000 ppm<br>50 (%) |
|------------|------------------------|---------------------------------------------|--------------------|--------------------|---------------------|
| kidney     | white                  | 0 ( 0)                                      | 1 (2)              | 0 ( 0)             | 0 ( 0)              |
|            | nodule                 | 0 ( 0)                                      | 1 ( 2)             | 1 ( 2)             | 1 ( 2)              |
|            | hydronephrosis         | 4 ( 8)                                      | 4 ( 8)             | 2 ( 4)             | 5 (10)              |
| rin bladd  | urine marked retention | 2 ( 4)                                      | 2 ( 4)             | 0 ( 0)             | 1 (2)               |
| oituitary  | enlarged               | 2 ( 4)                                      | 4 ( 8)             | 2 ( 4)             | 2 (4)               |
|            | red zone               | 1 ( 2)                                      | 3 (6)              | 1 (2)              | 1 (2)               |
|            | nodule                 | 5 (10)                                      | 2 ( 4)             | 2 (4)              | 2 (4)               |
| hyroid     | enlarged               | 0 ( 0)                                      | 0 ( 0)             | 0 ( 0)             | 1 (2)               |
| vary       | enlarged               | 3 ( 6)                                      | 7 (14)             | 8 (16)             | 5 (10)              |
|            | cyst                   | 4 ( 8)                                      | 2 ( 4)             | 5 (10)             | 2 (4)               |
| terus      | enlarged               | 0 ( 0)                                      | 1 ( 2)             | 0 ( 0)             | 0 ( 0)              |
|            | nodule                 | 9 (18)                                      | 14 (28)            | 9 (18)             | 14 (28)             |
|            | dilated lumen          | 0 ( 0)                                      | 0 ( 0)             | 1 (2)              | 0 ( 0)              |
| agina      | nodule                 | 0 ( 0)                                      | 0 ( 0)             | 0 ( 0)             | 1 (2)               |
| orain      | red zone               | 1 ( 2)                                      | 0 ( 0)             | 1 ( 2)             | 0 ( 0)              |
| eriph nerv | nodule                 | 0 ( 0)                                      | 0 ( 0)             | 0 ( 0)             | 1 (2)               |
| уө         | turbid                 | 0 ( 0)                                      | 0 ( 0)             | 1 (2)              | 1 (2)               |
| arder gl   | enlarged               | 1 ( 2)                                      | 0 ( 0)             | 0 ( 0)             | 1 (2)               |
|            | nodule                 | 2 ( 4)                                      | 0 ( 0)             | 0 ( 0)             | 2 (4)               |
| one        | nodule                 | 0 ( 0)                                      | 1 ( 2)             | 0 ( 0)             | 0 ( 0)              |
| ediastinum | mass                   | 2 ( 4)                                      | 1 ( 2)             | 3 (6)              | 3 (6)               |
| eritoneum  | mass                   | 0 ( 0)                                      | 0 ( 0)             | 0 ( 0)             | 1 (2)               |

PAGE : 5

## STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 SEX

~

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

| :  | FEMALE   |       |
|----|----------|-------|
|    |          | Grou  |
| an | Findings | NO. ( |

| Organ       | Findings      | Group Name<br>NO. of Animals | Control<br>50 (%) | 2500 ppm<br>50 (%) | 5000 ppm<br>50 (%) | 10000 ppm<br>50 (%) |
|-------------|---------------|------------------------------|-------------------|--------------------|--------------------|---------------------|
|             |               |                              |                   |                    |                    |                     |
| peritoneum  | thick         |                              | 0 ( 0)            | 1 ( 2)             | 0 ( 0)             | 2 (4)               |
| retroperit  | nodule        |                              | 0 ( 0)            | 1 (2)              | 0 ( 0)             | 0 ( 0)              |
|             | mass          |                              | 1 ( 2)            | 0 ( 0)             | 0 ( 0)             | 1 ( 2)              |
| abdominal c | hemorrhage    |                              | 0 ( 0)            | 1 (2)              | 4 (8)              | 4 ( 8)              |
|             | ascites       |                              | 9 (18)            | 12 (24)            | 7 (14)             | 13 ( 26)            |
| thoracic ca | pleural fluid |                              | 12 (24)           | 12 (24)            | 11 (22)            | 14 (28)             |
| other       | scab          |                              | 0 ( 0)            | 1 (2)              | 0 ( 0)             | 0 ( 0)              |
|             | tail:nodule   |                              | 0 ( 0)            | 1 (2)              | 0 ( 0)             | 0 ( 0)              |
|             | ear:nodule    |                              | 1 ( 2)            | 1 ( 2)             | 0 ( 0)             | 0 ( 0)              |
| whole body  | anemic        |                              | 1 ( 2)            | 0 ( 0)             | 0 ( 0)             | 1 ( 2)              |
|             |               |                              |                   |                    |                    |                     |

,

(HPT080)

\_\_\_\_\_

BAIS 4

PAGE : 6

TABLE J 5

# GROSS FINDINGS: FEMALE: DEAD AND MORIBUND ANIMALS

## STUDY NO. : 0613 ANIMAL : MO REPORT TYPE : A SEX : FEMALE

# GROSS FINDINGS (SUMMARY) ND ANIMALS (0-105W)

| 0010                        | anona Lination (n |
|-----------------------------|-------------------|
| MOUSE B6D2F1/Cr1j[Crj:BDF1] | DEAD AND MORIBUND |
| Λ1                          |                   |
| FEMALE                      |                   |

|         |                        |                                             |                    | ·                  |                     |
|---------|------------------------|---------------------------------------------|--------------------|--------------------|---------------------|
| gan     | Findings               | Group Name Control<br>NO. of Animals 21 (%) | 2500 ppm<br>24 (%) | 5000 ppm<br>19 (%) | 10000 ppm<br>30 (%) |
| n/app   | erosion                | 1 ( 5)                                      | 0 ( 0)             | 0 ( 0)             | 0 ( 0)              |
| cutis   | edema                  | 4 (19)                                      | 3 (13)             | 5 (26)             | 7 (23)              |
|         | mass                   | 3 (14)                                      | 3 (13)             | 1 ( 5)             | 2 (7)               |
| g       | red zone               | 1 (5)                                       | 0 ( 0)             | 1 (5)              | 1 ( 3)              |
|         | nodule                 | 1 ( 5)                                      | 1 ( 4)             | 0 ( 0)             | 2 (7)               |
| ph node | enlarged               | 4 (19)                                      | 8 (33)             | 7 (37)             | 10 (33)             |
| een     | enlarged               | 7 (33)                                      | 6 (25)             | 7 (37)             | 11 (37)             |
|         | white zone             | 0 ( 0)                                      | 0 ( 0)             | 0 ( 0)             | 1 ( 3)              |
| ər      | enlarged               | . 4 (19)                                    | 4 (17)             | 0 ( 0)             | 2 (7)               |
|         | white zone             | 6 (29)                                      | 9 (38)             | 4 (21)             | 7 (23)              |
|         | red zone               | 1 ( 5)                                      | 0 ( 0)             | 0 ( 0)             | 1 (3)               |
|         | nodule                 | I (5)                                       | 3 (13)             | 2 (11)             | 3 (10)              |
| creas   | red                    | 0 ( 0)                                      | 0 ( 0)             | 0 ( 0)             | 1 (3)               |
| ney     | pale                   | 1 ( 5)                                      | 0 ( 0)             | 0 ( 0)             | 0 ( 0)              |
|         | nodule                 | 0 ( 0)                                      | 0 ( 0)             | 0 ( 0)             | 1 (3)               |
|         | hydronephrosis         | 3 (14)                                      | 2 ( 8)             | 1 (5)              | 2 (7)               |
| n bladd | urine:marked retention | 2 (10)                                      | 2 ( 8)             | 0 ( 0)             | 1 (3)               |
| uitary  | enlarged               | 1 ( 5)                                      | 1 ( 4)             | 1 (5)              | 1 (3)               |
|         | red zone               | 1 ( 5)                                      | 1 (4)              | 0 ( 0)             | 0 ( 0)              |
|         | nodule                 | 1 ( 5)                                      | 1 ( 4)             | 0 ( 0)             | 2 (7)               |
| roid    | enlarged               | 0 ( 0)                                      | 0 ( 0)             | 0 ( 0)             | 1 (3)               |
| у       | enlarged               | 3 (14)                                      | 6 (25)             | 5 (26)             | 5 (17)              |

PAGE: 4

## STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 SEX : FEMALE

## GROSS FINDINGS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

.

1.

| SEX :       | FEMALE        |                                                 |                    |                    |                     |  |  |
|-------------|---------------|-------------------------------------------------|--------------------|--------------------|---------------------|--|--|
| Organ       | Findings      | <br>Group Name Control<br>NO. of Animals 21 (%) | 2500 ppm<br>24 (%) | 5000 ppm<br>19 (%) | 10000 ppm<br>30 (%) |  |  |
|             |               |                                                 |                    |                    |                     |  |  |
| ovary       | cyst          | 1 (5)                                           | 0 ( 0)             | 2 (11)             | 0 ( 0)              |  |  |
| iterus      | enlarged      | 0 ( 0)                                          | 1 ( 4)             | 0 ( 0)             | 0 ( 0)              |  |  |
|             | nodule        | 7 (33)                                          | 9 (38)             | 6 (32)             | 10 ( 33)            |  |  |
| agina       | nodule        | 0 ( 0)                                          | 0 ( 0)             | 0 ( 0)             | 1 ( 3)              |  |  |
| orain       | red zone      | 1 ( 5)                                          | 0 ( 0)             | 1 (5)              | 0 ( 0)              |  |  |
| эуе         | turbid        | 0 ( 0)                                          | 0 ( 0)             | 1 (5)              | 0 ( 0)              |  |  |
| larder gl   | enlarged      | 1 (5)                                           | 0 ( 0)             | 0 ( 0)             | 0 ( 0)              |  |  |
|             | nodule        | 0 ( 0)                                          | 0 ( 0)             | 0 ( 0)             | 1 ( 3)              |  |  |
| nediastinum | mass          | 2 (10)                                          | 1 ( 4)             | 3 (16)             | 3 (10)              |  |  |
| peritoneum  | mass          | 0 ( 0)                                          | 0 ( 0)             | 0 ( 0)             | 1 (3)               |  |  |
|             | thick         | 0 ( 0)                                          | 1 ( 4)             | 0 ( 0)             | 2 ( 7)              |  |  |
| etroperit   | nodule        | 0 ( 0)                                          | 1 ( 4)             | 0 ( 0)             | 0 ( 0)              |  |  |
|             | mass          | 1 ( 5)                                          | 0 ( 0)             | 0 ( 0)             | 1 ( 3)              |  |  |
| bdominal c  | hemorrhage    | 0 ( 0)                                          | 1 ( 4)             | 4 (21)             | 4 (13)              |  |  |
|             | ascites       | 8 (38)                                          | 9 (38)             | 5 (26)             | 10 (33)             |  |  |
| horacic ca  | pleural fluid | 10 (48)                                         | 10 (42)            | 9 (47)             | 13 (43)             |  |  |
| ther        | scab          | 0 ( 0)                                          | 1 ( 4)             | 0 ( 0)             | 0 ( 0)              |  |  |
|             | ear:nodule    | 1 (5)                                           | 1 ( 4)             | 0 ( 0)             | 0 ( 0)              |  |  |
| hole body   | anemic        | 1 (5)                                           | 0 ( 0)             | 0 ( 0)             | 1 (3)               |  |  |

BAIS 4

`

TABLE J 6

# GROSS FINDINGS: FEMALE: SACRIFICED ANIMALS

#### GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (105W)

## STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 SEX : FEMALE

#### 5000 ppm Group Name Control 2500 ppm 10000 ppm Findings\_ NO. of Animals 29 (%) 26 (%) 31 (%) 20 (%) nodule 1 (3) 0 ( 0) 1 (3) 0 ( 0) mass 0 ( 0) 2 (8) 0 ( 0) 1 (5) white zone 0 ( 0) 1 (4) 0 ( 0) 0 ( 0) nodule 1 (3) 2 (8) 0 ( 0) 1 (5) enlarged 3 (10) 5 (19) 6 (19) 4 (20) enlarged 3 (10) 3 (12) 3 (10) 1 (5) nodule 1 (3) 0 ( 0) 0 ( 0) 1 (5) deformed 0 ( 0) 0 ( 0) 1 (3) 0 ( 0) accentuation of white pulp 1 (3) 0 ( 0) 0 ( 0) 0 ( 0) nodule 1 (3) 0 ( 0) 0 ( 0) 0 ( 0) nodule 0 ( 0) 1 ( 4) 0 ( 0) 0 ( 0) ulcer 1 (3) 0 ( 0) 0 ( 0) 0 ( 0)

0 ( 0)

1 (4)

gl stomach liver white zone 1 (3) 0 ( 0) red zone 5 (17) 4 (15) nodule 4 (14) 1 (4) kidney white 0 ( 0) 1 (4) nodule 0 ( 0) 1 (4) hydronephrosis 1 (3) 2 (8) pituitary enlarged 1 (3) 3 (12) red zone 0 ( 0) 2 (8) nodule 4 (14) 1 (4)

Organ\_

skin/app

subcutis

lymph node

salivary gl

forestomach

spleen

lung

PAGE : 3

BAIS 4

0 ( 0)

0 ( 0)

1 (5)

0 ( 0)

0 ( 0)

3 (15)

1 (5)

1 (5)

0 ( 0)

0 ( 0)

0 ( 0)

3 (10)

7 (23)

0 ( 0)

1 (3)

1 (3)

1 (3)

1 (3)

2 (6)

3 (10)

ovary

enlarged

# GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (105W)

# BDF1]

ANIMAL : MOUSE B6D2F1/Cr1j[Crj;BDF1] REPORT TYPE : A1 SEX : FEMALE

STUDY NO. : 0613

| SEX :       | FEMALE        |                                             | ·                  |                    | PAGE :              |
|-------------|---------------|---------------------------------------------|--------------------|--------------------|---------------------|
| Organ       | Findings      | Group Name Control<br>NO. of Animals 29 (%) | 2500 ppm<br>26 (%) | 5000 ppm<br>31 (%) | 10000 ppm<br>20 (%) |
| ovary       | cyst          | 3 (10)                                      | 2 ( 8)             | 3 (10)             | 2 (10)              |
| uterus      | nodule        | 2 ( 7)                                      | 5 (19)             | 3 (10)             | 4 (20)              |
|             | dilated lumen | • 0 ( 0)                                    | 0 ( 0)             | 1 ( 3)             | 0 ( 0)              |
| periph nerv | nodule        | 0 ( 0)                                      | 0 ( 0)             | 0 ( 0)             | 1 ( 5)              |
| eye         | turbid        | 0 ( 0)                                      | 0 ( 0)             | 0 ( 0)             | 1 (5)               |
| Harder gl   | enlarged      | 0 ( 0)                                      | 0 ( 0)             | 0 ( 0)             | 1 (5)               |
|             | nodule        | 2 ( 7)                                      | 0 ( 0)             | 0 ( 0)             | 1 (5)               |
| polie       | nodule        | 0 ( 0)                                      | 1 ( 4)             | 0 ( 0)             | 0 ( 0)              |
| abdominal c | ascites       | 1 ( 3)                                      | 3 (12)             | 2 (6)              | 3 (15)              |
| horacic ca  | pleural fluid | 2 ( 7)                                      | 2 ( 8)             | 2 (6)              | 1 ( 5)              |
| other       | tail:nodule   | 0 ( 0)                                      | 1 (4)              | . 0 ( 0)           | 0 ( 0)              |

(HPT080)

# TABLE K 1

# ORGAN WEIGHT, ABSOLUTE: MALE

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 SEX : MALE UNIT: g

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

PAGE : 1 Group Name NO. of Body Weight ADRENALS TESTES HEART LUNGS KIDNEYS Animals 35 41.4± 8.0 Control 0.011± 0.002 0.200± 0.035 0.224± 0.018 0.212± 0.069 0.648± 0.047 5000 ppm 3244.4± 7.4  $0.010 \pm 0.002$  $0.223 \pm 0.033$ 0.221± 0.022 0.199± 0.057 0.695± 0.175 10000 թթա 36  $44.0 \pm 5.1$ 0.010± 0.002 0.216± 0.037  $0.221 \pm 0.025$  $0.202 \pm 0.030$  $0.786 \pm 0.576$ 20000 ppm 40 44.0± 6.8  $0.010 \pm 0.002$ 0.209± 0.042 0.219± 0.019 0.216± 0.141  $0.665 \pm 0.061$ 

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

Test of Dunnett

(HCL040)

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 SEX : MALE UNIT: g

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

\*\* : P ≦ 0.01

PAGE : 2 Group Name NO. of SPLEEN LIVER BRAIN Animals 35 0.452± 0.017 Control  $0.162 \pm 0.255$ 1.688± 0.721 5000 ppm 32 0.114± 0.079  $1.806 \pm 1.050$ 0.455± 0.017 10000 ppm 36 0.120± 0.092 1.812± 0.562 0.454± 0.015 20000 ppm 40  $0.095 \pm 0.078$  $1.585 \pm 0.279$  $0.452 \pm 0.022$ Significant difference ; \* : P ≦ 0.05

Test of Dunnett

(HCL040)

. ----

TABLE K 2

ORGAN WEIGHT, ABSOLUTE: FEMALE

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

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 SEX : FEMALE UNIT: g

PAGE : 3

| Group Name | NO. of<br>Animals | Body Weight       | ADRENALS     | OVARIES           | HEART        | LUNGS             | KIDNEYS      |  |
|------------|-------------------|-------------------|--------------|-------------------|--------------|-------------------|--------------|--|
|            |                   | W                 |              |                   |              |                   |              |  |
| Control    | 28                | 32.9± 5.9         | 0.014± 0.003 | 0.049± 0.094      | 0.182± 0.032 | 0.205± 0.057      | 0.470± 0.169 |  |
| 2500 ppm   | 25                | 30.6± 3.4         | 0.015± 0.003 | $0.041 \pm 0.044$ | 0.178± 0.031 | $0.215 \pm 0.067$ | 0.562± 0.269 |  |
| 5000 ppm   | 31                | 31.4± 4.8         | 0.014± 0.003 | 0.200± 0.659      | 0.176± 0.022 | 0.193± 0.023      | 0.552± 0.514 |  |
| 10000 ррм  | 19                | 28.9 <u>+</u> 3.9 | 0.013± 0.001 | 0.105± 0.243      | 0.164± 0.014 | 0. 198 ± 0. 040   | 0.475± 0.145 |  |

(HCL040)

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1;[Crj:BDF1] REPORT TYPE : A1 SEX : FEMALE UNIT: g

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

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

 $\sim \sim$ 

PAGE : 4 SPLEEN LIVER Group Name NO. of BRAIN Animals Control 28  $0.307 \pm 0.648$  $1.642 \pm 0.607$ 0.473± 0.018 2500 ppm 25 0.296± 0.363  $1.577 \pm 0.406$ 0.481± 0.018 5000 ppm 31 0.223± 0.159 1.430± 0.200 0.470± 0.018 10000 ppm 190.172± 0.116  $1.367 \pm 0.254$  $0.472 \pm 0.021$ 

Test of Dunnett

(HCL040)

# TABLE L 1

# ORGAN WEIGHT, RELATIVE: MALE

## STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1] 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    | 35                | 41. 4± 8. 0        | 0.027± 0.009         | 0.499± 0.127 | 0.563± 0.128 | 0.535± 0.207 | 1.630± 0.374 |  |
| 5000 ppm   | 32                | 44.4± 7.4          | 0.024± 0.008         | 0.514± 0.104 | 0.513± 0.107 | 0.464± 0.181 | 1.638± 0.651 |  |
| 10000 ppm  | 36                | 44.0± 5.1          | $0.022\pm 0.005$     | 0.495± 0.092 | 0.510± 0.080 | 0.466± 0.094 | 1.851± 1.554 |  |
| 20000 ppm  | 40                | 44.0± 6.8          | <b>0.024</b> ± 0.008 | 0.483± 0.101 | 0.508± 0.075 | 0.534± 0.569 | 1.538± 0.201 |  |

(HCL042)

BAIS 4

.

## STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1,j[Cr,j:BDF1] REPORT TYPE : Λ1 SEX : MALE UNIT: %

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

 $\overline{}$ 

PAGE : 2

| Group Name | NO. of<br>Animals | SPLEEN       | LIVER        | BRAIN          |  |
|------------|-------------------|--------------|--------------|----------------|--|
| Control    | 35                | 0.448± 0.789 | 4.195± 1.960 | 1. 138± 0. 262 |  |
| 5000 ppm   | 32                | 0.270± 0.229 | 4.160± 2.405 | 1.057± 0.218   |  |
| 10000 թթա  | 36                | 0.286± 0.247 | 4.204± 1.523 | 1.047± 0.132   |  |
| 20000 ppm  | 40                | 0.214± 0.158 | 3.662± 0.809 | 1.053± 0.182   |  |

(HCL042)

.

TABLE L 2

ORGAN WEIGHT, RELATIVE: FEMALE

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

| Group Name | NO. of<br>Animals | Body Weight<br>(g) | ADRENALS     | OVARIES      | HEART        | LUNGS        | KIDNEYS       |
|------------|-------------------|--------------------|--------------|--------------|--------------|--------------|---------------|
| Control    | 28                | 32.9± 5.9          | 0.044± 0.010 | 0.156± 0.316 | 0.565± 0.123 | 0.646± 0.227 | 1.465± 0.605  |
| 2500 ppm   | 25                | 30.6± 3.4          | 0.048± 0.012 | 0.136± 0.139 | 0.591± 0.140 | 0.714± 0.260 | 1.901± 1.133* |
| 5000 ppm   | 31                | 31.4± 4.8          | 0.045± 0.011 | 0.662± 2.166 | 0.567± 0.085 | 0.622± 0.095 | 1.797± 1.713  |
| 10000 ppm  | 19                | 28.9± 3.9          | 0.047± 0.007 | 0.401± 0.994 | 0.572± 0.062 | 0.699± 0.173 | 1.669± 0.562* |

(HCL042)

BAIS 4

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

~~

.

PAGE : 4

~~~

| Group Name        | NO. of<br>Animals | SPLEEN            | LIVER        | BRAIN             |  |
|-------------------|-------------------|-------------------|--------------|-------------------|--|
| Control           | 28                | 0.965± 1.956      | 5.051± 1.810 | 1.481± 0.255      |  |
| 2500 ppm          | 25                | 1.001± 1.315      | 5.179± 1.269 | 1.588± 0.179      |  |
| 5000 ppm          | 31                | $0.727 \pm 0.535$ | 4.618± 0.762 | $1.525 \pm 0.214$ |  |
| 100 <b>00</b> ppm | 19                | 0.609± 0.437      | 4.755± 0.821 | 1.652± 0.172*     |  |

(HCL042)

## TABLE M 1

## HISTOPATHOLOGICAL FINDINGS:

NON-NEOPLASTIC LESIONS:

MALE: ALL ANIMALS

.

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

•

| )rgan       | Group<br>- No. o<br>Grade<br>Findings      | f Animals on Study 50                                   | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | $\begin{array}{cccc} 20000 \text{ ppm} \\ 50 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ |
|-------------|--|---|---|---|---|
| Integumenta | cy system∕appandage}                       |   |   |   |   |
| kin/app     | ulcer                                      | <50><br>0 1 1 0<br>( 0) ( 2) ( 2) ( 0)                  | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0   |
|             | necrosis                                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                          | 0 i 0 0<br>( 0) ( 2) ( 0) ( 0)                        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0   |
|             | scab                                       | 2 1 0 0<br>(4)(2)(0)(0)                                 | 1 2 0 0<br>(2) (4) (0) (0)                            | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0)                        | 1 0 0 0<br>(2)(0)(0)(0)   |
| Respiratory | system}                                    |   |   |   |   |
| asal cavit  | eosinophilic change:olfactory epithelium   | $\langle 50 \rangle$<br>16 1 0 0<br>(32) (2) (0) (0)    | <50><br>23 0 1 0<br>(46) (0) (2) (0)                  | <50><br>18 1 0 0<br>(36) (2) (0) (0)                  | <50><br>15 0 0 0<br>(30) (0) (0) (0   |
|             | eosinophilic change:respiratory epithelium | 16     3     0     0       (32)     (6)     (0)     (0) | 9 0 1 0<br>(18) (0) (2) (0)                           | 10 0 0 0<br>(20)(0)(0)(0)                             | 12 0 0 0<br>(24) (0) (0) (0   |
|             | respiratory metaplasia                     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 1 0 0 0<br>(2)(0)(0)(0)                               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0   |
|             | inflammation foreign body                  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 1 0 0 0<br>(2)(0)(0)(0)                               | .0 0 0 0<br>( 0) ( 0) ( 0) ( 0  |

ь (c) с:b/а\*100

Significant difference ; \* : P  $\leq$  0.05 \*\* : P  $\leq$  0.01 Test of Chi Square

(HPT150)

BAIS4

•

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

1 0

(2)(0)(0)(0)

0 0

0

0 0 0

|              |  | oup Name Control<br>. of Animals on Study 50 |                | 5000 ррт<br>50   | 10000 ррт<br>50  | ענע 20000 ענש<br>50  |
|--------------|--|--|----------------|--|--|--|
| Organ        |  | ade <u>1 2</u>                               | 3 4<br>(%) (%) | $\frac{1}{(\%)}  \frac{2}{(\%)}  \frac{3}{(\%)}  \frac{4}{(\%)}$ | $\frac{1}{(\%)}  \frac{2}{(\%)}  \frac{3}{(\%)}  \frac{4}{(\%)}$ | $\frac{1}{(\%)} \begin{array}{c} 2 & 3 & 4 \\ (\%) & (\%) & (\%) & (\%) \end{array}$ |
| {Respiratory | system)                                  |  |                |  |  |  |
| nasal cavit  | inflammation:respiratory epithelium      | <50)<br>1 0<br>(2) (0) (                     | 0 0            | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                           | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                           | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
|              | respiratory metaplasia:olfactory epithel | ium 21 0<br>(42)(0)(                         | 0 0<br>0) ( 0) | 8 0 0 0 **<br>(16) (0) (0) (0)                                   | 11 0 0 0<br>(22)(0)(0)(0)  | 11 0 0 0<br>(22) (0) (0) (0)   |
|              | respiratory metaplasia:gland             | 24 0<br>(48) (0) (                           | 0 0<br>0) ( 0) | 13 1 0 0<br>(26) (2) (0) (0)                                     | 19 1 0 0<br>(38) (2) (0) (0)                                     | 19 1 0 0<br>(38) (2) (0) (0)   |
|              | squamous cell metaplasia:respiratory epi | thelium 0 0<br>( 0) ( 0) (                   | 0 0<br>0) ( 0) | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                   | 1 0 0 0<br>(2)(0)(0)(0)  | 1 0 0 0<br>(2) (0) (0) (0)   |
| nasopharynx  | eosinophilic change                      | <50><br>1 1<br>( 2) ( 2) (                   | 0 0            | <50><br>1 0 1 0<br>( 2) ( 0) ( 2) ( 0)                           | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                           | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)   |
| lung         | hemorrhage                               | <50><br>0 0<br>( 0) ( 0) (                   | 0 0            | <50><br>1 2 0 0<br>( 2) ( 4) ( 0) ( 0)                           | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                           | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |

0 0 0 0

0 0 0 0

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe ≺a≻ a : Number of animals examined at the site

b b: Number of animals with lesion

(c) c:b/a\*100

edema

Significant difference ; \* : P  $\leq$  0.05 \*\* : P  $\leq$  0.01 Test of Chi Square

(HPT150)

BAIS4

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

 $\sim$ 

 $\sim$ 

| Drgan       | Findings                              | Group Name         Control           No. of Animals on Study         50           Grade         1         2         3         4           (%)         (%)         (%)         (%) | 5000 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | $ \begin{array}{c} 20000 \text{ ppm} \\ 50 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ |
|-------------|---------------------------------------|---|---|---|---|
|             | Findings                              | (%) (%) (%)   |   | (%) (%) (%)   | (%) (%) (%) (%)   |
| Kespiratory | system}                               |   |   |   |   |
| Ing         | inflammatory infiltration             | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)              | <50><br>2 1 0 0<br>( 4) ( 2) ( 0) ( 0)                | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
|             | accumulation of foamy cells           | 1 0 0 0<br>(2)(0)(0)(0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
|             | bronchiolar-alveolar cell hyperplasia | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 2 0 0 0<br>(4)(0)(0)(0)                               | 2 1 0 0<br>(4)(2)(0)(0)   |
| Hematopoiet | ic system)                            |   |   |   |   |
| one marrow  | congestion                            | $\begin{array}{cccc} <50 \\ 1 & 0 & 0 & 0 \\ ( 2) & ( 0) & ( 0) & ( 0) \\ \end{array}$  | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)  |
|             | increased hematopoiesis               | 6 0 0 0<br>(12)(0)(0)(0)  | 6 0 0 0<br>(12) (0) (0) (0)                         | 7 0 0 0<br>(14) (0) (0) (0)                           | 6 0 0 0<br>(12) (0) (0) (0)   |
|             | myelofibrosis                         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 3 0 0 0<br>(6)(0)(0)(0)   |
|             | megakaryocyteincreased                | 1 0 0 0<br>(2)(0)(0)(0)(0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 1 0 0 0<br>(2)(0)(0)(0)                               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |

(c) c:b/a\*100

Significant difference ; \* : P  $\leq$  0.05 \*\* : P  $\leq$  0.01 Test of Chi Square

(HPT150)

BAIS4

## STUDY NO. : 0613 HISTOPATHOLOG ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] ALL ANIMALS (0 REPORT TYPE : A1 SEX : MALE

-----

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

|             |                              | Group Name Control<br>No. of Animals on Study 50     | 5000 ррт<br>50                         | 10000 ppm<br>50  | 20000 ррт<br>50                        |  |
|-------------|------------------------------|--|--|--|--|--|
| rgan        | Findings                     | Grade <u>1 2 3 4</u><br>(%) (%) (%) (%)              | <u>1 2 3 4</u><br>(%) (%) (%) (%)      | $\frac{1}{(\%)}  \frac{2}{(\%)}  \frac{3}{(\%)}  \frac{4}{(\%)}$ | <u>1 2 3 4</u><br>(%) (%) (%) (%)      |  |
| ematopoieti | c system)                    |  |  |  |  |  |
| one marrow  | granulopoiesis:increased     | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                           | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) |  |
| mph node    | lymphadenitis                | <50><br>0 1 0 0<br>( 0) ( 2) ( 0) ( 0)               | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0) | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                           | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) |  |
| een         | angiectasis                  | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                           | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0) |  |
|             | deposit of melanin           | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                   | 2 0 0 0<br>(4)(0)(0)(0)                |  |
|             | extramedullary hematopoiesis | 10 6 0 0<br>(20) (12) (0) (0)                        | 12 10 0 0<br>(24) (20) (0) (0)         | 15 6 0 0<br>(30) (12) (0) (0)                                    | 10 5 0 0<br>(20)(10)(0)(0)             |  |
|             | follicular hyperplasia       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       | 1 0 0 0<br>(2)(0)(0)(0)                | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0)                                   | 0 0 0 0<br>(0)(0)(0)(0)                |  |

{Circulatory system}

| heart          | <50>          | <50>         | <50>                | <50>                |
|----------------|---------------|--------------|---------------------|---------------------|
| mineralization | 2 	 0 	 0 	 0 | 2 1 0 0      | 0 0 0 0             | 0 0 0 0             |
|                | (4)(0)(0)(0)  | (4)(2)(0)(0) | ( 0) ( 0) ( 0) ( 0) | ( 0) ( 0) ( 0) ( 0) |

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

 ${\rm \langle a \, \rangle} \qquad {\rm a}$  : Number of animals examined at the site

b 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

 $\sim$ 

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

|            |                         | Group Name Control<br>No. of Animals on Study 50 |         |   | 20000 ppm<br>50                             |  |
|------------|-------------------------|--|---------|---|---|--|
| gan        | Findings                |  | 1 2 3 4 | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | $\frac{1  2  3  4}{(\%)  (\%)  (\%)  (\%)}$ |  |
| irculatory | system)                 |  |         |   |   |  |
| art        | arteritis               | <50><br>0 0 0<br>( 0) ( 0) ( 0) ( 0)             |         | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)      |  |
| ery/aort   | arteritis               | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)           |         | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)      |  |
| gestive sy | stem}                   |  |         |   |   |  |
| th         | dysplasia               | <50><br>1 0 0 (<br>2) ( 0) ( 0) ( 0)             |         | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)      |  |
| gue        | arteritis               | <50><br>0 0 0 (<br>( 0) ( 0) ( 0) ( 0)           |         | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)      |  |
| ivary gl   | abscess                 | <50><br>1 0 0 (<br>( 2) ( 0) ( 0) ( 0)           |         | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)      |  |
| mach       | hyperplasia:forestomach | <50><br>0 1 1 (<br>( 0) ( 2) ( 2) ( 0            |         | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                | <50><br>0 0 0 0<br>( 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 ;  $*:P \leq 0.05$   $**:P \leq 0.01$  Test of Chi Square

(HPT150)

BAIS4

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

 $\sim \sim$ 

| brgan        | Findings                      | Group Name         Control           No. of Animals on Study         50           Grade         1         2         3         4           (%)         (%)         (%)         (%) | 5000 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | 20000 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|--------------|-------------------------------|---|---|---|--|
| ligestive sy | stem)                         |   |   |   |  |
| omach        | erosion:glandular stomach     | $\begin{array}{cccc} <50 \\ 3 & 1 & 0 & 0 \\ ( & 6) & ( & 2) & ( & 0) & ( & 0) \end{array}$   | <50><br>8 0 0 0<br>(16) (0) (0) (0)                 | <50><br>8 0 0 0<br>(16) (0) (0) (0)                   | <50><br>7 0 0 0<br>(14) (0) (0) (0)                  |
|              | hyperplasia:glandular stomach | 17 0 0 0<br>(34) (0) (0) (0)  | 16 0 0 0<br>(32) (0) (0) (0)                        | 19 0 0 0<br>(38) (0) (0) (0)                          | 13 0 0 0<br>(26)(0)(0)(0)(0)                         |
| rge intes    | lymphoid hyperplasia          | <50><br>0 1 0 0<br>( 0) ( 2) ( 0) ( 0)  | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |
| ver          | necrosis:focal                | $\langle 50 \rangle$<br>1 1 0 0<br>( 2) ( 2) ( 0) ( 0)  | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)              | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |
|              | fatty change:central          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 1 0<br>( 0) ( 0) ( 2) ( 0)                      | 1 0 0 0<br>(2)(0)(0)(0)                               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |
|              | inflammatory infiltration     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 1 0 0 0<br>(2)(0)(0)(0)                               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |
|              | inflammatory cell nest        | 6 0 0 0<br>(12) (0) (0) (0)   | 3 0 0 0<br>(6)(0)(0)(0)                             | $\begin{array}{cccccccccccccccccccccccccccccccccccc$  | 1 0 0 0<br>(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  $\leq$  0.05 \*\* : P  $\leq$  0.01 Test of Chi Square

(HPT150)

.

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

|            |                        | Group Name Control   | 5000 muyu   | 10000 yym                              | 20000 ppm   |
|------------|------------------------|--|---|--|---|
| ,          |                        | No. of Animals on Study 50                                 | 50  | 50                                     | 50  |
|            | Findings               | Grade <u>1 2 3 4</u><br>(%) (%) (%) (%)                    | $\frac{1}{(\%)} \frac{2}{(\%)} \frac{3}{(\%)} \frac{4}{(\%)}$ | <u>1 2 3 4</u><br>(%) (%) (%) (%)      | $\begin{array}{c ccccccccccccccccccccccccccccccccccc$ |
| igestive s | system)                |  |   |  |   |
| ver        | clear cell focus       | <pre> &lt;50&gt;<br/>0 0 0 0<br/>( 0) ( 0) ( 0) ( 0)</pre> | <50><br>0 2 0 0<br>( 0) ( 4) ( 0) ( 0)                        | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                |
|            | acidophilic cell focus | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$      | 0 2 0 0<br>( 0) ( 4) ( 0) ( 0)                                | 2 0 1 0<br>( 4) ( 0) ( 2) ( 0)         | 2 1 0 0<br>( 4) ( 2) ( 0) ( 0)                        |
|            | basophilic cell focus  | 1 0 0 0<br>(2)(0)(0)(0)                                    | 2 0 0 0<br>(4)(0)(0)(0)                                       | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0)         | 3 0 0 0<br>(6)(0)(0)(0)                               |
|            | bile duct hyperplasia  | 1 0 0 0<br>(2)(0)(0)(0)                                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        |
|            | biliary cyst           | 0 0 0 0<br>(0)(0)(0)(0)                                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 1 0 0 0<br>(2)(0)(0)(0)                               |
| 11 bladd   | cyst                   | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                        | <49><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <49><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                |
|            | hyperplasia            | 2 0 0 0.<br>(4)(0)(0)(0)(0)                                | 1 0 0 0<br>(2)(0)(0)(0)(0)                                    | 2 0 0 0<br>(4)(0)(0)(0)                | 2 0 0 0<br>( 4) ( 0) ( 0) ( 0)                        |
| rinary sys | stem)                  |  |   |  |   |
| dney       | cyst                   | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                |

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

 $\langle a \rangle \qquad a$  : Number of animals examined at the site

b 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

2

.

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

| rgan       | Findings                  | Group Name<br>No. of Animals<br>Grade | $\begin{array}{c} \text{Control} \\ \text{on Study} & 50 \\ \underline{1  2  3  4} \\ \underline{-  (\%)  (\%)  (\%)  (\%)} \end{array}$ | 5000                                   | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | $\begin{array}{c} 20000 \text{ µpm} \\ 50 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ |
|------------|---------------------------|---------------------------------------|--|--|---|--|
|            |                           | · · · · · · · · · · · · · · · · · · · |  |  |   |  |
| Jrinary sy | rstem)                    |                                       |  |  |   |  |
| idney      | hyaline droplet           |                                       | <50><br>2 0 0 0<br>( 4) ( 0) ( 0) ( 0)   | <50><br>3 0 0 0<br>( 6) ( 0) ( 0) ( 0) | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                | <50><br>5 0 0 0<br>(10) (0) (0) (0)  |
|            | inflammatory infiltration |                                       | 1 0 0 0<br>(2)(0)(0)(0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 1 0 0 0<br>(2)(0)(0)(0)  |
|            | lymphocytic infiltration  |                                       | 2 1 0 0<br>(4) (2) (0) (0)   | 1 0 0 0<br>(2) (0) (0) (0)             | 4 0 0 0<br>(8)(0)(0)(0)                               | 2 0 0 0<br>( 4) ( 0) ( 0) ( 0)   |
|            | osseous metaplasia        |                                       | 1 0 0 0<br>(2) (0) (0) (0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
|            | scar                      |                                       | 2 1 0 0<br>( 4) ( 2) ( 0) ( 0)   | 3 1 0 0<br>(6)(2)(0)(0)                | 1 0 0 0<br>(2)(0)(0)(0)                               | 1 0 0 0<br>(2)(0)(0)(0)  |
|            | inflammatory polyp        |                                       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 0 2 0 0<br>( 0) ( 4) ( 0) ( 0)                        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
|            | hydronephrosis            |                                       | 0 0 0 1<br>( 0) ( 0) ( 0) ( 2)   | 1 0 4 0<br>(2)(0)(8)(0)                | 0 2 2 0<br>( 0) ( 4) ( 4) ( 0)                        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
|            | mineralization:cortex     |                                       | 3 0 0 0<br>(6)(0)(0)(0)  | i 0 0 0<br>(2)(0)(0)(0)                | $\begin{array}{cccccccccccccccccccccccccccccccccccc$  | 0 0 0 0<br>( 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  $\leq$  0.05 \*\* : P  $\leq$  0.01 Test of Chi Square

(HPT150)

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

|                |                              | Group Name<br>No. of Animals on S |          | ntrol<br>5(  | ) .    |                 |                 | 5000 | թրա<br>50 |        |       |   | 1               | 0000     | թթա<br>50 |          |                 |   |                 | 2000 | )0 pp<br>50 | n      |                 |  |
|----------------|------------------------------|-----------------------------------|----------|--------------|--------|-----------------|-----------------|------|-----------|--------|-------|---|-----------------|----------|-----------|----------|-----------------|---|-----------------|------|-------------|--------|-----------------|--|
| Organ          | Findings                     | Grade                             | <u> </u> | 2<br>(%)     | 3 (%)  | <u>4</u><br>(%) | <u>1</u><br>(%) | (9   |           | 3 (%)  | 4 (%) |   | <u>1</u><br>(%) | 2<br>(%) |           | 3<br>(%) | <u>4</u><br>(%) |   | <u>1</u><br>(%) |      | 2<br>(%)    | 3 (%)  | <u>4</u><br>(%) |  |
| {Urinary syste | em)                          |                                   |          |              |        |                 |                 |      |           |        |       |   |                 |          |           |          |                 |   |                 |      |             |        |                 |  |
| kidney         | regeneration proximal tubule |                                   | 2        | <50<br>1     | )>     | 0               | 2               |      | <50>      | ,<br>0 | 0     |   | 2               | <<br>0   | 50>       | 0        | 0               |   | 3               |      | <502<br>0   | ><br>0 | 0               |  |
|                |                              |                                   | (4)(     | (2)          | ( 0) ( | ( 0)            | (4)             |      | )) (      | 0)     | ( 0)  | ( | -<br>4)         | ( 0)     | (         | 0) (     | 0)              | ( | 6)              | (    | 0) (        | 0)     | ( 0)            |  |
| urin bladd     | dilatation                   |                                   | 0        | <50<br>2     | )>     | 0               | 0               |      | <50>      | >      | 0     |   | 1               | <<br>0   | 50>       | 0        | 0               |   | 0               |      | <50)<br>0   | ><br>0 |                 |  |
|                |                              |                                   | ( 0) (   | ( <u>4</u> ) | (2)    | (0)             | ( 0)            |      | ,<br>)) ( | 2)     | (0)   | ( | 1<br>2)         | ( 0)     |           | 0) (     | 0)              | ( | 0)              |      | 0) (        | 0)     | ( 0)            |  |
|                | lymphocytic infiltration     |                                   | 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)     | ( 0)            |  |

| urethra |              | <50>                | <50>                | <50>                | <50>                |
|---------|--------------|---------------------|---------------------|---------------------|---------------------|
|         | inflammation | 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) |

#### {Endocrine system}

| pituitary |              |   | <50>                           | <50>                    | <50>                    | <50>                    |
|-----------|--------------|---|--------------------------------|-------------------------|-------------------------|-------------------------|
|           | hyperplasia  |   | 0 2 0 0                        | 0 0 0 0                 | 0 0 0 0                 | 1 0 0 0                 |
|           |              |   | (0)(4)(0)(0)                   | ( 0) ( 0) ( 0) ( 0)     | ( 0) ( 0) ( 0) ( 0)     | (2)(0)(0)(0)            |
|           | Rathke pouch | • | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | 4 0 0 0<br>(8)(0)(0)(0) | 3 0 0 0<br>(6)(0)(0)(0) | 2 0 0 0<br>(4)(0)(0)(0) |

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

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

b b : Number of animals with lesion

(c) с:b/а\*100

Significant difference ; \* : P  $\leq$  0.05 \*\* : P  $\leq$  0.01 Test of Chi Square

(HPT150)

BAIS4

.

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

| Organ         | Findings                  |                            | <u>3 4</u><br>(%) (%) | 5000 ррт<br>-50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10000 ppm<br>50<br>(%) (%) (%) (%)<br>(%) (%) (%) | 20000 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|---------------|---------------------------|----------------------------|-----------------------|--|---|--|
| {Endocrine sy | stem}                     |                            |                       |  |   |  |
| thyroid       | cyst                      | <50><br>0 0<br>( 0) ( 0) ( | 0 0                   | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)               | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)            | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |
|               | follicular hyperplasia    | 1 0<br>( 2) ( 0) (         | 0 0<br>0) ( 0)        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0)                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |
|               | C-cell hyperplasia        | 2 0<br>(4)(0)(             | 0 0<br>0) ( 0)        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       | 1 0 0 0<br>(2)(0)(0)(0)                           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |
| parathyroid   | cyst                      | <50><br>0 0<br>( 0) ( 0) ( | 0 0                   | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)               | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)            | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)               |
| adrenal       | spindle-cell hyperplasia  | <50><br>3 0<br>( 6) ( 0) ( | 0 0<br>0) ( 0)        | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)               | <50><br>2 0 0 0<br>(4) (0) (0) (0)                | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |
|               | hyperplasia:cortical cell | 0 0<br>( 0) ( 0) (         | 0 0<br>0) ( 0)        | 1 0 0 0<br>(2)(0)(0)(0)                              | 0 0 1 0<br>( 0) ( 0) ( 2) ( 0)                    | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0)                       |
| {Reproductive | system)                   |                            |                       |  |   |  |
| testis        | atrophy                   | <50><br>0 0<br>( 0) ( 0) ( | 0 0<br>0) ( 0)        | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               | <50><br>2 0 0 0<br>( 4) ( 0) ( 0) ( 0)            | <50><br>1 0 0 0<br>(2) (0) (0) (0)                   |

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

 $\langle a \rangle$  a : Number of animals examined at the site

b 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

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

.

|             |                           | Group Name<br>No. of Animals on Stud |          | ontro]<br>F   | l<br>50    |           |         |   |   | 50             | 000     | թթm<br>50   |          |     |                |   | 10              | 0000           | թթո<br>50 |           |         |     |          | 200 | 00 pj<br>50    |                 |     |          |
|-------------|---------------------------|--------------------------------------|----------|---|------------|-----------|---------|---|---|----------------|---------|-------------|----------|-----|----------------|---|-----------------|----------------|-----------|-----------|---------|-----|----------|-----|----------------|-----------------|-----|----------|
| rgan        | Findings                  | Grade                                | <u> </u> | 2<br>(%)  |            | 3<br>%)   | 4 (%)   |   | ( | <u>1</u><br>%) | 2<br>(% |             | 3<br>(%) | (9  | <u>1</u><br>6) |   | <u>1</u><br>(%) | 2<br>(%)       |           | 3<br>%)   | 4 (%)   |     | <u> </u> |     | 2 (%)          | 3 (%)           |     | 4<br>(%) |
| eproductive | e system)                 |                                      |          |   |            |           |         | • |   |                |         |             |          |     |                |   |                 |                |           |           |         |     |          |     |                |                 |     |          |
| stis        | xanthogranuloma           | (                                    | 0<br>0)  | <td< td=""><td>50&gt;<br/>( 2</td><td></td><td>0<br/>0)</td><td></td><td></td><td>0<br/>0) (</td><td>0</td><td></td><td>0<br/>0)</td><td>( (</td><td></td><td>(</td><td>0<br/>0)</td><td>&lt;<br/>0<br/>( 0)</td><td></td><td>0<br/>0) (</td><td>0<br/>0)</td><td>(</td><td>0<br/>0)</td><td>(</td><td>&lt;50<br/>0<br/>0)</td><td>0&gt;<br/>0<br/>( 0)</td><td>• (</td><td>0<br/>0)</td></td<> | 50><br>( 2 |           | 0<br>0) |   |   | 0<br>0) (      | 0       |             | 0<br>0)  | ( ( |                | ( | 0<br>0)         | <<br>0<br>( 0) |           | 0<br>0) ( | 0<br>0) | (   | 0<br>0)  | (   | <50<br>0<br>0) | 0><br>0<br>( 0) | • ( | 0<br>0)  |
| ididymis    | inflammatory infiltration | (                                    | 0<br>0)  | <9<br>1<br>(2)  |            | D) (      | 0<br>0) |   |   | 0<br>0) (      | 0       | <50><br>) ( | 0<br>0)  | ( ( | )))            | ( | 0<br>0)         | 0              |           | 0<br>0) ( | 0<br>0) | (   | 2<br>4)  | (   | <50<br>0<br>0) | 0><br>0<br>( 0) |     | 0<br>0)  |
|             | spermatogenic granuloma   | (                                    | 0<br>0)  | 0<br>( 0)   |            | D<br>D) ( | 0<br>0) |   | ( | 1<br>2) (      | 0       | ) (         | 0<br>0)  | ( ( | )))            | ( | 1<br>2)         | 1<br>(2)       |           | 0<br>0) ( | 0<br>0) | (   | 1<br>2)  |     | 0<br>0)        | 0<br>( 0)       |     | 0<br>0)  |
|             | xanthogranuloma           | (                                    | 0<br>0)  | 0<br>( 0)   | ( 2        |           | 0<br>0) |   | ( | 0<br>0) (      | 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)  |
| nin ves     | inflammation              | (                                    | 0<br>0)  | <8<br>0<br>( 0)   |            | )<br>)) ( | 0<br>0) |   |   | 0<br>0) (      | 0       |             | 0<br>0)  | (   |                | ( | 1<br>2)         | 0              |           | 0<br>0) ( | 0<br>0) | (   | 0<br>0)  |     | <50<br>0<br>0) | 0><br>0<br>( 0) | (   | 0<br>0)  |
| ostate      | lymphocytic infiltration  | (                                    | 0<br>0)  | <8<br>0<br>( 0)   |            | )<br>(    | 0<br>0) |   | ( | 1<br>2) (      | 0       | <50><br>) ( | 0<br>0)  | ( ( | )              | ( | 0<br>0)         | 0              |           | 0<br>0) ( | 0<br>0) | . ( | 0<br>0)  |     | <50<br>0<br>0) | 0><br>0<br>( 0) | (   | 0<br>0)  |
|             | hyperplasia               | (                                    | 0<br>0)  | 0<br>( 0)   |            | )<br>)) ( | 0<br>0) |   |   | 0<br>0) (      | 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)  |

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

b (c) с:b/а\*100

Significant difference ; \* : P  $\leq$  0.05 \*\* : P  $\leq$  0.01 Test of Chi Square

(HPT150)

BAIS4

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

PAGE : 12

|               |                | Group Name Control<br>No. of Animals on Study 50<br>Grade <u>1</u> 234 | 5000 ppm<br>50<br>_1 2 3 4             | 10000 ррш<br>50<br>_1 2 3 4  | 20000 ppm<br>50<br>1 2 3 4             |
|---------------|----------------|--|--|--|--|
| )rgan         | Findings       | (%) (%) (%) (%)  | (%) (%) (%) (%)                        | (%) (%) (%)  | (%) (%) (%) (%)                        |
| (Reproductive | system)        |  |  |  |  |
| prep/cli gl   | cyst           | <50><br>0 0 1 0<br>( 0) ( 0) ( 2) ( 0)                                 | <50><br>2 0 0 0<br>( 4) ( 0) ( 0) ( 0) | $\begin{array}{cccc} <50> \\ 1 & 0 & 0 & 0 \\ ( 2) & ( 0) & ( 0) & ( 0) \end{array}$ | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) |
| Nervous syst  | em}            |  |  |  |  |
| orain         | hemorrhage     | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                 | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <50><br>0 0 1 0<br>( 0) ( 0) ( 2) ( 0) |
|               | mineralization | 16 0 0 0<br>(32) (0) (0) (0)   | 15 0 0 0<br>(30) (0) (0) (0)           | 9 0 0 0<br>(18) (0) (0) (0)  | 17 0 0 0<br>(34) (0) (0) (0)           |
|               | epidermal cyst | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 1 0 0 0<br>(2)(0)(0)(0)(0)             | 0 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0)         |
| pinal cord    | hemorrhage     | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                 | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0) |
|               | necrosis:focal | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 1 0 0 0<br>(2)(0)(0)(0)                | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         |

b 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

(HPT150)

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

|       |          | Group Name          | Control         | 5000 ppm                              | 10000 ppm       | 20000 µpm  |
|-------|----------|---------------------|-----------------|---------------------------------------|-----------------|------------|
|       |          | No. of Animals on S | tudy 50         | 50                                    | 50              | 50         |
|       |          | Grade               | 1 2 3 4         | 1  2  3  4                            | 1  2  3  4      | 1 2 3      |
| Organ | Findings |                     | (%) (%) (%) (%) | (%) (%) (%) (%)                       | (%) (%) (%) (%) | (%) (%) (% |
|       |          |                     |                 | · · · · · · · · · · · · · · · · · · · |                 |            |

#### {Special sense organs/appendage}

| Harder gl              |           |        | <50> | •    |    |   |      | <5 | 0>  |      |    |     |    |   | <50  | >  |   |    |   |      |      | <50> |    |      |  |
|------------------------|-----------|--------|------|------|----|---|------|----|-----|------|----|-----|----|---|------|----|---|----|---|------|------|------|----|------|--|
| hypern                 | plasia    | 1      | 0    | 0    | 0  |   | 0    | 0  | C   | )    | 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) |  |
|                        |           |        |      |      |    |   |      |    |     |      |    |     |    |   |      |    |   |    |   |      |      |      |    |      |  |
| {Musculoskeletal syste | em)       |        |      |      |    |   |      |    |     |      |    |     |    |   |      |    |   |    |   |      |      |      |    |      |  |
| muscle                 |           |        | <50> |      |    |   |      | <5 | 0>  |      |    |     |    |   | <50  | >  |   |    |   |      |      | <50> |    |      |  |
| necros                 | sis       | 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) |  |
| minera                 | alization | 1      | 0    | 0    | 0  |   | 0    | 0  | C   | )    | 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) |  |
|                        |           |        |      |      |    |   |      |    |     |      |    |     |    |   |      |    |   |    |   |      |      |      |    |      |  |

#### {Body cavities}

| pleura     |            | <50>  | <50>                                   | <50>                                   | <50>                                   |
|------------|------------|---|--|--|--|
|            | pleuritis  | 0 0 1 0<br>( 0) ( 0) ( 2) ( 0)              | 0 0 0 0 0<br>(0)(0)(0)(0)              | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         |
| retroperit | hemorrhage | -<br><50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <50><br>0 1 0 0<br>( 0) ( 2) ( 0) ( 0) | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <50><br>0 0 0 0<br>( 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  $\leq$  0.05 \*\* : P  $\leq$  0.01 Test of Chi Square

(HPT150)

BAIS4

PAGE : 13

4

(%) (%) TABLE M 2

# HISTOPATHOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS:

## MALE: DEAD AND MORIBUND ANIMALS

#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

 $\overline{\phantom{a}}$ 

| )rgan        | Group Na<br>No. of A<br>Grade              | ame Control<br>Animals on Study 15<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 5000 ppm<br>17<br><u>1 2 3 4</u><br>(%) (%) (%) (%)                           | $ \begin{array}{c} 10000 \text{ ppm} \\ 14 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ | 20000 ppm<br>9<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|--------------|--|---|---|---|---|
| gan          |  | (%) (%) (%) (%)   | (%) (%) (%)<br>   |   | (%) (%) (%) (%)                                     |
| Integumentar | ry system/appandage)                       |   |   |   |   |
| kin/app      | necrosis                                   | <15><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                  | <17><br>0 1 0 0<br>( 0) ( 6) ( 0) ( 0)  | <14><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              |
|              | scab                                       | 1 0 0 0<br>(7)(0)(0)(0)(0)  | 0 1 0 0<br>( 0) ( 6) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      |
| Respiratory  | system)                                    |   |   |   |   |
| asal cavit   | eosinophilic change:olfactory epithelium   | <15><br>3 0 0 0<br>( 20) ( 0) ( 0) ( 0)                                 | $\begin{array}{c} <17 \\ 2 & 0 & 1 & 0 \\ (12) & (0) & (6) & (0) \end{array}$ | $\langle 14 \rangle$<br>4 0 0 0<br>( 29) ( 0) ( 0) ( 0).  | <pre>&lt; 9&gt; 2 0 0 0 ( 22) ( 0) ( 0) ( 0)</pre>  |
|              | eosinophilic change respiratory epithelium | 3 0 0 0<br>(20) (0) (0) (0)   | 2 0 1 0<br>(12) (0) (6) (0)   | 2 0 0 0<br>(14) (0) (0) (0)   | 2 0 0 0<br>(22) ( 0) ( 0) ( 0)                      |
|              | respiratory metaplasia                     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 1 0 0 0<br>(7)(0)(0)(0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      |
|              | inflammation:foreign body                  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 1 0 0 0<br>(7)(0)(0)(0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      |
|              | inflammation:respiratory epithelium        | 1 0 0 0<br>(7)(0)(0)(0)(0)  | 0 0 0 0<br>(0)(0)(0)(0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>(0)(0)(0)(0)                             |

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

 $\langle a \rangle$  a : Number of animals examined at the site

b 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

(HPT150)

BAIS4

#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 2

| Organ                        | Group Name<br>No. of Anima<br>Grade<br>Findings  | Control           als on Study         15           1         2         3         4           (%)         (%)         (%)         (%) | 5000 ppm<br>17<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10000 ppm<br>14<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 20000 ppm<br>9<br><u>1 2 3 4</u><br>(%) (%) (%) (%)        |
|------------------------------|--|---|---|--|--|
| (p                           |  |   |   |  |  |
| {Respiratory                 | system)  |   |   |  |  |
| nasal cavit                  | respiratory metaplasia:olfactory epithelium  | <15><br>7 0 0 0<br>(47) (0) (0) (0)   | <17><br>1 0 0 0 *<br>( 6) ( 0) ( 0) ( 0)            | <14><br>5 0 0 0<br>(36) (0) (0) (0)                  | < 9><br>1 0 0 0<br>(11) ( 0) ( 0) ( 0)                     |
|                              | respiratory metaplasia:gland   | 4 0 0 0<br>(27) (0) (0) (0)   | 2 0 0 0<br>(12) (0) (0) (0)                         | 5 0 0 0<br>(36)(0)(0)(0)                             | 3 0 0 0<br>(33)(0)(0)(0)                                   |
| nasopharynx                  | eosinophilic change  | <15><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <17><br>0 0 1 0<br>( 0) ( 0) ( 6) ( 0)              | <14><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     |
| lung                         | hemorrhage   | <15><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <17><br>1 2 0 0<br>( 6) ( 12) ( 0) ( 0)             | <14><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               | <pre> &lt; 9&gt;<br/>0 0 0 0<br/>( 0) ( 0) ( 0) ( 0)</pre> |
|                              | edema  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 1 0 0 0<br>( 7) ( 0) ( 0) ( 0)                       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                             |
|                              | inflammatory infiltration  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 1 0 0 0<br>( 7) ( 0) ( 0) ( 0)                       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                             |
|                              | bronchiolar-alveolar cell hyperplasia  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       | 0 1 0 0<br>( 0) (11) ( 0) ( 0)                             |
| Grade<br>< a ><br>b<br>( c ) | 1 : Slight 2 : Moderate 3 : Marked<br>a : Number of animals examined at the site<br>b : Number of animals with lesion<br>c : b / a * 100<br>ifference : * : $P \le 0.05$ ** : $P \le 0.01$ Tes | 4 : Severe  |   |  |  |

(HPT150)

#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

| Findings                     | Group Name         Control           No. of Animals on Study         15           Grade         1         2         3         4           (%)         (%)         (%)         (%) | 5000 ppm<br>17<br><u>1 2 3 4</u><br>(%) (%) (%) (%)   | $\begin{array}{c} 10000 \text{ ppm} \\ 14 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | 20000 ppm<br>9<br><u>1 2 3 4</u><br>(%) (%) (%)  |
|------------------------------|---|---|--|--|
| : system)                    |   |   |  |  |
| increased hematopoiesis      | <15><br>3 0 0 0<br>( 20) ( 0) ( 0) ( 0)   | <17><br>3 0 0 0<br>( 18) ( 0) ( 0) ( 0)   | <pre> &lt;14&gt;</pre>   | < 9><br>4 0 0 0<br>( 44) ( 0) ( 0) ( 0)  |
| lymphadenitis                | <15><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <17><br>1 0 0 0<br>( 6) ( 0) ( 0) ( 0)  | <14><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
| extramedullary hematopoiesis | <15><br>2 4 0 0<br>(13) (27) (0) (0)  | <17><br>5 7 0 0<br>( 29) ( 41) ( 0) ( 0)  | <14><br>4 4 0 0<br>( 29) ( 29) ( 0) ( 0)   | < 9><br>0 3 0 0<br>( 0) ( 33) ( 0) ( 0)  |
| system)                      |   |   |  |  |
| mineralization               | <15><br>2 0 0 0<br>( 13) ( 0) ( 0) ( 0)   | <17><br>2 1 0 0<br>(12) (6) (0) (0)   | <14><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
| arteritis                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 1 0 0 0<br>( 6) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
| arteritis                    | <15><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <17><br>1 0 0 0<br>( 6) ( 0) ( 0) ( 0)  | <14><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <pre> &lt; 9&gt;     0 0 0 0     ( 0) ( 0) ( 0) ( 0)</pre>   |
|                              | : system)<br>increased hematopoiesis<br>lymphadenitis<br>extramedullary hematopoiesis<br>system)<br>mineralization<br>arteritis   | No. of Animals on Study       15         Grade $1 - 2 - 3 - 4$ Findings       (%)         increased hematopoiesis $3 - 0 - 0$ increased hematopoiesis $3 - 0 - 0$ lymphadenitis $0 - 0 - 0$ extramedullary hematopoiesis $(15)$ mineralization $(15)$ $2 - 4 - 0 - 0$ $(13)$ $(27)$ $(20)$ $(0)$ $(13)$ $(27)$ $(20)$ $(0)$ $(13)$ $(27)$ $(20)$ $(0)$ $(13)$ $(27)$ $(20)$ $(0)$ $(13)$ $(27)$ $(20)$ $(0)$ $(13)$ $(27)$ $(20)$ $(0)$ $(13)$ $(0)$ $(0)$ $(0)$ $(13)$ $(0)$ $(13)$ $(0)$ $(13)$ $(0)$ $(13)$ $(0)$ $(13)$ $(0)$ $(13)$ $(0)$ $(15)$ $(0)$ $(15)$ $(15)$ | No. of Animals on Study       15       17         Findings   | No. of Animals on Study       15       17       14         Indings       17       14         Findings       17       14         Findings       17       1       1       2       3       4         Findings       17       1       2       3       4         System         (155       (17)       (14)         (155       (17)       (14)         (155       (17)       (14)         (155       (17)       (14)         (15)       (17)       (14)         (15)       (17)       (14)         (15)       (17)       (14)         (13)       (27)       (14)         (13)       (21)       (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  $\leq 0.05$  \*\* : P  $\leq 0.01$  Test of Chi Square

(HPT150)

BAIS4

#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

|          |                               | Group Name Control<br>No. of Animals on Study 15<br>Grade <u>1 2 3 4</u>               | 5000 ppm<br>17<br><u>1 2 3 4</u>   | 10000 ppm<br>14<br>1 2 3 4             | 20000 ppm<br>9<br>1 2 3 4              |
|----------|-------------------------------|--|--|--|--|
| gan      | Findings                      | (%) (%) (%)  | (%) (%) (%)  | (%) (%) (%) (%)                        | `(%) (%) (%) (%)                       |
| igestive | system}                       |  |  |  |  |
| ngue     | arteritis                     | $\begin{array}{cccc} <15> \\ 0 & 0 & 0 & 0 \\ ( & 0) & ( & 0) & ( & 0) \\ \end{array}$ | $\begin{array}{cccc} <17>\\ 1 & 0 & 0 & 0\\ (6) & (0) & (0) & (0) \end{array}$ | <14><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) |
| omach    | hyperplasia:forestomach       | $\langle 15 \rangle$<br>0 0 1 0<br>( 0) ( 0) ( 7) ( 0)                                 | <17><br>1 1 0 0<br>( 6) ( 6) ( 0) ( 0)   | <14><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <pre></pre>                            |
|          | erosion:glandular stomach     | 1 0 0 0<br>(7)(0)(0)(0)  | 3 0 0 0<br>(18) (0) (0) (0)  | 1 0 0 0<br>(7)(0)(0)(0)                | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         |
|          | hyperplasia:glandular stomach | 1 0 0 0<br>(7)(0)(0)(0)(0)   | 4 0 0 0<br>(24) (0) (0) (0)  | 2 0 0 0<br>(14) (0) (0) (0)            | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         |
| ver      | necrosis:focal                | <15><br>1 1 0 0<br>( 7) ( 7) ( 0) ( 0)   | <17><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <14><br>1 0 0 0<br>( 7) ( 0) ( 0) ( 0) | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) |
|          | fatty change:central          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 1 0<br>( 0) ( 0) ( 6) ( 0)   | 1 0 0 0<br>(7)(0)(0)(0)                | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         |
|          | inflammatory cell nest        | 2 0 0 0<br>(13) (0) (0) (0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         |

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

(HPT150)

#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 5

------

| Organ        | Findings                     | Group Name         Control           No. of Animals on Study         15           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | $\begin{array}{c} 5000 \text{ ppm} \\ 17 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $\begin{array}{ccc} 10000 \text{ ppm} \\ 14 \\ \underline{1 & 2 & 3 & 4} \\ (\%) & (\%) & (\%) & (\%) \end{array}$ | 20000 ppm<br>9<br><u>1 2 3 4</u><br>(%) (%) (%) (%)   |
|--------------|------------------------------|---|---|--|---|
| {Digestive s | system)                      |   |   |  |   |
| liver        | acidophilic cell focus       | <15><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <17><br>0 1 0 0<br>( 0) ( 6) ( 0) ( 0)  | $ \begin{array}{c} <14 \\ 0 & 0 & 0 & 0 \\ ( & 0) & ( & 0) & ( & 0) & ( & 0) \end{array} $                         | <br><br><br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br>0<br> |
|              | bile duct hyperplasia        | 1 0 0 0<br>(7)(0)(0)(0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
| {Urinary sys | stem)                        |   |   |  |   |
| kidney       | hyaline droplet .            | <15><br>2 0 0 0<br>( 13) ( 0) ( 0) ( 0)   | <17><br>2 0 0 0<br>(12) (0) (0) (0)   | $\begin{array}{ccccc} <14 \\ 1 & 0 & 0 & 0 \\ ( 7) & ( 0) & ( 0) & ( 0) \end{array}$                               | < 9><br>4 0 0 0<br>( 44) ( 0) ( 0) ( 0)   |
|              | scar                         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 1 0 0 0<br>(6)(0)(0)(0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
|              | hydronephrosis               | 0 0 0 1<br>( 0) ( 0) ( 0) ( 7)  | 1 0 1 0<br>(6)(0)(6)(0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
|              | mineralization:cortex        | 2 0 0 0<br>(13) (0) (0) (0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
|              | regeneration:proximal tubule | 0 1 0 0<br>( 0) ( 7) ( 0) ( 0)  | 0 0 0 0<br>(0)(0)(0)(0)(0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |

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

 $\langle a \rangle$  a : Number of animals examined at the site

b 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

(HPT150)

#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

| EX :        | MALE                   | · · · · · · · · · · · · · · · · · · ·   |   | · · · · · · · · · · · · · · · · · · ·                | PAGE :  |
|-------------|------------------------|---|---|--|---|
| 'gan        | Findings               | Group Name         Control           No. of Animals on Study         15           Grade         1         2         3         4           (%)         (%)         (%)         (%) | 5000 ppm<br>17<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10000 ppm<br>14<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 20000 ppm<br>9<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
| rinary syst | em)                    |   |   |  |   |
| in bladd    | dilatation             | <15><br>0 2 1 0<br>( 0) ( 13) ( 7) ( 0)   | <17><br>0 0 1 0<br>( 0) ( 0) ( 6) ( 0)              | <14><br>1 0 0 0<br>( 7) ( 0) ( 0) ( 0)               | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              |
| ethra       | inflammation           | <15><br>0 1 0 0<br>( 0) ( 7) ( 0) ( 0)  | <17><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <14><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              |
| ndocrine sy | stem)                  |   |   |  |   |
| tuitary     | Rathke pouch           | <15><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <17><br>1 0 0 0<br>( 6) ( 0) ( 0) ( 0)              | <14><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              |
| yroid       | cyst                   | <15><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <17><br>1 0 0 0<br>( 6) ( 0) ( 0) ( 0)              | <14><br>· 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)             | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              |
|             | follicular hyperplasia | 1 0 0 0<br>(7)(0)(0)(0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      |
| rathyroid   | cyst                   | <15><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <17><br>1 0 0 0<br>( 6) ( 0) ( 0) ( 0)              | <pre> &lt;14&gt;</pre>                               | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              |

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

 $\langle a \rangle \qquad a$  : Number of animals examined at the site

b 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

(HPT150)

#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105%)

~~~

| Organ          | Findings                 | Group Name         Control           No. of Animals on Study         15           Grade         1         2         3         4           (%)         (%)         (%)         (%) | 5000 ppm<br>17<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | $\begin{array}{c} 10000 \text{ ppm} \\ 14 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \end{array}$ | 20000 ppm<br>9<br><u>1 2 3 4</u><br>(%) (%) (%) (%)    |
|----------------|--------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------|------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------|
| {Endocrine sys | tem)                     |                                                                                                                                                                                   |                                                     |                                                                                                                  |                                                        |
| adrenal        | spindle-cell hyperplasia | <15><br>2 0 0 0<br>( 13) ( 0) ( 0) ( 0)                                                                                                                                           | <17><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <14><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                           | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                 |
| {Reproductive  | system)                  |                                                                                                                                                                                   |                                                     |                                                                                                                  |                                                        |
| testis         | atrophy                  | <15><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                                            | <17><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <14><br>1 0 0 0<br>( 7) ( 0) ( 0) ( 0)                                                                           | <pre></pre>                                            |
|                | xanthogranuloma          | 0 0 1 0<br>( 0) ( 0) ( 7) ( 0)                                                                                                                                                    | 0 0 0 0<br>(0)(0)(0)(0)(0)                          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                         |
| epididymis     | spermatogenic granuloma  | $\langle 15 \rangle$<br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                                                            | <17><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <14><br>0 1 0 0<br>( 0) ( 7) ( 0) ( 0)                                                                           | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                 |
|                | xanthogranuloma          | 0 0 1 0<br>( 0) ( 0) ( 7) ( 0)                                                                                                                                                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                         |
| prep/cli gl    | cyst                     | <15><br>0 0 1 0<br>( 0) ( 0) ( 7) ( 0)                                                                                                                                            | <17><br>1 0 0 0<br>( 6) ( 0) ( 0) ( 0)              | <14><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                           | <pre> &lt; 9&gt; 0 0 0 0   ( 0) ( 0) ( 0) ( 0) .</pre> |

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

 $\langle a \rangle$  a : Number of animals examined at the site

b 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

(HPT150)

BAIS4

#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 8

|                              |                                                                                                                                                                         | Group Name<br>No. of Animals on Stu | Cont:<br>ly | 15                    |             |    |           | ) ppm<br>17       |           |                 |           | 1000 | 0 pp<br>14        |              |                 |     | 20         | 000 1    | opm<br>9        |            |
|------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|-------------|-----------------------|-------------|----|-----------|-------------------|-----------|-----------------|-----------|------|-------------------|--------------|-----------------|-----|------------|----------|-----------------|------------|
| Organ                        | Findings                                                                                                                                                                | Grade                               | <u> </u>    | 2 <u>3</u><br>%) (%   |             | Ī  |           | 2<br>(%)          | 3 (%)     | <u>4</u><br>(%) | <u> </u>  | (    | 2<br>%)           | 3<br>(%)     | <u>4</u><br>(%) | -   | 1<br>(%)   | 2<br>(%) | <u>3</u><br>(%) |            |
|                              | · · · · · · · · · · · · · · · · · · ·                                                                                                                                   |                                     |             |                       |             |    |           |                   |           |                 |           |      |                   |              |                 |     |            |          |                 |            |
| Nervous syst                 | em}                                                                                                                                                                     |                                     |             |                       |             |    |           |                   |           |                 |           |      |                   |              |                 |     |            |          |                 |            |
| orain                        | hemorrhage                                                                                                                                                              | (                                   | 0<br>0) (   | <15><br>0 0<br>0) ( 0 |             |    | 0<br>0) ( | <17)<br>0<br>0) ( | 0         | 0<br>0)         | 0<br>( 0) | (    | <14<br>0<br>0) (  | ><br>0<br>0) | 0<br>( 0)       |     | 0<br>0) (  |          | 9><br>1<br>(11) | 0<br>) ( 0 |
|                              | mineralization                                                                                                                                                          | (                                   | 3<br>20) (  | 0 0<br>0)(0           |             | (1 | 2<br>2) ( | 0<br>0) (         | 0<br>0) ( | 0<br>0)         | 3<br>(21) | (    | 0<br>0) (         | 0<br>0)      | 0<br>(0)        | ( : | 2<br>22) ( | 0<br>0)  | 0               | 0<br>) ( 0 |
|                              | epidermal cyst                                                                                                                                                          | (                                   | 0 (         | 0 0<br>0) ( 0         |             | (  | 1<br>6) ( | 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>11) | 0<br>( 0)       | 0<br>) ( 0 |
| spinal cord                  | hemorrhage                                                                                                                                                              | (                                   |             | <15><br>0 0<br>0) ( 0 |             | (  | D<br>D) ( | <17><br>0<br>0) ( | 0         | 0<br>0)         | 0<br>( 0) | (    | <14<br>0<br>0) (  | 0            | 0<br>( 0)       |     | 1<br>11) ( | 0        | 9><br>0<br>( 0) | 0<br>) ( 0 |
|                              | necrosis:focal                                                                                                                                                          | (                                   |             | 0 0<br>0) ( 0         | 0<br>) ( 0) | (  | 1<br>5) ( | 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 |
| {Musculoskele                | tal system)                                                                                                                                                             |                                     |             |                       |             |    |           |                   |           |                 |           |      |                   |              |                 |     |            |          |                 |            |
| nuscle                       | necrosis                                                                                                                                                                | (                                   |             | <15><br>0 0<br>0) ( 0 |             |    | )<br>)) ( | <172<br>1<br>6) ( | 0         | 0<br>0)         | ( 0)      |      | <14)<br>0<br>0) ( | 0            | 0<br>( 0)       |     | 0<br>0) (  | 0        |                 | 0<br>) ( 0 |
| Grade<br>〈 a 〉<br>b<br>( c ) | 1: Slight 2: Moderate 3<br>a: Number of animals examined at the s<br>b: Number of animals with lesion<br>c: $b / a * 100$<br>ifference: $* : P \le 0.05 **: P \le 0.05$ |                                     |             |                       |             |    |           |                   |           |                 |           |      |                   |              |                 |     |            | ,        |                 |            |

(HPT150)

#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

~~/

|                |                | Group Name Control<br>No. of Animals on Study 15 | 5000 ppm<br>17                           | 10000 ppm<br>14                                                                      | 20000 ppm<br>9                         |
|----------------|----------------|--------------------------------------------------|------------------------------------------|--------------------------------------------------------------------------------------|----------------------------------------|
| Organ          | Findings       | Grade <u>1 2 3 4</u><br>(%) (%) (%) (%)          | <u>1 2 3 4</u><br>(%) (%) (%) (%)        | 1 2 3 4<br>(%) (%) (%) (%)                                                           | <u>1 2 3 4</u><br>(%) (%) (%) (%)      |
| {Musculoskele  | tal system)    |                                                  |                                          |                                                                                      |                                        |
| muscle         | mineralization | <15><br>1 0 0 0<br>( 7) ( 0) ( 0) ( 0)           | <17><br>0 · 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <14><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                               | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) |
| (Body cavities | s}             |                                                  |                                          |                                                                                      |                                        |
| pleura         | pleuritis      | <15><br>0 0 1 0<br>( 0) ( 0) ( 7) ( 0)           | <17><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | $ \begin{array}{c} <14 \\ 0 & 0 & 0 & 0 \\ ( & 0) & ( & 0) & ( & 0) \\ \end{array} $ | < 9><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) |
| retroperit     | hemorrhage     | <15><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)           | <17><br>0 l 0 0<br>( 0) ( 6) ( 0) ( 0)   | <14><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                               | < 9><br>0 0 0 0<br>( 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  $\leq$  0.05 \*\* : P  $\leq$  0.01 Test of Chi Square

(HPT150)

TABLE M 3

HISTOPATHOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: MALE: SACRIFICED ANIMALS

#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

|              |                       | Group Name<br>No. of Animals on |      | ontrol<br>35 |          |       | !                   | 1q 000   | om<br>33 |                 |    | 100       | 100 pr<br>36 |          |                 | 20           | 0000 pj<br>4 | -         |       |
|--------------|-----------------------|---------------------------------|------|--------------|----------|-------|---------------------|----------|----------|-----------------|----|-----------|--------------|----------|-----------------|--------------|--------------|-----------|-------|
| Organ        | Findings              | Grade                           | (%)  | 2<br>(%)     | 3<br>(%) | 4 (%) | <u>    1</u><br>(%) | 2<br>(%) | 3<br>(%) | <u>4</u><br>(%) | (9 | ()<br>()  | 2<br>(%)     | 3<br>(%) | <u>4</u><br>(%) | <br>1<br>(%) | 2<br>(%)     | 3<br>(%)  | 4 (%) |
| {Integumenta | ary system/appandage} |                                 |      |              |          |       |                     |          |          |                 |    |           |              |          |                 |              |              |           |       |
| skin/app     | ulcer                 |                                 | 0    | <3           | 5>       | 0     | 0                   | <3<br>0  | 33>      | 0               |    | )         | <36<br>0     | i><br>0  | 0               | 0            | <4:<br>0     |           | 0     |
|              | urei                  |                                 | ( 0) | (3)          | (3)(     | 0)    | ( 0)                | ( 0)     | (0)      | (0)             |    | ,<br>)) ( | 0) (         | (0)(     | 0<br>0)         | 0) (         | (0)          | 0<br>( 0) | ( 0)  |
|              | scab                  |                                 | 1    | 1            | 0        | 0     | 1                   | 1        | 0        | 0               | (  | )         | 1            | 0        | 0               | 1            | 0            | 0         | 0     |

{Respiratory system}

| nasal cavit | eosinophilic change:olfactory epithelium        | <35><br>13 1 0 0<br>(37) (3) (0) (0) | <33><br>21 0 0 0<br>( 64) ( 0) ( 0) ( 0) | <36><br>14 1 0 0<br>(39) (3) (0) (0) | <41><br>13 0 0 0<br>( 32) ( 0) ( 0) ( 0) |
|-------------|-------------------------------------------------|--------------------------------------|------------------------------------------|--------------------------------------|------------------------------------------|
|             | eosinophilic change:respiratory epithelium      | 13 3 0 0<br>(37) (9) (0) (0)         | 7 0 0 0<br>(21)(0)(0)(0)                 | 8 0 0 0<br>(22) (0) (0) (0)          | 10 0 0 0<br>(24) (0) (0) (0)             |
|             | respiratory metaplasia:olfactory epithelium     | 14 0 0 0<br>(40)(0)(0)(0)            | 7 0 0 0<br>(21)(0)(0)(0)                 | 6 0 0 0<br>(17) (0) (0) (0)          | 10 0 0 0<br>(24) (0) (0) (0)             |
|             | respiratory metaplasia:gland                    | 20 0 0 0<br>(57)(0)(0)(0)            | 11 l 0 0<br>(33)(3)(0)(0)                | 14 1 0 0<br>(39)(3)(0)(0)            | 16 1 0 0<br>(39)(2)(0)(0)                |
|             | squamous cell metaplasia:respiratory epithelium | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)           | 1 0 0 0<br>(3)(0)(0)(0)              | 1 0 0 0<br>(2)(0)(0)(0)(0)               |

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

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

b b : Number of animals with lesion

с:b/а\*100 (c)

Significant difference ; \* : P  $\leq$  0.05 \*\* : P  $\leq$  0.01 Test of Chi Square /

(HPT150)

BAIS4

PAGE: 1

#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

PAGE : 2

`~~~

| Organ            | I                                                                                                                                                             | Group Name<br>No. of Animals on Stud<br>Grade |           | ntrol<br>3<br><u>2</u><br>(%) |          | 4 (%)   | - | 50<br><u>1</u><br>(%) | 00 p<br><u>2</u><br>(%) | 33  | 3<br>(%) | 4(%)      |   | <u> </u> |   | )0 p)<br>3(<br><u>2</u><br>(%) |                |   | <u>4</u><br>(%) |   | 2       | 0000<br>2<br>(% | 41  | 3<br>(%) | 4         |
|------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------|-----------|-------------------------------|----------|---------|---|-----------------------|-------------------------|-----|----------|-----------|---|----------|---|--------------------------------|----------------|---|-----------------|---|---------|-----------------|-----|----------|-----------|
| {Respiratory s   | system)                                                                                                                                                       |                                               |           |                               |          |         |   |                       |                         |     |          |           |   |          |   |                                |                |   |                 |   |         |                 |     |          |           |
| asopharynx       | eosinophilic change                                                                                                                                           | (                                             | 1<br>3) ( | <3<br>1<br>3)                 | 0        | 0<br>0) |   | 1<br>3) (             | 0                       |     | 0<br>0)  | 0<br>( 0) | ( | 1<br>3)  |   | <3)<br>0<br>0)                 | 6><br>0<br>(0) |   | 0<br>0)         |   | 1<br>2) | 0               |     | 0        | 0<br>( 0) |
| ung              | inflammatory infiltration                                                                                                                                     | . (                                           | 0<br>0) ( | <3<br>0<br>0)                 | 0        | 0<br>0) |   | 1<br>3) (             | 0                       | 33> |          | 0<br>( 0) | ( | 1<br>3)  |   | <3)<br>1<br>3)                 | 5><br>0<br>(0) |   | 0<br>0)         | ( | 0<br>0) | 0               |     | 0        | 0<br>( 0) |
|                  | accumulation of foamy cells                                                                                                                                   | (                                             | 1<br>3) ( | 0<br>0)                       | 0        | 0<br>0) | ( | 0<br>0) (             | 0<br>0)                 |     | 0<br>0)  | 0<br>( 0) | ( | 0<br>0)  | ( | 0<br>0)                        | 0              | ( | 0<br>0)         | ( | 0<br>0) | 0<br>( 0)       |     | 0<br>0)  | 0<br>( 0) |
|                  | bronchiolar-alveolar cell hyperplasia                                                                                                                         | . (                                           | 0<br>0) ( | 0<br>0)                       | 0<br>( 0 | 0<br>0) | ( | 0<br>0) (             | 0<br>0)                 | (   | 0<br>0)  | 0<br>( 0) | ( | 2<br>6)  | ( | 0<br>0)                        | 0<br>( 0)      | ( | 0<br>0)         | ( | 2<br>5) | 0               | ) ( | 0<br>0)  | 0<br>( 0) |
| Hematopoietic    | ; system)                                                                                                                                                     |                                               |           |                               |          |         |   |                       |                         |     |          |           |   |          |   |                                |                |   |                 |   |         |                 |     |          |           |
| one marrow       | congestion                                                                                                                                                    | (                                             | 1<br>3) ( | <3<br>0<br>0)                 | 0        | 0<br>0) | ( | 0<br>0) (             | 0                       |     | 0<br>0)  | 0<br>(0)  | ( | 0<br>0)  | ( | <30<br>0<br>0)                 | 6><br>0<br>(0) | ( | 0<br>0)         |   | 1<br>2) | 0               |     | 0        | 0<br>( 0) |
|                  | increased hematopoiesis                                                                                                                                       | (                                             | 3<br>9) ( | 0<br>0)                       | 0<br>( 0 | 0<br>0) |   | 3<br>9) (             | 0<br>0)                 |     | 0<br>0)  | 0<br>( 0) | ( | 4<br>11) | ( | 0<br>0)                        | 0<br>( 0)      | ( | 0<br>0)         | ( | 2<br>5) | 0               |     | 0<br>0)  | 0<br>( 0) |
| (a ><br>b<br>(c) | I : Slight2 : Moderate3a : Number of animals examined at the sib : Number of animals with lesionc : b / a * 100fference ;* : $P \leq 0.05$ ** : $P \leq 0.05$ |                                               |           |                               |          | <br>    |   |                       |                         |     |          |           |   |          |   |                                |                |   |                 |   |         |                 |     |          |           |

.

(HPT150)

.

#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

| )rgan          | Findings                     | Group Name<br>No. of Animals on Stu<br>Grade | $ \begin{array}{c} \text{Control} \\ \text{idy} & 35 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ | 5000 ppm<br>33<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10000 ppm<br>36<br><u>1 2 3 4</u><br>(%) (%) (%) (%)       | 20000 ppm<br>41<br><u>1 2 3 4</u><br>(%) (%) (%) (%)       |
|----------------|------------------------------|----------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------|------------------------------------------------------------|------------------------------------------------------------|
| (Hematopoietic | system)                      |                                              |                                                                                                                                     |                                                     |                                                            |                                                            |
| oone marrow    | myelofibrosis                | (                                            | <35><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                              | <33><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <pre> &lt;36&gt;<br/>0 0 0 0<br/>( 0) ( 0) ( 0) ( 0)</pre> | <pre> &lt;41&gt;     3 0 0 0     ( 7) ( 0) ( 0) ( 0)</pre> |
|                | megakaryocyte:increased      | (                                            | 1 0 0 0<br>(3)(0)(0)(0)(0)                                                                                                          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 1 0 0 0<br>(3)(0)(0)(0)(0)                                 | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                             |
|                | granulopoiesis:increased     | . (                                          | 0 0 0 0<br>(0)(0)(0)(0)                                                                                                             | 0 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 1 0 0 0<br>(3)(0)(0)(0)(0)                                 | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                             |
| ymph node      | lymphadenitis                | (                                            | <35><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0)                                                                                              | <33><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <36><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     |
| pleen          | angiectasis                  | (                                            | <35><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                                                              | <33><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <36><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     | <41><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                     |
|                | deposit of melanin           | (                                            | 1 0 0 0<br>(3)(0)(0)(0)                                                                                                             | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                             | 2 0 0 0<br>( 5) ( 0) ( 0) ( 0)                             |
|                | extramedullary hematopoiesis | (                                            | 8 2 0 0<br>(23) (6) (0) (0)                                                                                                         | 7 3 0 0<br>(21) (9) (0) (0)                         | 11 2 0 0<br>(31) (6) (0) (0)                               | 10 2 0 0<br>(24) (5) (0) (0)                               |

Significant difference ; \* : P  $\leq$  0.05 \*\* : P  $\leq$  0.01 Test of Chi Square

(HPT150)

BAIS4

#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

| Organ         | Findings                      | Group Name Co<br>No. of Animals on Study<br>Grade <u>1</u><br>(%) | ntrol<br>35<br><u>2</u><br>(%) | 3<br>(%) | <u>4</u><br>(%) | <u>1</u><br>(%) | 5000 pj<br>2<br>(%) | pm<br>33<br>3<br>(% |           | 4 (%)   | <u>    1</u><br>(% |      | 000 pr<br>36<br><u>2</u><br>(%) |           | 4 (%)     | <u>    1</u><br>(% |     | )00 pr<br>41<br>2<br>(%) |           | <u>4</u><br>(%) |
|---------------|-------------------------------|-------------------------------------------------------------------|--------------------------------|----------|-----------------|-----------------|---------------------|---------------------|-----------|---------|--------------------|------|---------------------------------|-----------|-----------|--------------------|-----|--------------------------|-----------|-----------------|
| {Hematopoieti | c system}                     |                                                                   |                                |          |                 |                 |                     |                     |           |         |                    |      |                                 |           |           |                    |     |                          |           |                 |
| spleen        | follicular hyperplasia        | 0                                                                 | <35<br>0<br>0) (               | 0        | 0<br>( 0)       | 1<br>( 3)       | 0                   | 33><br>0<br>( 0     | )<br>)) ( | 0<br>0) | 0                  | )) ( | <36<br>1<br>3)                  | 0         | 0<br>( 0) | 0                  | ) ( | <41<br>0<br>0) (         | 0         | 0<br>( 0)       |
| {Digestive sy | stem}                         |                                                                   |                                |          |                 |                 |                     |                     |           |         |                    |      |                                 |           |           |                    |     |                          |           |                 |
| tooth         | dysplasia                     | 1                                                                 | <35<br>0<br>0) (               | 0        | 0<br>( 0)       | 0<br>( 0)       | 0                   | 33><br>0<br>( 0     | )<br>)) ( | 0<br>0) | 0                  | ) (  | <36<br>0<br>0) (                | 0         | 0<br>( 0) | 0<br>( 0)          |     | <41<br>0<br>0) (         | 0         | 0<br>( 0)       |
| salivary gl   | abscess                       | 1<br>(-3)                                                         | <35<br>0<br>0) (               | 0        | 0<br>( 0)       | 0<br>( 0)       | 0                   | 33><br>0<br>( 0     | )<br>)) ( | 0<br>0) | 0<br>( 0)          | ) (  | <36<br>0<br>0) (                | 0         | 0<br>( 0) | 0<br>( 0)          | ) ( | <41<br>0<br>0) (         | 0         | 0<br>( 0)       |
| stomach       | hyperplasia:forestomach       | 0<br>( 0) (                                                       | <35<br>1<br>3) (               | 0        | 0<br>( 0)       | 0<br>( 0)       | 0                   |                     |           | 0<br>0) | 1<br>( 3)          | ) (  | <36<br>0<br>0) (                | 0         | 0<br>( 0) | 0<br>( 0)          |     | <41<br>0<br>0) (         | 0         | 0<br>( 0)       |
|               | erosion:glandular stomach     | 2<br>( 6) (                                                       | 1<br>3) (                      | 0<br>0)  | 0<br>( 0)       | 5<br>(15)       | 0<br>( 0)           | 0<br>( 0            | )<br>)) ( | 0<br>0) | 7<br>(19)          | ) (  | 0<br>0) (                       | 0<br>( 0) | 0<br>( 0) | 7<br>(17)          | ) ( | 0<br>0) (                | 0<br>( 0) | 0<br>( 0)       |
|               | hyperplasia:glandular stomach | 16<br>(46)                                                        | 0<br>0) (                      | 0<br>0)  | 0<br>( 0)       | 12<br>(36)      | 0<br>( 0)           | 0                   |           | 0<br>0) | 17<br>(47)         |      | 0<br>0) (                       | 0<br>( 0) | 0<br>( 0) | 13<br>( 32)        |     | 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

b

(c) с:b/а\*100

Significant difference ;  $*: P \leq 0.05$   $**: P \leq 0.01$  Test of Chi Square

(HPT150)

BAIS4

#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

PAGE: 5

|              |                           | Group Name<br>No. of Animals on Study<br>Grade | 1         | ntrol<br>3<br>2 | 5<br>3    | 4         |     | 1         |   | ppm<br>33<br>2   | 3       | 4         |   | 1       | 2         | 86<br>3                    |             |   | 1       |     | 0 ppm<br>41<br>2  | 3       | 4         |
|--------------|---------------------------|------------------------------------------------|-----------|-----------------|-----------|-----------|-----|-----------|---|------------------|---------|-----------|---|---------|-----------|----------------------------|-------------|---|---------|-----|-------------------|---------|-----------|
| rgan         | Findings                  | (                                              | %)        | (%)             | (%)       | (%)       |     | (%)       | ( | %)               | (%)     | (%)       |   | (%)     | (%)       | (%)                        | ) (%)       |   | (%)     | (9  | 6)<br>            | (%)     | (%)       |
| Digestive sy | ystem)                    |                                                |           |                 |           |           |     |           |   |                  |         |           |   |         |           |                            |             |   |         |     |                   |         |           |
| arge intes   | lymphoid hyperplasia      |                                                | 0<br>0) ( | <3:<br>1<br>3)  | 0         | 0<br>( 0) | ,   | 0<br>( 0) |   | <33<br>0<br>0) ( | 0       | 0<br>( 0) | ( | 0<br>0) | 0         | 86><br>0<br>( 0)           | 0<br>) ( 0) | ( | 0<br>0) |     | <41><br>0<br>0) ( | 0       | 0<br>( 0) |
| iver         | necrosis:focal            |                                                | 0<br>0) ( | <3:<br>0<br>0)  | 0         | 0<br>( 0) | . 1 | 1<br>(3)  | ( | <33<br>0<br>0) ( | 0       | 0<br>( 0) | ( | 0<br>0) | 0         | 86><br>0<br>( 0)           | 0<br>) ( 0) | ( | 0<br>0) | (   | <41><br>0<br>0) ( | 0       | 0<br>( 0) |
|              | inflammatory infiltration |                                                | 0<br>0) ( | 0<br>0)         | 0<br>( 0) | 0<br>( 0) | I   | 0<br>( 0) |   | 0<br>0) (        | 0<br>0) | 0<br>( 0) | ( | 1<br>3) | 0<br>( 0) | 0<br>( 0)                  | 0<br>) ( 0) | ( | 0<br>0) |     | 0<br>0) (         | 0<br>0) | 0<br>( 0) |
|              | inflammatory cell nest    |                                                | 4<br>1) ( | 0<br>0)         | 0<br>( 0) | 0<br>( 0) | I   | 3<br>(9)  | ( | 0<br>0) (        | 0<br>0) | 0<br>( 0) | ( | 1<br>3) | 0<br>( 0) | 0<br>( 0)                  | 0<br>) ( 0) | ( | 1<br>2) | ( ) | 0<br>0) (         | 0<br>0) | 0<br>( 0) |
|              | clear cell focus          | (                                              | 0<br>0) ( | 0<br>0)         | 0<br>( 0) | 0<br>( 0) |     | 0<br>( 0) | ( | 2<br>6) (        | 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         |
|              | acidophilic cell focus    |                                                | 1<br>3) ( | 1<br>3)         | 0<br>( 0) | 0         | i   | 0<br>( 0) | ( | 1<br>3) (        | 0<br>0) | 0<br>( 0) | ( | 2<br>6) | 0<br>( 0) | ( <u>1</u><br>( <u>3</u> ) | 0<br>) ( 0) | ( | 2<br>5) | ( ; | 1<br>2) (         | 0<br>0) | 0<br>( 0) |
|              | basophilic cell focus     |                                                | 1<br>3) ( | 0<br>0)         | 0<br>( 0) | 0<br>( 0) | I   | 2<br>(6)  | ( | 0<br>0) (        | 0<br>0) | 0<br>( 0) | ( | 0<br>0) | 1<br>(3)  | 0<br>( 0)                  | 0<br>) ( 0) | ( | 3<br>7) |     | 0<br>0) (         | 0<br>0) | 0<br>( 0) |
|              | biliary cyst              |                                                | 0<br>0) ( | 0<br>0)         | 0<br>( 0) | 0<br>( 0) | I   | 0<br>( 0) |   | 0<br>0) (        | 0<br>0) | 0<br>( 0) | ( | 0<br>0) | 0<br>( 0) | 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

 $\langle \, a \, \rangle \qquad a$  : Number of animals examined at the site

b 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

(HPT150)

#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

PAGE : 6

| Organ          | Findings                  | Group Name<br>No. of Animals on Stud<br>Grade | 1 2                      | <u>3 4</u><br>%) (%) | 5000 ppm<br>33<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10000 ppm<br>36<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 20000 ppm<br>41<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|----------------|---------------------------|-----------------------------------------------|--------------------------|----------------------|-----------------------------------------------------|------------------------------------------------------|------------------------------------------------------|
|                |                           |                                               |                          |                      |                                                     |                                                      |                                                      |
| {Digestive sys | stem}                     |                                               |                          |                      |                                                     |                                                      |                                                      |
| gall bladd     | cyst                      | . (                                           | <35><br>0 0<br>0) ( 0) ( | 0 0<br>0) ( 0)       | <33><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)              | <36><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               | <41><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)               |
|                | hyperplasia               | . (                                           | 2 0<br>6) ( 0) (         | 0 0<br>0) ( 0)       | 1 0 0 0<br>(3)(0)(0)(0)                             | 2 0 0 0<br>( 6) ( 0) ( 0) ( 0)                       | 2 0 0 0<br>(5)(0)(0)(0)                              |
| {Urinary syste | em)                       |                                               |                          |                      |                                                     |                                                      |                                                      |
| kidney         | cyst                      | (                                             | <35><br>0 0<br>0) ( 0) ( | 0 0<br>0) ( 0)       | <33><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <36><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               | <41><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)               |
|                | hyaline droplet           | (                                             | 0 0<br>0) ( 0) (         | 0 0<br>0) ( 0)       | 1 0 0 0<br>(3)(0)(0)(0)                             | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       | 1 0 0 0<br>(2) (0) (0) (0)                           |
|                | inflammatory infiltration | (                                             | 1 0<br>3) ( 0) (         | 0 0<br>0) ( 0)       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       | 1 0 0 0<br>(2)(0)(0)(0)                              |
|                | lymphocytic infiltration  | . (                                           | 2 1<br>6) ( 3) (         | 0 0<br>0) ( 0)       | 1 0 0 0<br>(3)(0)(0)(0)                             | 4 0 0 0<br>(11) (0) (0) (0)                          | 2 0 0 0<br>(5)(0)(0)(0)                              |
|                | osseous metaplasia        | (                                             | 1 0<br>3) ( 0) (         | 0 0<br>0) ( 0)       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |

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

 $\langle a \rangle$  a : Number of animals examined at the site

b 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

(HPT150)

| STUDY NO. : 0613<br>ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] |                              | HISTOPATHOLOGICAL FINDING<br>SACRIFICED ANIMALS (105W)           | RY)                                                        | •<br>•                                 |                                                                                            |
|----------------------------------------------------------|------------------------------|------------------------------------------------------------------|------------------------------------------------------------|----------------------------------------|--------------------------------------------------------------------------------------------|
| REPORT TYPE<br>SEX                                       | : A1<br>: MALE               |                                                                  |                                                            |                                        | PAGE :                                                                                     |
|                                                          |                              | Group Name Control<br>No. of Animals on Study 35<br>Grade1 2 3 4 | 5000 ppm<br>33<br>1 2 3 4                                  | 10000 ppm<br>36<br>1 2 3 4             | 20000 ppm<br>41<br>1 2 3 4                                                                 |
| Organ                                                    | Findings                     | (%) (%) (%)                                                      | (%) (%) (%)                                                | (%) (%) (%) (%)                        | (%) (%) (%) (%)                                                                            |
| {Urinary syst                                            | tem)                         |                                                                  |                                                            |                                        |                                                                                            |
| kidney                                                   | scar                         | <pre> &lt;35&gt;     2 1 0 0     ( 6) ( 3) ( 0) ( 0)</pre>       | <pre> &lt;33&gt;<br/>2 1 0 0<br/>( 6) ( 3) ( 0) ( 0)</pre> | <36><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0) | $\begin{array}{cccc} <41>\\ 1 & 0 & 0 & 0\\ ( \ 2) & ( \ 0) & ( \ 0) & ( \ 0) \end{array}$ |
|                                                          | inflammatory polyp           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                             | 0 2 0 0<br>( 0) ( 6) ( 0) ( 0)         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                             |
|                                                          | hydronephrosis               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                   | 0 0 3 0<br>( 0) ( 0) ( 9) ( 0)                             | 0 2 2 0<br>( 0) ( 6) ( 6) ( 0)         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                             |
|                                                          | mineralization:cortex        | 1 0 0 0<br>(3)(0)(0)(0)                                          | 1 0 0 0<br>(3)(0)(0)(0)                                    | 1 0 0 0<br>(3)(0)(0)(0)                | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                             |
|                                                          | regeneration:proximal tubule | 2 0 0 0<br>( 6) ( 0) ( 0) ( 0)                                   | 2 0 0 0<br>( 6) ( 0) ( 0) ( 0)                             | 2 0 0 0<br>(6)(0)(0)(0)                | 3 0 0 0<br>(7)(0)(0)(0)                                                                    |
| urin bladd                                               | lymphocytic infiltration     | <35><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                           | <33><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)                     | <36><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                     |
| {Endocrine sy                                            | vstem)                       |                                                                  |                                                            |                                        |                                                                                            |
| pituitary                                                | hyperplasia                  | $\langle 35 \rangle$<br>0 2 0 0<br>(0) (5) (0) (0) (2)           |                                                            |                                        | <41><br>1 0 0 0<br>( 2) ( 2) ( 2) ( 2)                                                     |

| Grade | l : Slight | 2 : Moderate | 3 : Marked | 4 : Severe |
|-------|------------|--------------|------------|------------|
|-------|------------|--------------|------------|------------|

 $\langle a \rangle$  a : Number of animals examined at the site

b 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

(HPT150)

BAIS4

(2)(0)(0)(0)

.

.

( 0) ( 0) ( 0) ( 0)

( 0) ( 0) ( 0) ( 0)

#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

~~~

| rgan         | Findings                  | Group Name<br>No. of Animals on Stu<br>Grade | 1 2 3                           | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | 20000 ppm<br>41<br>1 2 3 4<br>(%) (%) (%) (%) |
|--------------|---------------------------|--|---------------------------------|---|---|---|
| indocrine sy | stem}                     |  |                                 |   |   |   |
| tuitary      | Rathke pouch              | (  | <35><br>0 0 0<br>0) ( 0) ( 0) ( | <pre>&lt;33&gt; 0 3 0 0 0 0) (9) (0) (0) (0)</pre>    | <36><br>3 0 0 0<br>(8) (0) (0) (0)                    | <41><br>2 0 0 0<br>( 5) ( 0) ( 0) ( 0)        |
| yroid        | cyst                      | (  | <35><br>0 0 0<br>0) ( 0) ( 0) ( | <33><br>0 0 0 0 0<br>0) ( 0) ( 0) ( 0) ( 0)           | <36><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)                | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)        |
|              | follicular hyperplasia    | . (  | 0 0 0<br>0)(0)(0)(0)(           | 0 0 0 0 0<br>0) ( 0) ( 0) ( 0) ( 0)                   | 0 1 0 0<br>( 0) ( 3) ( 0) ( 0)                        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |
|              | C-cell hyperplasia        | (  | 2 0 0<br>6) ( 0) ( 0) (         | 0 0 0 0 0<br>0) ( 0) ( 0) ( 0) ( 0)                   | 1 0 0 0<br>(3)(0)(0)(0)                               | 0 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              |
| rathyroid    | cyst                      | . (  | <35><br>0 0 0<br>0) ( 0) ( 0) ( | <33><br>0 0 0 0 0<br>0) ( 0) ( 0) ( 0) ( 0)           | <36><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <41><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)        |
| renal        | spindle-cell hyperplasia  | (  | <35><br>1 0 0<br>3) ( 0) ( 0) ( | <33><br>0 1 0 0 0<br>0) (3) (0) (0) (0)               | <36><br>2 0 0 0<br>( 6) ( 0) ( 0) ( 0)                | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)        |
|              | hyperplasia:cortical cell | (  | 0 0 0<br>0) ( 0) ( 0) (         | 0 1 0 0 0<br>0) (3)(0)(0)(0)                          | 0 0 1 0<br>( 0) ( 0) ( 3) ( 0)                        | 0 1 0 0<br>( 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  $\leq$  0.05 \*\* : P  $\leq$  0.01 Test of Chi Square

(HPT150)

BAIS4

#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

 $\sim$ 

| SEX :         | MALE                      | · · ·   |   |  | PAGE : 9   |
|---------------|---------------------------|---|---|--|--|
| Organ         | Findings                  | Group Name         Control           No. of Animals on Study         35           Grade         1         2         3         4           (%)         (%)         (%)         (%) | 5000 ppm<br>33<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10000 ppm<br>36<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 20000 ppm<br>41<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
| {Reproductive | system)                   |   |   |  |  |
| testis        | atrophy                   | <35><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <333><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)             | <36><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)               | <41><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)               |
| epididymis    | inflammatory infiltration | 0 1 0 0<br>( 0) ( 3) ( 0) ( 0)  | <33><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <36><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               | <41><br>2 0 0 0<br>( 5) ( 0) ( 0) ( 0)               |
|               | spermatogenic granuloma   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 1 0 0 0<br>(3)(0)(0)(0)                             | 1 0 0 0<br>(3)(0)(0)(0)                              | 1 0 0 0<br>(2)(0)(0)(0)                              |
| semin ves     | inflammation              | <35><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <33><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <36><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)               | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |
| prostate      | lymphocytic infiltration  | <35><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <33><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)              | <36><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               | <11><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |
|               | hyperplasia               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 1 0 0 0<br>(3)(0)(0)(0)(0)                           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |
| prep/cli gl   | cyst                      | 35>       0     0       0     0       0     0       0     0       0     0       0     0   | <33><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)              | <36><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)               | <41><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |

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

 $\langle a \rangle$  a : Number of animals examined at the site

b 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

(HPT150)

# HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

|                |                   | Group Name<br>No. of Animals | Control<br>on Study 35            | 5000 ppm<br>33                    | 10000 ррм<br>36                   | 20000 ppm<br>41                   |
|----------------|-------------------|------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|
| Organ          | Findings          | Grade                        | <u>1 2 3 4</u><br>(%) (%) (%) (%) |
|                |                   |                              |                                   | ~                                 |                                   |                                   |
| Nervous system | n                 |                              |                                   |                                   |                                   |                                   |
| brain          | mineralization    |                              | <35><br>13 0 0 0                  | <33><br>13 0 0 0                  | <36><br>6 0 0 0                   | <41><br>15 0 0 0                  |
|                |                   |                              | (37) (0) (0) (0)                  | (39) (0) (0) (0)                  | (17) (0) (0) (0)                  | (37) (0) (0) (0                   |
| {Special sense | organs/appendage) |                              |                                   |                                   |                                   |                                   |
| Harder gl      |                   |                              | <35>                              | <33>                              | <36>                              | <41>                              |
| 0              | hyperplasia       |                              | 1 0 0 0                           | 0 0 0 0                           | 1 0 0 0                           | 0 0 0 0                           |
|                |                   |                              | (3)(0)(0)(0)                      | ( 0) ( 0) ( 0) ( 0)               | (3)(0)(0)(0)                      | (0)(0)(0)(0)                      |

(HPT150)

BAIS4

TABLE M 4

# HISTOPATHOLOGICAL FINDINGS:

NON-NEOPLASTIC LESIONS:

FEMALE: ALL ANIMALS

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

 $\sim$ 

| )rgau         | Findings              | Group Name<br>No. of Animals on Stu<br>Grade | tudy<br>_1<br>(% | L | ntro<br>{<br>2<br>(%) | 50 | 3         | 4 (%)     | <u>1</u><br>(%) | 0 pp<br>5<br><u>2</u><br>(%) | m<br>0<br>3<br>(% | 4 (%)     |   | <u>1</u><br>(%) | ppm<br>50<br><u>2</u><br>%) |              |     | <u>4</u><br>%) | - | 10<br><u>1</u><br>(%) | 0000<br><u>2</u><br>(%) | 50 | <u>3</u><br>(%) | <u>4</u><br>(%) |
|---------------|-----------------------|--|------------------|---|-----------------------|----|-----------|-----------|-----------------|------------------------------|-------------------|-----------|---|-----------------|-----------------------------|--------------|-----|----------------|---|-----------------------|-------------------------|----|-----------------|-----------------|
| Integumentary | / system/appandage}   |  |                  |   |                       |    |           |           |                 |                              |                   |           |   |                 |                             |              |     |                |   |                       |                         |    |                 |                 |
| kin/app       | ulcer                 | . 1  | 1<br>( 2         |   | 0                     |    | 0<br>0) ( | 0<br>( 0) | 0<br>( 0)       | 0                            | i0><br>0<br>( 0   | 0<br>( 0) | ( | 0<br>0)         | <50<br>0<br>0) (            | ><br>0<br>0) |     | D<br>D)        |   | 0<br>0) (             | 0                       |    | 0<br>0) (       | 0               |
|               | scab                  |  | 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)         | 0<br>0) (                   | 0<br>0)      |     | 0<br>D)        |   | 0<br>0) (             | 0<br>( 0)               |    | 0<br>0) (       | 0               |
|               | sebaceous hyperplasia |  | 1                |   | 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               |
| ubcutis       | hemorrhage            |  | 0                |   | 0                     |    | 0<br>0) ( | 0<br>( 0) | 1<br>(2)        | 0<br>0<br>0)                 | 0                 | 0<br>( 0) | ( | 0<br>0)         | <50<br>0<br>0) (            | ><br>0<br>0) |     | D<br>D)        |   | 0<br>0) (             | 0                       |    | 0<br>0) (       | 0               |
|               | inflammation          |  | 0<br>( 0         |   | 0<br>0)               |    | 1<br>2) ( | 0<br>(0)  | 0<br>( 0)       | 0<br>0)                      | 0                 | 0<br>( 0) | ( | 0<br>0)         | 0<br>0) (                   | 0<br>0)      | ( ) |                |   | 0<br>0) (             | 0<br>( 0)               |    | 0<br>0) (       | 0               |
| Respiratory s | system)               |  |                  |   |                       |    |           |           |                 |                              |                   |           |   |                 |                             |              |     |                |   |                       |                         |    |                 |                 |
| nasal cavit   | exudate               |  | 0                |   | 0                     |    | 0<br>0) ( | 0<br>( 0) | 0<br>( 0)       | 0                            | 0><br>0<br>( 0    | 0<br>( 0) | ( | 1<br>2)         | <50<br>0<br>0) (            | ><br>0<br>0) |     | )<br>)         |   | 0<br>0) (             | 0                       |    | 0<br>0) (       | 0               |

Significant difference ; \* : P  $\leq$  0.05 \*\* : P  $\leq$  0.01 Test of Chi Square

(HPT150)

~

BAIS4

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

 $\sim$ 

~----

| rgau       | Group N<br>No. of<br>Grade                    | ame Control<br>Animals on Study 50<br>(%) (%) (%) (%) | 2500 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%)  | 5000 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | $\begin{array}{cccc} 10000 & \text{ppm} & & \\ & 50 & \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) & (\%) \end{array}$ |
|------------|---|---|--|---|---|
| espiratory | system)                                       |   |  |   |   |
| sal cavit  | inflammatory infiltration                     | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)              | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  |
|            | eosinophilic change:olfactory epithelium      | 15 1 0 0<br>(30)(2)(0)(0)                             | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | 9 0 0 0<br>(18) (0) (0) (0)                         | 9 0 0 0<br>(18) (0) (0) (0)   |
|            | eosinophilic change:respiratory epithelium    | 26 8 0 0<br>(52)(16)(0)(0)                            | 28 3 0 0<br>(56)(6)(0)(0)                            | 35 2 0 0<br>(70) (4) (0) (0)                        | 33 1 0 0<br>(66)(2)(0)(0)   |
|            | inflammation:respiratory epithelium           | 2 0 0 0<br>( 4) ( 0) ( 0) ( 0)                        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       | 6 0 0 0<br>(12) (0) (0) (0)                         | 2 0 0 0<br>( 4) ( 0) ( 0) ( 0)  |
|            | respiratory metaplasia:olfactory epithelium   | 15 0 0 0<br>(30)(0)(0)(0)                             | 6 0 0 0 *<br>(12) ( 0) ( 0) ( 0)                     | 11 0 0 0<br>(22) (0) (0) (0)                        | 10 0 0 0<br>(20) (0) (0) (0)  |
|            | respiratory metaplasia:gland                  | 22 1 0 0<br>(44) (2) (0) (0)                          | 22 0 0 0<br>(44) (0) (0) (0)                         | 18 2 0 0<br>(36) (4) (0) (0)                        | 21 0 0 0<br>(42)(0)(0)(0)   |
|            | squamous cell metaplasia:respiratory epitheli | um 1 0 0 0<br>(2)(0)(0)(0)                            | 1 0 0 0<br>(2)(0)(0)(0)                              | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 1 0 0 0<br>(2)(0)(0)(0)   |
| sopharynx  | eosinophilic change                           | <50><br>9 2 0 0<br>(18) (4) (0) (0)                   | <50><br>4 1 0 0<br>( 8) ( 2) ( 0) ( 0)               | <50><br>3 1 0 0<br>( 6) ( 2) ( 0) ( 0)              | <50><br>2 0 0 0 =<br>( 4) ( 0) ( 0) ( 0)  |

b : Number of animals with lesion b

с:b/а\*100 (c)

Significant difference ; \* : P  $\leq$  0.05 \*\* : P  $\leq$  0.01 Test of Chi Square

(HPT150)

PAGE : 15 \_\_\_\_

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

| SEX :         | FEMALE                                |  |  |  | PAGE :                                 |
|---------------|---------------------------------------|--|--|--|--|
|               | Group N<br>No. of<br>Grade            | ame Control<br>Animals on Study 50<br><u>I 2</u> 3 4 | 2500 ppm<br>50<br>1 2 3 4              | 5000 ppm<br>50<br>1 2 3 4              | 10000 ppm<br>50<br><u>1 2 3 4</u>      |
| Organ         | Findings                              | (%) (%) (%)  | (%) (%) (%) (%)                        | (%) (%) (%) (%)                        | (%) (%) (%) (%)                        |
| {Respiratory  | system)                               |  |  |  |  |
| lung          | inflammatory infiltration             | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)               | <50><br>2 0 0 0<br>( 4) ( 0) ( 0) ( 0) | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0) | <50><br>2 0 0 0<br>( 4) ( 0) ( 0) ( 0) |
|               | lymphocytic infiltration              | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 1 0 0 0<br>(2)(0)(0)(0)                | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         |
|               | bronchiolar-alveolar cell hyperplasia | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       | 1 0 0 0<br>(2)(0)(0)(0)                | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         |
|               | arteritis                             | 0 0 0 0<br>(0)(0)(0)(0)                              | 1 0 0 0<br>(2) (0) (0) (0)             | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         |
| (Hematopoieti | c system)                             |  |  |  |  |
| oone marrow   | increased hematopoiesis               | <50><br>5 0 0 0<br>( 10) ( 0) ( 0) ( 0)              | <50><br>9 0 0 0<br>(18) (0) (0) (0)    | <50><br>6 0 0 0<br>(12) (0) (0) (0)    | <50><br>5 0 0 0<br>(10) (0) (0) (0)    |
|               | myelofibrosis                         | 1 0 0 0<br>(2)(0)(0)(0)                              | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0)         | 2 0 0 0<br>(4)(0)(0)(0)                | 2 0 0 0<br>( 4) ( 0) ( 0) ( 0)         |
|               | megakaryocyte:increased               | 0 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

 $\langle a \rangle$  a : Number of animals examined at the site

b 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

(HPT150)

BAIS4

( 0) ( 0) ( 0) ( 0)

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

~

PAGE : 17

| Organ       | Findings                     | Group Name         Control           No. of Animals on Study         50           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) |  | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | 10000 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|-------------|------------------------------|---|--|---|--|
| {Hematopoie | tic system}                  |   |  |   |  |
| spleen      | fibrosis:focal               | <50><br>0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                | <50><br>0 0 1 0<br>( 0) ( 0) ( 2) ( 0)               |
|             | extramedullary hematopoiesis | $\begin{array}{cccccccccccccccccccccccccccccccccccc$  | 10 10 1 0<br>(20) (20) (2) (0)         | 11 7 0 0<br>(22) (14) (0) (0)                         | 8 5 つ0 0<br>(16) (10) (0) (0)                        |
|             | follicular hyperplasia       | 1 0 0 0<br>(2)(0)(0)(0)   | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0)         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |
| {Circulator | y system)                    |   |  |   |  |
| heart       | thrombus                     | <50><br>0 0 1 0<br>( 0) ( 0) ( 2) ( 0)  | <50><br>0 0 1 0<br>( 0) ( 0) ( 2) ( 0) | <50><br>0 1 0 0<br>( 0) ( 2) ( 0) ( 0)                | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |
|             | mineralization               | $\begin{array}{cccccccccccccccccccccccccccccccccccc$  | 1 0 0 0<br>(2)(0)(0)(0)(0)             | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 5 0 0 0<br>(10) (0) (0) (0)                          |
|             | inflammatory cell nest       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 2 0 0 0<br>(4)(0)(0)(0)(0)                            | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |
|             | myocardial fibrosis          | $\begin{array}{cccccccccccccccccccccccccccccccccccc$  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | 1 0 0 0<br>(2)(0)(0)(0)                              |

b 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

(HPT150)

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

 $\sim$ 

PAGE : 18

|              |                          | Group Name Control<br>No. of Animals on Study 50<br>Grade <u>1 2 3 4</u> | 2500 ppm<br>50<br><u>1 2 3 4</u>       | 5000 ppm<br>50<br><u>1 2 3 4</u>       | 10000 ppm<br>50<br><u>1 2 3 4</u>      |
|--------------|--------------------------|--|--|--|--|
| )rgan        | Findings                 | (%) (%) (%) (%)  | (%) (%) (%) (%)                        | (%) (%) (%) (%)                        | (%) (%) (%) (%)                        |
| Circulatory  | system)                  |  |  |  |  |
| neart        | arteritis                | <pre>&lt;50&gt; 0 0 0 0 ( 0) ( 0) ( 0) ( 0)</pre>                        | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0) | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0) | <50><br>0 1 0 0<br>( 0) ( 2) ( 0) ( 0) |
| rtery/aort   | arteritis                | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                   | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <50><br>0 0 1 0<br>( 0) ( 0) ( 2) ( 0) | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) |
| Digestive sy | stem)                    |  |  |  |  |
| tongue       | arteritis                | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                                   | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0) | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0) | <50><br>2 0 0 0<br>( 4) ( 0) ( 0) ( 0) |
| salivary gl  | lymphocytic infiltration | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)                                   | <49><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0) | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0) |
| stomach      | ulcer:forestomach        | <50><br>2 0 0 0<br>( 4) ( 0) ( 0) ( 0)                                   | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) |
|              | hyperplasia:forestomach  | 1 0 0 0<br>(2) (0) (0) (0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 2 0 0 0<br>( 4) ( 0) ( 0) ( 0)         | 4 0 0 0<br>( 8) ( 0) ( 0) ( 0)         |

ь (с) с: b/а\*100

Significant difference ; \*:  $P \leq 0.05$  \*\* :  $P \leq 0.01$  Test of Chi Square

(HPT150)

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

PAGE: 19

| )rgan       | Findings                      | Group Name         Control           No. of Animals on Study         50           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | $\begin{array}{cccc} 2500 \text{ ppm} \\ 50 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | 5000 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10000 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|-------------|-------------------------------|---|--|---|--|
| Digestive s | ystem)                        |   |  |   |  |
| tomach      | erosion:glandular stomach     | <50><br>5 2 0 0<br>(10) (4) (0) (0)   | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)   | <50><br>7 0 0 0<br>(14). ( 0) ( 0) ( 0)             | 2 0 0 0<br>(4)(0)(0)(0)                              |
|             | ulcer:glandular stomach       | 1 0 0 0<br>( 2) ( 0) ( 0) ( 0)  | 1 0 0 0<br>(2)(0)(0)(0)(0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |
|             | hyperplasia:glandular stomach | 15 0 0 0<br>(30) (0) (0) (0)  | 16 0 0 0<br>(32) (0) (0) (0)   | 12 0 0 0<br>(24) (0) (0) (0)                        | 8 0 0 0<br>(16) (0) (0) (0)                          |
| iver        | angiectasis                   | <50><br>0 1 1 0<br>( 0) ( 2) ( 2) ( 0)  | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <50><br>4 0 0 0<br>(8) (0) (0) (0)                  | <50><br>1 0 0 0<br>(2)(0)(0)(0)                      |
|             | necrosis:central              | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |
|             | necrosis:focal                | 1 0 0 0<br>(2)(0)(0)(0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 2 0 0 0<br>(4)(0)(0)(0)                             | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |
|             | inflammatory infiltration     | 1 0 0 0<br>(2)(0)(0)(0)   | 2 0 0 0<br>(4)(0)(0)(0)  | 1 0 0 0<br>(2) (0) (0) (0)                          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |
|             | inflammatory cell nest        | 11 0 0 0<br>(22) (0) (0) (0)  | 7 0 0 0<br>(14) (0) (0) (0)  | 12 0 0 0<br>(24) (0) (0) (0)                        | 8 0 0 0<br>(16)(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  $\leq$  0.05 \*\* : P  $\leq$  0.01 Test of Chi Square

(HPT150)

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

| :BDF1] | ALL ANIMALS | 1011 11201 240120 | 000 |
|--------|-------------|-------------------|-----|
|        |             |                   |     |

PAGE : 20

| )rgan        | Findings                     | Group Name<br>No. of Animals on Stu<br>Grade | Contro<br>dy<br><u>1 2</u><br>(%) (%) | 50<br>3          | 4 (%)     | 2<br>     | 500 pp<br>5<br><u>2</u><br>(%) | m<br>60<br><u>3</u><br>(%) | 4(%)      | <u> </u> |     | ) ppm<br>50<br><u>2</u><br>(%) |                | 4 (%)     |   | 10<br>1<br>(%) | 000 p<br>5<br><u>2</u><br>(%) |                 | 4        |
|--------------|------------------------------|--|---------------------------------------|------------------|-----------|-----------|--------------------------------|----------------------------|-----------|----------|-----|--------------------------------|----------------|-----------|---|----------------|-------------------------------|-----------------|----------|
| rgan         | r maings                     |  | (%) (%)                               | (%)              | (%)       | (%)       | (%)                            | (%)                        | (%)       | (%)      | )   | (%)                            | (%)            | (%)       |   | (%)            | (%)                           | (%)             |          |
| Digestive sy | stem)                        |  |                                       |                  |           |           |                                |                            |           |          |     |                                |                |           |   |                |                               |                 |          |
| iver         | extramedullary hematopoiesis | (  | <<br>0 0<br>0) ( 0)                   | 50><br>0<br>( 0) | 0<br>( 0) | 1<br>(2)  | <5<br>0<br>( 0)                | 0                          | 0<br>( 0) | 1<br>( 2 |     | <50<br>0<br>0) (               | ><br>0<br>0) ( | 0<br>( 0) | ( | 0<br>0) (      | <5<br>0<br>( 0)               | 0><br>0<br>( 0) | 0<br>( 0 |
| ,            | clear cell focus             | (  | 0 0<br>0) ( 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) |   | 1<br>2) (      |                               | 0<br>( 0)       | 0<br>( 0 |
|              | acidophilic cell focus       | (  | 0 2<br>0) ( 4)                        | 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) | ( | 1<br>2) (      | 1<br>2)                       | 0<br>( 0)       | 0<br>( 0 |
|              | basophilic cell focus        | (  | 0 0<br>0) ( 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 |
|              | biliary cyst                 | (  | 0 0<br>0) ( 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<br>( 0)       | 0<br>( 0 |
| gall bladd   | lıyperplasia                 | (  | <<br>1 0<br>2) ( 0)                   | 49><br>0<br>( 0) | 0<br>( 0) | 0<br>( 0) | <4<br>0<br>( 0)                | 0                          | 0<br>( 0) | 0        |     | <50<br>0<br>0) (               | ><br>0<br>0) ( | 0<br>( 0) | ( | 1<br>2) (      | <5<br>0<br>( 0)               | 0><br>0<br>( 0) | 0<br>( 0 |
| oancreas     | fibrosis:focal               | . (  | <<br>0 0<br>0) ( 0)                   | 50><br>0<br>( 0) | 0<br>( 0) | 0<br>( 0) | <5<br>0<br>( 0)                | 0                          | 0<br>( 0) | 0<br>( 0 |     | <50<br>0<br>0) (               | ><br>0<br>0) ( | 0<br>( 0) | ( | 0<br>0) (      |                               | 0><br>1<br>(2)  | 0<br>( 0 |

Significant difference ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$  Test of Chi Square

(HPT150)

.

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

PAGE : 21

| Organ          | Findings                  | Group Name<br>No. of Animals on Stud<br>Grade |            | 1trol<br>50<br><u>2</u><br>(%) | 3 (%)     | 4 (%)     |     | 2<br>1<br>(%) | 500 p<br>2<br>(%) | 50 | 3<br>(%)   | 4(%)    |   | 5<br>- <u>1</u><br>(%) | 000 p<br><u>2</u><br>(%) | 50               | 3<br>%)   | 4 (%)   | - | 10<br><u>1</u><br>(%) | )000<br>2<br>(%) | 50<br>3  | ;) (      | <u>4</u><br>(%) |
|----------------|---------------------------|---|------------|--------------------------------|-----------|-----------|-----|---------------|-------------------|----|------------|---------|---|------------------------|--------------------------|------------------|-----------|---------|---|-----------------------|------------------|----------|-----------|-----------------|
| {Urinary syste | m) .                      |   |            |                                |           |           |     |               |                   |    |            |         |   |                        |                          |                  |           |         |   |                       |                  |          |           |                 |
| kidney         | cyst                      | (   | 0<br>0) (  | <50<br>0<br>0) (               | 0         | 0<br>( 0) | (   | 1<br>2)       | 0                 |    | 0<br>0) (  | 0<br>0) | ( | 0<br>0)                | 0                        | :50><br>(<br>( ( | )<br>)) ( | 0<br>0) |   | 0<br>0) (             | 0                |          | )<br>)) ( | 0<br>0)         |
| ·              | hyaline droplet           | (   | 7<br>14) ( | 0<br>0) (                      | 0<br>( 0) | 0<br>( 0) | (   | 14<br>28)     | 0<br>( 0)         | (  | 0<br>0) (  | 0<br>0) | ( | 5<br>10)               | 0<br>( 0)                | ( (              | )<br>)) ( | 0<br>0) |   | 14<br>28) (           | 0<br>( 0)        | 0<br>( 0 | )<br>)) ( | 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) | ( | 1<br>2)                | 0<br>( 0)                | ( (              | )<br>) (  | 0<br>0) | ( | 0<br>0) (             | 0<br>0)          | 0<br>( 0 | )<br>)) ( | 0<br>0)         |
|                | inflammatory infiltration | (   | 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)                | ( (              | )<br>)) ( | 0<br>0) | ( | 0<br>0) (             | 0<br>( 0)        | 0<br>( 0 | )<br>)) ( | 0<br>0)         |
|                | lymphocytic infiltration  | . (   | 4<br>8) (  | 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) | ( | 2<br>4) (             | 0<br>( 0)        | ( 0      | )<br>)) ( | 0<br>0)         |
|                | scar                      | (   | 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)                | ( (              | )<br>)) ( | 0<br>0) | ( | 2<br>4) (             | 0<br>( 0)        | 0<br>( 0 | )<br>)) ( | 0<br>0)         |
|                | inflammatory polyp        | (   | 0<br>0) (  | 2<br>4) (                      | 0<br>0)   | 0<br>( 0) | . ( | 2<br>4)       | 1<br>(2)          | (  | 0<br>0) (  | 0<br>0) | ( | 1<br>2)                | 0<br>( 0)                |                  | )<br>)) ( | 0<br>0) | ( | 0<br>0) (             | 2<br>( 4)        | 0<br>( 0 | )))(      | 0<br>0)         |
|                | hydronephrosis            | (   | 0<br>0) (  | 0<br>0) (                      | 2<br>4)   | 2<br>( 4) | (   | 1<br>2)       | 1<br>(2)          | (  | 2<br>4) (  | 0<br>0) | ( | 0<br>0)                | 0<br>( 0)                | ( 4              | 2<br>4) ( | 0<br>0) |   | 1<br>2) (             | 3<br>( 6)        |          | 2) (      | 0<br>0)         |

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

 $\langle a \rangle$  a : Number of animals examined at the site

b 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

(HPT150)

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

|              |                            | Group Name<br>No. of Animals on |              | ntrol<br>50      |           |         |   | 25        | 00 pp<br>5    |           |           |   |   | 50        | 1q 00           | om<br>50        |     |                 |   | 10        | 0000            | ppm<br>50        |            |
|--------------|----------------------------|---------------------------------|--------------|------------------|-----------|---------|---|-----------|---------------|-----------|-----------|---|---|-----------|-----------------|-----------------|-----|-----------------|---|-----------|-----------------|------------------|------------|
| Organ        | Findings                   | Grade                           | <u> </u> (%) | 2<br>(%)         | 3 (%)     | 4 (%)   |   | 1<br>(%)  | 2 (%)         | 3<br>(%)  | 4<br>(%)  | - | - | 1<br>(%)  | 2 (%)           | 3 (%            |     | <u>4</u><br>(%) | - | 1<br>(%)  | 2<br>(%)        | 3                |            |
| {Urinary sys | stem}                      |                                 |              |                  |           |         |   |           |               |           |           |   |   |           |                 |                 |     |                 |   |           |                 |                  |            |
| kidney       | pyelonephritis             |                                 | 0<br>( 0) (  | <50<br>0<br>0) ( | 1         | 0<br>0) | ( | 0<br>0) ( | <5<br>0<br>0) | 0         | 0<br>( 0) |   | ( | 0<br>0) ( | <(<br>0<br>( 0) | i0><br>0<br>( 0 | ) ( | 0<br>0)         | ( | 0<br>0) ( |                 | 50><br>0<br>(0)  | ) ( (      |
|              | arthritis                  |                                 | 0<br>( 0) (  | 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)        | () ( (     |
|              | hyaline droplet:glomerulus |                                 | 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               | ) ( | 0<br>0)         | ( | 0<br>0) ( | 0<br>( 0)       | 0<br>( 0)        | (<br>) ( ( |
| urin bladd   | dilatation                 |                                 | 0<br>( 0) (  | <50<br>1<br>2) ( | 1         | 0<br>0) | ( | 1<br>2) ( | <5<br>2<br>4) | 0         | 0<br>( 0) |   | ( | 0<br>0) ( | <(<br>0<br>( 0) | i0><br>0<br>( 0 | ) ( | 0<br>0)         | ( | 0<br>0) ( | <:<br>1<br>( 2) | 50><br>0<br>( 0) | (<br>) ( ( |
|              | inflammatory infiltration  |                                 | 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               | ) ( | 0<br>0)         | ( | 0<br>0) ( | 0<br>0)         | 0<br>( 0)        | (<br>) ( ( |
|              | lymphocytic infiltration   |                                 | 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               | ) ( | 0<br>0)         | ( | 0<br>0) ( | 0<br>0)         | 0<br>· ( 0)      | (<br>) ( ( |

### {Endocrine system}

| pituitary   | <50>                | <50>         | <50>         | <50>         |
|-------------|---------------------|--------------|--------------|--------------|
| angiectasis | 0 0 0 0             | 1 0 0 0      | 1 0 0 0      | 1 0 0 0      |
|             | ( 0) ( 0) ( 0) ( 0) | (2)(0)(0)(0) | (2)(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  $\leq$  0.05 \*\* : P  $\leq$  0.01 Test of Chi Square

(HPT150)

BAIS4

#### STUDY NO. : 0613 HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] ALL ANIMALS (0-105W) REPORT TYPE : A1 : FEMALE SEX Group Name Control 2500 ppm No. of Animals on Study 50 50 2 2 Grade 3 3 1 4 1 4 Findings\_ (%) (%) Organ\_\_\_ (%) (%) (%) (%) (%) (%) (%)

| {Endocrine sys | stem)              |   |  |  |
|----------------|--------------------|---|--|--|
| pituitary      | cyst               | <50>     <50>       0     0     0     0     0       (0)     (0)     (0)     (0)     (0)     (0)   | <50><br>2 0 0 0<br>( 4) ( 0) ( 0) ( 0) | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
|                | hyperplasia        | 7       2       1       0       4       5       3       0         (14)       (4)       (2)       (0)       (8)       (10)       (6)       (0) | 9 2 3 0<br>(18) (4) (6) (0)            | 5 2 4 0<br>(10) (4) (8) (0)              |
|                | Rathke pouch       | 1       0       0       0       0       0       0         (2)       (0)       (0)       (0)       (0)       (0)       (0)       (0)           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 1 0 0 0<br>(2)(0)(0)(0)                  |
| thyroid        | cyst               | $\begin{array}{cccccccccccccccccccccccccccccccccccc$  | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | . <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) |
|                | C-cell hyperplasia | 3       0       0       0       0       0       0         (6)       (0)       (0)       (0)       (0)       (0)       (0)       (0)           | 1 0 0 0<br>(2)(0)(0)(0)                | 1 0 0 0<br>(2)(0)(0)(0)                  |
| parathyroid    | hyperplasia        | <50> <50><br>1 0 0 0 0 0 0 0<br>( 2) ( 0) ( 0) ( 0) ( 0) ( 0) ( 0) ( 0)   | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
| adrena1        | degeneration       | <50>     <50>       0     0     0     0     1     0       (0)     (0)     (0)     (0)     (0)     (0)   | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |

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

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

b b : Number of animals with lesion

(c) с: b / а \* 100

Significant difference ; \* : P  $\leq$  0.05 \*\* : P  $\leq$  0.01 Test of Chi Square

(HPT150)

BAIS4

PAGE : 23

4

(%)

10000 ppm

2

(%)

50

(%) (%)

3

5000 ppm

2 3

(%)

50

(%)

4

(%)

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

 $\sim$ 

PAGE : 24

|               |                           | Group Name<br>No. of Animals c |              | trol<br>50        |                   |                 | 250          | 0 pp<br>5      |             |                 | 5  | ар 000<br>1 | om.<br>50        |                 |   | 10          | 000° pj<br>51  |           |           |
|---------------|---------------------------|--------------------------------|--------------|-------------------|-------------------|-----------------|--------------|----------------|-------------|-----------------|--|-------------|------------------|-----------------|---|-------------|----------------|-----------|-----------|
| Organ         | Grade                     | Grade                          | 1            | 2                 | <u>3</u><br>(%) ( | <u>4</u><br>(%) | 1(%)         | 2<br>(%)       | 3<br>(%)    | <u>4</u><br>(%) | <u> </u>                                 | 2<br>(%)    | 3<br>(%)         | <u>4</u><br>(%) | ( | 1<br>(%)    | 2 (%)          | 3<br>(%)  | 4<br>(%)  |
| Endocrine sys | tem)                      |                                |              |                   |                   |                 |              |                |             |                 |  |             |                  |                 |   |             |                |           |           |
| adrenal       | spindle-cell hyperplasia  |                                | 32<br>(64) ( | <50><br>2<br>4) ( |                   | 0<br>0)         | 32<br>(64) ( | <50<br>1<br>2) | 0           | 0<br>( 0)       | 30<br>(60)                               | 1           | 50><br>0<br>( 0) | 0<br>( 0)       |   | :5<br>i0) ( | <50<br>2<br>4) | 0         | 0<br>( 0) |
|               | focal fatty change:cortex |                                | 0<br>( 0) (  | 3<br>6) (         |                   | 0<br>0)         | 1<br>(2)(    | 1<br>2)        | 0<br>( 0) ( | 0               | 0<br>( 0)                                | 1<br>(2)    | 0<br>( 0)        | 0<br>( 0)       |   |             | 0<br>· 0)      | 0<br>( 0) | 0<br>( 0) |
| Reproductive  | system)                   |                                |              |                   |                   |                 |              |                |             |                 |  |             |                  |                 |   |             |                |           |           |
| ovary         | angiectasis               |                                | 0<br>( 0) (  | <50><br>0<br>0) ( |                   | 0<br>0)         | 1<br>(2)(    | <50<br>0<br>0) | 0           | 0               | 0<br>( 0)                                |             | 50><br>0<br>(0)  | 0<br>( 0)       | ( | 0<br>0) (   | <50<br>0<br>0) | 0         | 0<br>( 0) |
|               | cyst                      |                                | 5<br>(10) (  | 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)       |   | 2<br>4) (   | 3<br>6)        | 0<br>( 0) | 0<br>( 0) |
|               | hyperplasia               |                                | 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) |
| iterus        | dilatation                |                                | 0<br>( 0) (  |                   |                   | 0<br>0)         | 0<br>( 0) (  |                | • 0         | 0               | $\begin{pmatrix} 1 \\ (2) \end{pmatrix}$ | 0           | i0><br>0<br>(0)  | 0<br>( 0)       |   | 0<br>0) (   | <50<br>0<br>0) | 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 :  $*: P \leq 0.05$   $**: P \leq 0.01$  Test of Chi Square

(HPT150)

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

| rgan        | Findings                       | Group Name         Control           No. of Animals on Study         50           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | 2500 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%)                              | 5000 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10000 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|-------------|--------------------------------|---|--|---|--|
| Reproductiv | ve system)                     |   |  |   |  |
| terus       | thrombus                       | <50><br>0 1 0 0<br>( 0) ( 2) ( 0) ( 0)  | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |
|             | inflammatory infiltration      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 1 0 0 0<br>(2)(0)(0)(0)(0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |
|             | stromal hyperplasia            | I 0 0 0<br>(2)(0)(0)(0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0                        |
|             | cystic endometrial hyperplasia | 26 0 0 0<br>(52) (0) (0) (0)  | 16 1 0 0<br>(32)(2)(0)(0)  | 22 I 0 0<br>(44)(2)(0)(0)                           | 16 1 0 0<br>(32) (2) (0) (0)                         |
| gina        | polyp                          | . <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <50><br>0 1 0 0<br>( 0) ( 2) ( 0) ( 0)              | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |
| mmary gl    | cyst                           | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)   | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0                |
| ep∕cli gl   | cyst                           | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <50>       0     0     0       (     0)     (     0)       (     0)     (     0) | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)              | <50><br>0 0 0 0<br>( 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  $\leq$  0.05 \*\* : P  $\leq$  0.01 Test of Chi Square

(IIPT150)

BAIS4

PAGE : 25

 $\sim$ 

 STUDY NO.
 : 0613

 ANIMAL
 : MOUSE B6D2F1/Cr1j[Crj:BDF1]

 REPORT TYPE
 : A1

 SEX
 : FEMALE

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

|                | Group Name<br>No. of Animals | Control<br>on Study 50                            | 2500 ppm<br>50                    | 5000 ppm<br>50                    | 10000 ppm<br>50                   |
|----------------|------------------------------|---|-----------------------------------|-----------------------------------|-----------------------------------|
| Findings       | Grade                        | <u>    1   2   3   4</u><br>(%)   (%)   (%)   (%) | <u>1 2 3 4</u><br>(%) (%) (%) (%) | <u>1 2 3 4</u><br>(%) (%) (%) (%) | <u>1 2 3 4</u><br>(%) (%) (%) (%) |
| tem)           |                              | <50>  | <50>                              | <50>                              | <50>                              |
| hemorrhage     |                              | 0 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)    | 1 0 0 0<br>(2)(0)(0)(0)           |
| mineralization |                              | 5 0 0 0<br>(10) (0) (0) (0)                       | 7 0 0 0<br>(14) (0) (0) (0)       | 5 0 0 0<br>(10) (0) (0) (0)       | 7 0 0 0<br>(14) (0) (0) (0)       |

{Special sense organs/appendage}

0rgan\_\_\_

brain

{Nervous system}

| еуе       |                           | <50> <50>  | <50>                                   | <50>                                   |
|-----------|---------------------------|--|--|--|
|           | inflammatory infiltration | 0 0 0 0 0 0 0 0<br>( 0) ( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 0 1 0 0<br>( 0) ( 2) ( 0) ( 0)         |
|           | cataract                  | 0       0       0       0       0       0       0         (       0)       (       0)       (       0)       (       0)       (       0)       (       0)  | 1 0 0 0<br>(2) (0) (0) (0)             | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         |
|           | retinal atrophy           | 0       0       0       0       0       0       0         (       0)       (       0)       (       0)       (       0)       (       0)       (       0)  | 0 0 1 0<br>( 0) ( 0) ( 2) ( 0)         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         |
|           | keratitis                 | 0       0       0       0       0       0       0         (       0) <td>0 0 0 0 0<br/>( 0) ( 0) ( 0) ( 0)</td> <td>1 0 1 0<br/>(2)(0)(2)(0)</td> | 0 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)       | 1 0 1 0<br>(2)(0)(2)(0)                |
| Harder gl | degeneration              | $\begin{array}{cccccccccccccccccccccccccccccccccccc$   | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0) | <50><br>0 0 0 0<br>( 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  $\leq$  0.05 \*\* : P  $\leq$  0.01 Test of Chi Square

(HPT150)

BAIS4

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

 $\sim$ 

PAGE : 27

 $\sim \sim \sim$ 

| )rgan          | Findings            | Group Name         Control           No. of Animals on Study         50           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | 2500 ppm<br>50<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | $\begin{array}{cccc} 5000 \text{ ppm} \\ 50 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |
|----------------|---------------------|---|---|--|---|
| {Special sense | e organs/appendage} | ······································  |   |  |   |
| larder gl      | hyperplasia         | <pre> &lt;50&gt;     0 0 0 0     ( 0) ( 0) ( 0) ( 0)</pre>  | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)   | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |
| Musculoskelet  | tal system)         |   |   |  |   |
| uscle          | mineralization      | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <50><br>1 0 · 0 0<br>( 2) ( 0) ( 0) ( 0)            | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <50><br>2 0 0 0<br>( 4) ( 0) ( 0) ( 0)                |
| DINE           | osteosclerosis      | <50><br>1 0 0 0<br>( 2) ( 0) ( 0) ( 0)  | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |
| Body cavities  | 5)                  |   |   |  |   |
| ediastinum     | inflammation        | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <50><br>0 1 0 0<br>( 0) ( 2) ( 0) ( 0)                |
| eritoneum      | peritonitis         | <50><br>0 0 1 0<br>( 0) ( 0) ( 2) ( 0)  | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <50><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |

(HPT150)

TABLE M 5

# HISTOPATHOLOGICAL FINDINGS:

NON-NEOPLASTIC LESIONS:

FEMALE: DEAD AND MORIBUND ANIMALS

# HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

 $\sim$ 

PAGE : 10

| Organ   | Group<br>No. of<br>Grade  | Name         Control           21         21           1         2         3         4           (%)         (%)         (%)         (%) | 2500 ppm<br>24<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 5000 ppm<br>19<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10000 ppm<br>30<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|---|---|--|---|---|--|
| {Integumentar                                 | ry system/appandage)  |  |   |   |  |
| skin/app                                      | ulcer   | <21><br>1 0 0 0<br>( 5) ( 0) ( 0) ( 0)   | <24><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <19><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <30><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |
|   | scab  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 2 0 0<br>(0)(8)(0)(0)                             | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |
| subcutis                                      | inflammation  | $\begin{array}{c} <21 \\ 0 & 0 & 1 & 0 \\ ( & 0) & ( & 0) & ( & 5) & ( & 0) \end{array}$   | <24><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <19><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <30><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |
| {Respiratory                                  | system)   |  |   |   |  |
| nasal cavit                                   | exudate   | <21><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | <24><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <19><br>1 0 0 0<br>( 5) ( 0) ( 0) ( 0)              | <30><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |
|   | eosinophilic change:olfactory epithelium  | 5 1 0 0<br>(24)(5)(0)(0)   | 5 0 0 0<br>(21) (0) (0) (0)                         | 2 0 0 0<br>(11) (0) (0) (0)                         | 4 0 0 0<br>(13) (0) (0) (0)                          |
|   | eosinophilic change:respiratory epithelium  | 9 2 0 0<br>(43)(10)(0)(0)  | 12 0 0 0<br>(50) (0) (0) (0)                        | 10 1 0 0<br>(53)(5)(0)(0)                           | 20 0 0 0<br>(67) ( 0) ( 0) ( 0)                      |
| Grade<br>< a ><br>b<br>( c )<br>Significant d | <ul> <li>1: Slight 2: Moderate 3: Mark</li> <li>a: Number of animals examined at the site</li> <li>b: Number of animals with lesion</li> <li>c: b / a * 100 ,</li> <li>lifference; *: P ≤ 0.05 ** : P ≤ 0.01</li> </ul> | ted 4: Severe<br>Test of Chi Square  |   |   |  |

(HPT150)

•

BAIS4

-

# HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

~\_\_\_\_\_

PAGE : 11

| )rgan          | Group Name<br>No. of Animals on<br>Grade<br>Findings | Control<br>Study 21<br>(%) (%) (%) (%)  | 2500 ppm<br>24<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 5000 ppm<br>19<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10000 ppm<br>30<br><u>1 2 3 4</u><br>(%) (%) (%) (%)       |
|----------------|--|---|---|---|--|
| {Respiratory s | vstam)   |   |   |   |  |
| nasal cavit    | inflammation:respiratory epithelium                  | <21><br>1 0 0 0<br>( 5) ( 0) ( 0) ( 0)  | <24><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | 2 0 0 0<br>( 11) ( 0) ( 0) ( 0)                     | <30><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     |
|                | respiratory metaplasia:olfactory epithelium          | 6 0 0 0<br>(29)(0)(0)(0)                | 2 0 0 0<br>( 8) ( 0) ( 0) ( 0)                      | 2 0 0 0<br>(11) (0) (0) (0)                         | 2 0 0 0<br>(7)(0)(0)(0)                                    |
|                | respiratory metaplasia:gland                         | 11 0 0 0<br>(52) ( 0) ( 0) ( 0)         | 6 0 0 0<br>(25)(0)(0)(0)                            | 5 0 0 0<br>(26) (0) (0) (0)                         | 12 0 0 0<br>(40)(0)(0)(0)                                  |
|                | squamous cell metaplasia:respiratory epithelium      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)          | 1 0 0 0<br>( 4) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                             |
| ıasopharynx    | eosinophilic change                                  | <21><br>3 1 0 0<br>(14) (5) (0) (0)     | <24><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)              | <19><br>3 1 0 0<br>( 16) ( 5) ( 0) ( 0)             | <30><br>2 0 0 0<br>( 7) ( 0) ( 0) ( 0)                     |
| lung           | inflammatory infiltration                            | <21><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <24><br>2 0 0 0<br>( 8) ( 0) ( 0) ( 0)              | <19><br>1 0 0 0<br>( 5) ( 0) ( 0) ( 0)              | <pre> &lt;30&gt;     1 0 0 0     ( 3) ( 0) ( 0) ( 0)</pre> |
| (Hematopoietic | system)  |   |   |   |  |
| oone marrow    | increased hematopoiesis                              | <21><br>4 0 0 0<br>( 19) ( 0) ( 0) ( 0) | <24><br>5 0 0 0<br>( 21) ( 0) ( 0) ( 0)             | <19><br>6 0 0 0<br>(32) (0) (0) (0)                 | <30><br>5 0 0 0<br>(17) (0) (0) (0)                        |

Significant difference ; \* : P  $\leq$  0.05 \*\* : P  $\leq$  0.01 Test of Chi Square

.

# HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

| SEX :          | FEMALE                       |   |   |  | PAGE : 12  |
|----------------|------------------------------|---|---|--|--|
| Organ          | Findings                     | Group Name         Control           No. of Animals on Study         21           Grade         1         2         3         4           (%)         (%)         (%)         (%) | 2500 ppm<br>24<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | $ \begin{array}{c} 5000 \text{ ppm} \\ 19 \\ \underline{1 \ 2 \ 3 \ 4} \\ (\%) \ (\%) \ (\%) \ (\%) \ (\%) \end{array} $ | 10000 ppm<br>30<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
| (Hematopoietic | c system)                    |   |   |  |  |
| spleen         | extramedullary hematopoiesis | <21><br>4 4 2 0<br>(19) (19) (10) (0)   | <24><br>1 9 1 0<br>( 4) ( 38) ( 4) ( 0)             | <19><br>2 7 0 0<br>(11) (37) (0) (0)   | <30><br>3 5 0 0<br>(10) (17) (0) (0)                 |
| {Circulatory   | system}                      |   |   |  |  |
| heart          | thrombus                     | <21><br>0 0 1 0<br>( 0) ( 0) ( 5) ( 0)  | <24><br>0 0 1 0<br>( 0) ( 0) ( 4) ( 0)              | <19><br>0 1 0 0<br>( 0) ( 5) ( 0) ( 0)   | <30><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |
|                | mineralization               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 1 0 0 0<br>( 4) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 5 0 0 0<br>(17) (0) (0) (0)                          |
|                | inflammatory cell nest       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 1 0 0 0<br>(5)(0)(0)(0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |
|                | myocardial fibrosis          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 1 0 0 0<br>(3)(0)(0)(0)                              |
|                | artoritis                    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 1 0 0 0<br>(4)(0)(0)(0)                             | 1 0 0 0<br>(5)(0)(0)(0)  | 0 1 0 0<br>( 0) ( 3) ( 0) ( 0)                       |
| artery/aort    | arteritis                    | <21><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <24><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <19><br>0 0 1 0<br>( 0) ( 0) ( 5) ( 0)   | <30><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |

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

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

b 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

(HPT150)

#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

| 1 |  |  |
|---|--|--|
|   |  |  |
|   |  |  |

| 0rgan         | Findings                      | Group Name         Control           No. of Animals on Study         21           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | 2500 ppm<br>24<br><u>1 2 3 4</u><br>(%) (%) (%) (%)   | 5000 ppm<br>19<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |
|---------------|-------------------------------|---|---|---|---|
| {Digestive sy | rstem}                        |   |   |   |   |
| tongue        | arteritis                     | $\langle 21 \rangle$<br>1 0 0 0<br>( 5) ( 0) ( 0) ( 0)  | $\begin{array}{cccc} <24 \\ 1 & 0 & 0 & 0 \\ ( \ 4 ) & ( \ 0 ) & ( \ 0 ) & ( \ 0 ) \end{array}$ | <19><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <30><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)                |
| stomach       | ulcer:forestomach             | $\begin{array}{cccc} & <21 \\ 1 & 0 & 0 & 0 \\ ( 5) & ( 0) & ( 0) & ( 0) \end{array}$   | <24><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <19><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <30><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |
| ••<br>•       | hyperplasia:forestomach       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 1 0 0 0<br>(3)(0)(0)(0)                               |
|               | erosion:glandular stomach     | 1 0 0 0<br>(5)(0)(0)(0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 1 0 0 0<br>(5)(0)(0)(0)                             | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        |
|               | ulcer:glandular stomach       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 1 0 0 0<br>( 4) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        |
|               | hyperplasia:glandular stomach | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 1 0 0 0<br>(5)(0)(0)(0)                             | 2 0 0 0<br>(7)(0)(0)(0)                               |
| liver         | necrosis:central              | <21><br>0 1 0 0<br>( 0) ( 5) ( 0) ( 0)  | <24><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <19><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <30><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                |

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

 $\langle a \rangle$  a : Number of animals examined at the site

b b: Number of animals with lesion

(c) c:b/a\*100

(HPT150)

BAIS4

.

# HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

`\_\_\_\_

 $\sim$ 

| Organ     | Findings                  | Group Name         Control           No. of Animals on Study         21           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | 2500 ppm<br>24<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | $\begin{array}{c} 5000 \text{ ppm} \\ 19 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | 10000 ppm<br>30<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|-----------|---------------------------|---|---|---|--|
| Digestive | system}                   |   |   |   |  |
| iver      | necrosis:focal            | $\begin{array}{cccc} & <21 \\ 1 & 0 & 0 & 0 \\ ( & 5) & ( & 0) & ( & 0) \end{array}$  | <24><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <19><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <30><br>0 0 0 0<br><( 0) ( 0) ( 0) ( 0)              |
|           | inflammatory infiltration | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 1 0 0 0<br>( 4) ( 0) ( 0) ( 0)                      | 1 0 0 0<br>(5)(0)(0)(0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |
|           | inflammatory cell nest    | 2 0 0 0<br>(10) (0) (0) (0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 1 0 0 0<br>(5)(0)(0)(0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |
|           | acidophilic cell focus    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 1 1 0 0<br>(3)(3)(0)(0)                              |
| rinary sy | stem)                     |   |   |   |  |
| dney      | hyaline droplet           | $\begin{array}{c} <21> \\ 6 & 0 & 0 \\ (29) & (0) & (0) \\ \end{array}$   | <24><br>12 0 0 0<br>(50) (0) (0) (0)                | <19><br>5 0 0 0<br>( 26) ( 0) ( 0) ( 0)   | <30><br>12 0 0 0<br>(40) (0) (0) (0)                 |
|           | scar                      | 1 0 0 0<br>(5)(0)(0)(0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |
|           | inflammatory polyp        | 0 1 0 0<br>( 0) ( 5) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 1 0 0 0<br>(5)(0)(0)(0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |

(c) c : b / a \* 100

Significant difference ; \* : P  $\leq$  0.05 \*\* : P  $\leq$  0.01  $\,$  Test of Chi Square

(HPT150)

BAIS4

# HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

PAGE : 15

|   |  | Group Name Control<br>No. of Animals on Study 21 | 2500 ppm<br>24 | 5000 ррт<br>19                         | 10000 ррт<br>30                        |
|---|--|--|----------------|--|--|
| )rgan   | Findings   | Grade <u>1 2 3 4</u><br>(%) (%) (%) (%)          |                | <u>1 2 3 4</u><br>(%) (%) (%) (%)      | 1 2 3 4<br>(%) (%) (%) (%)             |
| {Urinary syst                                 | tem)   |  |                |  |  |
| kidney  | hydronephrosis   | 0 0 1 2<br>( 0) ( 0) ( 5) ( 10                   |                | <19><br>0 0 1 0<br>( 0) ( 0) ( 5) ( 0) | <30><br>0 1 1 0<br>( 0) ( 3) ( 3) ( 0) |
|   | arthritis  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0                    |                | 0 1 0 • 0<br>( 0) ( 5) ( 0) ( 0)       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         |
| ırin bladd                                    | dilatation   | <21><br>0 1 1 0<br>( 0) ( 5) ( 5) ( 0            |                | <19><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <30><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0) |
| {Endocrine sy                                 | ystem)   |  |                |  |  |
| oituitary                                     | angiectasis  | <21><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0            |                | <19><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <30><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0) |
|   | hyperplasia  | 2 0 0 0<br>(10) (0) (0) (0                       |                | 1 1 0 0<br>(5)(5)(0)(0)                | 1 2 2 0<br>(3)(7)(7)(0)                |
|   | Rathke pouch   | 1 0 0 0<br>(5)(0)(0)(0)                          |                | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         |
| Grade<br>< a ><br>b<br>( c )<br>Significant d | l : Slight 2 : Moderate<br>a : Number of animals examined at th<br>b : Number of animals with lesion<br>c : b / a * 100<br>lifference ; * : P ≤ 0.05 **: |  |                |  |  |

(HPT150)

# HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105%)

| PAGE | : | 16 |
|------|---|----|
|------|---|----|

|                        |   | Group Name<br>No. of Animals on Study<br>Grade | 21                     | 4     | 2          | 500 pp           | 4              | 4               |            |                 | 9               |                 |   | 100         | 000 pp<br>30     | I              | 4               |
|------------------------|---|--|------------------------|-------|------------|------------------|----------------|-----------------|------------|-----------------|-----------------|-----------------|---|-------------|------------------|----------------|-----------------|
| Organ                  | Findings  |  | 2 <u>3</u><br>%) (%)   | 4 (%) | (%)        | 2<br>(%)         | 3<br>(%)       | <u>4</u><br>(%) | <u> </u>   | 2<br>(%)        | 3<br>(%)        | <u>4</u><br>(%) |   | (%)         | 2<br>(%)         | 3<br>(%)       | <u>4</u><br>(%) |
| {Endocrine sys         | stem)   |  |                        |       |            |                  |                |                 |            |                 |                 |                 |   |             |                  |                |                 |
| thyroid                | cyst  |  | <21><br>0 0<br>0) ( 0) |       | 1<br>( 4)  | <2<br>0<br>( 0)  |                | 0<br>( 0)       | 0<br>( 0)  | <1<br>0<br>( 0) | 9><br>0<br>(0)  | 0<br>(0)        | ( | 0<br>0) ·(  | <30<br>0<br>0) ( | ><br>0<br>0)   | 0<br>( 0)       |
|                        | C-cell hyperplasia  |  | 0 0<br>0)(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>3) (   | 0<br>0) (        | 0<br>0)        | 0<br>( 0)       |
| parathyroid            | hyperplasia   | (  | <21><br>0 0<br>0) ( 0) |       | 0<br>( 0)  |                  | 4><br>0<br>(0) | 0<br>( 0)       | 0<br>( 0)  | 0               | 9><br>0<br>( 0) | 0<br>( 0)       |   | 0<br>0) (   | <30<br>0<br>0) ( | ><br>0<br>0)   | 0<br>(0)        |
| adrenal                | degeneration  |  | <21><br>0 0<br>0) ( 0) |       | 0<br>( 0)  | <2<br>1<br>( 4)  | 0              | 0<br>( 0)       | 0<br>( 0)  | 0               | 9><br>0<br>( 0) | 0<br>( 0)       | ( | 0<br>0) (   | <30<br>0<br>0) ( | ><br>0<br>0)   | 0<br>( 0)       |
|                        | spindle-cell hyperplasia  |  | 0 0<br>0)(0)           |       | 12<br>(50) | 0<br>( 0)        | 0<br>( 0)      | 0<br>( 0)       | 10<br>(53) | 0<br>( 0)       | 0<br>( 0)       | 0<br>( 0)       |   | 10<br>33) ( | 0<br>0) (        | 0<br>0)        | 0*<br>(0)       |
| {Reproductive          | system)   |  |                        |       |            |                  |                |                 |            |                 |                 |                 |   |             |                  |                |                 |
| ovary                  | angiectasis   |  | <21><br>) 0<br>)) ( 0) |       | 1<br>( 4)  | <2-<br>0<br>( 0) | 0              | 0<br>( 0)       | 0<br>( 0)  | Λ               | 9><br>0<br>(0)  | 0<br>( 0)       | ( | 0<br>0) (   | <30<br>0<br>0) ( | ><br>0<br>0) ( | 0<br>( 0)       |
| <a>)<br/>b<br/>(c)</a> | 1 : Slight 2 : Moderate<br>a : Number of animals examined at th<br>b : Number of animals with lesion<br>c : b / a * 100<br>ifference : $* : P \leq 0.05 $ **: |  |                        | · .   |            |                  |                |                 |            |                 |                 |                 |   |             |                  |                |                 |

(HPT150)

# HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

 $\sim$ 

PAGE : 17

|                 |  | roup Name Control ,<br>b. of Animals on Study 21  | 2500 ppm<br>24   | 5000 ppm<br>19                          | 10000 ppm<br>30                        |
|-----------------|--|---|--|---|--|
| )rgan           |  | ade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | $\frac{1}{(\%)} \frac{2}{(\%)} \frac{3}{(\%)} \frac{4}{(\%)} \frac{4}{(\%)}$ | <u>1 2 3 4</u><br>(%) (%) (%) (%)       | <u>1 2 3 4</u><br>(%) (%) (%) (%)      |
| Reproductive    | system)  |   |  |   |  |
| ovary           | cyst   | <21><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <24><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                       | <19><br>3 0 0 0<br>( 16) ( 0) ( 0) ( 0) | <30><br>0 2 0 0<br>( 0) ( 7) ( 0) ( 0) |
| terus           | stromal hyperplasia  | $\langle 21 \rangle$<br>1 0 0 0<br>( 5) ( 0) ( 0) ( 0)  | <24><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                       | <19><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <30><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) |
|                 | cystic endometrial hyperplasia   | 4 0 0 0<br>(19) (0) (0) (0)   | 3 0 0 0<br>(13) (0) (0) (0)  | 2 0 0 0<br>(11) (0) (0) (0)             | 3 0 0 0<br>(10) (0) (0) (0             |
| rep/cli gl      | cyst   | <pre>&lt;21&gt; 0 0 0 0 ( 0) ( 0) ( 0) ( 0)</pre>   | <24><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                       | <19><br>1 0 0 0<br>( 5) ( 0) ( 0) ( 0)  | <30><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) |
| Nervous syste   | em)  |   |  |   |  |
| rain            | hemorrhage   | $\begin{array}{cccc} & <21 \\ 0 & 0 & 0 & 0 \\ ( & 0) & ( & 0) & ( & 0) \\ \end{array}$                   | <pre> &lt;24&gt;<br/>0 0 0 0<br/>( 0) ( 0) ( 0) ( 0)</pre>                   | <19><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <30><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0) |
|                 | mineralization   | 1 0 0 0<br>(5)(0)(0)(0)   | 2 0 0 0<br>( 8) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)          | 3 0 0 0<br>(10) (0) (0) (0)            |
| a ><br>b<br>(c) | 1: Slight 2: Moderate 3:<br>a: Number of animals examined at the site<br>b: Number of animals with lesion<br>c: $b / a * 100$<br>(forence; $*: P \leq 0.05 \Rightarrow **: P \leq 0$ |   |  |   |  |

(HPT150)

#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

|             |                      | Group Name<br>No. of Animals o<br>Grade | Control<br>n Study 21<br>1 2 3 4       | 2500 ppm<br>24<br>1 2 3 4              | 5000 ppm<br>19<br>1 2 3 4  | 10000 ppm<br>30<br>1 2 3 4                   |
|-------------|----------------------|---|--|--|--|--|
| gan         | Findings             |   | (%) (%) (%)                            | (%) (%) (%) (%)                        | $\frac{1}{(\%)}  (\%)  (\%)  (\%)$   | $\frac{1}{(\%)}$ $(\%)$ $(\%)$ $(\%)$ $(\%)$ |
| ecial sen   | se organs/appendage) |   |  |  |  |  |
|             | cataract             |   | <21><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <24><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | $\begin{array}{c} <19 \\ 1 & 0 & 0 & 0 \\ (5) & (0) & (0) & (0) \end{array}$ | <30><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)       |
|             | retinal atrophy      |   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 0 0 1 0<br>(0)(0)(5)(0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |
| der gl      | degeneration         |   | <21><br>1 0 0 0<br>( 5) ( 0) ( 0) ( 0) | <24><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <19><br>1 0 0 0<br>( 5) ( 0) ( 0) ( 0)                                       | <30><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0        |
|             | hyperplasia          |   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 1 0 0 0<br>(5)(0)(0)(0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |
| sculoskel   | ətal system)         |   |  |  |  |  |
| cle         | mineralization       |   | <21><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <24><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0) | <19><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                       | <30><br>2 0 0 0<br>( 7) ( 0) ( 0) ( 0)       |
| ody cavitie | es]                  |   |  |  |  |  |
| liastinum   | inflammation         |   | <21><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <24><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <19><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                       | <30><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0)       |

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

b b : Number of animals with lesion

c:b/a\*100 (c)

Significant difference ; \* : P  $\leq$  0.05 \*\* : P  $\leq$  0.01 Test of Chi Square

(HPT150)

BAIS4

# HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) DEAD AND MORIBUND ANIMALS (0-105W)

|             |   | Group Name<br>No. of Animals | Control<br>on Study 21            | 2500 ppm<br>24                    | 5000 ррт<br>19                    | 10000 ppm<br>30   |  |
|-------------|---|------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|---|--|
| rgan        | Findings  | Grade                        | <u>1 2 3 4</u><br>(%) (%) (%) (%) | <u>1 2 3 4</u><br>(%) (%) (%) (%) | <u>1 2 3 4</u><br>(%) (%) (%) (%) | $\frac{1}{(\%)}  \begin{array}{cccc} 2 & 3 & 4 \\ (\%) & (\%) & (\%) & (\%) \\ \end{array}$ |  |
|             | 1   |                              |                                   |                                   |                                   |   |  |
| ody cavitie | S)  |                              |                                   |                                   |                                   |   |  |
| ritoneum    |   |                              | <21>                              | <24>                              | <19>                              | <30>  |  |
|             | peritonitis   |                              | 0 0 1 0<br>(0)(0)(5)(0)           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)    | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)    | 0 0 0 0<br>(0)(0)(0)(0)   |  |
| rade<br>a≻  | 1 : Slight 2 : Moderate<br>a : Number of animals examined a |                              | 4 : Severe                        |                                   |                                   |   |  |
| b<br>(c)    | b : Number of animals with lesic<br>c : b / a * 100         | n                            |                                   |                                   |                                   |   |  |

(HPT150)

BAIS4

.

TABLE M 6

HISTOPATHOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: FEMALE: SACRIFICED ANIMALS

#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

|                         |  | Control<br>als on Study 29  | 2500 ррм<br>26   | 5000 ррт<br>31   | 10000 ppm<br>20                          |
|-------------------------|--|---|--|--|--|
| rgan                    | Grade  | <u> </u>  | $\frac{1}{(\%)}  \frac{2}{(\%)}  \frac{3}{(\%)}  \frac{4}{(\%)}$ | <u>1 2 3 4</u><br>(%) (%) (%) (%)                          | <u>1 2 3 4</u><br>(%) (%) (%) (%)        |
| [ntegumenta]            | ry system/appandage}   |   |  |  |  |
| kin/app                 | sebaceous hyperplasia  | $\begin{array}{cccc} & <29 \\ 1 & 0 & 0 & 0 \\ ( 3) & ( 0) & ( 0) & ( 0) \end{array}$ | <26><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                           | <pre> &lt;31&gt;<br/>0 0 0 0<br/>( 0) ( 0) ( 0) ( 0)</pre> | <20><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
| ubcutis                 | hemorrhage   | <29><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <26><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)                           | <31><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     | . <20><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) |
| Respiratory             | system)  |   |  |  |  |
| sal cavit               | inflammatory infiltration  | <29><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <pre> &lt;26&gt;<br/>0 0 0 0<br/>( 0) ( 0) ( 0) ( 0)</pre>       | <pre> &lt;31&gt;     1 0 0 0     ( 3) ( 0) ( 0) ( 0)</pre> | <20><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   |
|                         | eosinophilic change:olfactory epithelium   | 10 0 0 0<br>(34) (0) (0) (0)  | 5 1 0 0<br>(19) (4) (0) (0)                                      | 7 0 0 0<br>(23) (0) (0) (0)                                | 5 0 0 0<br>(25) ( 0) ( 0) ( 0)           |
|                         | eosinophilic change:respiratory epithelium   | 17 6 0 0<br>(59) (21) (0) (0)   | 16 3 0 0<br>(62)(12)(0)(0)                                       | 25 1 0 0<br>(81) (3) (0) (0)                               | 13 1 0 0<br>(65)(5)(0)(0)                |
|                         | inflammation:respiratory epithelium  | 1 0 0 0<br>(3)(0)(0)(0)(0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                   | 4 0 0 0<br>(13) (0) (0) (0)                                | 2 0 0 0<br>(10) (0) (0) (0)              |
| rade<br>a ≻<br>b<br>c ) | <ul> <li>1 : Slight 2 : Moderate 3 : Marked</li> <li>a : Number of animals examined at the site</li> <li>b : Number of animals with lesion</li> <li>c : b / a * 100</li> </ul> | 4 : Severe  |  |  |  |

(HPT150)

BAIS4

# HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

~~

~~~

|            | No.                                        | np Name Control<br>of Animals on Study 29                                                    | 2500 ppm<br>26                                                               | 5000 ppm<br>31                                                   | 10000 ppm<br>20                        |
|------------|--------------------------------------------|----------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|------------------------------------------------------------------|----------------------------------------|
| gan        | Grad                                       | (%) (%) (%) (%)                                                                              | $\frac{1}{(\%)}  \frac{2}{(\%)}  \frac{3}{(\%)}  \frac{4}{(\%)}$             | $\frac{1}{(\%)}  \frac{2}{(\%)}  \frac{3}{(\%)}  \frac{4}{(\%)}$ | <u>1 2 3 4</u><br>(%) (%) (%) (%)      |
| espiratory | system)                                    |                                                                                              |                                                                              |                                                                  |                                        |
| sal cavit  | respiratory metaplasia:olfactory epitheliu | m (29)<br>9 0 0 0<br>(31) (0) (0) (0)                                                        | <pre> &lt;26&gt;     4     0     0     0     ( 15) ( 0) ( 0) ( 0) ( 0)</pre> | <31><br>9 0 0 0<br>(29) (0) (0) (0)                              | <pre> &lt;20&gt;</pre>                 |
|            | respiratory metaplasia:gland               | $\begin{array}{cccccccccccccccccccccccccccccccccccc$                                         | 16 0 0 0<br>(62) (0) (0) (0)                                                 | 13 2 0 0<br>(42) (6) (0) (0)                                     | 9 0 0 0<br>(45)(0)(0)(0)               |
|            | squamous cell metaplasia:respiratory epith | nelium 1 0 0 0<br>(3)(0)(0)(0)                                                               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                   | 1 0 0 0<br>(5)(0)(0)(0)                |
| sopharynx  | eosinophilic change                        | $\begin{array}{c} \langle 29 \rangle \\ 6 & 1 & 0 & 0 \\ (21) & (3) & (0) & (0) \end{array}$ | $\begin{array}{c} <26 \\ 3 & 1 & 0 \\ (12) & (4) & (0) & (0) \end{array}$    | <31><br>0 0 0 0 *<br>( 0) ( 0) ( 0) ( 0)                         | <20><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) |
| ng         | inflammatory infiltration                  | <29><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)                                                       | <26><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                       | <31><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                           | <20><br>1 0 0 0<br>( 5) ( 0) ( 0) ( 0) |
|            | lymphocytic infiltration                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                               | 1 0 0 0<br>(3) (0) (0) (0)                                       | - 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)       |
|            | bronchiolar—alveolar cell hyperplasia      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                               | 1 0 0 0<br>( 4) ( 0) ( 0) ( 0)                                               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         |

b 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

(HPT150)

BAIS4

# HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

~~~

|             |                              | Group Name Control<br>No. of Animals on Study 29<br>Grade 1 2 3 4                     | 2500 ppm<br>26<br>1 2 3 4                         | 5000 ppm<br>31<br>1 2 3 4              | 10000 ppm<br>20  |
|-------------|------------------------------|---|---|--|--|
| rgalı       | Findings                     | Grade $1$ $2$ $3$ $4$ (%)         (%)         (%)         (%)         (%)         (%) | 1 2 3 4<br>(%) (%) (%) (%)                        | 1 2 3 4<br>(%) (%) (%) (%)             | <u>1 2 3 4</u><br>(%) (%) (%) (%)                          |
| espiratory  | system)                      |   |   |  |  |
| Ing         | arteritis                    | <29><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <26><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)            | <31><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <pre> &lt;20&gt;<br/>0 0 0 0<br/>( 0) ( 0) ( 0) ( 0)</pre> |
| ematopoieti | c system)                    |   |   |  |  |
| ne marrow   | increased hematopoiesis      | $\begin{array}{c} <29 > \\ 1 & 0 & 0 & 0 \\ ( 3) & ( 0) & ( 0) & ( 0) \end{array}$    | <26><br>4 0 0 0<br>(15) (0) (0) (0)               | <31><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <20><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                     |
|             | myelofibrosis                | 1 0 0 0<br>(3)(0)(0)(0)   | 0 1 0 0<br>(0)(4)(0)(0)                           | 2 0 0 0<br>. ( 6) ( 0) ( 0) ( 0)       | 2 0 0 0<br>(10) (0) (0) (0)                                |
|             | megakaryocyte:increased      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                    | 1 0 0 0<br>(3)(0)(0)(0)                | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                             |
| leen        | fibrosis:focal               | <29><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <pre>&lt;26&gt; 0 0 0 0 ( 0) ( 0) ( 0) ( 0)</pre> | <31><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <20><br>0 0 1 0<br>( 0) ( 0) ( 5) ( 0)                     |
|             | extramedullary hematopoiesis | 8 0 0 0<br>(28) (0) (0) (0)   | 9 1 0 0<br>(35) (4) (0) (0)                       | 9 0 0 0<br>(29) (0) (0) (0)            | 50000<br>(25)(0)(0)(0)                                     |

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

b 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

(HPT150)

. •

#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

~~~~

|             |                        | Group Name Control<br>No. of Animals on Study 29 |                                                               | 2500 ppm<br>26                                                | 5000 ppm<br>31                                                               | 10000 ppm<br>20                                 |
|-------------|------------------------|--------------------------------------------------|---------------------------------------------------------------|---------------------------------------------------------------|------------------------------------------------------------------------------|-------------------------------------------------|
| rgan        | Findings               | Grade                                            | $\frac{1}{(\%)} \frac{2}{(\%)} \frac{3}{(\%)} \frac{4}{(\%)}$ | $\frac{1}{(\%)} \frac{2}{(\%)} \frac{3}{(\%)} \frac{4}{(\%)}$ | $\frac{\begin{array}{ccccccccccccccccccccccccccccccccccc$                    | $\frac{1}{(\%)} \frac{23}{(\%)} \frac{4}{(\%)}$ |
| Hematopoiet | ic system)             |                                                  |                                                               |                                                               |                                                                              |                                                 |
| pleen       | follicular hyperplasia |                                                  | <29><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)                        | <26><br>0 1 0 0<br>( 0) ( 4) ( 0) ( 0)                        | <31><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                       | <20><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)          |
| Circulatory | system)                | X                                                |                                                               |                                                               |                                                                              |                                                 |
| eart        | mineralization         |                                                  | <29><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)                        | <26><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | <pre></pre>                                                                  | <20><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0           |
|             | inflammatory cell nest |                                                  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                | 1 0 0 0<br>(3)(0)(0)(0)                                                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0                   |
|             | myocardial fibrosis    |                                                  | 1 0 0 0<br>(3)(0)(0)(0)                                       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                  |
| Digestive s | ystem)                 |                                                  |                                                               |                                                               |                                                                              |                                                 |
| ongue       | arteritis              |                                                  | <29><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | <26><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                        | $\begin{array}{c} <31 \\ 1 & 0 & 0 & 0 \\ (3) & (0) & (0) & (0) \end{array}$ | <20><br>1 0 0 0<br>( 5) ( 0) ( 0) ( 0)          |

(HPT150)

c:b/a\*100

Significant difference ; \* :  $P \leq 0.05$  \*\* :  $P \leq 0.01$  Test of Chi Square

(c)

BAIS4

#### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

~~~

PAGE : 15

|              |                               | Group Name Control<br>No. of Animals on Study 29 |                 | 2500 ppm<br>26 |           |          | 5000 ppm<br>31 |             |               |           |   | 10000 ppm<br>20 |          |           |               |           |   |                 |   |           |                 |          |                |          |
|--------------|-------------------------------|--|-----------------|----------------|-----------|----------|----------------|-------------|---------------|-----------|---|-----------------|----------|-----------|---------------|-----------|---|-----------------|---|-----------|-----------------|----------|----------------|----------|
| rgan         | Findings                      | Grade  | <u>1</u><br>(%) | 2 (%)          | 3         | 4        | -              | 1<br>(%)    | 2 (%)         | 3<br>(%)  |   | <u>4</u><br>(%) | (        | 1<br>%)   | 2 (%)         | 3 (%)     |   | <u>4</u><br>(%) | ( | 1<br>%)   | 2 (%)           | :        | <u>3</u><br>%) | 4<br>(%) |
| Digestive sy | stem)                         |  |                 |                |           |          |                |             |               |           |   |                 |          |           |               |           |   |                 |   |           |                 |          |                |          |
| alivary gl   | lymphocytic infiltration      |  | 1<br>(3) (      | <29<br>0<br>0) | 0         | ( (      | (              | 0<br>0) (   | <2<br>0<br>0) | 0         | ( | 0<br>0)         |          | 1<br>3) ( | <3<br>0<br>0) | 0         | ( | 0               |   | 1<br>5) ( | <2<br>0<br>( 0) |          | 0<br>0) (      | 0<br>0)  |
| tomach       | ulcer:forestomach             |  | 1<br>( 3) (     | <29<br>0<br>0) | 0         | ( (      | (              | 0<br>0) (   | <2<br>0<br>0) | 0         |   | 0               |          | )<br>) (  | <3<br>0<br>0) | 0         |   | 0<br>0)         |   | 0<br>0) ( | <2<br>0<br>0)   |          | 0<br>0) (      | 0<br>0)  |
|              | hyperplasia:forestomach       |  | 1<br>( 3) (     | 0<br>0)        | 0<br>( 0) | ( (      | (              | 0<br>0) (   | 0<br>0)       | 0<br>( 0) | ( | 0<br>0)         | (        | 2<br>6) ( | 0<br>0)       | 0<br>( 0) |   | 0<br>0)         |   | 3<br>5) ( | 0<br>0)         |          | 0<br>0) (      | 0<br>0   |
|              | erosion:glandular stomach     |  | 4<br>(14) (     | 2<br>7)        | 0<br>( 0) |          | (              | 1<br>4) (   | 0<br>0)       | 0<br>( 0) |   | 0<br>0)         |          | i<br>)) ( | 0<br>0)       | 0<br>( 0) | ( | 0<br>0)         |   | 2<br>0) ( | 0<br>0)         |          | 0<br>0) (      | 0<br>0)  |
|              | ulcer:glandular stomach       |  | 1<br>( 3) (     | 0<br>0)        | 0<br>( 0) | 0<br>( 0 | (              | 0<br>0) (   | 0<br>0)       | 0<br>( 0) | ( | 0<br>0)         | ( )      | )<br>)) ( | 0<br>0)       | 0<br>( 0) | ( | 0<br>0)         |   | 0<br>0) ( | 0<br>0)         |          | 0<br>0) (      | 0<br>0)  |
|              | hyperplasia:glandular stomach |  | 15<br>(52) (    | 0<br>0)        | 0<br>( 0) | 0<br>( 0 |                | 16<br>52) ( | 0<br>0)       | 0<br>( 0) |   | 0<br>0)         | 1<br>(3) |           | 0<br>0)       | 0<br>( 0) | ( | 0<br>0)         |   | 6<br>0) ( | 0<br>0)         |          | 0<br>0) (      | 0<br>0)  |
| iver         | angiectasis                   |  | 0               | <29<br>1<br>3) | 1         | 0<br>( 0 | (              | 0<br>0) (   | <2<br>0<br>0) | 0         |   | 0<br>0)         |          | 1<br>3) ( | <3<br>0<br>0) | 0         | ( | 0<br>0)         | ( | 1<br>5) ( | <2<br>0<br>0)   | 20><br>( |                | 0<br>0)  |

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

 $\langle a \rangle$  a : Number of animals examined at the site

b 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

(HPT150)

# HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

| PAGE | : | 16 |
|------|---|----|
|      |   |    |

|            |                              | Group Name Control<br>No. of Animals on Study 29<br>Grade <u>1 2 3 4</u> | 2500 ppm<br>26<br><u>1 2 3 4</u>       | 5000 ppm<br>31<br><u>1 2 3 4</u>   | 10000 ppm<br>20<br><u>1 2 3 4</u>      |
|------------|------------------------------|--|--|------------------------------------|--|
| Organ      | Findings                     | (%) (%) (%)  | (%) (%) (%)                            | (%) (%) (%) (%)                    | (%) (%) (%) (%)                        |
| {Digestive | system)                      |  |  |                                    |  |
| liver      | necrosis:focal               | <pre></pre>  | <26><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <31><br>2 0 0 0<br>(6) (0) (0) (0) | <20><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) |
|            | inflammatory infiltration    | 1 0 0 0<br>( 3) ( 0) ( 0) ( 0)   | 1 0 0 0<br>(4)(0)(0)(0)                | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         |
|            | inflammatory cell nest       | 9 0 0 0<br>(31)(0)(0)(0)   | 7 0 0 0<br>(27)(0)(0)(0)               | 11 0 0 0<br>(35) (0) (0) (0)       | 8 0 0 0<br>(40) ( 0) ( 0) ( 0)         |
|            | extramedullary hematopoiesis | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | i 0 0 0<br>(4)(0)(0)(0)                | 1 0 0 0<br>(3) (0) (0) (0)         | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         |
|            | clear cell focus             | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 0 1 0 0<br>( 0) ( 3) ( 0) ( 0)     | 1 1 0 0<br>(5)(5)(0)(0)                |
|            | acidophilic cell focus       | 0 2 0 0<br>( 0) ( 7) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 3 0 0 0<br>(10) (0) (0) (0)        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         |
|            | basophilic cell focus        | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         | 0 1 0 0<br>(0)(3)(0)(0)            | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         |
|            | biliary cyst                 | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)   | 1 0 0 0<br>(4)(0)(0)(0)                | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)     | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)         |

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

 $\langle a \rangle$  a : Number of animals examined at the site

b 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

(HPT150)

# HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

~~~

PAGE : 17

| Organ                    |                                                                                                                                                                                 | p Name Control<br>of Animals on Study 29<br>e <u>1 2 3 4</u><br>(%) (%) (%) (%) | 2500 ppm<br>26<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 5000 ppm<br>31<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10000 ppm<br>20<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|--------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------|-----------------------------------------------------|-----------------------------------------------------|------------------------------------------------------|
| {Digestive sy            | /stem)                                                                                                                                                                          |                                                                                 |                                                     | •                                                   |                                                      |
| gall bladd               | hyperplasia                                                                                                                                                                     | <28><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)                                          | <25><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <31><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <20><br>1 0 0 0<br>( 5) ( 0) ( 0) ( 0)               |
| pancreas                 | fibrosis:focal                                                                                                                                                                  | <29><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                          | <26><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <31><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <20><br>0 0 1 0<br>( 0) ( 0) ( 5) ( 0)               |
| {Urinary syst            | tem)                                                                                                                                                                            |                                                                                 |                                                     |                                                     |                                                      |
| idney                    | cyst                                                                                                                                                                            | <29><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                          | <26><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)              | <31><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <pre> &lt;20&gt; 0 0 0 0   ( 0) ( 0) ( 0) ( 0)</pre> |
|                          | hyaline droplet                                                                                                                                                                 | 1 0 0 0<br>( 3) ( 0) ( 0) ( 0)                                                  | 2 0 0 0<br>(8)(0)(0)(0)                             | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 2 0 0 0<br>(10) (0) (0) (0)                          |
|                          | deposit of hemosiderin                                                                                                                                                          | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 1 0 0 0<br>(3)(0)(0)(0)                             | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |
|                          | inflammatory infiltration                                                                                                                                                       | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                                                  | 2 0 0 0<br>(8)(0)(0)(0)                             | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |
| Grade<br>(a)<br>b<br>(c) | <pre>1 : Slight 2 : Moderate 3 : Ma a : Number of animals examined at the site b : Number of animals with lesion c : b / a * 100 lifterence ; * : P ≤ 0.05 *** : P ≤ 0.05</pre> |                                                                                 |                                                     | ······                                              |                                                      |

(HPT150)

BAIS4

.

### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

 $\searrow$ 

PAGE : 18

|              |                            | Group Name Co<br>No. of Animals on Study |                         |         | 2               | 500 ppm<br>26           |              | 5000 ppm<br>31 |                        |           | 10000                | ppm<br>20                  |
|--------------|----------------------------|------------------------------------------|-------------------------|---------|-----------------|-------------------------|--------------|----------------|------------------------|-----------|----------------------|----------------------------|
| 0rgan        | Findings                   | Grade <u>1</u> (%)                       | <u>2</u> 3<br>(%) (%    |         | <u>1</u><br>(%) | <u>2</u> 3<br>(%) (%    |              | <u> </u>       | 2 3<br>(%) (%)         | 4(%)      | <u>1</u> 2<br>(%) (% | 3 4                        |
| Urinary syst | em)                        |                                          |                         |         |                 |                         |              |                |                        |           |                      |                            |
| idney        | lymphocytic infiltration   | 4 (14)                                   | <29><br>0 0<br>( 0) ( 0 |         | 3<br>(12)       | <26><br>0 0<br>( 0) ( 0 |              | 3<br>(10) (    | <31><br>0 0<br>0) ( 0) | 0<br>( 0) | 2 0                  | <20><br>0 0<br>) ( 0) ( 0) |
|              | scar                       | 0<br>( 0) (                              | 0 0<br>(0) (0           |         | 0<br>( 0)       | 0 0<br>( 0) ( 0         |              | 1<br>( 3) (    | 0 0<br>0) ( 0)         | 0<br>( 0) | 20<br>(10) (0        | 00)<br>(0)(0)              |
|              | inflammatory polyp         | 0<br>( 0) (                              | 1 0<br>3)(0             |         | 2<br>( 8)       | 1 0<br>(4)(0            | 0<br>) ( 0)  | 0<br>( 0) (    | 0 0<br>0) ( 0)         | 0<br>( 0) | 0 2<br>( 0) ( 10     | 00)<br>(0)(0)              |
|              | hydronephrosis             | 0<br>( 0) (                              | 0 1<br>( 0) ( 3         | 0) ( 0) | 0<br>( 0)       | 1 1<br>(4)(4            | 0<br>) ( 0)  | 0<br>( 0) (    | 0 1<br>0) ( 3)         | 0<br>( 0) | 1 2<br>(5)(10        | 00)<br>(0)(0)              |
|              | pyelonephritis             | 0<br>( 0) (                              | 0 1<br>0)(3             |         | 0<br>( 0)       | 00<br>(0)(0             |              | 0<br>( 0) (    | 0 0<br>0) ( 0)         | 0<br>( 0) | 00<br>(0)(0)         | 00<br>)(0)(0)              |
|              | hyaline droplet:glomerulus | 0 ( 0) (                                 | 0 0<br>0)(0             |         | 0<br>( 0)       | 1 0<br>(4)(0            | 0.<br>) ( 0) | 0<br>( 0) (    | 0 0<br>0) ( 0)         | 0<br>( 0) | 00<br>(0)(0          | 00<br>(0)(0)               |
| rin bladd    | dilatation                 | 0<br>( 0) (                              | <29><br>0 0<br>0) ( 0   |         | 1<br>( 4)       | <26><br>0 0<br>( 0) ( 0 |              | 0<br>( 0) (    | <31><br>0 0<br>0) ( 0) | 0<br>( 0) | 0 0                  | <20><br>0 0<br>) ( 0) ( 0) |
|              | inflammatory infiltration  | 0<br>( 0) (                              | 0 0<br>0) ( 0           |         | 1<br>( 4)       | 00                      |              | 0<br>( 0) (    | 0 0<br>0) ( 0)         | 0<br>( 0) | 0 0<br>( 0) ( 0)     | 00<br>)(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

(HPT150)

### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

~~~~

|  |  | <br> |  |
|--|--|------|--|
|  |  |      |  |
|  |  |      |  |
|  |  |      |  |

~----

PAGE: 19

| )rgan          | Findings                 | rol<br>29<br>2 <u>34</u><br>%) (%) (%) | 2500 ppm<br>26<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | $\begin{array}{c} 5000 \text{ ppm} \\ 31 \\ \hline 1 & 2 & 3 & 4 \\ \hline (\%) & (\%) & (\%) & (\%) \end{array}$ | 10000 ppm<br>20<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|----------------|--------------------------|--|---|---|--|
| (Urinary syste | em)                      |  |   |   |  |
| urin bladd     | lymphocytic infiltration | <29><br>0 0 0<br>0) ( 0) ( 0)          | <26><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)              | <31><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <20><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |
| Endocrine sys  | stem)                    |  |   |   |  |
| oituitary      | angiectasis              | <29><br>0 0 0<br>0) ( 0) ( 0)          | <26><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)              | <31><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)  | <20><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |
|                | cyst                     | 0 0 0<br>0)(0)(0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 2 0 0 0<br>(6)(0)(0)(0)   | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |
|                | hyperplasia              | 2 1 0<br>7) (3) (0)                    | 3 4 3 0<br>(12) (15) (12) (0)                       | 8 1 3 0<br>(26) (3) (10) (0)  | 4 0 2 0<br>(20) ( 0) (10) ( 0)                       |
|                | Rathke pouch             | 0 0 0<br>0)(0)(0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                      | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 1 0 0 0<br>(5)(0)(0)(0)                              |
| hyroid         | C-cell hyperplasia       | <29><br>0 0 0<br>0) ( 0) ( 0)          | <26><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <31><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)  | <20><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |

Significant difference ;  $*: P \leq 0.05$   $**: P \leq 0.01$  Test of Chi Square

(HPT150)

BAIS4

•

### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

 $\sim \sim$ 

| Organ        | Findings                  | Group Name Control<br>No. of Animals on Study 29<br>Grade <u>1 2 3 4</u><br>(%) (%) (%) (%) | 2500 ppm<br>26<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 5000 ppm<br>31<br><u>1 2 3 4</u><br>(%) (%) (%) (%)      | 10000 ppm<br>20<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|--------------|---------------------------|---|---|--|--|
| {Endocrine s | system)                   |   |   |  |  |
| adrenal      | spindle-cell hyperplasia  | $\begin{array}{c} <29 \\ 18 & 2 & 0 & 0 \\ (62) & (7) & (0) & (0) \end{array}$              | <pre>&lt;26&gt; 20 l 0 0 (77) (4) (0) (0)</pre>     | <pre> &lt;31&gt;     20 1 0 0     (65) (3) (0) (0)</pre> | <20><br>15 2 0 0<br>(75) (10) (0) (0)                |
|              | focal fatty change:cortex | 0 3 0 0<br>( 0) ( 10) ( 0) ( 0)   | 1 1 0 0<br>(4)(4)(0)(0)                             | 0 1 0 0<br>( 0) ( 3) ( 0) ( 0)                           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |
| {Reproductiv | ve system]                |   |   |  |  |
| ovary        | cyst                      | <29><br>5 0 0 0<br>(17) (0) (0) (0)   | <pre>&lt;26&gt; 2 0 0 0 ( 8) ( 0) ( 0) ( 0)</pre>   | <pre> &lt;31&gt;     2 0 0 0     (6) (0) (0) (0) </pre>  | <20><br>2 1 0 0<br>(10) (5) (0) (0)                  |
|              | hyperplasia               | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0).                     | 0 1 0 0<br>( 0) ( 3) ( 0) ( 0)                           | 0 0 0 0<br>( 0) ( 0) ( 0) ( 0)                       |
| uterus       | dilatation                | <29><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <pre>&lt;26&gt; 0 0 0 0 ( 0) ( 0) ( 0) ( 0)</pre>   | <31><br>1 0 0 0<br>( 3) ( 0) ( 0) ( 0)                   | <pre> &lt;20&gt; 0 0 0 0 ( 0) ( 0) ( 0) ( 0)</pre>   |
|              | thrombus                  |   |   | 0 0 0 0  | 0 0 0 0  |

(0)(3)(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</a>

b 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

(HPT150)

BAIS4

### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

 $\sim$ 

~~

| lrgan               | Findings  | Group Name         Control           No. of Animals on Study         29           Grade         1         2         3         4           (%)         (%)         (%)         (%)         (%) | 2500 ppm<br>26<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 5000 ppm<br>31<br><u>1 2 3 4</u><br>(%) (%) (%) (%) | 10000 ppm<br>20<br><u>1 2 3 4</u><br>(%) (%) (%) (%) |
|---------------------|---|---|---|---|--|
|                     |   |   |   |   |  |
| {Reproductiv        | e system)   |   |   |   |  |
| ıterus              | inflammatory infiltration   | <pre>&lt;29&gt; 0 0 0 0 ( 0) ( 0) ( 0) ( 0)</pre>   | <26><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)              | <31><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <20><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |
|                     | cystic endometrial hyperplasia  | 22 0 0 0<br>(76)(0)(0)(0)   | 13 1 0 0<br>(50) (4) (0) (0)                        | 20 1 0 0<br>(65)(3)(0)(0)                           | 13 1 0 0<br>(65)(5)(0)(0)                            |
| vagina              | polyp   | <pre>&lt;29&gt; 0 0 0 0 ( 0) ( 0) ( 0) ( 0) </pre>  | <26><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <31><br>0 1 0 0<br>( 0) ( 3) ( 0) ( 0)              | <20><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)               |
| mammary gl          | cyst  | <29><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <26><br>1 0 0 0<br>( 4) ( 0) ( 0) ( 0)              | <31><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <20><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0                |
| {Nervous sys        | tem)  |   |   |   |  |
| brain               | mineralization  | <29><br>4 0 0 0<br>(14) (0) (0) (0)   | <26><br>5 0 0 0<br>(19) (0) (0) (0)                 | <31><br>5 0 0 0<br>(16) (0) (0) (0)                 | <20><br>4 0 0 0<br>( 20) ( 0) ( 0) ( 0)              |
| {Special sen        | se organs/appendage)  |   |   |   |  |
| еуе                 | inflammatory infiltration   | <29><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | <26><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <31><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)              | <20><br>0 1 0 0<br>( 0) ( 5) ( 0) ( 0)               |
| Grade<br>< a ><br>b | l : Slight 2 : Moderate<br>a : Number of animals examined at the<br>b : Number of animals with lesion | 3 : Marked 4 : Severe<br>e site   |   |   |  |

### HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (105W)

|                                | Group Nam<br>No. of An   | e Control<br>imals on Study 29  | 2500 ppm<br>26                         | 5000 ppm<br>31                         | 10000 ppm<br>20                        |  |  |
|--------------------------------|--|---|--|--|--|--|--|
| Organ                          | Grade<br>_ Findings  | <u>    1   2   3   4</u><br>(%)  (%)  (%)  (%)                                      | <u>1 2 3 4</u><br>(%) (%) (%) (%)      | <u>1 2 3 4</u><br>(%) (%) (%) (%)      | <u>1 2 3 4</u><br>(%) (%) (%) (%)      |  |  |
| {Special s                     | ense organs/appendage)   |   |  |  |  |  |  |
| еуе                            | keratitis  | <29><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0)  | (26><br>0 0 0 0<br>(0) (0) (0) (0)     | <31><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <20><br>1 0 1 0<br>( 5) ( 0) ( 5) ( 0) |  |  |
| {Musculosk                     | eletal system)   |   |  |  |  |  |  |
| bone                           | osteosclerosis   | $\begin{array}{cccc} <29 \\ 1 & 0 & 0 & 0 \\ ( 3) & ( 0) & ( 0) & ( 0) \end{array}$ | <26><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <31><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) | <20><br>0 0 0 0<br>( 0) ( 0) ( 0) ( 0) |  |  |
| Grade<br><a><br/>b<br/>(c)</a> | 1 : Slight 2 : Moderate 3 : Marked<br>a : Number of animals examined at the site<br>b : Number of animals with lesion<br>c : b / a * 100<br>t difference ; $* : P \leq 0.05 *** : P \leq 0.01$ | 4 : Severe<br>Test of Chi Square  |  |  |  |  |  |

.

(HPT150)

BAIS4

### TABLE N 1

## NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS-TIME RELATED: MALE

NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS - TIME RELATED

### STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 SEX : MALE

| 0 - 52         NO. OF EXAMINED ANIMALS         0         1         0         0           NO. OF ANIMALS WITH TUNORS<br>NO. OF ANIMALS WITH STURIES TWINKS         0         0         0         0         0           NO. OF ANIMALS WITH STURIES TWINKS<br>NO. OF ANIMALS WITH STURIES TWINKS         0         0         0         0         0           NO. OF EXAMINED ANIMALS         0         0         0         0         0         0           NO. OF EXAMINED ANIMALS         0         0         0         0         0         0           NO. OF EXAMINED ANIMALS         3         3         2         1         1         1           So of ANIMALS WITH STORES<br>NO. OF ANIMALS WITH STORES TWO STORES         3         2         1         1           NO. OF EXAMINED ANIMALS         3         2         1         1         1           NO. OF ANIMALS WITH STORE TWORES<br>NO. OF ANIMALS WITH STORES TWO STORES         3         2         1         1           NO. OF EXAMINED ANIMALS         12         13         12         8           NO. OF EXAMINED ANIMALS         12         13         12         8           NO. OF EXAMINED ANIMALS         12         13         12         1           NO. OF EXAMINED | 10000 ppm 20000 ppm | 10000 ppm | 5000 ppm | Control | Group Name   | Items                                   | Time-related Ite |
|--|---------------------|-----------|----------|---------|--------------|---|------------------|
| NO. OF ANTIMALS WITH NUMER TINORS         0  | 0 0                 | 0         |          | 0       |              | NO. OF EXAMINED ANIMALS                 | 0 – 52 NO.       |
| No. OF BENIGN TWORES         0   |                     |           | •        | 0<br>0  |              |   |                  |
| NO. OF MALICRANT TRAVES         0  | 0 0                 | 0         | 0        | 0       |              |   |                  |
| 53 - 78       NO. OF EXMINED ANIMALS       3       3       2       1         NO. OF ANIMALS WITH TUMORS       3       2       1       1         NO. OF ANIMALS WITH SUNCE TUMORS       1       2       1       1         NO. OF ANIMALS WITH MULTIPLE TUMORS       2       0       0       0         NO. OF ANIMALS WITH MULTIPLE TUMORS       2       0       0       1         NO. OF ANIMALS WITH MULTIPLE TUMORS       2       0       0       1         NO. OF ANIMALS WITH MULTIPLE TUMORS       2       0       0       1         NO. OF ANIMALS WITH MULTIPLE TUMORS       2       0       0       1         79 - 104       NO. OF EXAMINED ANIMALS       12       13       12       8         NO. OF ANIMALS WITH TUMORS       10       12       10       8         NO. OF ANIMALS WITH TUMORS       10       12       10       8         NO. OF ANIMALS WITH TUMORS       10       12       12       12         NO. OF ANIMALS WITH MURTIPLE TUMORS       4       4       3       0         NO. OF ANIMALS WITH MURTIPLE TUMORS       10       12       12       12         NO. OF ANIMALS WITH MURTIPLE TUMORS       10       12  | 0 0                 | 0         | 0        |         |              | NO. OF MALIGNANT TUMORS                 | NO.              |
| N0. OF         ANIMALS WITH TUMORS         3         2         1         1           N0. OF         ANIMALS WITH SINCLE TUMORS         1         2         1         1           N0. OF         ANIMALS WITH MULTIPLE TUMORS         2         0         0         0           N0. OF         ANIMALS WITH MULTIPLE TUMORS         2         0         0         1           N0. OF         DENTISH TUMORS         2         0         0         1           N0. OF         MALIGNANT TUMORS         2         0         0         1           N0. OF         FAMIMALS WITH TUMORS         3         2         1         0           N0. OF         ANIMALS         TITH MULTIPLE TUMORS         3         2         1         1           79 - 104         N0. OF         EXAMINED ANIMALS         12         13         12         8           N0. OF         ANIMALS WITH TUMORS         10         12         10         8         5           N0. OF ANIMALS WITH MULTIPLE TUMORS         4         4         3         0         12         12         12           N0. OF ANIMALS WITH MULTIPLE TUMORS         14         16         15         12         12         12  |                     |           |          |         |              | , <u>, ,</u> , , ,, , , , , , , , , , , |                  |
| N0. OF ANIMALS WITH SINCLE TUMORS       1       2       1       1         N0. OF ANIMALS WITH MULTIPLE TUMORS       2       0       0       0         N0. OF BENIGN TUMORS       2       0       0       1         N0. OF BENIGN TUMORS       2       0       0       1         N0. OF DUAL TUMORS       3       2       1       1         79 - 104       N0. OF EXAMINED ANIMALS       12       13       12       8         N0. OF ANIMALS WITH TUMORS       10       12       10       8         N0. OF ANIMALS WITH TUMORS       6       9       6       5         N0. OF ANIMALS WITH TUMORS       10       12       10       8         N0. OF ANIMALS WITH TUMORS       4       3       0       0         N0. OF ANIMALS WITH MULTIPLE TUMORS       4       3       0       0         N0. OF ANIMALS WITH MULTIPLE TUMORS       14       15       12       12         105 - 105       N0. OF EXAMINED ANIMALS       35       33       36       41         N0. OF ANIMALS WITH SINGLE TUMORS       21       23       26       22         N0. OF ANIMALS WITH SINGLE TUMORS       12       10       17       17   |                     |           |          |         |              |   |                  |
| NO. OF ANIMALS WITH MULTIPLE TUMORS       2       0       0       0         NO. OF BENIEN TUMORS       2       0       0       1         NO. OF BENIEN TUMORS       3       2       1       0         NO. OF MALIGNANT TUMORS       3       2       1       0         NO. OF TUTAL TUMORS       3       2       1       0         79 - 104       NO. OF EXAMINED ANIMALS       12       13       12       8         NO. OF ANIMALS WITH TUMORS       10       12       10       8         NO. OF ANIMALS WITH TUMORS       6       9       6       5         NO. OF BENIENT TUMORS       4       3       0       3         NO. OF BENIENT TUMORS       4       4       3       0         NO. OF BENIENT TUMORS       14       16       15       12         105 - 105       NO. OF EXAMINED ANIMALS       35       33       36       41         NO. OF ANIMALS WITH MULTIPLE TUMORS       21       23       26       22         105 - 105       NO. OF EXAMINED ANIMALS       35       33       36       41         NO. OF ANIMALS WITH MULTIPLE TUMORS       21       23       26       22       22  |                     |           |          | 3       |              |   |                  |
| NO. OF MALIGNANT TUMORS         3         2         1         0           NO. OF TOTAL TUMORS         5         2         1         1           79 - 104         NO. OF EXAMINED ANIMALS         12         13         12         8           NO. OF ANIMALS WITH TUMORS         10         12         10         8           NO. OF ANIMALS WITH TUMORS         6         9         6         5           NO. OF ANIMALS WITH MULTIPLE TUMORS         4         3         4         3           NO. OF ANIMALS WITH MULTIPLE TUMORS         4         4         3         0           NO. OF ANIMALS WITH MULTIPLE TUMORS         4         4         3         0           NO. OF BENICH TUMORS         4         4         3         0           NO. OF TOTAL TUMORS         10         12         12         12           NO. OF TOTAL TUMORS         14         16         15         12           105 - 105         NO. OF EXAMINED ANIMALS         35         33         36         41           NO. OF ANIMALS WITH TUMORS         21         23         26         22           NO. OF ANIMALS WITH MULTIPLE TUMORS         9         13         9         5  | * *                 |           |          | 2       |              |   |                  |
| NO. OF TOTAL TUMORS         5         2         1         1           79 - 104         NO. OF EXAMINED ANIMALS         12         13         12         8           NO. OF ANIMALS WITH TUMORS         10         12         10         8           NO. OF ANIMALS WITH TUMORS         6         9         6         5           NO. OF ANIMALS WITH SINGLE TUMORS         4         3         4         3           NO. OF ANIMALS WITH MULTIPLE TUMORS         4         4         3         0           NO. OF BENIGN TUMORS         4         4         3         0           NO. OF MALIGNANT TUMORS         10         12         12         12           NO. OF MALIGNANT TUMORS         10         12         12         12           NO. OF MALIGNANT TUMORS         14         16         15         12           105 - 105         NO. OF EXAMINED ANIMALS         35         33         36         41           NO. OF ANIMALS WITH TUMORS         21         23         26         22           NO. OF ANIMALS WITH SINGLE TUMORS         12         10         17         17           NO. OF ANIMALS WITH MULTIPLE TUMORS         9         13         9         5  |                     | 0         |          | =       |              |   |                  |
| 79 - 104       NO. OF EXAMINED ANIMALS       12       13       12       8         NO. OF ANIMALS WITH TUMORS       10       12       10       8         NO. OF ANIMALS WITH TUMORS       6       9       6       5         NO. OF ANIMALS WITH MULTIPLE TUMORS       4       3       4       3         NO. OF ANIMALS WITH MULTIPLE TUMORS       4       4       3       0         NO. OF ANIMALS WITH MULTIPLE TUMORS       4       4       3       0         NO. OF BENICH TUMORS       4       4       3       0         NO. OF MALIGNANT TUMORS       10       12       12       12         NO. OF TOTAL TUMORS       14       16       15       12         105 - 105       NO. OF EXAMINED ANIMALS       35       33       36       41         NO. OF ANIMALS WITH TUMORS       21       23       26       22         NO. OF ANIMALS WITH MULTIPLE TUMORS       12       10       17       17         NO. OF ANIMALS WITH MULTIPLE TUMORS       9       13       9       5  |                     | , -       |          |         | $\checkmark$ |   |                  |
| 13       12       13       12       8         N0. OF ANIMALS WITH TUMORS       10       12       10       8         N0. OF ANIMALS WITH SINGLE TUMORS       6       9       6       5         N0. OF ANIMALS WITH SINGLE TUMORS       6       9       6       5         N0. OF ANIMALS WITH MULTIPLE TUMORS       4       3       4       3         N0. OF BENIGN TUMORS       4       4       3       0         N0. OF MALIGNANT TUMORS       10       12       12       12         N0. OF TOTAL TUMORS       10       12       12       12         N0. OF TOTAL TUMORS       10       12       12       12         N0. OF TOTAL TUMORS       14       16       15       12         105 - 105       N0. OF EXAMINED ANIMALS       35       33       36       41         .       N0. OF ANIMALS WITH TUMORS       21       23       26       22         .       N0. OF ANIMALS WITH SINGLE TUMORS       12       10       17       17         .       N0. OF ANIMALS WITH MULTIPLE TUMORS       9       13       9       5   |                     | . 1       | 2        |         |              |   |                  |
| NO. OF ANIMALS WITH SINGLE TUMORS6965NO. OF ANIMALS WITH MULTIPLE TUMORS4343NO. OF BENIGN TUMORS4430NO. OF MALIGNANT TUMORS10121212NO. OF MALIGNANT TUMORS14161512105 - 105NO. OF EXAMINED ANIMALS35333641NO. OF ANIMALS WITH TUMORS21232622NO. OF ANIMALS WITH TUMORS12101717NO. OF ANIMALS WITH SINGLE TUMORS91395   | 12 8                | 12        | 13       | . 12    |              | NO. OF EXAMINED ANIMALS                 | 79 - 104 NO.     |
| NO. OF ANIMALS WITH MULTIPLE TUMORS4343NO. OF BENIGN TUMORS4430NO. OF MALIGNANT TUMORS10121212NO. OF TOTAL TUMORS14161512105 - 105NO. OF EXAMINED ANIMALS35333641NO. OF ANIMALS WITH TUMORS21232622NO. OF ANIMALS WITH SINGLE TUMORS12101717NO. OF ANIMALS WITH MULTIPLE TUMORS91395   |                     | 10        |          |         |              |   |                  |
| NO. OF BENIGN TUMORS       4       4       4       3       0         NO. OF MALIGNANT TUMORS       10       12       12       12         NO. OF TOTAL TUMORS       10       12       12       12         105 - 105       NO. OF EXAMINED ANIMALS       35       33       36       41         .       NO. OF ANIMALS WITH TUMORS       21       23       26       22         NO. OF ANIMALS WITH SINGLE TUMORS       12       10       17       17         NO. OF ANIMALS WITH MULTIPLE TUMORS       9       13       9       5   |                     |           |          |         |              |   |                  |
| NO. OF MALIGNANT TUMORS       10       12       12       12         NO. OF TOTAL TUMORS       14       16       15       12         105 - 105       NO. OF EXAMINED ANIMALS       35       33       36       41         NO. OF ANIMALS WITH TUMORS       21       23       26       22         NO. OF ANIMALS WITH SINGLE TUMORS       12       10       17       17         NO. OF ANIMALS WITH MULTIPLE TUMORS       9       13       9       5  | 4 3                 | 4         | 3        | 4       |              | NO. OF ANIMALS WITH MOLTH LE TOMORS     | 110.             |
| NO. OF TOTAL TUMORS         14         16         15         12           105 - 105         NO. OF EXAMINED ANIMALS         35         33         36         41           NO. OF ANIMALS WITH TUMORS         21         23         26         22           NO. OF ANIMALS WITH SINGLE TUMORS         12         10         17         17           NO. OF ANIMALS WITH MULTIPLE TUMORS         9         13         9         5  | 3 0                 | 3         |          | 4       |              |   |                  |
| 105 - 105NO. OF EXAMINED ANIMALS35333641NO. OF ANIMALS WITH TUMORS21232622NO. OF ANIMALS WITH SINGLE TUMORS12101717NO. OF ANIMALS WITH MULTIPLE TUMORS91395  |                     |           |          |         |              |   |                  |
| NO. OF ANIMALS WITH TUMORS21232622NO. OF ANIMALS WITH SINGLE TUMORS12101717NO. OF ANIMALS WITH MULTIPLE TUMORS91395  | 15 12               | 15        | 16       | . 14    |              | NO. OF TOTAL TORORS                     | NO.              |
| NO. OF ANIMALS WITH SINGLE TUMORS12101717NO. OF ANIMALS WITH MULTIPLE TUMORS91395  | 36 41               | 36        | 33       | 35      |              | NO. OF EXAMINED ANIMALS                 | 105 - 105 NO.    |
| NO. OF ANIMALS WITH SINGLE TUMORS12101717NO. OF ANIMALS WITH MULTIPLE TUMORS91395  | 26 22               | 26        | 23       | 21      |              |   |                  |
|  | 17 17               |           | 10       |         |              |   |                  |
|  | 9 5                 | 9         | 13       | 9       |              | NO. OF ANIMALS WITH MULTIPLE TUMORS     | NO.              |
| 18 14 17 14  | 17 14               | 17        | 14       | 18      |              | NO. OF BENIGN TUMORS                    | NO.              |
| NO. OF MALIGNANT TUMORS 18 26 20 16  | 20 16               | 20        | . 26     | 18      |              |   |                  |
| NO. OF TOTAL TUMORS 36 40 37 30  | 37 30               | 37        | 40       | 36      |              | NO. OF TOTAL TUMORS                     | NO.              |

PAGE : 1

.

(HPT070)

### MENDED OF ANTIMA C WITH THUODE AND

### STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 SEX : MALE

|--|

| e-related<br>_Weeks | Items                               | Group Name | Control | 5000 ppm | 10000 ppm | 20000 ppm |  |
|---------------------|-------------------------------------|------------|---------|----------|-----------|-----------|--|
| ×                   |                                     |            |         |          |           |           |  |
| 0 - 105             | NO. OF EXAMINED ANIMALS             |            | 50      | 50       | 50        | 50        |  |
|                     | NO. OF ANIMALS WITH TUMORS          |            | 34      | 37       | 37        | 31        |  |
|                     | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 19      | 21       | 24        | 23        |  |
|                     | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 15      | 16       | 13        | 8         |  |
|                     | NO. OF BENIGN TUMORS                |            | 24      | 18       | 20        | 15        |  |
|                     | NO. OF MALIGNANT TUMORS             |            | 31      | 40       | 33        | 28        |  |
|                     | NO. OF TOTAL TUMORS                 |            | 55      | 58       | 53        | 43        |  |

(HPT070)

BAIS4

.

TABLE N 2

### NUMBER OF ANIMALS WITH TUMORS AND

### NUMBER OF TUMORS-TIME RELATED: FEMALE

### NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS - TIME RELATED

#### STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 SEX : FEMALE

### rj:BDF1j

Time-related Items\_\_\_ Group Name 2500 ppm Control 5000 ppm 10000 ppm \_\_\_\_Weeks\_ 0 - 52 NO. OF EXAMINED ANIMALS 2 . NO. OF ANIMALS WITH TUMORS NO. OF ANIMALS WITH SINGLE TUMORS NO. OF ANIMALS WITH MULTIPLE TUMORS NO. OF BENIGN TUMORS Û NO. OF MALIGNANT TUMORS NO. OF TOTAL TUMORS 53 - 78 NO. OF EXAMINED ANIMALS NO. OF ANIMALS WITH TUMORS NO. OF ANIMALS WITH SINGLE TUMORS NO. OF ANIMALS WITH MULTIPLE TUMORS NO. OF BENIGN TUMORS NO. OF MALIGNANT TUMORS NO. OF TOTAL TUMORS 79 - 104 NO. OF EXAMINED ANIMALS NO. OF ANIMALS WITH TUMORS NO. OF ANIMALS WITH SINGLE TUMORS NO. OF ANIMALS WITH MULTIPLE TUMORS NO. OF BENIGN TUMORS NO. OF MALIGNANT TUMORS NO. OF TOTAL TUMORS 105 - 105 NO. OF EXAMINED ANIMALS NO. OF ANIMALS WITH TUMORS NO. OF ANIMALS WITH SINGLE TUMORS NO. OF ANIMALS WITH MULTIPLE TUMORS NO. OF BENIGN TUMORS NO. OF MALIGNANT TUMORS NO. OF TOTAL TUMORS (HPT070)

BAIS4

### NUMBER OF ANIMALS WITH TUMORS AND NUMBER OF TUMORS - TIME RELATED

~~~

#### STUDY NO. : 0613 : MOUSE B6D2F1/Cr1j[Crj:BDF1] ANIMAL REPORT TYPE : A1 SEX FEMALE

| `ime-related<br>Weeks | Items                               | Group Name | Control | 2500 ppm | 5000 ppm | 10000 ppm |  |
|-----------------------|-------------------------------------|------------|---------|----------|----------|-----------|--|
| 0 - 105               | NO. OF EXAMINED ANIMALS             |            | 50      | 50       | 50       | 50        |  |
| 0 100                 |                                     |            | 50      | 00       | 50       | 50        |  |
|                       | NO. OF ANIMALS WITH TUMORS          |            | 37      | 42       | 42       | 40        |  |
|                       | NO. OF ANIMALS WITH SINGLE TUMORS   |            | 25      | 27       | 32       | 29        |  |
|                       | NO. OF ANIMALS WITH MULTIPLE TUMORS |            | 12      | 15       | 10       | 11        |  |
|                       | NO. OF BENIGN TUMORS                |            | 25      | 21       | 20       | 15        |  |
|                       | NO. OF MALIGNANT TUMORS             |            | 29      | 37       | 33       | 40        |  |
|                       | NO. OF TOTAL TUMORS                 |            | 54      | 58       | 53       | 55        |  |

(HPT070)

TABLE O 1

### HISTOPATHOLOGICAL FINDINGS:

NEOPLASTIC LESIONS: MALE

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

 $\sim$ 

| Organ ·        | Findings                       | Group Name Control<br>No. of animals on Study 50 | 5000 ppm<br>50  | 10000 ррт<br>50 | 20000 ppm<br>50  |
|----------------|--------------------------------|--------------------------------------------------|-----------------|-----------------|------------------|
| {Integumentary | y system/appandage)            |                                                  |                 |                 |                  |
| subcutis       | lipoma                         | <50><br>1 ( 2%)                                  | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <50><br>0 ( 0%)  |
|                | schwannoma                     | 1 ( 2%)                                          | 0 ( 0%)         | 0 ( 0%)         | 0 ( 0%)          |
|                | schwannoma malignant           | 0 ( 0%)                                          | 1 ( 2%)         | 1 ( 2%)         | 1 ( 2%)          |
|                | histiocytic sarcoma            | 0 ( 0%)                                          | 1 ( 2%)         | 0 ( 0%)         | 0 ( 0%)          |
|                | mastcytoma:malignant           | 0 ( 0%)                                          | 1 ( 2%)         | 0 ( 0%)         | 0 ( 0%)          |
|                | hemangiosarcoma                | 1 ( 2%)                                          | 0 ( 0%)         | 0 ( 0%)         | 0 ( 0%)          |
| Respiratory    | system)                        |                                                  |                 |                 |                  |
| asal cavit     | histiocytic sarcoma            | . <50><br>0 ( 0%)                                | <50><br>1 ( 2%) | <50><br>1 ( 2%) | <50><br>0 ( 0%)  |
| ung            | bronchiolar-alveolar adenoma   | <50><br>7 (14%)                                  | <50><br>4 ( 8%) | <50><br>4 ( 8%) | <50><br>3 ( 6%)  |
|                | bronchiolar-alveolar carcinoma | 4 ( 8%)                                          | 10 ( 20%)       | 7 (14%)         | 5 (10%)          |
| (Hematopoietic | c system)                      |                                                  |                 |                 |                  |
| one marrow     | hemangioma                     | <50><br>0 ( 0%)                                  | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%)  |
| lymph node     | malignant lymphoma             | <50><br>13 ( 26%)                                | <50><br>6 (12%) | <50><br>6 (12%) | <50><br>6 ( 12%) |

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

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

(HPT085)

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

|                |                          |                                          |       |               |        |               |       |               |       |               | TAGE 2 |
|----------------|--------------------------|------------------------------------------|-------|---------------|--------|---------------|-------|---------------|-------|---------------|--------|
| Organ          | Findings                 | Group Name Cc<br>No. of animals on Study | ontro | 1<br>50       | 5000 p | opm<br>50     | 10000 | ppm<br>50     | 20000 | ррт<br>50     |        |
| {Hematopoieti  | c system)                |                                          |       |               |        |               |       |               |       |               |        |
| spleen         | histiocytic sarcoma      |                                          | 1     | <50><br>(2%)  | 0      | <50><br>( 0%) | 1     | <50><br>(2%)  | 0     | <50><br>( 0%) |        |
|                | malignant lymphoma       |                                          | 0     | ( 0%)         | 0      | ( 0%)         | 0     | ( 0%)         | 2     | ( 4%)         |        |
|                | hemangiosarcoma          |                                          | 1     | (2%)          | 1      | ( 2%)         | 2     | ( 4%)         | 1     | (2%)          |        |
| {Digestive sys | stem)                    |                                          |       |               |        |               |       |               |       |               |        |
| salivary gl    | histiocytic sarcoma      |                                          | 0     | <50><br>(0%)  | 1      | <50><br>(2%)  | 0     | <50><br>( 0%) | 0     | <50><br>( 0%) |        |
| stomach        | squamous cell papilloma  |                                          | 0     | <50><br>(0%)  | 1      | <50><br>( 2%) | 0     | <50><br>( 0%) | 1     | <50><br>( 2%) |        |
| small intes    | adenocarcinoma           |                                          | 0     | <50><br>( 0%) | 1      | <50><br>( 2%) | 1     | <50><br>(2%)  | 0     | <50><br>( 0%) |        |
| liver          | hemangioma               |                                          | 0     | <50><br>( 0%) | 1      | <50><br>(2%)  | 0     | <50><br>( 0%) | 0     | <50><br>( 0%) |        |
|                | hepatocellular adenoma   |                                          | 12    | (24%)         | 7      | ( 14%)        | 14    | (28%)         | 7     | (14%)         |        |
|                | histiocytic sarcoma      |                                          | 3     | ( 6%)         | 3      | ( 6%)         | 1     | ( 2%)         | 4     | ( 8%)         |        |
|                | hemangiosarcoma          |                                          | 1     | (2%)          | 2      | ( 4%)         | 3     | ( 6%)         | 1     | ( 2%)         |        |
|                | hepatocellular carcinoma |                                          | 6     | (12%)         | 9      | ( 18%)        | 6     | ( 12%)        | 6     | ( 12%)        |        |
| gall bladd     | papillary adenoma        |                                          | 0     | <50><br>( 0%) | 0      | <50><br>( 0%) | 1     | <49><br>( 2%) | 1     | <49><br>( 2%) |        |

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

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

(HPT085)

# STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : Λ1 SEX : MALE

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

~

|                | MALL                | · · · · · · · · · · · · · · · · · · · |                                       |              |               |        |                 |       |               |       |               | PAGE : |
|----------------|---------------------|---------------------------------------|---------------------------------------|--------------|---------------|--------|-----------------|-------|---------------|-------|---------------|--------|
| 0rgan          | Findings            |                                       | Group Name<br>_ No. of animals on Stu | Contro<br>dy | 1<br>50       | 5000 p | opm<br>50       | 10000 | ppm<br>50     | 20000 | ррт<br>50     |        |
| {Urinary syste | em)                 |                                       |                                       |              |               |        |                 |       |               |       |               |        |
| kidney         | histiocytic sarcoma |                                       |                                       | 0            | <50><br>( 0%) | 0      | <50><br>( 0%)   | 0     | <50><br>( 0%) | 1     | <50><br>(2%)  |        |
| urin bladd     | histiocytic sarcoma |                                       |                                       | 0            | <50><br>( 0%) | 0      | <50><br>( 0%)   | 1     | <50><br>(2%)  | 1     | <50><br>( 2%) |        |
| {Endocrine sys | stem)               |                                       |                                       |              |               |        |                 |       |               |       |               |        |
| pituitary      | adenoma             |                                       |                                       | 0            | <50><br>( 0%) | 2      | <50><br>-(, 4%) | 0     | <50><br>( 0%) | 0     | <50><br>( 0%) |        |
| thyroid        | C-cell carcinoma    |                                       |                                       | 1            | <50><br>( 2%) | 0      | <50><br>( 0%)   | 0     | <50><br>( 0%) | 0     | <50><br>( 0%) |        |
| {Reproductive  | system}             |                                       |                                       |              |               |        |                 |       |               |       |               |        |
| epididymis     | histiocytic sarcoma |                                       |                                       | 0            | <50><br>( 0%) | 1      | <50><br>( 2%)   | 0     | <50><br>( 0%) | 0     | <50><br>( 0%) |        |
| semin ves      | histiocytic sarcoma |                                       |                                       | 0            | <50><br>( 0%) | 0      | <50><br>( 0%)   | 1     | <50><br>(2%)  | 0     | <50><br>( 0%) |        |
| {Nervous syste | em)                 |                                       |                                       |              |               |        |                 |       |               |       |               |        |
| periph nerv    | histiocytic sarcoma |                                       |                                       | 0            | <50><br>( 0%) | 0      | <50><br>( 0%)   | 1     | <50><br>(2%)  | 0     | <50><br>( 0%) |        |
| {Special sense | e organs/appendage) |                                       |                                       |              |               |        |                 |       |               |       |               |        |
| Harder gl      | adenoma             |                                       |                                       | 2            | <50><br>( 4%) | 2      | <50><br>( 4%)   | 1     | <50><br>(2%)  | 2     | <50><br>( 4%) |        |
|                | adenocarcinoma      |                                       |                                       | 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

(HPT085)

BAIS4

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

5000 ppm Group Name Control 10000 ppm 20000 ppm Organ\_ Findings\_ No. of animals on Study 50 50 50 50 {Musculoskeletal system} bone <50> <50> <50> <50> osteoma 1 (2%) 0 ( 0%) 0 ( 0%) 0 (0%) 0 ( 0%) 1 (2%) 0 ( 0%) 0 ( 0%) osteosarcoma {Body cavities}

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

(HPT085)

BAIS4

.

PAGE : 4

~~

TABLE O 2

### HISTOPATHOLOGICAL FINDINGS:

NEOPLASTIC LESIONS: FEMALE

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

~~~~

·----

| SEX :          | FEMALE                         |  |                  |                  | PAGE :            |
|----------------|--------------------------------|--|------------------|------------------|-------------------|
| Organ          | Findings                       | Group Name Control<br>No. of animals on Study 50 | 2500 ppm<br>50   | 5000 ppm<br>50   | 10000 מספס<br>50  |
| [Integumentary | y system/appandage)            |  |                  |                  |                   |
| subcutis       | schwannoma                     | <50><br>0 ( 0%)                                  | <50><br>1 ( 2%)  | <50><br>0 ( 0%)  | <50><br>0 ( 0%)   |
|                | hemangioma                     | 1 ( 2%)  | 0 ( 0%)          | 0 ( 0%)          | 0 ( 0%)           |
|                | fibrosarcoma                   | 0 ( 0%)  | 1 (2%)           | 1 ( 2%)          | 0 ( 0%)           |
| Respiratory s  | system)                        |  |                  |                  |                   |
| ung            | bronchiolar-alveolar adenoma   | 、<br><50><br>2 ( 4%)                             | <50><br>1 ( 2%)  | <50><br>0 ( 0%)  | <50><br>0 ( 0%)   |
|                | bronchiolar-alveolar carcinoma | 2 ( 4%)  | 2 (4%)           | 1 ( 2%)          | 3 ( 6%)           |
| lematopoietio  | c system)                      |  |                  |                  |                   |
| one marrow     | hemangioma                     | <50><br>0 ( 0%)                                  | <50><br>0 ( 0%)  | <50><br>0 ( 0%)  | <50><br>1 ( 2%)   |
| ymph node      | malignant lymphoma             | <50><br>12 (24%)                                 | <50><br>18 (36%) | <50><br>19 (38%) | <50><br>16 ( 32%) |
| pleen          | hemangioma                     | <50><br>0 ( 0%)                                  | <50><br>0 ( 0%)  | <50><br>0 ( 0%)  | <50><br>1 ( 2%)   |
|                | malignant lymphoma             | 1 ( 2%)  | 0 ( 0%)          | 1 ( 2%)          | 1 ( 2%)           |
| )igestive sys  | stem)                          |  |                  |                  |                   |
| alivary gl     | histiocytic sarcoma            | <50><br>1 ( 2%)                                  | <49><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 с: b / а \* 100

(HPT085)

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

~~

| SEX          | : FEMALE                 |                                 |                     | · · · · · · · · · · · · · · · · · · · |                  | PAG              | E : |
|--------------|--------------------------|---------------------------------|---------------------|---------------------------------------|------------------|------------------|-----|
| Organ        | Findings                 | Group Name<br>No. of animals on | Control<br>Study 50 | 2500 ppm<br>50                        | 5000 ppm<br>50   | 10000 ppm<br>50  |     |
|              |                          |                                 |                     |                                       |                  |                  |     |
| {Digestive s | system)                  |                                 |                     |                                       |                  |                  |     |
| stomach      | squamous cell papilloma  |                                 | <50><br>0 ( 0%)     | <50><br>1 ( 2%)                       | <50><br>0 ( 0%)  | <50><br>0 ( 0%)  |     |
| liver        | hemangioma               |                                 | <50><br>3 ( 6%)     | <50><br>3 ( 6%)                       | <50><br>3 ( 6%)  | <50><br>1 ( 2%)  |     |
|              | hepatocellular adenoma   |                                 | 3 ( 6%)             | 1 ( 2%)                               | 4 ( 8%)          | 1 (2%)           |     |
|              | histiocytic sarcoma      |                                 | 2 ( 4%)             | 0 ( 0%)                               | 0 ( 0%)          | 1 ( 2%)          |     |
|              | hemangiosarcoma          |                                 | 0 ( 0%)             | 0 ( 0%)                               | 1 ( 2%)          | 0 ( 0%)          |     |
|              | hepatocellular carcinoma |                                 | 1 ( 2%)             | 1 ( 2%)                               | 1 ( 2%)          | 2 ( 4%)          |     |
| {Endocrine s | system)                  |                                 |                     |                                       |                  |                  |     |
| pituitary    | adenoma                  |                                 | <50><br>12 (24%)    | <50><br>9 ( 18%)                      | <50><br>5 ( 10%) | <50><br>6 ( 12%) |     |
|              | adenocarcinoma           |                                 | 0 ( 0%)             | 0 ( 0%)                               | 0 ( 0%)          | 1 ( 2%)          |     |
| thyroid      | C-cell carcinoma         |                                 | <50><br>0 ( 0%)     | <50><br>0 ( 0%)                       | <50><br>0 ( 0%)  | <50><br>1 ( 2%)  |     |
| {Reproductiv | re system)               |                                 |                     |                                       |                  |                  |     |
| ovary        | cystadenoma              |                                 | <50><br>0 ( 0%)     | <50><br>0 ( 0%)                       | <50><br>3 ( 6%)  | <50><br>1 ( 2%)  |     |
|              | hemangioma               |                                 | 0 ( 0%)             | 1 ( 2%)                               | 4 ( 8%)          | 0 ( 0%)          |     |
|              | . در                     |                                 |                     |                                       |                  |                  |     |
|              |                          |                                 |                     |                                       |                  |                  |     |

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

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

(HPT085)

BAIS4

| ANIMAL<br>REPORT TYPE | : 0013<br>: MOUSE B6D2F1/Cr1,j[Cr,j:BDF1]<br>: A1<br>: FEMALE | HISTOPATHOLOGICAL FINDINGS : NEOPLASTIC LES.<br>ALL ANIMALS (0-105W) | IUNS (SUMMART)  |                 | PAGE :          |
|-----------------------|---|--|-----------------|-----------------|-----------------|
| Organ                 | Findings  | Group Name Control<br>No. of animals on Study 50                     | 2500 ppm<br>50  | 5000 ppm<br>50  | 10000 ppm<br>50 |
| {Reproductive         | e system)   |  |                 |                 |                 |
| uterus                | leiomyoma   | <50><br>1 ( 2%)  | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) |
|                       | endometrial stromal polyp                                     | 0 ( 0%)  | 1 ( 2%)         | 1 ( 2%)         | 0 ( 0%)         |
|                       | histiocytic sarcoma   | 8 (16%)  | 14 (28%)        | 7 (14%)         | 14 (28%)        |
|                       | hemangiosarcoma   | 0 ( 0%)  | 0 ( 0%)         | 1 ( 2%)         | 0 ( 0%)         |
|                       | endometrial stromal sarcoma                                   | 0 ( 0%)  | 0 ( 0%)         | 1 ( 2%)         | 0 ( 0%)         |
| mammary gl            | adenocarcinoma  | <50><br>1 ( 2%)  | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>1 ( 2%) |
| {Nervous syst         | tem}  |  |                 |                 |                 |
| brain                 | meningioma:malignant  | <50><br>1 ( 2%)  | <50><br>0 ( 0%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) |
| {Special sens         | se organs/appendage)  |  |                 |                 |                 |
| Harder gl             | adenoma   | <50><br>3 (6%)   | <50><br>2 ( 4%) | <50><br>0 ( 0%) | <50><br>4 ( 8%) |
| {Musculoskele         | etal system}  |  | -               |                 |                 |
| muscle                | rhabdomyosarcoma  | <50><br>0 ( 0%)  | <50><br>1 ( 2%) | <50><br>0 ( 0%) | <50><br>0 ( 0%) |
| bone                  | osteoma   | <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 с:b/а\*100

(HPT085)

STUDY NO. : 0613

BAIS4

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

7

### TABLE P 1

### NEOPLASTIC LESIONS-INCIDENCE AND

### STATISTICAL ANALYSIS: MALE

#### STUDY No. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]

### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

SEX : MALE

Group Name Control 5000 ppm 10000 ppm 20000 ppm SITE : lung TUMOR : bronchiolar-alveolar adenoma Tumor rate Overall rates(a) 7/50(14.0) 4/50( 8.0) 4/50(8.0)3/50(6,0)Adjusted rates(b) 20.00 12.12 11.11 7.32 Terminal rates(c) 7/35(20.0) 4/33(12.1) 4/36(11.1) 3/41 ( 7.3) Statistical analysis Peto test Standard method(d) P = ----Prevalence method(d) P = 0.9414Combined analysis(d) P = -----Cochran-Armitage test(e) P = 0.2102Fisher Exact test(e) P = 0.2623P = 0.2623P = 0.1589SITE : lung TUMOR : bronchiolar-alveolar carcinoma Tumor rate Overall rates(a) 4/50( 8.0) 10/50(20.0) 5/50( 10.0) 7/50(14.0) Adjusted rates(b) 9.76 24.24 13.16 10.64 Terminal rates(c) 3/35( 8.6) 8/33(24.2) 4/36(11.1) 3/41 ( 7.3) Statistical analysis Peto test Standard method(d) P = 0.5791Prevalence method(d) P = 0.6094Combined analysis(d) P = 0.6373Cochran-Armitage test(e) P = 0.8311Fisher Exact test(e) P = 0.0739P = 0.2623P = 0.5000SITE : lung TUMOR : bronchiolar-alveolar adenoma, bronchiolar-alveolar carcinoma Tumor rate Overall rates(a) 11/50(22.0) 14/50 (28.0) 11/50(22.0)8/50(16.0) Adjusted rates(b) 28.57 36.36 23.6817.02 Terminal rates(c) 10/35(28.6) 12/33 ( 36. 4) 8/36(22.2) 6/41(14.6)Statistical analysis Peto test Standard method(d) P = 0.5791Prevalence method(d) P = 0.9016Combined analysis(d) P = 0.9071Cochran-Armitage test(e) P = 0.2989Fisher Exact test(e) P = 0.3224P = 0.5952P = 0.3055

(HPT360A)

BAIS4

### STUDY No. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]

SEX : MALE

### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE: 2

| Group Name                      | Control                                | 5000 ppm                              | 10000 ppm    | 20000 ppm      |
|---------------------------------|--|---------------------------------------|--------------|----------------|
|                                 | SITE : lymph node                      |                                       |              |                |
|                                 | TUMOR : malignant lymphoma             |                                       |              |                |
| Tumor rate                      |  |                                       |              |                |
| Overall rates(a)                | 13/50(26.0)                            | 6/50(12.0)                            | 6/50(12.0)   | 6/50(12.0)     |
| Adjusted rates(b)               | 17.14                                  | 12. 12                                | 8.33         | 14.63          |
| Terminal rates(c)               | 6/35(17.1)                             | 4/33 ( 12. 1)                         | 3/36( 8.3)   | 6/41(14.6)     |
| Statistical analysis            |  |                                       |              |                |
| Peto test<br>Standard method(d) | P = 0.9976                             |                                       |              |                |
| Prevalence method(d)            | P = 0.5755                             |                                       |              |                |
| Combined analysis(d)            | P = 0.9697                             |                                       |              |                |
| Cochran-Armitage test(e)        | P = 0.1056                             |                                       |              |                |
| Fisher Exact test(e)            | 1 - 0.1000                             | P = 0.0624                            | P = 0.0624   | P = 0.0624     |
|                                 |  | 1 - 0.0024                            | 1 - 0.0024   | r - 0.0024     |
|                                 | SITE : liver                           |                                       |              |                |
|                                 | TUMOR : hepatocellular adenoma         |                                       |              |                |
| Tumor rate                      | Tomon nepatocorratar adenoma           |                                       |              |                |
| Overall rates(a)                | 12/50(24.0)                            | 7/50(14.0)                            | 14/50(28.0)  | 7/50(14.0)     |
| Adjusted rates(b)               | 25. 71                                 | 16. 22                                | 33. 33       | 14.63          |
| Terminal rates(c)               | 9/35 ( 25, 7)                          | 5/33 (15.2)                           | 12/36(33.3)  | 6/41 ( 14. 6)  |
| Statistical analysis            |  | .,,                                   | 10,000,0000, | () I ( I I ()) |
| Peto test                       |  |                                       |              |                |
| Standard method(d)              | P = 0.8050                             |                                       |              |                |
| Prevalence method(d)            | P = 0.7987                             |                                       |              |                |
| Combined analysis(d)            | P = 0.8594                             |                                       |              |                |
| Cochran-Armitage test(e)        | P = 0.4028                             |                                       |              |                |
| Fisher Exact test(e)            |  | P = 0.1540                            | P = 0.4100   | P = 0.1540     |
|                                 | ······································ |                                       |              |                |
|                                 | SITE : liver                           |                                       |              |                |
|                                 | TUMOR : histiocytic sarcoma            |                                       |              |                |
| lumor rate                      |  |                                       |              |                |
| Overall rates(a)                | 3/50( 6.0)                             | 3/50 ( 6.0)                           | 1/50(2.0)    | 4/50 ( 8.0)    |
| Adjusted rates(b)               | 2.86                                   | 3. 03                                 | 2.78         | 0.0            |
| Terminal rates(c)               | 1/35(2.9)                              | 1/33( 3.0)                            | 1/36( 2.8)   | 0/41( 0.0)     |
| Statistical analysis            |  |                                       |              |                |
| Peto test                       | D 0.0010                               |                                       |              |                |
| Standard method(d)              | P = 0.2212                             |                                       |              |                |
| Prevalence method(d)            | P = 0.8247                             |                                       |              |                |
| Combined analysis(d)            | P = 0.4353                             |                                       |              |                |
| Cochran-Armitage test(e)        | P = 0.7136                             | $\mathbf{p} = \mathbf{o} \cdot cct 1$ | D 0.0007     |                |
| Fisher Exact test(e)            |  | P = 0.6611                            | P = 0.3087   | P = 0.5000     |

(HPT360A)

STUDY No. : 0613 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1] SEX : MALE

#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

~~~

PAGE : 3

.

| Group Name                                       | Control                     | 5000 ppm               | 10000 ppm             | 20000 ppm     |  |
|--------------------------------------------------|-----------------------------|------------------------|-----------------------|---------------|--|
|                                                  | SITE : liver                |                        |                       |               |  |
|                                                  | TUMOR : hemangiosarcoma     |                        |                       |               |  |
| umor rate                                        |                             |                        |                       |               |  |
| Overall rates(a)                                 | 1/50( 2.0)                  | 2/50( 4.0)             | 3/50( 6.0)            | 1/50( 2.0)    |  |
| Adjusted rates(b)                                | 2.86                        | 6.06                   | 2.78                  | 0.0           |  |
| Terminal rates(c)                                | 1/35( 2.9)                  | 2/33(6.1)              | 1/36( 2.8)            | 0/41( 0.0)    |  |
| tatistical analysis                              |                             |                        |                       |               |  |
| Peto test                                        |                             |                        |                       |               |  |
| Standard method(d)                               | P = 0.1735                  |                        |                       |               |  |
| Prevalence method(d)                             | P = 0.8679                  |                        |                       |               |  |
| Combined analysis(d)                             | P = 0.5743                  |                        |                       |               |  |
| Cochran-Armitage test(e)                         | P = 0.9481                  |                        |                       |               |  |
| Fisher Exact test(e)                             |                             | P = 0.5000             | $\mathbf{P} = 0.3087$ | P = 0.7525    |  |
|                                                  | SITE : liver                |                        |                       |               |  |
|                                                  | TUMOR : hepatocellular card | -i                     |                       |               |  |
| umor rate                                        | Tomok - nepatoceriurar card |                        |                       |               |  |
| Overall rates(a)                                 | 6/50(12.0)                  | 9/50 (18,0)            | 6 (50 ( 10 0)         | C (FO ( 10 0) |  |
|                                                  | 15. 79                      |                        | 6/50(12.0)            | 6/50(12.0)    |  |
| Adjusted rates(b)<br>Terminal rates(c)           | 15.79<br>5/35(14.3)         | 14. 29<br>4/33 (12. 1) | 13.89                 | 9.09          |  |
| tatistical analysis                              | 5/35(14.3)                  | 4/33(12.1)             | 5/36(13.9)            | 2/41 ( 4.9)   |  |
| Peto test                                        |                             |                        |                       |               |  |
| Standard method(d)                               | P = 0.3664                  |                        |                       |               |  |
| Prevalence method(d)                             | P = 0.3004<br>P = 0.8232    |                        |                       |               |  |
| Combined analysis(d)                             | P = 0.8232<br>P = 0.7299    |                        |                       |               |  |
| Combined analysis(d)<br>Cochran-Armitage test(e) |                             |                        |                       |               |  |
| Cochran-Armitiage test(e)                        | P = 0.7529                  |                        |                       |               |  |

(HPT360A)

#### STUDY No. : 0613 ANIMAL : MOUSE B6D2F1/Cr1;[Crj:BDF1] SEX : MALE

#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

| Group Name               | Control                    | 5000 ppm                       | 10000 ppm   | 20000 ppm   |
|--------------------------|----------------------------|--------------------------------|-------------|-------------|
|                          | SITE : liver               |                                |             |             |
|                          | TUMOR : hepatocellular ade | noma, hepatocellular carcinoma |             |             |
| 'umor rate               | -                          |                                |             |             |
| Overall rates(a)         | 16/50(32.0)                | 16/50 ( 32.0)                  | 18/50(36.0) | 13/50(26.0) |
| Adjusted rates(b)        | 34. 29                     | 30. 56                         | 41.67       | 22.92       |
| Terminal rates(c)        | 12/35(34.3)                | 9/33 (27.3)                    | 15/36(41.7) | 8/41(19.5)  |
| tatistical analysis      |                            |                                |             |             |
| Peto test                |                            |                                |             |             |
| Standard method(d)       | P = 0.5794                 |                                |             |             |
| Prevalence method(d)     | P = 0.8183                 |                                |             |             |
| Combined analysis(d)     | P = 0.8187 ·               |                                |             |             |
| Cochran-Armitage test(e) | P = 0.5201                 |                                |             |             |
| Fisher Exact test(e)     |                            | P = 0.5848                     | P = 0.4165  | P = 0.3299  |

(HPT360A)

(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.

BAIS4

PAGE :

4

STUDY No. : 0613 ANIMAL : MOUSE B6D2F1/Cr1,j[Cr,j:BDF1] SEX : MALE

### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 1

| Group Name               | Control                                        | 5000 ppm    | 10000 ppm  | 20000 ppm    |
|--------------------------|------------------------------------------------|-------------|------------|--------------|
|                          |                                                |             |            |              |
|                          | SITE : ALL SITE<br>TUMOR : histiocytic sarcoma |             |            |              |
| ſumor rate               | TOMOR · HISTICCYTIC Salcoma                    |             |            |              |
| Overall rates(a)         | 4/50( 8.0)                                     | 7/50 (14.0) | 6/50(12.0) | 6/50(12.0)   |
| Adjusted rates(b)        | 2.86                                           | 15. 15      | 11.11      | 4. 88        |
| Terminal rates(c)        | 1/35( 2.9)                                     | 5/33 (15.2) | 4/36(11.1) | 2/41 ( 4, 9) |
| Statistical analysis     | 1,000                                          | 0,00 (10.2) | 1,00(11.1) | 2/11( 1.0)   |
| Peto test                |                                                |             |            |              |
| Standard method(d)       | P = 0.3428                                     |             |            |              |
| Prevalence method(d)     | P = 0.5921                                     |             |            |              |
| Combined analysis(d)     | P = 0.4560                                     |             |            |              |
| Cochran-Armitage test(e) | P = 0.6803                                     |             |            |              |
| Fisher Exact test(e)     | 1 0.0000                                       | P = 0.2623  | P = 0.3703 | P = 0.3703   |
|                          | · · · · · · · · · · · · · · · · · · ·          |             |            |              |
|                          | SITE : ALL SITE                                |             |            |              |
|                          | TUMOR : malignant lymphoma                     |             |            |              |
| umor rate                |                                                |             |            |              |
| Overall rates(a)         | 13/50(26.0)                                    | 6/50(12.0)  | 6/50(12.0) | 8/50(16.0)   |
| Adjusted rates(b)        | 17.14                                          | 12. 12      | 8. 33      | 19.51        |
| Terminal rates(c)        | 6/35(17.1)                                     | 4/33(12.1)  | 3/36( 8.3) | 8/41 ( 19.5) |
| Statistical analysis     |                                                |             |            |              |
| Peto test                | D 0.0050                                       |             |            |              |
| Standard method(d)       | P = 0.9976                                     |             |            |              |
| Prevalence method(d)     | P = 0.3175                                     |             |            |              |
| Combined analysis(d)     | P = 0.9017                                     |             |            |              |
| Cochran-Armitage test(e) | P = 0.3182                                     | D 0 0000    |            |              |
| Fisher Exact test(e)     |                                                | P = 0.0624  | P = 0.0624 | P = 0.1631   |

(HPT360A)

#### STUDY No. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]

SEX : MALE

### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 2

| Group Name               | Control                                    | 5000 ppm     | 10000 ppm  | 20000 ppm  |  |
|--------------------------|--------------------------------------------|--------------|------------|------------|--|
|                          | SITE : ALL SITE<br>TUMOR : hemangiosarcoma |              |            |            |  |
| Tumor rate               | Tomore - Hemangrosar coma                  |              |            |            |  |
| Overall rates(a)         | 3/50(6.0)                                  | 3/50 ( 6, 0) | 4/50( 8.0) | 2/50(4.0)  |  |
| Adjusted rates(b)        | 8.57                                       | 9.09         | 2.78       | 2.44       |  |
| Terminal rates(c)        | 3/35( 8, 6)                                | 3/33 ( 9, 1) | 1/36(2.8)  | 1/41(2.4)  |  |
| Statistical analysis     |                                            |              | 2,000      |            |  |
| Peto test                |                                            |              |            |            |  |
| Standard method(d)       | P = 0.1846                                 |              |            |            |  |
| Prevalence method(d)     | P = 0.9198                                 |              |            |            |  |
| Combined analysis(d)     | P = 0.7177                                 |              |            |            |  |
| Cochran-Armitage test(e) | P = 0.6872                                 |              |            |            |  |
| Fisher Exact test(e)     |                                            | P = 0.6611   | P = 0.5000 | P = 0.5000 |  |

#### (HPT360A)

(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 P 2

### NEOPLASTIC LESIONS-INCIDENCE AND

### STATISTICAL ANALYSIS: FEMALE

### STUDY No. : 0613 ANIMAL : MOUSE B6D2F1/Cr1,j[Cr,j:BDF1]

SEX : FEMALE

### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 5

~

| Group Name               | Control                      | 2500 ppm                               | 5000 ppm              | 10000 ppm   |  |
|--------------------------|------------------------------|----------------------------------------|-----------------------|-------------|--|
|                          | SITE : lung                  |                                        |                       |             |  |
|                          | TUMOR : bronchiolar-alveolar | carcinoma                              |                       |             |  |
| Tumor rate               |                              |                                        |                       |             |  |
| Overall rates(a)         | 2/50( 4.0)                   | 2/50( 4.0)                             | 1/50( 2.0)            | 3/50(6.0)   |  |
| Adjusted rates(b)        | 5.26                         | 7.69                                   | 3. 23                 | 6.90        |  |
| Terminal rates(c)        | 1/29( 3.4)                   | 2/26(7.7)                              | 1/31( 3.2)            | 1/20( 5.0)  |  |
| Statistical analysis     |                              |                                        |                       |             |  |
| Peto test                |                              |                                        |                       |             |  |
| Standard method(d)       | P = 0.1155                   |                                        |                       |             |  |
| Prevalence method(d)     | P = 0.4665                   |                                        |                       |             |  |
| Combined analysis(d)     | P = 0.2751                   |                                        |                       |             |  |
| Cochran-Armitage test(e) | P = 0.6256                   |                                        |                       |             |  |
| Fisher Exact test(e)     |                              | P = 0.6913                             | $\mathbf{P} = 0.5000$ | P = 0.5000  |  |
|                          | SITE : lung                  |                                        |                       |             |  |
|                          | <del>-</del>                 | adenoma, bronchiolar-alveolar carcinom | าล                    |             |  |
| Tumor rate               |                              | ,                                      |                       |             |  |
| Overall rates(a)         | 4/50 ( 8.0)                  | 3/50(6,0)                              | 1/50( 2.0)            | 3/50( 6.0)  |  |
| Adjusted rates(b)        | 10. 53                       | 8.82                                   | 3.23                  | 6.90        |  |
| Terminal rates(c)        | 2/29 ( 6, 9)                 | 2/26(7.7)                              | 1/31(-3,2)            | 1/20( 5.0)  |  |
| Statistical analysis     |                              |                                        |                       |             |  |
| Peto test                |                              |                                        |                       |             |  |
| Standard method(d)       | P = 0.1155                   |                                        |                       |             |  |
| Prevalence method(d)     | P = 0.7930                   |                                        |                       |             |  |
| Combined analysis(d)     | P = 0.6173                   | •                                      |                       |             |  |
| Cochran-Armitage test(e) | P = 0.6370                   |                                        |                       |             |  |
| Fisher Exact test(e)     |                              | P = 0.5000                             | P = 0.1811            | P = 0.5000  |  |
| <u> </u>                 |                              |                                        |                       |             |  |
|                          | SITE : lymph node            |                                        |                       |             |  |
|                          | TUMOR : malignant lymphoma   |                                        |                       |             |  |
| Tumor rate               |                              |                                        |                       |             |  |
| Overall rates(a)         | 12/50(24.0)                  | 18/50 ( 36.0)                          | 19/50( 38.0)          | 16/50(32.0) |  |
| Adjusted rates(b)        | 20. 69                       | 30. 77                                 | 32.26                 | 20.00       |  |
| Terminal rates(c)        | 6/29(20.7)                   | 8/26(30.8)                             | 10/31(32.3)           | 4/20( 20.0) |  |
| Statistical analysis     |                              |                                        |                       |             |  |
| Peto test                |                              | <i>v</i>                               |                       |             |  |
| Standard method(d)       | P = 0.0718                   |                                        |                       |             |  |
| Prevalence method(d)     | P = 0.5195                   |                                        |                       |             |  |
| Combined analysis(d)     | P = 0.1217                   |                                        |                       |             |  |
| Cochran-Armitage test(e) | P = 0.5235                   |                                        |                       |             |  |
| Fisher Exact test(e)     |                              | P = 0.1376                             | P = 0.0971            | P = 0.2522  |  |
| (HPT360A)                |                              |                                        |                       |             |  |

.

•

(HPT360A)

### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

STUDY No. : 0613 ANIMAL : MOUSE B6D2F1/Cr1,j[Cr,j:BDF1]

SEX : FEMALE

PAGE: 6

 $\sim \sim$ 

| Group Name                        | Control                      | 2500 ppm                    | 5000 ррм              | 10000 ppm             |     |
|-----------------------------------|------------------------------|-----------------------------|-----------------------|-----------------------|-----|
|                                   | SITE : liver                 |                             |                       |                       |     |
| n                                 | TUMOR : hemangioma           |                             |                       |                       |     |
| Tumor rate<br>Overall rates(a)    | 3/50(6.0)                    | 3/50(6.0)                   |                       | 1/50/ 0.0)            |     |
| Adjusted rates (b)                | 8.33                         | 11. 11                      | 3/50 ( 6.0)<br>9.68   | 1/50(2.0)             |     |
| Terminal rates(c)                 | 2/29(6.9)                    | 2/26 ( 7.7)                 | 3/31(9.7)             | 0/20(0.0)             |     |
| Statistical analysis              | 2/20( 0.0)                   | b/ b( ( 1.1)                | 5/51( 5.17            | 0/20( 0:0)            |     |
| Peto test                         |                              |                             |                       |                       |     |
| Standard method(d)                | P =                          |                             |                       |                       |     |
| Prevalence method(d)              | P = 0.8274                   |                             |                       |                       |     |
| Combined analysis(d)              | P =                          |                             |                       |                       |     |
| Cochran-Armitage test(e)          | P = 0.3236                   |                             |                       |                       |     |
| Fisher Exact test(e)              |                              | P = 0.6611                  | $\mathbf{P} = 0.6611$ | $\mathbf{P} = 0.3087$ |     |
|                                   |                              | <b>x</b>                    |                       |                       |     |
|                                   | SITE : liver                 |                             |                       |                       |     |
|                                   | TUMOR : hepatocellular adenc | ma                          | •                     |                       |     |
| fumor rate                        |                              |                             |                       |                       |     |
| Overall rates(a)                  | 3/50( 6.0)                   | 1/50 ( 2.0)                 | 4/50( 8.0)            | 1/50( 2.0)            |     |
| Adjusted rates(b)                 | 10.34                        | 3.70                        | 11. 43                | 5.00                  |     |
| Terminal rates(c)                 | 3/29(10.3)                   | 0/26( 0.0)                  | 3/31( 9.7)            | 1/20( 5.0)            |     |
| Statistical analysis<br>Peto test |                              |                             |                       |                       |     |
| Standard method(d)                | P =                          |                             |                       |                       |     |
| Prevalence method(d)              | P = 0.6815                   |                             |                       |                       |     |
| Combined analysis(d)              | P =                          |                             |                       |                       |     |
| Cochran-Armitage test(e)          | P = 0.5259                   |                             |                       |                       |     |
| Fisher Exact test(e)              | 1 - 0. 5259                  | P = 0.3087                  | P = 0.5000            | P = 0.2097            |     |
| TISHEL EXACT LEST(e)              |                              | r - 0.3001                  | F - 0. 5000           | P = 0.3087            |     |
|                                   | SITE : liver                 |                             |                       |                       | . * |
|                                   | TUMOR : hepatocellular adeno | ma,hepatocellular carcinoma |                       |                       |     |
| lumor rate                        |                              |                             |                       |                       |     |
| Overall rates(a)                  | 4/50( 8.0)                   | 2/50( 4.0)                  | 4/50( 8.0)            | 3/50(6.0)             |     |
| Adjusted rates(b)                 | 10.34                        | 7.41                        | 9.68                  | 5.88                  |     |
| Terminal rates(c)                 | 3/29(10.3)                   | 1/26( 3.8)                  | 3/31 ( 9.7)           | 1/20( 5.0)            |     |
| Statistical analysis              |                              |                             |                       |                       |     |
| Peto test                         |                              |                             |                       |                       |     |
| Standard method(d)                | P = 0.3485                   |                             |                       |                       |     |
| Prevalence method(d)              | P = 0.5490                   |                             |                       |                       |     |
| Combined analysis(d)              | P = 0.4708                   |                             |                       |                       |     |
| Cochran-Armitage test(e)          | P = 0.8844                   | B 0 9900                    |                       |                       |     |
| Fisher Exact test(e)              |                              | P = 0.3389                  | P = 0.6425            | P = 0.5000            |     |

(HPT360A)

### STUDY No. : 0613 ANIMAL : MOUSE B6D2F1/Cr1;[Crj:BDF1]

SEX : FEMALE

### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

~

 $\overline{\phantom{a}}$ 

PAGE: 7

| Group Name                                   | Control                                 | 2500 ppm   | 5000 ppm     | 10000 ppm  |  |
|----------------------------------------------|-----------------------------------------|------------|--------------|------------|--|
|                                              | SITE : pituitary gland                  |            |              |            |  |
|                                              | TUMOR : adenoma                         |            |              |            |  |
| Tumor rate                                   |                                         |            |              |            |  |
| Overall rates(a)                             | 12/50(24.0)                             | 9/50(18.0) | 5/50(10.0)   | 6/50(12.0) |  |
| Adjusted rates(b)                            | 30. 56                                  | 25. 71     | 15.15        | 25.00      |  |
| Terminal rates(c)                            | 8/29(27.6)                              | 6/26(23.1) | 4/31 ( 12.9) | 5/20(25.0) |  |
| Statistical analysis                         |                                         |            |              |            |  |
| Peto test                                    | D 0.0017 9                              |            |              |            |  |
| Standard method(d)                           | P = 0.8917 ?                            |            |              |            |  |
| Prevalence method(d)<br>Combined analysis(d) | P = 0.9072<br>P = 0.9362                |            |              |            |  |
| Cochran-Armitage test(e)                     | P = 0.0900                              |            |              |            |  |
| Fisher Exact test(e)                         | 1 - 0.0900                              | P = 0.3121 | P = 0.0542   | P = 0.0961 |  |
|                                              |                                         | 1 = 0.5121 | r - 0.0342   | P - 0.0901 |  |
|                                              | SITE : pituitary gland                  |            |              |            |  |
|                                              | TUMOR : adenoma, adenocarcinoma         |            |              |            |  |
| Tumor rate                                   | - · · · · · · · · · · · · · · · · · · · |            |              |            |  |
| Overall rates(a)                             | 12/50(24.0)                             | 9/50(18,0) | 5/50(10.0)   | 7/50(14.0) |  |
| Adjusted rates(b)                            | 30.56                                   | 25. 71     | 15.15        | 25.00      |  |
| Terminal rates(c)                            | 8/29(27.6)                              | 6/26(23.1) | 4/31 ( 12.9) | 5/20(25.0) |  |
| Statistical analysis                         |                                         |            |              |            |  |
| Peto test                                    |                                         |            |              |            |  |
| Standard method(d)                           | P = 0.3751                              |            |              |            |  |
| Prevalence method(d)                         | P = 0.9072                              |            |              |            |  |
| Combined analysis(d)                         | P = 0.8835                              |            |              |            |  |
| Cochran-Armitage test(e)                     | P = 0.1662                              |            |              |            |  |
| Fisher Exact test(e)                         |                                         | P = 0.3121 | P = 0.0542   | P = 0.1540 |  |
|                                              | SITE : ovary                            |            |              |            |  |
|                                              | TUMOR : cystadenoma                     |            |              |            |  |
| lumor rate                                   |                                         |            |              |            |  |
| Overall rates(a)                             | 0/50(0.0)                               | 0/50(0,0)  | 3/50(6,0)    | 1/50( 2.0) |  |
| Adjusted rates(b)                            | 0.0                                     | 0.0        | 9.68         | 2.13       |  |
| Terminal rates(c)                            | 0/29( 0.0)                              | 0/26( 0.0) | 3/31(9.7)    | 0/20( 0.0) |  |
| Statistical analysis                         |                                         |            | · · ·        |            |  |
| Peto test                                    |                                         |            |              |            |  |
| Standard method(d)                           | P =                                     |            |              |            |  |
| Prevalence method(d)                         | P = 0.1470                              |            |              |            |  |
| Combined analysis(d)                         | P =                                     |            |              |            |  |
| Cochran-Armitage test(e)                     | P = 0.3056                              |            |              |            |  |
| Fisher Exact test(e)                         |                                         | P = N.C.   | P = 0.1212   | P = 0.5000 |  |

(HPT360A)

### STUDY No. : 0613

ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]

SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

 $\overline{}$ 

|                          | Control                                      | 2500 ppm       | 5000 ppm              | 10000 ppm                              |
|--------------------------|----------------------------------------------|----------------|-----------------------|----------------------------------------|
|                          | SITE : ovary                                 |                |                       |                                        |
|                          | TUMOR : hemangioma                           |                |                       |                                        |
| umor rate                |                                              |                |                       |                                        |
| Overall rates(a)         | 0/50( 0.0)                                   | 1/50(2.0)      | 4/50( 8.0)            | 0/50( 0.0)                             |
| Adjusted rates(b)        | 0.0                                          | 3. 85          | 8.57                  | 0.0                                    |
| Terminal rates(c)        | 0/29( 0.0)                                   | 1/26( 3.8)     | 2/31(6.5)             | 0/20( 0.0)                             |
| tatistical analysis      |                                              |                |                       |                                        |
| Peto test                |                                              |                |                       |                                        |
| Standard method(d)       | P = 0.4037                                   | ,              |                       |                                        |
| Prevalence method(d)     | P = 0.4525                                   |                |                       |                                        |
| Combined analysis(d)     | P = 0.4291                                   |                |                       |                                        |
| Cochran-Armitage test(e) | P = 0.9390                                   |                |                       |                                        |
| Fisher Exact test(e)     |                                              | $P = 0.\ 5000$ | $\mathbf{P} = 0.0587$ | $\mathbf{P} = \mathbf{N}. \mathbf{C}.$ |
|                          | SITE : uterus<br>TUMOR : histiocytic sarcoma |                |                       |                                        |
| umor rate                | TOMOR · HIStrocytic sarcouna                 |                |                       |                                        |
| Overall rates(a)         | 8/50(16.0)                                   | 14/50 (28.0)   | 7/50(14.0)            | 14/50(28.0)                            |
| Adjusted rates(b)        | 6.90                                         | 15.38          | 6.45                  | 14/30(28.0)                            |
| Terminal rates(c)        | 2/29( 6.9)                                   | 4/26 ( 15. 4)  | 2/31(6.5)             | 3/20(15.0)                             |
| tatistical analysis      | 2/29( 0.9)                                   | 4/20(15.4)     | 2/31( 0.3)            | 3/20(15.0)                             |
| Peto test                |                                              |                |                       |                                        |
| Standard method(d)       | P = 0.2268                                   |                |                       |                                        |
| Prevalence method(d)     | P = 0.2208<br>P = 0.1735                     |                |                       |                                        |
| Combined analysis(d)     | P = 0.1331                                   |                |                       |                                        |
| Cochran-Armitage test(e) | P = 0.1331<br>P = 0.3085                     |                |                       | S                                      |
| Fisher Exact test(e)     | r - 0.3003                                   | P = 0.1105     | $\mathbf{P} = 0$ F000 |                                        |
| TSHEL EXACT (est(e)      |                                              | P = 0.1135     | P = 0.5000            | P = 0.1135                             |
| PT360A)                  |                                              |                |                       |                                        |

### STUDY No. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]

### SEX : FEMALE

### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE: 9

| Group Name               | Control                                   | 2500 ppm    | 5000 ppm   | 10000 ppm  |  |
|--------------------------|-------------------------------------------|-------------|------------|------------|--|
| · .                      | SITE : Harderian gland<br>TUMOR : adenoma |             |            |            |  |
| Tumor rate               |                                           |             |            |            |  |
| Overall rates(a)         | 3/50 ( 6.0)                               | 2/50 ( 4.0) | 0/50(0.0)  | 4/50( 8.0) |  |
| Adjusted rates(b)        | 8. 33                                     | 7.69        | 0.0        | 10.00      |  |
| Terminal rates(c)        | 2/29 ( 6.9)                               | 2/26 (7.7)  | 0/31( 0.0) | 2/20(10.0) |  |
| Statistical analysis     |                                           |             |            |            |  |
| Peto test                |                                           |             |            |            |  |
| Standard method(d)       | P =                                       |             |            |            |  |
| Prevalence method(d)     | P = 0.3053                                |             |            |            |  |
| Combined analysis(d)     | P =                                       |             |            |            |  |
| Cochran-Armitage test(e) | P = 0.6038                                |             |            |            |  |
| Fisher Exact test(e)     |                                           | P = 0.5000  | P = 0.1212 | P = 0.5000 |  |

#### (HPT360A)

(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.

### STUDY No. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]

SEX : FEMALE

PAGE : 3

| Group Name               | Control                               | 2500 ppm      | 5000 ppm    | 10000 ppm    |
|--------------------------|---------------------------------------|---------------|-------------|--------------|
|                          | SITE : ALL SITE<br>TUMOR : hemangioma |               |             |              |
| lumor rate               | Tomore Honking Long                   |               |             |              |
| Overall rates(a)         | 3/50(6.0)                             | 4/50 ( 8.0)   | 7/50(14.0)  | 2/50(4.0)    |
| Adjusted rates(b)        | 8.33                                  | 14.81         | 17.14       | 5.00         |
| Terminal rates(c)        | 2/29(6,9)                             | 3/26(11.5)    | 5/31(16.1)  | 1/20( 5.0)   |
| Statistical analysis     |                                       |               |             | -, , , ,     |
| Peto test                |                                       |               |             |              |
| Standard method(d)       | P = 0.4037                            |               |             |              |
| Prevalence method(d)     | P = 0.6299                            |               |             |              |
| Combined analysis(d)     | P = 0.6085                            |               |             |              |
| Cochran-Armitage test(e) | P = 0.7245                            |               |             |              |
| Fisher Exact test(e)     |                                       | P = 0.5000    | P = 0.1589  | P = 0.5000   |
|                          | SITE : ALL SITE                       |               |             |              |
|                          | TUMOR : histiocytic sarcoma           |               |             |              |
| Tumor rate               |                                       |               |             |              |
| Overall rates(a)         | 11/50(22.0)                           | 14/50 ( 28.0) | 7/50(14.0)  | 15/50( 30.0) |
| Adjusted rates(b)        | 17.24                                 | 15. 38        | 6.45        | 15.00        |
| Terminal rates(c)        | 5/29(17.2)                            | 4/26 (15.4)   | 2/31 ( 6.5) | 3/20(15.0)   |
| Statistical analysis     |                                       |               |             |              |
| Peto test                |                                       |               |             |              |
| Standard method(d)       | P = 0.1595                            |               |             |              |
| Prevalence method(d)     | P = 0.5142                            |               |             |              |
| Combined analysis(d)     | P = 0.2043                            | •             |             |              |
| Cochran-Armitage test(e) | P = 0.5168                            |               |             |              |
| Fisher Exact test(e)     |                                       | P = 0.3224    | P = 0.2178  | P = 0.2472   |

(HPT360A)

#### STUDY No. : 0613 ANIMAL : MOUSE B6D2F1/Cr1,j[Cr,j:BDF1] SEX : FEMALE

#### NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

PAGE : 4

| Group Name               | Control                    | 2500 ppm      | 5000 ppm    | 10000 ppm   |  |  |
|--------------------------|----------------------------|---------------|-------------|-------------|--|--|
|                          | SITE : ALL SITE            |               |             |             |  |  |
|                          | TUMOR : malignant lymphoma |               |             |             |  |  |
| ľumor rate               |                            |               |             |             |  |  |
| Overall rates(a)         | 13/50(26.0)                | 18/50 ( 36.0) | 20/50(40.0) | 17/50(34.0) |  |  |
| Adjusted rates(b)        | 24.14                      | 30. 77        | 35.48       | 25.00       |  |  |
| Terminal rates(c)        | 7/29(24.1)                 | 8/26 ( 30.8)  | 11/31(35.5) | 5/20(25.0)  |  |  |
| Statistical analysis     |                            |               |             |             |  |  |
| Peto test                |                            |               |             |             |  |  |
| Standard method(d)       | P = 0.0718                 |               |             |             |  |  |
| Prevalence method(d)     | P = 0.4440                 |               |             |             |  |  |
| Combined analysis(d)     | P = 0.1029                 |               |             |             |  |  |
| Cochran-Armitage test(e) | P = 0.4799                 |               |             |             |  |  |
| Fisher Exact test(e)     |                            | P = 0.1937    | P = 0.1008  | P = 0.2565  |  |  |

### (HPT360A)

(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 Q 1

### HISTOPATHOLOGICAL FINDINGS:

METASTASIS OF TUMOR: MALE

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

~~

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1;[Cr;:BDF1] REPORT TYPE : A1 SEX : MALE

| rgan          |                                                                               | Group Name Control<br>No. of Animals on Study 50 | 5000 ppm<br>50 | 10000 ppm<br>50 | 20000 ppm<br>50                       |
|---------------|-------------------------------------------------------------------------------|--------------------------------------------------|----------------|-----------------|---------------------------------------|
| r gan         | rinuings                                                                      |                                                  |                |                 | · · · · · · · · · · · · · · · · · · · |
| Integumentary | system/appandage)                                                             |                                                  |                |                 |                                       |
| ubcutis       | metastasis:spleen tumor                                                       | <50>                                             | <50><br>0      | <50>            | <50>                                  |
|               | metastasis:epididymis tumor                                                   | 0                                                | 1              | 0               | 0                                     |
| kespiratory s | us tom)                                                                       |                                                  |                |                 |                                       |
|               | ystenij                                                                       |                                                  |                |                 |                                       |
| asal cavit    | metastasis:subcutis tumor                                                     | <50><br>0                                        | <50><br>1      | <50><br>0       | <50><br>0                             |
|               | metastasis∶epididymis tumor                                                   | 0                                                | 1              | 0               | 0                                     |
| lig           |                                                                               | <50>                                             | <50>           | (50)            |                                       |
| ng            | leukemic cell infiltration                                                    | 3                                                | 2              | <50><br>2       | <50><br>0                             |
|               | metastasis:liver tumor                                                        | 3                                                | 3              | 1               | 3                                     |
|               | metastasis:subcutis tumor                                                     | 0                                                | 0              | 0               | 1                                     |
|               | metastasis:bone tumor                                                         | 0                                                | 1              | 0               | 0                                     |
|               | metastasis spleen tumor                                                       | 1                                                | 0              | 0               | 0                                     |
| lematopoietic | system)                                                                       |                                                  |                |                 |                                       |
| one marrow    |                                                                               | <50>                                             | <50>           | <50>            | <50>                                  |
|               | leukemic cell infiltration                                                    | 5                                                | 1              | 1               | 1                                     |
|               | metastasis:liver tumor                                                        | 2                                                | 1              | 0               | 2                                     |
|               | metastasis:subcutis tumor                                                     | 1                                                | 0              | 0               | 0                                     |
|               | metastasis:spleen tumor                                                       | I                                                | 0 .            | 2               | 0                                     |
| a><br>b       | a : Number of animals examined at the si<br>b : Number of animals with lesion | te                                               |                |                 |                                       |

(JPT150)

BAIS4

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

~

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 SEX : MALE

| SEX :         | MALE                                                                     |                                                  |                |                 | PAGE :          |
|---------------|--------------------------------------------------------------------------|--------------------------------------------------|----------------|-----------------|-----------------|
| Organ         | -<br>Findings                                                            | Group Name Control<br>No. of Animals on Study 50 | 5000 ppm<br>50 | 10000 ppm<br>50 | 20000 ppm<br>50 |
|               |                                                                          | · · · · · · · · · · · · · · · · · · ·            |                |                 |                 |
| (Hematopoieti | c system)                                                                |                                                  |                |                 |                 |
| ymph node     | metastasis:liver tumor                                                   | <50><br>0                                        | <50><br>1      | <50><br>0       | <50><br>0       |
|               | metastasis spleen tumor                                                  | 1                                                | 0              | 0               | 0               |
|               | metastasis:urinary bladder tumor                                         | 0                                                | 0              | 1               | 0               |
| hymus         | leukemic cell infiltration                                               | <50><br>1                                        | <50><br>0      | <50><br>0       | <50><br>0       |
| pleen         | leukemic cell infiltration                                               | <50><br>10                                       | <50><br>5      | <50><br>2       | <50><br>1       |
|               | metastasis:liver tumor                                                   | 1                                                | 1              | 0               | 4               |
|               | metastasis:subcutis tumor                                                | 1                                                | 0              | 0               | 0               |
| Circulatory   | system}                                                                  |                                                  |                |                 |                 |
| eart          | leukemic cell infiltration                                               | <50><br>2                                        | <50><br>0      | <50><br>0       | <50><br>0       |
|               | metastasis:subcutis tumor                                                | 0                                                | 0              | 0               | i               |
| Digestive sy  | stem}                                                                    |                                                  |                |                 |                 |
| alivary gl    | leukemic cell infiltration                                               | <50><br>0                                        | <50><br>1      | <50><br>1       | <50><br>0       |
| nall intes    | leukemic cell infiltration                                               | <50><br>3                                        | <50><br>0      | <50><br>2       | <50><br>0       |
| arge intes    | leukemic cell infiltration                                               | <50><br>1                                        | <50><br>0      | <50><br>0       | <50><br>0       |
| ≺a≻<br>b      | a : Number of animals examined at t<br>b : Number of animals with lesion | he site                                          |                |                 |                 |

PAGE : 2

(JPT150)

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 SEX : MALE

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

|               |                                      | Group Name Control<br>No. of Animals on Study 50 | 5000 ppm<br>50 | 10000 ppm<br>50 | 20000 ppm<br>50 |
|---------------|--------------------------------------|--------------------------------------------------|----------------|-----------------|-----------------|
| rgan          | Findings                             |                                                  |                |                 |                 |
| Digestive sys | stem)                                |                                                  |                |                 |                 |
| iver          |                                      | <50>                                             | <50>           | <50>            | <50>            |
|               | leukemic cell infiltration           | 6                                                | 3              | 1               | 0               |
|               | metastasis:spleen tumor              | 1                                                | 0              | х<br>1          | 0               |
| ancreas       |                                      | <50>                                             | <50>           | <50>            | <50>            |
|               | leukemic cell infiltration           | 0                                                | 1              | 0               | 1               |
|               | metastasis:liver tumor               | 1                                                | 0              | 0               | 0               |
|               |                                      |                                                  |                |                 |                 |
| Urinary syste | em)                                  |                                                  |                |                 |                 |
| idney         |                                      | <50>                                             | <50>           | <50>            | <50>            |
|               | leukemic cell infiltration           | 3                                                | 2              | 0               | 0               |
|               | metastasis:liver tumor               | 1                                                | 0              | 0               | 1               |
|               | metastasis:subcutis tumor            | 0                                                | 0              | 0               | 1               |
| rin bladd     |                                      | <50>                                             | <50>           | <50>            | <50>            |
|               | metastasis:liver tumor               | 1                                                | 0              | 0               | 0               |
| Indocrine sys |                                      |                                                  |                |                 |                 |
| ituitary      |                                      | <50>                                             | <50>           | <50>            | <50>            |
| <b>,</b>      | metastasis:peripheral nerve tumor    | 0                                                | 0              | 1               | 0               |
| Reproductive  | system)                              |                                                  |                |                 |                 |
| estis         |                                      | <50>                                             | <50>           | <50>            | <50>            |
|               | metastasis:liver tumor               | 0                                                | 1              | 0               | 0               |
|               | metastasis:epididymis tumor          | 0                                                | 1              | 0               | 0               |
| a >           | a : Number of animals examined at th |                                                  |                |                 |                 |

(JPT150)

BAIS4

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 SEX : MALE

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

1

~~~

| SEX :          | MALE  |  |                |                 | PAGE : 4        |
|----------------|---|--|----------------|-----------------|-----------------|
| Organ          | Findings  | Group Name Control<br>No. of Animals on Study 50 | 5000 ppm<br>50 | 10000 ppm<br>50 | 20000 ppm<br>50 |
|                |   |  |                |                 |                 |
| {Reproductive  | e system)   |  |                |                 |                 |
| epididymis     | metastasis:liver tumor  | <50><br>0  | <50><br>1      | <50><br>0       | <50><br>1       |
| semin ves      | leukemic cell infiltration  | <50><br>1  | <50><br>0      | <50><br>0       | <50><br>0       |
| prostate       | leukemic cell infiltration  | <50><br>1  | <50><br>1      | <50><br>0       | <50><br>0       |
|                | metastasis:liver tumor  | 0  | 0              | 0               | 1               |
| {Nervous syst  | tem}  |  |                |                 |                 |
| brain          | metastasis:subcutis tumor   | <50><br>0  | <50><br>1      | <50><br>0       | <50><br>0       |
|                | metastasis:peripheral merve tumor                                       | 0  | 0              | 1               | 0               |
| {Body cavitie  | əs}   |  |                |                 |                 |
| peritoneum     | leukemic cell infiltration  | <50><br>0  | <50><br>0      | <50><br>0       | <50><br>1       |
|                | metastasis:liver tumor  | I  | 0              | 0               | 0               |
| <a>→<br/>b</a> | a : Number of animals examined at the b : Number of animals with lesion | e site   |                | •               |                 |

(JPT150)

TABLE Q 2

# HISTOPATHOLOGICAL FINDINGS:

METASTASIS OF TUMOR: FEMALE

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1,j[Cr,j:BDF1] REPORT TYPE : A1 SEX : FEMALE

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

| rgan         | Findings                   | Group Name Control<br>No. of Animals on Study 50 | 2500 ppm<br>50 | 5000 ppm<br>50 | 10000 ppm<br>50 |
|--------------|----------------------------|--|----------------|----------------|-----------------|
|              |                            | · · · · · · · · · · · · · · · · · · ·            |                |                |                 |
| [ntegumentar | v system/appandage)        |  |                |                |                 |
| in/app       | leukemic cell infiltration | <50><br>0  | <50><br>0      | <50><br>0      | <50><br>1       |
| bcutis       | leukemic cell infiltration | <50><br>1  | <50><br>1      | <50><br>0      | <50><br>0       |
|              | metastasis:uterus tumor    | 0  | 0              | 0              | 1               |
| espiratory : | system)                    |  |                |                |                 |
| sal cavit    | leukemic cell infiltration | <50><br>1  | · <50><br>2    | <50><br>1      | <50><br>1       |
| ng           | leukemic cell infiltration | <50><br>8  | <50><br>9      | <50><br>9      | <50><br>8       |
|              | metastasis:liver tumor     | 1  | 0              | 0              | 1               |
|              | metastasis uterus tumor    | 2  | 6              | 1              | 5               |
|              | metastasis:thyroid tumor   | 0  | 0              | 0              | 1               |
| ematopoietio | : system)                  |  |                |                |                 |
| ne marrow    | leukemic cell infiltration | <50><br>5  | <50><br>5      | <50><br>10     | <50><br>7       |
|              | metastasis:liver tumor     | 0  | 0              | 0              | . 1 .           |
|              | metastasis:uterus tumor    | 5  | 5              | 1              | 4               |
| mph node     | metastasis uterus tumor    | <50><br>1  | <50><br>3      | <50><br>1      | <50><br>1       |

(JPT150)

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

 $\sim$ 

~

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 SEX : FEMALE

| Organ        | Findings                   | Group Name Cont<br>No. of Animals on Study | ro1<br>50 | 2500 ppm<br>50 | 5000 ppm<br>50 | 10000 ppm<br>50 |
|--------------|----------------------------|--|-----------|----------------|----------------|-----------------|
| organ        |                            |  |           |                |                |                 |
|              |                            |  |           |                |                |                 |
| Hematopoieti | c system)                  |  |           |                |                |                 |
| pleen        | leukemic cell infiltration |  | <50><br>7 | <50><br>12     | <50><br>11     | <50><br>13      |
|              | metastasis:liver tumor     |  | 0         | 0              | 0              | 1               |
|              | metastasis:uterus tumor    |  | 1         | 2              | 1              | 7               |
| Circulatory  | system)                    |  |           |                |                |                 |
| neart        | leukemic cell infiltration |  | <50><br>2 | <50><br>1      | <50><br>2      | <50><br>1       |
|              | metastasis:uterus tumor    |  | 0         | 1              | 3              | 1               |
| Digestive sy | vstem)                     |  |           |                |                |                 |
| ongue        | leukemic cell infiltration |  | <50><br>0 | <50><br>0      | <50><br>0      | <50><br>1       |
| alivary gl   | leukemic cell infiltration |  | <50><br>3 | <50><br>1      | <50><br>6      | <50><br>2       |
|              | metastasis:uterus tumor    |  | 0         | 1              | 0              | 0               |
| tomach       | leukemic cell infiltration |  | <50><br>0 | <50><br>0      | <50><br>0      | <50><br>1       |
| mall intes   | metastasis:uterus tumor    |  | <50><br>0 | <50><br>1      | <50><br>0      | <50><br>0       |
| iver         | leukemic cell infiltration |  | <50><br>8 | <50><br>9      | <50><br>12     | <50><br>11      |
|              | metastasis:uterus tumor    |  | 6         | 10             | 5              | 11              |

(JPT150) .

BAIS4

#### STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 SEX : FEMALE

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

 $\sim \sim$ 

| rgan        | Findings                     | Group Name Control<br>No. of Animals on Study 50 | 2500 ppm<br>50 | 5000 ppm<br>50 | 10000 ppm<br>50 |
|-------------|------------------------------|--|----------------|----------------|-----------------|
|             |                              |  |                |                |                 |
| igestive s  | ystem}                       |  |                |                |                 |
| ll bladd    | leukemic cell infiltration   | <50><br>0  | <50><br>0      | <50><br>1      | <50><br>0       |
| ncreas      | leukemic cell infiltration   | <50><br>0  | <50><br>0      | <50><br>4      | <50><br>3       |
|             | metastasis uterus tumor      | 1  | 1              | 0              | 0               |
| rinary sys  | tem}                         |  |                |                |                 |
| dney        | leukemic cell infiltration   | <50><br>2  | <50><br>6      | <50><br>9      | <50><br>4       |
|             | metastasis:uterus tumor      | 2  | 4              | 0.             | 4               |
| in bladd    | leukemic cell infiltration . | <50><br>3  | <50><br>1      | <50><br>5      | <50><br>3       |
| ndocrine s  | ystem)                       |  |                |                |                 |
| tuitary     | leukemic cell infiltration   | <50><br>0  | <50><br>0      | <50><br>1      | <50><br>1       |
| renal       | leukemic cell infiltration   | <50><br>1  | <50><br>0      | <50><br>0      | <50><br>2       |
| eproductive | e system)                    |  |                |                |                 |
| ary         | leukemic cell infiltration   | <50><br>1  | <50><br>3      | <50><br>6      | <50><br>7       |
|             | metastasis:uterus tumor      | 4  | 10             | 3              | 8               |

(JPT150)

STUDY NO. : 0613 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 SFY : FEMALE

•

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

~----

|                 |                            | Group Name Control         | 2500 ppm  | 5000 ppm  | 10000 ppm   |
|-----------------|----------------------------|----------------------------|-----------|-----------|-------------|
| galı            | Findings                   | No. of Animals on Study 50 | 50        | 50        | 50          |
| · -             |                            |                            |           |           |             |
| eproductive sy  | stem}                      |                            |           |           |             |
| erus            | leukemic cell infiltration | <50><br>3                  | <50><br>1 | <50><br>0 | <50><br>3   |
| gina            | metastasis:uterus tumor    | <50><br>0                  | <50><br>0 | <50><br>0 | <50><br>. 1 |
| Vervous system) |                            |                            |           |           |             |
| ain             | leukemic cell infiltration | <50><br>1                  | <50><br>2 | <50><br>1 | <50><br>0   |
| pecial sense o  | rgans/appendage)           |                            |           |           |             |
| rder gl         | leukemic cell infiltration | <50><br>0                  | <50><br>0 | <50><br>1 | <50><br>1   |
| lusculoskeletal | system)                    |                            |           |           |             |
| scle            | leukemic cell infiltration | <50><br>0                  | <50><br>0 | <50><br>2 | <50><br>1   |
| ody cavities}   |                            |                            |           |           |             |
| diastinum       | leukemic cell infiltration | <50><br>1                  | <50><br>0 | <50><br>0 | <50><br>0   |
|                 | metastasis:uterus tumor    | 0                          | 0         | 0         | 1           |
| ritoneum        | leukemic cell infiltration | <50><br>0                  | <50><br>1 | <50><br>0 | <50><br>3   |
| ŕ               | metastasis:uterus tumor    | 0                          | 0         | 0         | 1           |

(JPT150)

|               | 0613<br>MOUSE B6D2F1/Crlj[Crj:BDF1]<br>A1                              | HISTOPATHOLOGICAL FINDINGS : METASTASIS OF TUMOR (SUMMARY)<br>ALL ANIMALS (0-105W) |                 |                |                |                 |
|---------------|--|--|-----------------|----------------|----------------|-----------------|
| SEX           | FEMALE   |  |                 |                |                | PAGE :          |
|               |  | Group Name<br>No. of Animals on Study  | Control<br>y 50 | 2500 ppm<br>50 | 5000 ppm<br>50 | 10000 ppm<br>50 |
| Organ         | Findings   | ······   |                 |                |                |                 |
| {Body cavitie | [22  |  |                 |                |                |                 |
| ·             |  |  |                 |                |                |                 |
| retroperit    | leukemic cell infiltration   |  | <50><br>1       | <50><br>1      | <50><br>0      | <50><br>0       |
| ≺a><br>b      | a : Number of animals examined at<br>b : Number of animals with lesion |  |                 |                |                |                 |
| (JPT150)      |  |  |                 |                |                | BAIS            |

# TABLE R 1

# CAUSE OF DEATH: MALE

| STUDY NO. | : 0613                        | COUSE OF DEATH (SUMMARY) |
|-----------|-------------------------------|--------------------------|
| ANIMAL    | : MOUSE B6D2F1/Cr1j[Crj:BDF1] | (0-105%)                 |
| SEX       | : MALE                        |                          |
|           |                               |                          |

| Group Name                            | Control | 5000 ppm | 10000 ppm | 20000 ppm |      |                                       |
|---------------------------------------|---------|----------|-----------|-----------|------|---------------------------------------|
| Number of Dead and<br>Moribund Animal | 15      | 17       | 14        | 9         |      |                                       |
| no microscop confirm                  | 1       | 0        | 3         | 0         | <br> | · · · · · · · · · · · · · · · · · · · |
| hepatic lesion                        | 0       | 1        | 0         | 0         |      |                                       |
| oody cavity lesion                    | 1       | 0        | 0         | 0         |      |                                       |
| central nervo lesion                  | 0       | 0        | 0         | 1         |      |                                       |
| urinary retention                     | 2       | . 1      | 0         | 0         |      |                                       |
| erteritis                             | 0       | 1        | 0         | 0         |      |                                       |
| nydronephrosis                        | 0       | · 1      | 0         | 0         |      |                                       |
| cumor d:leukemia                      | 7       | 2        | 3         | 0         |      |                                       |
| cumor d:subcutis                      | 0       | 1        | 0         | . 1       |      |                                       |
| tumor d:lung                          | 0       | 1        | 1         | 0         |      |                                       |
| tumor displeen                        | 1       | 0        | 1         | 0         |      |                                       |
| umor d:liver                          | 3       | 7        | 4         | 7         |      |                                       |
| tumor d∶urin bladd                    | 0       | 0        | 1         | 0         |      |                                       |
| tumor d:periph nerv                   | 0       | 0        | 1         | 0         |      |                                       |
| umor d:bone                           | 0       | 1        | 0         | 0         |      |                                       |
| tumor d:pleura                        | 0       | 1        | 0         | 0         |      |                                       |

(BI0120)

.

BAIS4

# TABLE R 2

# CAUSE OF DEATH: FEMALE

| STUDY NO.<br>ANIMAL | : 0613<br>: MOUSE B6D2F1/Crlj[Crj:BDF1] | COUSE OF DEATH (SUMMARY)<br>(0-105W) |
|---------------------|---|--------------------------------------|
| SEX                 | : FEMALE                                |                                      |
|                     |   |                                      |

 $\sim$ 

| Group Name                            | Control | 2500 ppm | 5000 ppm | 10000 ppm |
|---------------------------------------|---------|----------|----------|-----------|
| Number of Dead and<br>Moribund Animal | 21      | 24       | 19       | 30        |
| cardiovascular les                    | 0       | 1        | 0        | 0         |
| eproductive sy les                    | 0       | 0        | 0        | 1         |
| ody cavity lesion                     | 0       | 0        | 0        | 1         |
| rinary retention                      | 2       | 1        | 0        | 0         |
| rteritis                              | 0       | 0        | 1        | 0         |
| nydronephrosis                        | 3       | 0        | 1        | 1         |
| peritonitis                           | 1       | 0        | 0        | 0         |
| tumor d:leukemia                      | 6       | 10       | 9        | 12        |
| tumor d:subcutis                      | 0       | 1        | 0        | 0         |
| tumor d:lung                          | 0       | 0        | 0        | 1         |
| tumor d:liver                         | 1       | 0        | 1        | 2         |
| tumor d:pituitary                     | 1       | 0        | 0        | 1         |
| tumor d:thyroid                       | 0       | . 0      | 0        | 1         |
| tumor d:ovary                         | 0       | 0        | 1        | 0         |
| tumor d:uterus                        | 6       | 10       | 6        | 10        |
| tumor d:brain                         | 1       | 0        | 0        | 0         |
| tumor d:muscle                        | 0       | 1        | 0        | 0         |
|                                       |         |          |          |           |

(BI0120)

BAIS4